ISSN 2521-3113 (Online)
ISSN 1024-8714 (Print)

BMDC RECOGNIZED

BANGLADESH HEART JOURNAL

VOL. 35 NO. 2 JULY 2020

CONTENTS

Original Article

Percutaneous Coronary Intervention (PCI) of Left Main (LM) Stem Disease: Our Experiences in a Tertiary Care Hospital 78
AHM Waliul Islam, Shams Munwar, AQM Reza, Shahabuddin Talukder, Tamzeed Ahmed, Azfar H Bhuiyan, Kazi Atiqur Rahman

Systematic Review and Pooled Meta-analysis of the Current Status of Coronary Revascularization Surgery in Bangladesh 87
Faizus Sazzad, Ashlynn Ai Li Ler, Geetha Ganesh, Marcus Kung, Theo Kofidis

Arteriovenous Fistula Creation for Hemodialysis: Evaluation of Complications 100
Motiur Rahman Sarkar, Nazmul Hosain, Moynul Islam, Saffait Jamil, Muhammad Mahmudul Hoque

Association between Circulating Fibrinogen Level and Severity of Coronary Artery Disease in Type 2 Diabetic Patients with Chronic Stable Angina 106
Md. Sadaqul Islam Sikdar, Md Mamunur Rashid, Md Khalekuzzaman, Iftekhar Alam, Mst. Nazmun Nahar, Md. Shariful Islam, Lipi Debnath, Abdullah Al Masud

Comparative Assessment of Serum Homocysteine and High Sensitivity C-reactive Protein in type 2 Diabetic and non Diabetic Patients with ACS 114
Lipi Debnath, Abdul Wadud Chowdhury, Iftekhar Alam, Md Mamunur Rashid, Md Sadaqul Islam Sikder, Bijan Kumar Nath

Clinical, Electrocardiographic and Echocardiographic Profile of Ischemic Cardiomyopathy: An analysis of 100 cases 121
Mainul Islam, M.Atahar Ali, Umme Habiba Ferdaushi, Shaila Nabi, Sayeedur Rahman Khan, Md. Shariful Islam, Hasan Mahmoud

Serum Potassium and Angiographic Severity of Coronary Artery Disease in Non-ST Elevation Myocardial Infarction 128
Maimuna Sultana, Afzalur Rahman, Pradip Kumar Karmakar, AKM Monwarul Islam, Al-Mamun, Khondaker Aisha Siddika, Kazi Md. Rubayet Anwar, Gokul Chandra Datta, Deb Dulal Debnath, Shaikat Chowdhury, Md. Nazmul Islam

Association of Haemoglobin A1c Level with the Severity of Coronary Artery Disease in Non-diabetic Patients with Non-ST-Segment Elevation Myocardial Infarction 134
Md. Mamunuzzaman, Mahboob Ali, Mir Jamal Uddin, Shaila Nabi, Kajal Kumar Karmoker, Muhammed Aminur Razzaque, Pinaki Ranjan Das, Md. Sazzad Masum, Mohammad Bazlur Rashid, Syed Mohammad Ali Romel

Short and Long Term Outcome In Patients with Calcified Lesions Requiring Rotational Artherectomy 140
Lima Asrin Sayami, Al-Fazir Omar, Sheikh Ziarat Islam, Subasni Govindan, Zulaikha Zainal, Rosli Mohd Ali

Review Article

Anticipating the Challenging and Unpredictable Long Term Cardiovascular Effects of COVID-19: A Review 147
Mohammad Arifur Rahman, Afzalur Rahman, Mohsin Ahmed, AKM Monwarul Islam, Md. Mesbahul Islam, Muhammad Salim Mahmod, Tanveer Ahmad

Case Report

Percutaneous Closure of Acquired Hole- First Case Report from Bangladesh 155
Tawfiq Shahriar Haq, Naharuma Aive Hyder Chowdhury, Abdul Mazid khan, Jesmin Hossain, Fazila-Tun-Nesa Malik

Obituary

Our Teacher: Prof Abu Zafor 159
Abdullah Al Shafi Majumder

Official Journal of
Bangladesh Cardiac Society

BANGLADESH HEART JOURNAL

VOL. 35, NO. 2, JULY 2020

Published by :
Prof. M.G. Azam
Publicity Secretary
Bangladesh Cardiac Society
Karukaj Hashim Heritage (1st Floor)
21/8, Khiljee Road, Block-B, Mohammadpur
Dhaka-1207, Bangladesh
Tel: 01799925522 (Office)
E-mail: bcs@bol-online.com
Website: www.banglacardio.org

Printed by :
Asian Colour Printing
130, DIT Extension Road
Fakirerpool, Dhaka-1000
Phone : 49357726, 58313186
E-mail: asianclr@gmail.com

BANGLADESH CARDIAC SOCIETY

EXECUTIVE COMMITTEE

President	:	Prof. AKM Mohibullah MD, FRCP, FACC, FESC
Vice-President	:	Prof. Mir Jamal Uddin MD, FACC, FRCP Prof. Abdul Wadud Chowdhury FCPS, MD Prof. H.I. Lutfur Rahman Khan MD Prof. AKM Fazlur Rahman MD, FACC, FRCP Prof. Abu Azam FRCPE, FESC, FACC Prof. Sajal Krishna Banerjee MD, FRCP, FACC, FESC
Treasurer	:	Prof. Md. Mamunur Rashid MD, FSCAI, AFACC
Secretary General	:	Prof. Abdullah A. Shafi Majumder MD, FACC, FRCPE, FESC
Joint Secretary	:	Dr. Kajal Kumar Karmoker D-Card, FSCAI Dr. Md. Mahbubur Rahman D-Card
Organising Secretary	:	Dr. Bijoy Dutta MD, FSCAI Prof. Syed Md. Mostafa Kamal D-Card, FACC Dr. Md. Towhiduz Zaman MD, FACC, FSCAI Dr. S M Habibullah Selim D-Card, MD Dr. Quazi Abul Azad MS Dr. S.M. Quamrul Huq MD
Publicity Secretary	:	Prof. M.G. Azam MD, FSCAI
Scientific Secretary	:	Dr. Mohsin Ahmed MD, FACC, FESC
Social & Cultural Secretary	:	Dr. Nur Alam MD, FSCAI
Office Secretary	:	Dr. Md. Zillur Rahman MD, FACC
Secretary International Affairs	:	Dr. Suman Nazmul Hosain MS
Members	:	Prof. Md. Afzalur Rahman MD, Ph.D, FRCP, FACC Prof. Amal Kumar Choudhury MD, FACC, FESC, FSCAI Dr. Mohammad Arifur Rahman MD Prof. Nawazesh Farid D-Card Prof. Mohd. Zahid Hussain FCPS Prof. Muhammad Shahabuddin MD Dr. Md. Shamsul Alam D-Card, FSCAI Prof. Liakat Hossain Tapan, D.Card, M Sc. Dr. Abu Mohammed Shafique MD

Correspondence: Bangladesh Cardiac Society, Karukaj Hashim Heritage (1st Floor)
21/8, Khiljee Road, Block-B, Mohammadpur, Dhaka-1207, Bangladesh
Tel: 01799925522 (Office), E-mail: bcs@bol-online.com, Website: www.banglacardio.org

INSTRUCTION TO AUTHORS

A. Introduction

Bangladesh Heart Journal is the official journal of Bangladesh Cardiac Society, and accepts articles for publication from home and abroad. This is a biannual, peer-reviewed journal and aims to publish work of the highest quality from all sub-specialties of cardiology and cardiovascular surgery. The aim of the publication is to promote research in Bangladesh and serve as platform for dissemination of scientific information in cardiology.

B. Categories of Articles

The journal accepts original research, review articles, case reports, cardiovascular images and letters to the editor, for publication.

Original Research:

Original, in-depth research article that represents new and significant contributions to medical science. Each manuscript should be accompanied by a structured abstract of up to 250 words using the following headings: Objective, Methods, Results, and Conclusions. Three to 5 keywords to facilitate indexing should be provided in alphabetical order below the abstract. The text should be arranged in sections on INTRODUCTION, METHODS, RESULTS and DISCUSSION. The typical text length for such contributions is up to 3000 words (including title page, abstract, tables, figures, acknowledgments and key messages). Numberof references should be limited to 50.

Review Articles:

Generally review articles are by invitation only. But unsolicited reviews will be considered for publication on merit basis. Following types of articles can be submitted under this category: Newer drugs, new technologies and review of a current concept.The manuscript should not exceed 5000 words (including tables and figures). A review article should include an abstract of up to 250 words describing the need and purpose of review,methods used for locating, selecting, extracting and synthesizing data, and main conclusions. The number of references should be limited to 50.

Case Reports:

Only case reports of exceptional quality will be published in the case report format. The text should not exceed 1500 words and is arranged as introduction, case report and discussion. Include a brief abstract of about 150 words. Number of tables/figures should be limited to 3. Include up to 10 most recent references. The patient's written consent, or that of the legal guardian, to publication must be obtained.

Cardiovascular Images:

Only clinical photographs with or without accompanying skiagrams, pathological images, echocardiographic images, angiographic images etc. are considered for publication. Image should clearly identify the condition and have the classical characteristics of the clinical condition. Clinical photographs of condition which are very common, where diagnosis is obvious, or where diagnosis is not at all possible on images alone would not be considered. Photographs should be of high quality, usually 127 × 173 mm (5 × 7 in) but no larger than 203 × 254 mm (8 × 10 in). A short text of up to 250 words depicting the condition is needed. Figures should be placed exactly at a logical place in the manuscript. The submitted images should be of high resolution (>300 dpi). The following file types are acceptable: JEPG and TIFF. The number of authors should not exceed 3. The authors should ensure that images of similar nature have not been published earlier. Authors must obtain signed informed consent from the patient, or the legal guardian.

Letter to the Editor:

Letters commenting upon recent articles in Bangladesh Heart Journal are welcome.Such letters should be received within 16 weeks of the article's publication. Letters should be up to 250 words; should contain no more than 1 figure/table and upto 5 most recent references. The text need not be divided into sections. The number of authors should not exceed 3.

C. Criteria for Acceptance

All manuscripts should meet the following criteria: the material is original, study methods areappropriate, data are sound, conclusions are reasonable and supported by the data, and the information is important; the topic has general cardiology interest; and that the article is written in reasonably good English. Manuscripts which do not follow the guidelines of Bangladesh Heart Journal are likely to be sent back to authors without initiating the peer-review process. All accepted manuscripts are subject to editorial modifications to suit the language and style of Bangladesh Heart Journal and suggestions may be made to the authors by the Editorial Board to improve the scientific value of the journal.

D. Editorial Process

The Bangladesh Heart Journal commits to high ethical and scientific standards. Submitted manuscripts are considered with the understanding that they have not been published previously in print or electronic format (except

in abstract or poster form) and are not under consideration by another publication or electronic medium. Statements and opinions expressed in the articles published in the Journal are those of the authors and not necessarily of the Editor. Neither the Editor nor the Publisher guarantees, warrants, or endorses any product or service advertised in the Journal. Bangladesh Heart Journal follows the guidelines on editorial independence produced by the International Committee of Medical Journal Editors (ICMJE). All manuscripts correctly submitted to the Bangladesh Heart Journal are first reviewed by the Editors. Manuscripts are evaluated according to their scientific merit, originality, validity of the material presented and readability. Some manuscripts are returned back to the authors at this stage if the paper is deemed inappropriate for publication in the Bangladesh Heart Journal, if the paper does not meet the submission requirements, or if the paper is not deemed to have a sufficiently high priority. All papers considered suitable by the Editors for progress further in the review process, undergo peer review by at least two reviewers. If there is any gross discrepancy between the comments of two reviewers, it is sent to a third reviewer. Peer reviewers' identities are kept confidential; authors' identities are also not disclosed to the reviewers. Accepted articles are edited, without altering the meaning, to improve clarity and understanding. Decision about provisional or final acceptance is communicated within 8 weeks.

E. Cover Letter

The cover letter should outline the importance and uniqueness of the work. It should include the signed declaration from all authors on:

1. Category of manuscript (original research, review article, case report, cardiovascular image, letter to the Editor)
2. Statement that the material has not been previously published or submitted elsewhere for publication (this restriction does not apply to abstracts published in connection with scientific meetings.)
3. Transfer of copyright to the Bangladesh Heart Journal upon the acceptance of the manuscript for publication
4. All authors have reviewed the article and agree with its contents
5. Information of any conflicts of interest (of any) of the authors.
6. Sources of research support, if any, including funding, equipment, and drugs.

The cover letter should also include the mailing address, telephone and fax numbers, and e-mail address of the corresponding author.

F. Manuscript Preparation

The manuscripts should comply with the prescribed guidelines. It should be well organized and written in simple and correct English under appropriate headings. The abbreviations and acronyms should be spelled out when they occur first time.

The Introduction should address the subject of the paper. The Methods section should describe in adequate detail the laboratory or study methods followed and state the statistical procedures employed in the research. This section should also identify the ethical guidelines followed by the investigators with regard to the population, patient samples or animal specimens used. A statement should be made, where applicable, that their study conforms to widely accepted ethical principles guiding human research (such as the Declaration of Helsinki) AND also that their study has been approved by a local ethics committee.The Results section should be concise and include pertinent findings and necessary tables and figures.The Discussion should contain conclusions based on the major findings of the study, a review of the relevant literature, clinical application of the conclusions and future research implications. Following the Discussion, Acknowledgements of important contributors and funding agencies may be given.

a. Title page information

- Title. Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations where possible.
- Author names and affiliations. Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower case superscript letter immediately after the author's name and in front of the appropriate address. Provide the e-mail address of each author.
- Corresponding author. Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.

b. Abstract

A concise and factual abstract is required. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. References should be avoided. Also, non-standard or uncommon abbreviations should be

avoided, but if essential they must be defined at their first mention in the abstract itself.

c. Keywords

Immediately after the abstract, provide a maximum of 5 keywords. Keywords should be the listed terms in the Medical Subject's Headings (MeSH) of the National Library of Medicine (NLM), available at https://www.nlm.nih.gov/mesh.

d. Abbreviations

Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

e. Acknowledgements

Collate acknowledgements in a separate section at the end of the article before the references. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

f. Units

Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI. Generic rather than trade names of drugs should be used.

g. Figures and graphics

- For graphics, a digital picture of 300 dpi or higher resolution in JPEG or TIFF format should be submitted.
- Figures should be numbered consecutively according to the order in which they have been first cited in the text, if there is more than 1 figure. Each figure should be cited in the text.
- Each figure/illustration should be provided with a suitable legend that includes enough information to permit its interpretation without reference to the text.
- All photomicrographs should indicate the magnification of the prints.
- When symbols, arrows, numbers or letters are used to identify parts of the illustrations, each one should be explained clearly in the legend.

h. Tables

Tables should be placed next to the relevant text in the article.

- Number tables consecutively in accordance with their appearance in the text. Each table should be cited in the text in Arabic numerals.
- Titles should be brief and a short or abbreviated heading for each column should be given.
- Explanatory matter should be placed in footnotes and not in the heading.
- Abbreviations in each table should be explained in footnotes.
- The data presented in a table should not be repeated in the text or figure.

i. References

References should follow the standards summarized in the NLM's International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals (ICMJE recommendations), available at: http://www.icmje.org/recommendations/. The titles of journals should be abbreviated according to the style used for MEDLINE (www.ncbi.nlm.nih.gov/nlmcatalog/journals). Journals that are not indexed should be written in full.

- References should be numbered consecutively in the order in which they are first mentioned in the text.
- References in text, tables and legends should be identified by superscript Arabic numerals at the end of the sentence outside any punctuation. If several different studies or papers are cited within one sentence, the number should be placed where it will accurately identify the correct study.
- The names of authors in the text should concur with the reference list.
- References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration.
- Abstracts as references may be used; "unpublished observations" and "personal communications" may not be used as references, although references to written, not oral, communications may be inserted (in parentheses) in the text.
- Papers accepted but not yet published may be included as references by adding "In press" after the journal name. Information from manuscripts submitted but not yet accepted should be cited in the text as "unpublished observations" (in parentheses).
- In general: All authors/editors should be listed unless the number exceeds six, when you should give six followed by "et al."

Examples of correct forms of references are given below:

Articles in Journals (see also *Journal article on the Internet*)

1. *Standard journal article*

List the first six authors followed by et al.

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25;347(4):284-7.

More than six authors:
Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.

2. *Organization as author*

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance.Hypertension. 2002;40(5): 679-86.

3. *Both personal authors and organization as author* (List all as they appear in the byline.)

Vallancien G, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1,274 European men suffering from lower urinary tract symptoms. J Urol. 2003;169(6):2257-61.

4. *Volume with supplement*

Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42Suppl 2:S93-9.

5. *Issue with supplement*

Glauser TA. Integrating clinical trial data into clinical practice.Neurology. 2002;58(12 Suppl 7):S6-12.

6. *Type of article indicated as needed*

Tor M, Turker H. International approaches to the prescription of long-term oxygen therapy [letter]. Eur Respir J. 2002;20(1):242.

Lofwall MR, Strain EC, Brooner RK, Kindbom KA, Bigelow GE. Characteristics of older methadone maintenance (MM) patients [abstract]. Drug Alcohol Depend. 2002;66Suppl 1:S105.

7. *Article published electronically ahead of the print version*

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. Blood. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

Books and Other Monographs

1. *Personal author(s)*

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

2. *Editor(s), compiler(s) as author*

Gilstrap LC 3rd, Cunningham FG, VanDorsten JP, editors.Operative obstetrics. 2nd ed. New York: McGraw-Hill; 2002.

3. *Organization(s) as author*

Advanced Life Support Group. Acute medical emergencies: the practical approach. London: BMJ Books; 2001. 454 p.

4. *Chapter in a book*

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

5. *Conference proceedings*

Harnden P, Joffe JK, Jones WG, editors.Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer; 2002.

6. *Dissertation or thesis*

Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

Other Published Material

Newspaper article

Tynan T. Medical improvements lower homicide rate: study sees drop in assault rate. The Washington Post. 2002 Aug 12;Sect. A:2 (col. 4).

Unpublished Material

In press or Forthcoming

Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. ProcNatlAcadSci U S A. Forthcoming 2002.

Electronic Material

1. *Journal article on the Internet*

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle

Article published electronically ahead of the print version:

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells.Blood. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

Article with document number in place of traditional pagination:

Williams JS, Brown SM, Conlin PR. Videos in clinical medicine.Blood-pressure measurement. N Engl J Med. 2009 Jan 29;360(5):e6. PubMed PMID: 19179309.

Article with a Digital Object Identifier (DOI):

Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. BMJ. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752. PubMed PMID: 19129307; PubMed Central PMCID: PMC2615549.

2. *Monograph on the Internet*

Foley KM, Gelband H, editors. Improving palliative care for cancer [Internet]. Washington: National Academy Press; 2001 [cited 2002 Jul 9]. Available from: http://www.nap.edu/books/0309074029/html/.

3. *Homepage/Web site*

Cancer-Pain.org [Internet]. New York: Association of Cancer Online Resources, Inc.; c2000-01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: http://www.cancer-pain.org/.

G. Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. The submission has not been previously published elsewhere, is original and has been written by the stated authors.
2. The article is not currently being considered for publication by any other journal and will not be submitted for such review while under review by the Bangladesh Heart Journal.
3. The submission file is in Microsoft Word file format, and the figures are in JEPG or TIFF format.
4. The text is single-spaced; uses a 12-point font; employs italics, rather than underlining (except with URL addresses); and all illustrations, figures, and tables are placed within the text at the appropriate points, rather than at the end.
5. The text adheres to the stylistic and bibliographic requirements outlined in the Instruction to Authors. Make sure that the references have been written according to the ICMJE Recommendations Style.
6. Spell and grammar checks have been performed.
7. All authors have read the manuscript and agree to publish it.

H. Submission

Papers should be submitted to the Editor. Three copies of manuscript should be submitted duly signed by all authors with a copy of CD, to:

Prof. Hl Lutfur Rahman Khan
The Editor, Bangladesh Heart Journal
Professor of Cardiology
Room No. 458, Block B, Anwer Khan Medical College
House No. 17, Road No 8, Dhanmondi, Dhaka 1205
Bangladesh.

Papers can also be submitted via the email using the following address:

Email: bangladeshheartj@yahoo.com

Original Article

Percutaneous Coronary Intervention (PCI) of Left Main (LM) Stem Disease: Our Experiences in a Tertiary Care Hospital

AHM Waliul Islam[1], Shams Munwar[2], AQM Reza[2], Shahabuddin Talukder[2], Tamzeed Ahmed[2], Azfar H Bhuiyan[3], Kazi Atiqur Rahman[2]

Abstract:

Background: It is well known that coronary artery bypass graft (CABG) is considered as gold standard treatment of left main (LM) stem disease. Over the years PCI of left main (LM) stem disease, proved its non-inferiority to CABG in treating LM stem disease

Objectives: Exact data of LM stem PCI and its procedural success, in-hospital, and post-procedural one-year survival outcome in-terms of repeat hospitalization due to re-infarction, LVF and death, in our population not known clearly. Therefore, we have carried out this prospective observational cohort to see the overall outcomes of LM Stem, PCI in our population

Methods and materials: Patients who underwent elective CAG and found LM stem disease and planned for PCI, were enrolled in this non-randomized observational study between November 2013 to September 2019. Total 146 patient (F 29; Male 117) were enrolled in this study.

Results: Out of 146 patients, female :19.8% (n=29) vs Male: 80.1% (n=117). Among, these patient females were more obese (BMI: Female 29.8 ± 3.6 vs male 26.8 ± 3.8). Male patients were older than female; Male 59 yrs. vs female 56 yrs. Among the CAD risk factors Hypertension (HTN) 67.8% (n=99), dyslipidemia 56.2% (n=82), Diabetes Mellitus (DM) 51.4% (n=75), smoking 31.5% (n=46), Family history of CAD (FH) 21.2% (n=31). In this study, 19.2%(n=28) patient had CABG in the past. Common Stented territories were ostial LM 6.8%(n=10), shaft of LM 28.8% (n=42), distal LM-LAD 47.3% (n=69), distal LM-LCX 15.1% (n=22) and distal LM-RI 2.7% (n=4). Common DES were Everolimus 69.9% (n=102), Sirolimus 12.3% (n=18), Zotarolimus 9.6%(n=14), BMS 4.8% (n=7), Sirolimus with Epithelial Progenitor Cell 3.4% (n=5), and Biolimus 2.1% (n=3). In terms of post procedural dual antiplatelet therapy (DAPT), patients receiving Clopidogrel were 57.5% (n=85), Ticagrelor 28.8% (n=42), and Prasugrel 13.7% (n=20). Total 12 patient died due to acute, sub-acute stent thrombosis or re-infarction with or without arrhythmia. Relook CAG done was only in 14.4% (n=21) patients, Stent patency 80.9% (n=17), significant ISR, later went to CABG 14.3%(n=3) and mild ISR 4.7% (n=1). IVUS guided PCI were done only in 10.9% (n=16) patients. Major adverse cardiac events in terms of periprocedural MI, repeat hospitalization or death were not common in this study.

Conclusion: PCI of LM stem disease is one of the important treatment modalities over CABG in our patient population. Very few patients developed re-stenosis, that needs repeat revascularization either by PCI or CABG. Thus, we may conclude, PCI of LM stem disease might be an alternative to CABG and needs comparative multicenter study to justify its superiority outcome in our patient population.

Key Words: LM, PCI, CABG

(Bangladesh Heart Journal 2020; 32(2): 78-86)

1. Consultant, Interventional Cardiology, Evercare Hospital, Dhaka.
2. Senior Consultant, Interventional cardiology, Evercare Hospital, Dhaka.
3. Specialist, Interventional cardiology, Evercare Hospital, Dhaka.

Address of Correspondence: Prof. Dr. AHM Waliul Islam, Interventional cardiology Department, Evercare Hospitals Dhaka. E-mail: Waliul.islam@evercarebd.com

Introduction:

Coronary artery bypass grafting (CABG) is considered as the gold standard in treating unprotected left main stem coronary artery (LMCA) disease.[1] Whereas percutaneous coronary intervention (PCI) was previously only performed as salvage treatment. Significant benefit

DOI: https://doi.org/10.3329/bhj.v35i2.52893

of LM stem PCI with CABG over PCI and medical treatment shown has been shown in several studies.[2-3] Over the last 20 years, advancement of PCI technique, improvement of stent technology and adjunctive drug therapy has led to progressively improved PCI outcomes for LMCA disease.[4] In addition to different imaging modalities with intravascular ultrasound (IVUS), optical coherence tomography (OCT) and individual operators expertise has improved PCI of ULMCA. ULMCA disease is seen in 5-7% patients undergoing coronary angiography.,[5] 50% mortality those treated medically.[6-7]

Historically, the first reported balloon angioplasty of the LMCA was performed in 1979 by Gruntzig.[8] Later, in 1989, a series of 129 patients' cases were reported,[9] with 10% in hospital and 64% 3-year mortality. By the mid-1990s, development of stenting techniques, DAPT allowed interventionist to do LM stem PCI again. LM stem PCI by BMS characterized high procedural success rate with 17-20% and 10-20% mortality in 1st year.[10-11] The availability of drug eluting stents for the treatment of ULMCA stenosis showed significant reduction of restenosis and target lesion revascularization (TLR).[12-14] Several observational single and multicenter registries showed that PCI of ULMCA by second or third generation DES had a good efficacy and safety profile.

Bangladesh is a densely populated country where death from Cardiovascular disease is number one in all-cause mortality. Many of the centers, with the availability of imaging modalities IVUS, OCT, many of the centers are routinely doing LM stem PCI. There is insufficient data regarding the safety, in-hospital mortality, and morbidity. Therefore, we have carried out this prospective observational study, to investigate the outcome of PCI of ULMCA in our population, a single center experience.

Method:

Materials: Patients who underwent elective CAG and found to have significant LM stem disease and later, percutaneous coronary intervention by deploying drug eluting stent, were enrolled in the observational non-randomized prospective cohort study. Total 146 patient (F 29; Male 117) were enrolled in this study.

PCI Procedures:

LM stem PCI performed by using standard 6F guide catheter, guide wires, balloon catheters and DES via both Femoral and Radial routes. Patients received 5000-unit bolus of heparin, followed by an additional 2000 units during the procedure. Coronary stenting was performed with standard technique with contrast dose left to individual operator discretion. Further, stent optimization was done by post-dilatation whenever required. Successful PCI was defined as a visually assessed 20-30% residual stenosis with TIMI-III distal flow (ref0. After the PCI, patients were shifted to CCU. Patient were pre-loaded with either Ticagrelor or clopidogrel along with Aspirin. Most of the patients received loading and maintenance doses of GP IIb/IIIa receptor blocker abciximab unless any contraindication as a common strategy in our lab.

Statistical Analysis

All data were summarized and displayed as mean ± standard deviation and in percentage of distribution. No statistical comparison was made.

Results:

Total 146 patients were enrolled in this observational prospective cohort study. Among them, 19.8%(n=29) were female vs 80.1% (n=117) were male. Table 1. Shows the demographic profile of studied patient. Among, these patient females were more obese (BMI: Female 29.8 ± 3.6 vs male 26.8 ± 3.8). Male patients were older than females (59 vs 56 years respectively). Fig. 1 shows the distribution of CAD risk factors. Among the coronary artery

Table-I

Demographic Profile of patient

	Male	Female
Number	117	29
Age (yrs.)	59.0±11.0	56.0±14.0
BMI (kg/m^2)	26.8±3.8	29.8±3.6
SBP(mmHg)	125.0±14.8	124.0±17.7
DBP(mmHg)	76.2±8.9	75.0±9.9
No. of CAD Risk Factor	3.0±1.0	2.0±1.0
LVEF %	52.0±8.9	53.6±8.1

Data were presented as Mean±SD

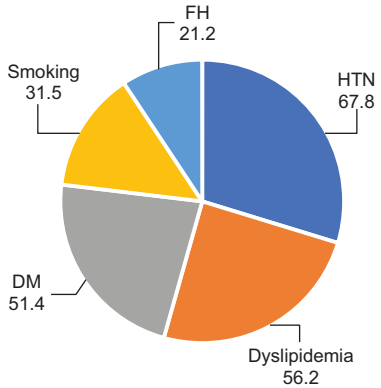


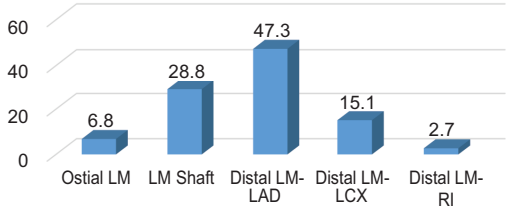
Fig.-1: *Percentage Distribution of CAD Risk Factors*

disease (CAD) risk factors for hypertension (HTN) 67.8% (n=99), Dyslipidemia 56.2% (n=82), diabetes mellitus (DM) 75 (51.4%), smoking 31.5% (n=46), family history (FH) 21.2% (n=31). Number of CAD risk factors were more in male, as all smokers in this study were male. In this study, 19.2%(n=28) patient had CABG in the past and not considered as or belong to UPLMCA. Table 2. Shows the average stent diameter according to location for ostial LM and LM shaft 3.7 mm, LM-LAD 3.4 mm, LM-LCX 3.3 mm and LM-RI 2.8 mm., indicating small size coronary vessel in this part of world. LVEF is almost same in both sex; in male 52 vs female 53%. Figure 2. Showed the distribution of lesion in the studied population.

Table-II
Average Size of Stent & Inflation Pressure at each segment of LM

	Diameter (mm)	Length (mm)	Inflation Pressure (ATM)
Ostial LM	3.7±0.4	14.9±5.9	16.0±1.13
LM Shaft	3.7±0.4	15.5±7.4	16.8±2.0
Distal LM-LAD	3.4±0.4	25.9±9.3	17.8±1.9
Distal LM-LCX	3.3±0.4	22.2±6.6	18.2±2.4
Distal LM-RI	2.8±0.7	26.7±8.1	16.5±4.1

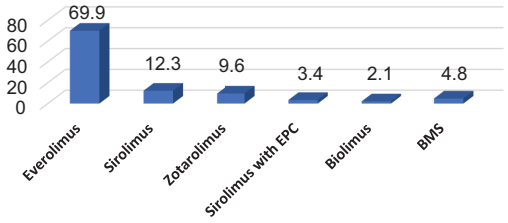
Data were presented as Mean ± SD



Common Stented territories were ostial LM 6.8%(n=10), shaft of LM 28.8% (n=42), distal LM-LAD 47.3% (n=69), distal LM-LCX 15.1% (n=22) and distal LM-RI 2.7% (n=4)

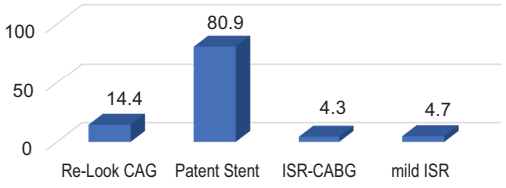
Fig.-2: *Percentage Distribution of Stented Territory of LM*

Common Stented territory were, Ostial LM 6.8% (n=10), shaft of LM 28.8% (n=42), distal LM-LAD 47.3% (n=69), distal LM-LCX 15.1% (n=22) and distal LM-RI 2.7% (n=4). LM-LAD lesion PCI followed by LM shaft lesion are the commonest LM segment lesions stented. Figure 3. Showed the distribution of common drug eluting stents. Common DES were, Everolimus 69.9% (n=102), Sirolimus 12.3% (n=18), Zotarolimus 9.6%(n=14), BMS 4.8%(n=7), Sirolimus with Epithelial Progenitor Cell 3.4% (n=5), Biolimus 2.1% (n=3). Among the P2Y12 inhibitors Clopidogrel were given in 57.5% (n=85), Ticagrelor in 28.8%(n=42), Prasugrel in 20 (13.7%). Total 8.2% (n=12) patient died due to acute, sub-acute stent thrombosis or re-infarction with or without arrythmia. Figure 4. Showed the findings of relook CAG done in a very small percentage of patients i.e., 14.4% (n=21). Among them, stent was patent in 80.9%(n=17), significant ISR, later went to CABG 14.3%(n=3) and mild ISR was found in in 4.7%(n=1). IVUS guided PCI were done only in 10.9%(n=16). Figure 5. Shows distribution of oral anticoagulant, Clopidogrel followed by Ticagrelor an Prasugrel were the commonest used oral P2Y12 inhibitors. Figure 6. Showed percentage distribution of status post CABG or who had CABG in the past were in 19.2%(n=28), IVUS guided PCI were done in 10.9% (n=16) and patient died after LM stem PCI in 8.2% (n=12). Figure 7. Showed IVUS guided LM stem PCI in a patient with 90% stenotic lesion from its distal 2/3rd segment by deploying a 3.5 x 48 mm Everolimus Eluting stents covering the LM ostium to proximal LAD lesion. Figure 8. Showed pre and Post PCI IVUS image of the same patient with well apposed expanded stent in LM stem. Figure 9. Shows PCI of LM-LAD and LCX by kissing (DK crush) technique. After ballooning both LM-LAD and LCX,



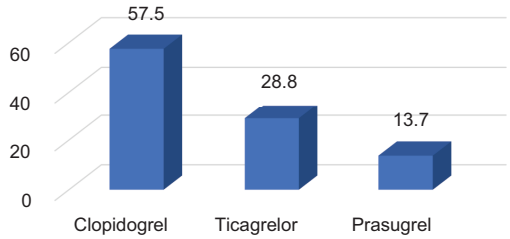
Common DES were Everolimus 69.9% (n=102), Sirolimus 12.3% (n=18), Zotarolimus 9.6%(n=14), BMS 4.8% (n=7), Sirolimus with Epithelial Progenitor Cell 3.4% (n=5), and Biolimus 2.1% (n=3)

Fig.-3: *Percentage distribution of different Drug Eluting Stents used*



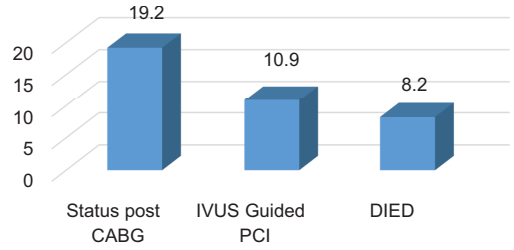
Relook CAG done was only in 14.4% (n=21) patients, Stent patency 80.9% (n=17), significant ISR, later went to CABG 14.3%(n=3) and mild ISR 4.7% (n=1)

Fig.-4: *Percentage Distribution of Re-look CAG in the Studied Patient*



Dual antiplatelet therapy (DAPT), patients receiving Clopidogrel were 57.5% (n=85), Ticagrelor 28.8% (n=42), and Prasugrel 13.7% (n=20)

Fig.-5: *Percentage Distribution of P2Y12 inhibitor as component of DAPT (n=146)*



status post CABG or who had CABG in the past were in 19.2%(n=28), IVUS guided PCI were done in 10.9% (n=16) and patient died after LM stem PCI in 8.2% (n=12)

Fig.-6: *Percentage distribution of SP CABG, IVUS guided PCI and patient died*

Fig.-7: *Showed LM stem lesion PCI in a patient with LM stem Disease*

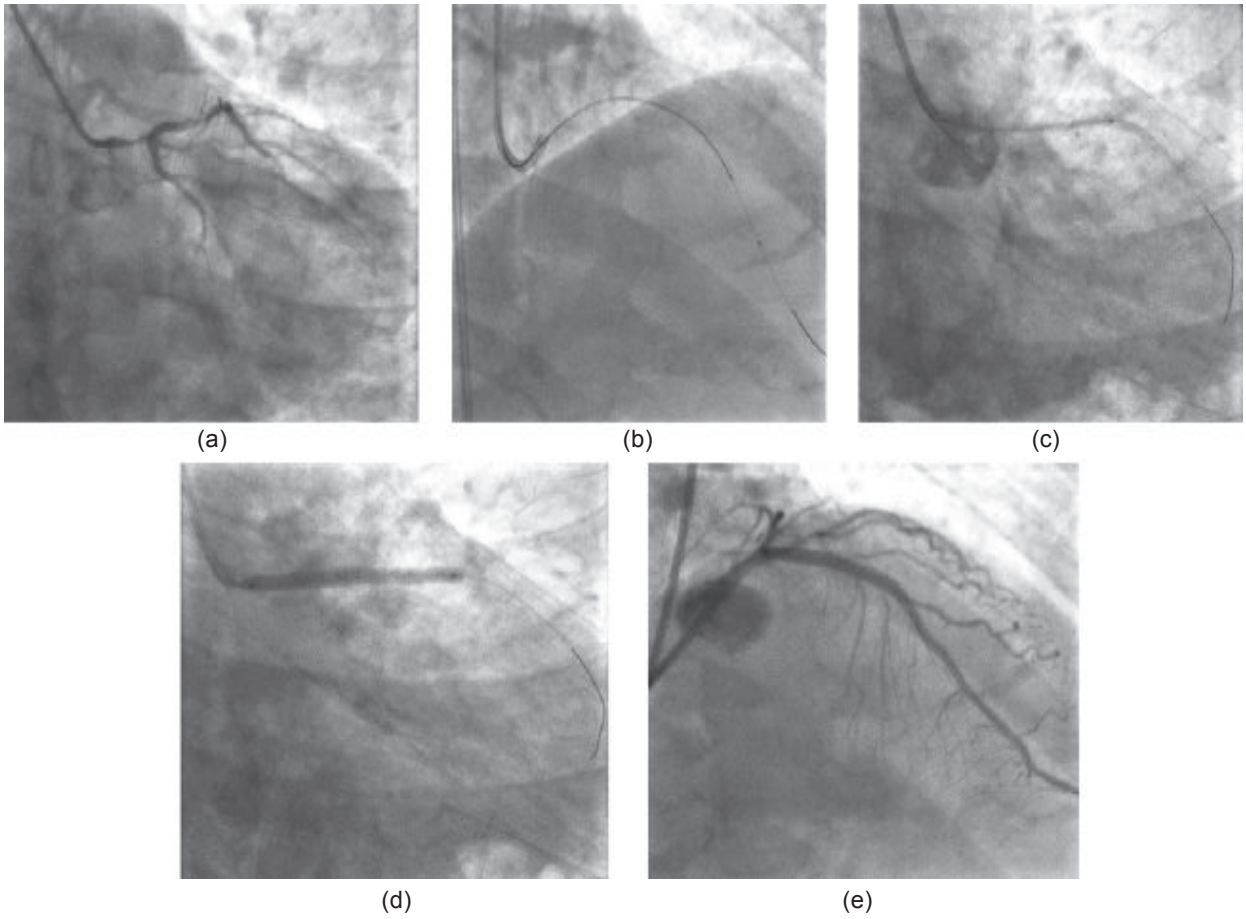
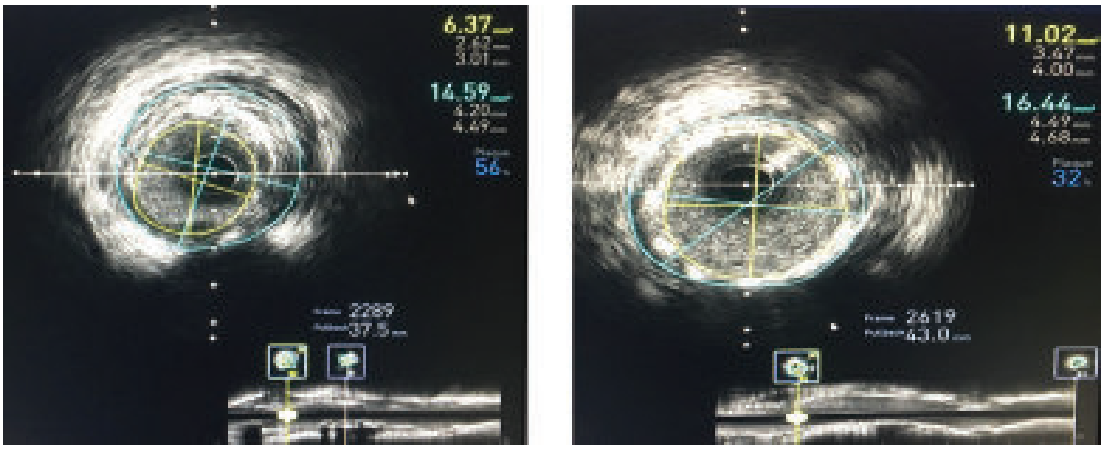


Fig.-7: *(a). 90% distal LM and 70Proximal LAD lesion, (b & c). 3.5 x 48 Everolimus Eluting Stent positioning, (d). Deployment of stent, while JL Catheter tip hanging at LM ostium, (e). Final cine after post dilation by 4.0 x 10mm NC balloon, showed well apposed stent*

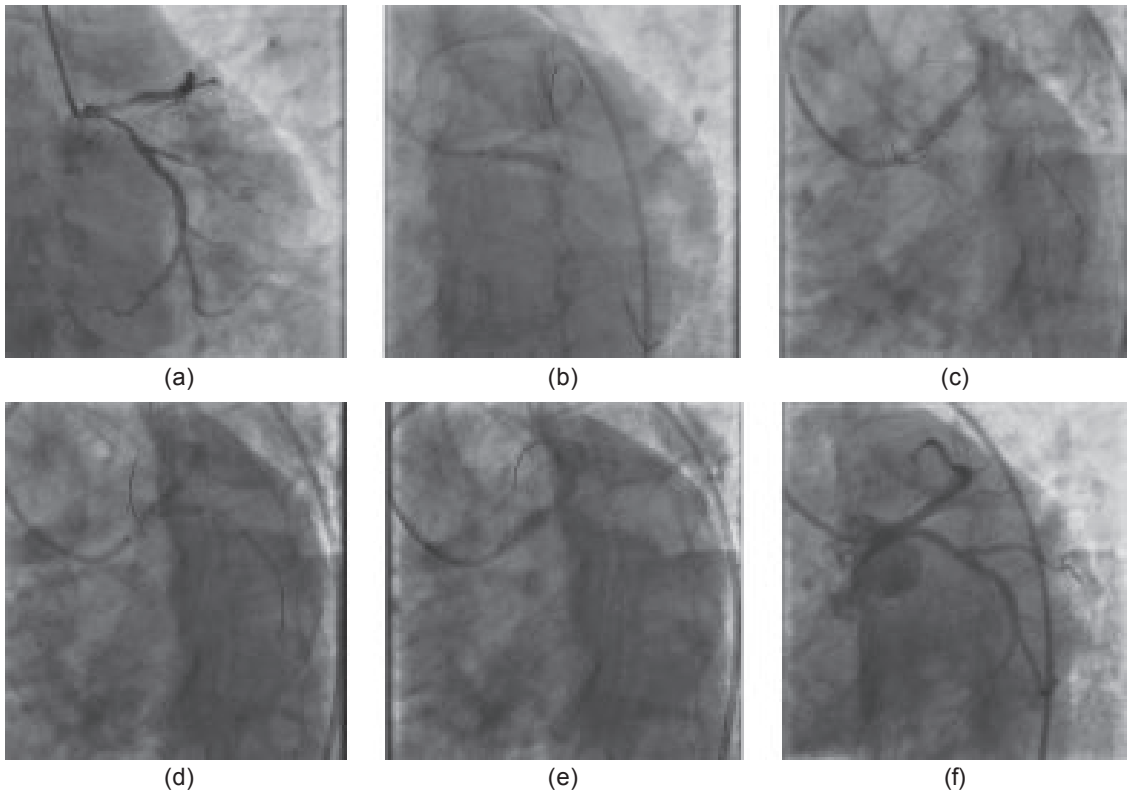
Figure 8. Shows both pre-post PCI IVUS Image of LM stem PCI
Left panel **Fig 8a**; showed Pre PCI IVUS images, showed stenotic lesion, Right Pane **Fig 8b.** post PCI IVUS image; well expanded stent and next one showed with complete apposition of and expansion of stent without edge tear.



(a) (b)

Fig.-8: *a. Pre PCI IVUS image of culprit LM lesion,* ***b.*** *Post PCI IVUS Image of LM Lesion*

Figure 9. Shows PCI of LM-LAD and LCX by Kissing (DK Crush) Technique



(a) (b) (c)

(d) (e) (f)

Fig.-9: *a. 50% distal LM and 90%Proximal LAD and 70% Proximal LCX lesion, b. 3.5 x 15 Everolimus Eluting stent in LCX deployed after kissing balloon, c. LM-LAD stenting by a 4.0 x23 Everolimus Eluting Stent, d. Further Kissing of both stent, e. POT of LM stent by 4.5 x 10 mm balloon at 18ATM, f. Final cine after post dilation by 4.0 x 10mm NC balloon showed well apposed stent.*

Everolimus Eluting 2.5 x 15 mm stent deployed covering the LCX ostium. Then, LM-LAD stenting done by 4 x 23 mm Everolimus eluting stent. Further optimization by kissing ballooning of both stent and POT of LM by a 4.5 x 10 mm balloon at 18ATM done. IVUS was done in LM-LAD which was showed LM-LAD & LCX were well dilated with clear bifurcation area.

Discussion:

With the growing number of cardiac catheterization laboratory facilities and the amount of expertise in the field of interventional cardiology, now a days many of the centers are performing percutaneous interventional procedures throughout the country. Availability of IVUS, OCT imaging facility and imaging physiology study by FFR, aids the needs of interventional procedures like stenting and details study of the lesion characterization and further stent optimization, thus, improving the quality of intervention and reduce the mortality and morbidity. We have carried out this observational prospective non-randomized study of LM stem PCI at our tertiary care center.

The *LMCA is responsible* for *supplying* about *75%* of the *left ventricular* (LV) *cardiac* mass in patients with *right dominant* type and 100% in the case of *left dominant* type. As a result, significant LM stem stenosis either, ostial, in shaft or distal segment disease will reduce flow to large portion of myocardium, thus may place patient at high risk for life threatening events of LV dysfunction or life-threatening arrhythmia. As we know, atherosclerotic lesion tends to occur where flow is disturbed specially in area of low shear stress.[15] In LMCA bifurcation, intimal atherosclerosis is accelerated in low shear stress area in lateral wall close to LAD/ LCX bifurcation.

Coronary artery bypass graft (CABG) or percutaneous coronary Intervention (PCI) are the well-known modalities in revascularizing the LM stem disease. Although, it is debatable, the superiority of CABG and PCI, and guideline recommendation has been updated time to time. Recent comparative studies of PCI and surgical revascularization for unprotected LM Stem PCI, demonstrated that PCI may be an alternative to CABG in treating ULMCA.[16] Clinical outcome may vary according to LM lesion site and complexity. Specially, disease of distal LM bifurcation increases PCI related complexity and is associated with worse clinical outcome compared to ostial LM or shaft segments.[17-18] Non-distal LM stem PCI is associated with favorable clinical outcomes.[19] Simple bifurcation lesions treated with one stent strategy more favorable than complex lesion treated with two-stent approach.[20-21] High plaque burden, patients with distal ULMCA PCI with two-stent approach showed TLR 25% with restenosis. two stents technique either crush, culotte, V- or T-stenting are mostly operator driven.

In the early era of DES, several randomized clinical trials, suggested that PCI achieved similar mortality and composite outcomes, more repeat frequent revascularization in PCI and frequent stroke in CABG.[21] These trials have been adequately powered or have included second generation DES with better safety and efficacy profile compared with first generation DES.[22] The EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Graft Surgery for Effectiveness of Left Main Revascularization) trial and the Noble (Nordic Baltic British left main revascularization study) trial are notable clinical trial on revascularization of LM stem disease. Excel found that PCI is noninferior to CABG and NOBLE shows CABG is superior to PCI.[23-24] The EXCEL trial shows similar 3-year outcomes for the composite primary endpoint of death, MI or stroke with PCI by using CoCr-EES compared with CABG. Repeat revascularization with 3 years for ischemia were more frequent in distal LM bifurcation PCI in previously reported studies distal LM lesion is shown as an important predictor of TLR after PCI.[25]

Multicenter registry study reported that patients with ostial or mid shaft LM CAD had a favorable prognosis after PCI with first Generation DES,[19] worse outcome in distal LM bifurcation lesion PCI than ostium or shaft.[26] In our present study, distal LM-LAD lesion represents 47.3% followed by shaft of LM 28.8%, distal LM-LCX lesion 15.1% , ostial LM 6.8% and distal LM-RI 2.7% and distal LM-LAD lesion PCI followed by LM shaft lesion are the commonest LM segment lesions stented. Although, many of the centers doing LM stem PCI routinely, exact data on survival outcome, stent patency or repeat revascularization is not well known in our patient perspectives. Average size of stent used for LM ostium and shaft 3.7 mm, LM-LAD / LM-LCX were 3.4 / 3.3 mm, indicating small size vessel in this part of world.[27]

Repeat revascularization rates during follow up after PCI compared to CABG were greater for lesion in distal LM but similar for LM ostium or shaft in previous studies. Metanalysis of several RCTS (PRE-COMBAT, SYNTAX, NOBLE, EXCEL) reported primary safety endpoint of death, MI, stroke was similar between PCI and CABG. Patients with UPLMCA disease, CABG and PCI results similar safety composite endpoint of death, myocardial infarction, or stroke. Among patients with isolated LM or + 1 vessel CAD PCI is associated with lower all-cause

mortality compared to CABG.[28] In our present observational study, only 14.4% (n=21) patients had relooked CAG and none of them underwent PCI, only three underwent CABG due to significant ISR. So, based on this finding, is very primitive to say that PCI is superior to CABG in our patient population. We need to have a set protocol for mandatory check CAG at least 3-6 months after PCI of LM and, need a multicenter LM registry. So, as to compare and better analyze, PCI outcome according to lesion location (shaft vs ostial vs distal LM).

ACC/AHA guideline recommends PCI of LMCA with stents a Class IIa recommendation for a SYNTAX score <22 and a class II b in patients with condition that associated with low risk in PCI or increased risk of surgical outcome with SYNTAX score 33.[29-30] Based on cumulative evidence of comparative studies of LMCA revascularization, guideline recommendation for LMCA PCI has been less stringent. CABG considered the standard of care in treating ULMC disease.[31] In ESC 2018 guideline CABG is a class of recommendation / Level of evidence IB for LM revascularization and PCI is IB, but a IIa recommendation, level of evidence B or III B based on SYNTAX score (SYNTAX score 23 to 32).[32]

The advent of coronary stents along with the evolutions of dual antiplatelet therapy has dramatically lowered the incidence of abrupt vessel closure, and the drug eluting stents further decreased the risk of in-stent restenosis.[33] PCI is increasingly used to treat ULMCA disease.[34] IVUS guidance is helpful in assessing vessel size, adequate stent expansion and absence of stent malapposition. In the MAIN-COMPARE registry, IVUS guidance was associated with improved 3-year mortality compared with angiography guided PCI.[35] OCT has been reported to assess vascular response to LMCA stenting.[36] Available IVUS and FFR and OCT guided PCI of LM stem diseases is associated with reduced major adverse cardiac events with further stent optimization.[37] Only 10.9% (n=16) of our patient had IVUS guided PCI in the studied group. Due to financial restrain, IVUS guided LM stem PCI was not carried out many of the patients of this study.

Unprotected LM stem disease is a heterogenous condition that includes various degrees of anatomic location and severity of LM lesions, and various possible sets of concurrent lesions of other coronary segments.[38]

Age is also an important predictor of LM stem PCI. Mortality was high > 60% in isolated LM PCI in patients over 75 years of age, as high as 75% in those with associated other coronary involvement among with LM stem, while being lower in younger patients.[39] when performing LM PCI, patient comorbidities such as diabetes, renal failure, acute coronary syndrome on presentation, left ventricular dysfunction, concomitant valvular disease, previous cerebro-vascular events are possible key important factor for procedural outcomes.

A recent metanalysis reported that based on totality of randomized clinical trial data (SYNTAX, EXCEL and NOBLE), at a mean follow up time of 5.6 years, there was no significant difference in overall mortality after PCI with DES and CABG for the treatment of LM coronary disease. There was no significant long-term difference between CABG and PCI for cardiac death MI or stroke.[1]

Conclusion:

In this preliminary observational prospective cohort study of LM stem PCI, we found that PCI is a reasonable option in LM lesion. LM stem disease is one of the important predictors of cardiovascular mortality and morbidity. Several studies have shown that revascularization of LM stem disease by PCI is not inferior to CABG. Although, LM stem PCI carries a risk of stent thrombosis or significant ISR development. Individual operator expertise, availability of IVUS, OCT, FFR helped to determine, character, lesion type and subsequent stent optimization. Proper size stent uses, pre- and post-dilation with upsize balloon may help well apposition of stent, thus reduce the risk of ISR and subsequent repeat revascularization.

We recommend check or relook CAG for all LM stem PCI patient at 3-6 months interval, if not possible, then at one year after PCI. We recommend, multicenter national database on LM stem PCI to better define outcomes in Bangladeshi population, facilitate comparative registry-based studies with CABG.

Limitations:

Due to financial issue, IVUS guided LM stem PCI with better lesion characterization and stent optimization not possible in most of the patients with LM stem disease. Limited numbers underwent relook CAG, no comparison of outcomes with CABG.

Acknowledgement:

Akhter Hossain, Sr. Cath Technician for IVUS assistance

References:

1. Jean Fajadet and Alaide Chieffo et al. Current management of left main coronary artery disease. European Heart Journal (2012) 33, 36–50
2. Ahmad Y, Howard JP, Arnold AD et al. Mortality after drug eluting stents vs coronary artery bypass grafting for left main coronary artery disease; a

meta-analysis of randomized controlled trials. Eu Heart J 2020; 41:3228-3235

3. Chaitman BR, Fisher LD, Bourassa MG et al. effect of coronary bypass surgery on survival patterns in subset of patients with left main coronary artery disease report of the collaborative study in coronary artery surgery (CASS). Am J Cardiol 1981; 48: 765-777
4. Lee PH. Ahn JM, Chang M et al. Left main coronary artery disease: secular trends in patient characteristics, treatments, and outcomes. J Am Coll Cardiol. 2016; 68:1233-1246
5. Stone P, Goldschalger N. Left main coronary artery disease: review and appraisal. Cardiovasc med 1979; 4:165-177
6. Taylor H, Deumite N, Chaitman B et al. Asymptomatic left main coronary artery disease in the coronary artery surgery study (CASS) registry. Circulation 1989; 79:1171-1179
7. Cohen M, Gorlin R. Main left coronary artery disease; clinical experience from 1964-1974. Circulation;1975; 52:275-285
8. Gruentzig AR, Stenning A, Siegeuthaler WE. Non-operative dilatation of coronary artery stenosis. Percutaneous transluminal coronary angiography. N Eng J Med. 1979; 301:61-8
9. O'Keefe JH, Jr., Hartzler GO, Rutherford BD et al. Left main coronary angio0plasty; early and late results of 127 acute and elective procedures. Am J Cardiol 1989; 64:144-147
10. Park SJ, Park SW, Hong MK et al. outcome after stenting of unprotected left main coronary stenosis in patients with normal left ventricular function. Am J Cardiol 2003; 91:12-16
11. Takagi T, Stakovic G, Finci L et al. Result and long-term predictors of adverse clinical events after elective percutaneous interventions on unprotected left main coronary artery. Circulation 2002;106;698-702
12. Park SJ Kim YH Lee BK et al. Sirolimus eluting stents implantation for unprotected left main coronary stenosis; comparison with bare metal stents implantation. J Am Coll Cardiol 2005; 45:351-356
13. Price MJ, Cristea E, Sawhney N et al. Serial angiographic follow-up of sirolimus eluting stents for unprotected left main coronary artery revascularization J Am Coll Cardiol 2006;47: 871-877
14. Chieffo A Park SJ Meliga E et al. Late and very late stent thrombosis following drug eluting stents implantation in ULMCA; a multicenter registry Eur Heart J 2008; 29:2108-2115
15. Kalbfleisch H. Hort W. Quantitative study on the size of coronary artery supplying areas postmortem Am Heart J 1977;94:183-188
16. Nerlekar N, Ha FJ, Verma KP et al. percutaneous coronary intervention using drug eluting stents versus coronary artery bypass grafting for unprotected left main coronary artery stenosis: a meta-analysis of randomized trials. Circ Cardiovasc interv 2016;9e04729. Doi:10.1161/circinterventions. 16.004729
17. Valgimigli M, Maslagutti P, Rodriguez-Granillo GA et al. Distal LM coronary artery disease is a major predictir of outcomes in patients undergoing PCI in the drug eluting stent era: a RESEARCH and T-SEARCH registries. J AM Coll Cardiol 2006; 47:1530-1537
18. Biondi-Zoccai GG, Lotrionte M et al. A collaborative systemic review and meta-analysis of 1278 patients undergoing percutaneous drug-eluting stenting for unprotected left main coronary artery disease. Am Heart J 2008; 155:274-283 doi:10.1016/ ahj.207.10.09
19. Chieffo A, Park SJ, Valgimigli M. et al. A favorable long-term outcome after drug-eluting stent implantation in non- bifurcation lesions that involve unprotected left main coronary artery: a multicenter registry. Circulation 2007:116:158-162
20. Meliga E, Garcia-Garcia HM, Valgimigili M et al. Longer available clinical outcomes after drug eluting stent implantation for unprotected left main coronary artery disease.: the DELFT Registry. J Am Coll cardiol. 2008:51:2212-2219
21. Morice MC, Serruyus PW, Kappetein AP et al. outcomes in patients de novo left main disease left main disease treated with either PCI with paclitaxel stents or CABG treatment in the SYNERGY between PCI with TAXUS and Cardiac surgery (SYNTAX) trial, Circulation 2010;121;2645-2653
22. Palmerinin T, Benedetto U, Biondi-Zoccai G et al, Long term safety of drug eluting and bare metal stent or bypass surgery for left main coronary artery disease. J Am Coll Cardiol 2015; 65:2496-25047. Doi; 10.1016/j.jacc.2015.04.017

23. Stone GW, Sabik JF, Serruyus PW, Simonton CA et al. EXCEL Trial investigators. Everolimus eluting stents or bypass surgery for left main coronary disease. N Eng HJ Med 2016; 375:2223-2235 Doi 10.1056/NEJMoa1610227

24. Makikallio T, Holm NR, Lindsay M et al. NOBLER Study. A prospective, randomized, open-label, non-inferiority trial. Lancet 2016; 388:2743-2752

25. Song PS, Song Y Bin, Lee JM et al. Major predictors pf long term clinical outcomes after percutaneous coronary interventions for coronary bifurcation lesions with 2-stent strategy. J Am Coll Cardiol Interv 2016; 9:1879-86

26. Naganuma T, Chieffo A, Meliga A et al. Long-term clinical outcomes after percutaneous coronary intervention for ostial/ mid shaft lesions versus distal bifurcation lesions in unprotected left main coronary artery. The DELTA registry: a multicenter intervention registry

27. AHM Waliul Islam, Shams Munwar et al. Percutaneous Coronary Intervention (PCI) in Small Vessel Coronary Artery Disease (CAD) in patient with Diabetes Mellitus. Bangladesh Heart Journal 2007;22(2): 70-75

28. Rafael Cavalcante, Stomi Y, Lee WC etal. Outcomes after percutaneous intervention or bypass surgery in patients with unprotected left main disease. J Am Coll Cardiol 2016; 68:999-1009

29. Levine GN, Bates ER, Blankship JC et al. 2011 ACC/ AHA/ SCAI guidelines for percutaneous coronary intervention: a report of American College of Cardiology Foundation or American Heart Association task force on practice guidelines and the society for Cardiovascular Angiography and Interventions. JACC 2001;58: e44-122

30. Kushner FG, Hand M, Smith Sc Jr aet al. ACC/AHA guidelines for the management patients with ST elevation MI. Circulation 2009;120:2271-2306

31. Takaro T, Peduzzui P, Detre KM et al. Survival in subgroups of patients with Left main coronary artery disease: veterans Administration cooperative study of surgery in coronary arterial occlusive disease. Circulation 1982:66L:14-22

32. Windecker S, Kolh P, Alfonso F et al. 2018 ESC/ EACTS Guideline on myocardial revascularization: The task force on Myocardial revascularization of the European society of Cardiology (ESC) and European association for cardiothoracic surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Intervention (EAPCI). Eur Heart J 2018; 00:1-96

33. Taggart DP, Kaul S, Boden WE et al. Revascularization of unprotected left main stem coronary artery stenosis: stenting or surgery. J Am Coll Cardiol 2008:51:885-92

34. Kandzari DE, Colombio A. Park SJ et al. Revascularization for unprotected left main disease-Evolution of the evidence basis to redefine treatment standards. J Am Coll Cardiol. 2009; 54:1576-88

35. Park SJ Kim YH Park DW et al. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. Circ Cardiovasc Interv 2009; 2:167-177

36. Parodi G, Maehara A, Giuliani G et al. Optical coherence tomography in unprotected left main coronary artery stenting. Euro intervention 2010; 6:94-99

37. Bech GJ, Droste H, Pijls NH et al. Value of fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Eng J Med 2009; 360:213-24

38. Corti R, Toggweiler S. PCI in acute LM stem disease: a paradigm shift or a new reality? Eur Heart J 2009; 30:2295-6

39. Dzavik V, Sleeper LA, Picard MH et al. Outcome of patient aged>75 years in the SHOCK trial: do elderly patients with acute myocardial infarction complicated by cardiogenic shock respond differently to emergent revascularization? Am Heart J 2005; 149:1128-34.

Original Article

Systematic Review and Pooled Meta-analysis of the Current Status of Coronary Revascularization Surgery in Bangladesh

Faizus Sazzad[1], Ashlynn Ai Li Ler[2], Geetha Ganesh[3], Marcus Kung[4], Theo Kofidis[5]

Abstract

Background: There is no consensus on the role of beating heart coronary artery bypass graft surgery (BECAB) in adult Bangladeshi patients requiring coronary revascularization surgery. We aimed to conduct a systematic review on all literature related to BECAB and/or conventional (CCAB) to determine the comparability of the patient outcomes of BECAB with that of a controlled cohort.

Method: We carried out a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. A meta-analysis was conducted to compare clinical outcomes between the BECAB and CCAB cohorts. Pooled analyses were also performed to determine the incidence rates of any adverse outcomes related to CABG.

Results: We observed significantly lower rates of operation time (MD: -52.30, CI: -67.73 to -36.86, p<0.0001), ventilation time (MD: -8.64, CI: -9.47 to -7.82, p<0.0001) and ICU stay (MD: -17.47, CI: -33.57 to -1.38, p=0.03) associated with BECAB. From our pooled analyses of the BECAB cohort, we observed that the average blood loss was 500.303 [352.099, 648.507], while the average rates of perioperative MI (0.020 [0.002, 0.049]), stroke/TIA (0.015 [0.000, 0.042]), AKI (0.006 [0.002, 0.012]), respiratory complications (0.020 [0.000, 0.058]) and low output syndrome (0.123 [0.106, 0.141]) were all lower than the averages observed in the CCAB cohort.

Conclusion: In an adult Bangladeshi CABG population, the clinical outcomes of patients that underwent BECAB were non-inferior to, if not better than, patients who underwent CCAB.

Keywords: *BECAB: Beating heart coronary artery bypass surgery; CCAB: Conventional coronary artery bypass surgery; Coronary Artery Bypass, Bangladesh*

(Bangladesh Heart Journal 2020; 32(2): 87-99)

Introduction:

In the era of changing prospects of clinical practice in coronary revascularization surgery, beating heart coronary artery bypass surgery (BECAB) is gaining popularity worldwide as well as in Bangladesh. On

1. Research Fellow/Cardiac Surgeon, Assistant Director, Cardiac Surgery Experimental Lab, Cardiovascular Research Institute (CVRI), National University of Singapore, Singapore.
2. Research Intern, Cardiac Surgery Experimental Lab, NUS, Singapore and School of Medicine, National University of Ireland, Galway, Ireland
3. Consultant, Cardiac Surgery Experimental Lab, National University of Singapore, Singapore and Indian Institute of Technology Madras, Chennai, India
4. School of Biomedical Engineering, Temasek Polytechnique, Singapore
5. Chairman, Initiative for Research and Innovation of Surgery, Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore and Head & Senior Consultant, Department of Cardiac, Thoracic and Vascular Surgery, National University Heart Centre, Singapore

Address of Correspondence: Faizus Sazzad, Research Fellow/Cardiac Surgeon, Department of Surgery (CTVS), Yong Loo Lin School of Medicine, National University of Singapore, MD-6 Building, Level-08 #South, 14, Medical Drive, Singapore 117599, Office: +65-66011434, Fax: +65-6775 8538, e-mail: surmfs@nus.edu.sg

DOI: https://doi.org/10.3329/bhj.v35i2.52894

average, more than 10,000 patients undergo coronary artery bypass graft (CABG) surgery each year.[1] As coronary artery disease continues to remain one of the most common forms of heart disease and is the single most significant cause of death in the adult Bangladeshi population,[2] the volume of CABG surgeries has only been increasing over the last decade.

As CABG surgery continues to evolve, developments in the field of CABG research has seen more focus on the arterial conduit with the introduction of newer long-acting cardioplegia and modifications to the surgical technique i.e. the minimally invasive approach.[3] Nevertheless, conventional CABG (CCAB) remains the more popular surgical procedure as a result of institutional practice and surgeon's preference.[4] Additionally, the overall patient outcomes of CABG have improved recently, but revascularisation of the heart still poses a greater risk of perioperative and postoperative death and morbidity.[3,4]

Changes in the practice of CABG in Bangladesh are up-to-date with the current research climate. In particular, recent reports have demonstrated that off-pump CABG is now widespread and has produced good clinical outcomes even in patients with left main coronary artery disease.[5] However, there is a paucity of studies reporting outcomes in larger patient cohorts that have been published within the last decade, with even fewer reports on BECAB being published in indexed medical journals.

Hence, there is a need for further research to be done in this area. A comparison of the named technique was therefore warranted. The objective of the present analysis was to quantify the clinical outcomes of coronary revascularization surgery in a standard adult Bangladeshi CABG cohort to reflect the incidence of early postoperative major adverse events (AEs) including myocardial infarction (MI), stroke, acute kidney injury (AKI), need for blood transfusion, atrial fibrillation (AF) and death. To achieve this objective, we systematically reviewed all relevant published literature in order to determine the average rates of each AE as well as discuss the comparability of off-pump CABG with conventional CABG in terms of patient outcomes.

Methods:

Search Strategy: A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standard.[6] We conducted electronic searches on Medline (via PubMed), Embase, Cochrane database records from the date of inception to 20 March 2020. On the PubMed database, a repetitive and exhaustive combination of the following 'Medical Subject Headings' (MeSH) search terms were used: "Aortocoronary Bypass", "Bypass Surgery", "Coronary Artery Bypass", "Coronary Artery Bypass Grafting", "Coronary Artery Bypass Surgery", "Coronary Artery Bypass, Off-Pump", "Beating Heart Coronary Artery Bypass", "Beating Heart Off-Pump Coronary Artery Bypass" and "Bangladesh". An alternative search on The Ubiquity Partner Network (UPN) via Bangladesh Journal Online (BanglaJOL)[7] was also performed using following search terms: "Aortocoronary Bypass, Bangladesh", "Bypass Surgery, Bangladesh", "Coronary Artery Bypass, Bangladesh" and other Mesh terms were repeated as mentioned above.

Inclusion criteria and exclusion criteria: Any prospective observational, interventional studies, retrospective cohort studies, case-control study, cross-sectional study and randomised controlled trials that reported clinical outcomes of both BECAB and/or CCAB surgery for coronary revascularization were included. Animal studies, experimental studies, survey results, small case series, case reports and studies that were not written in the English language were excluded.

Study selection: Three reviewers (F.S, A.L, G.G) screened and assessed the studies independently for inclusion. The scientific papers were first screened by their titles and abstracts, where the criteria used was purposely broad to include all relevant studies. The full text review was performed on articles if the reviewer was unable to confirm the relevance of the study for inclusion.

Three authors (F.S, A.L, M.K) independently abstracted the details of the study population, including preoperative baseline characteristics. In addition, data on all relevant clinical outcomes was obtained from each study for the generation of forest plots.

Quality of evidence and risk of bias assessment: As illustrated in chapter 11 of the Cochrane handbook of reviews to validate the quality of evidence found in our systematic review,[8] GRADEpro was used to evaluate the quality of evidence in the included studies (Table 1). As recommended in chapter 25 (section 25.3) of the online Cochrane Handbook version 5.1,[9] the software ROBINS-I tool[10] (Risk of Bias in Non-randomized Studies-of Interventions) was utilised to assess the risk of bias for non-randomized studies as seen in Table 2.

Table-I

Risk of bias of the included study for coronary revascularization surgery in Bangladesh

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Beating	Arrested	Relative (95% CI)	Absolute (95% CI)		
A. Assessed with: Trop I[11], BMI, AF, DM & Euroscore[11,14,16,28,34]												
5	NCC NCT	serious [a]	serious [b]	not serious	not serious	none	120/120 (100.0%)	180/240 (75.0%)	not estimable		⊕⊕◯◯ LOW	CRITICAL
B. Assessed with: Low EF, Radial Artery[12,32]												
2	RCT	serious [b]	serious [b]	not serious	not serious	publication bias strongly suspected [b]	30/200 (15.0%)	30/60 (50.0%)	not estimable		⊕◯◯◯ VERY LOW	CRITICAL
C. Assessed with: BIMA, Coronary Endarterectomy[17,33]												
2	RCS RSS	serious [a]	serious [c]	not serious	not serious	strong association	134/2781 (4.8%)	0/0	not estimable		⊕⊕⊕◯ MODERATE	CRITICAL
D. Assessed with: NCD HS-CRP[29]												
2	CSS	serious [a]	serious [b]	not serious	not serious	none	30/30 (100.0%)	100/100 (100.0%)	not estimable		⊕⊕◯◯ LOW	CRITICAL
E. Assessed with: MPV, Skeletonized IMA, BT, CEA, Aspirin Use, AF, RD, Low EF, DM, Euroscore, Tranexamic Acid use, Syntax Score and LM disease[15,18-27,30,31,35]												
14	POS PIS PCS	serious [a]	serious [a]	not serious	not serious	strong association	2204/3304 (66.7%)	362/362 (100.0%)	not estimable		⊕⊕⊕◯ MODERATE	CRITICAL

a. The study is an observational study with high risk of bias in confounding factors, b. Unspecified grouping of the study participants, c. Bias in selection of participants due to retrospective nature.

NCC: Nonrandomized controlled clinical study, **NCT**: Non-randomized Clinical Trail, **RCT**: Randomized Controlled Trail, **RSS**: Retrospective Study, **RCS**: Retrospective cross-sectional study, **CSS**: Cross sectional Study, **POS**: Prospective Observational Study, **PCS**: Prospective Cohort Study, **PIS**: Prospective Interventional Study. **CI:** Confidence Interval, **BMI:** Body Mass Index **AF:** Atrial Fibrillation, **DM:** Diabetes Mellitus, **EF:** Ejection Fraction, **BIMA:** Bilateral Internal Mammary Artery, **MPV:** Mean Platelet Volume, **CEA:** Carotid Endarterectomy, **HS-CRP:** High Sensitive C-Reactive Protein, **IMA:** Internal Mammary Artery, **BT:** Blood Transfusion, **RD:** Renal Dysfunction, **NCD**: Neurocognitive Dysfunction

Table-II

Summary of Included Studies

Sl	Author	Year	Study Design	Patients	BECAB	CCAB	Place of Study	Interest variable
BECAB and CCAB								
1	Badruzzaman et. al[11]	2010	Nonrandomized controlled clinical study	120	60	60	National Institute of Cardiovascular Diseases	Troponin I
2	Roy et. al[12]	2013	Randomized Controlled Trail	60	30	30	National Institute of Cardiovascular Diseases	Low Ejection Fraction
3	Ahmed et. al[13]	2018	Cross sectional Study	60	30	30	National Institute of Cardiovascular Diseases	Neurocognitive Dysfunction
4	Karim et. al[14]	2018	Non-randomized Clinical Trail	60	30	30	National Institute of Cardiovascular Diseases	Atrial Fibrillation
5	Alauddin et. al[15]	2019	Prospective Observational Study	100	50	50	Bangabandhu Sheikh Mujib Medical University	Renal Dysfunction
6	Kabir et. al[16]	2019	Nonrandomized controlled clinical study	60	30	30	National Institute of Cardiovascular Diseases	Euroscore
BECAB								
7	Saydur el al[17]	2016	Retrospective cross sectional study	134	134	0	United Hospital, Dhaka	Bilateral IMA
8	Sazzad et. al[18]	2016	Prospective Interventional Study	60	60	0	National heart Foundation Hospital & Research Institute	Skeletonized IMA
9	M Begum et. al[19]	2017	Prospective Observational Study	40	40	0	NICVD and BSMMU	Blood Transfusion
10	Ranjan et. al[20]	2017	Prospective Cohort Study	15	15	0	BSMMU and Al-Helal Specialized Hospital	Carotid Endarterectomy
11	R Karim et. al[21]	2018	Prospective Observational Study	48	48	0	National Institute of Cardiovascular Diseases	Use of Aspirin
12	Alam et. al[22]	2018	Prospective Interventional Study	100	100	0	National Institute of Cardiovascular Diseases	Atrial Fibrillation
13	Salekin et. al[23]	2018	Prospective Cohort Study	60	60	0	Bangabandhu Sheikh Mujib Medical University	Low Ejection Fraction
14	Ranjan et. al[24]	2019	Prospective Cohort Study	1403	1403	0	Bangabandhu Sheikh Mujib Medical University	Euroscore
15	Biswas et. al[25]	2020	Prospective Observational Study	428	428	0	National heart Foundation Hospital & Research Institute	Left main disease
CCAB								
16	Hasan et. al[26]	2016	Prospective Observational Study	81	0	81	National Institute of Cardiovascular Diseases	Mean Platelet Volume
17	Sazzad et. al[27]	2018	Prospective Observational Study	101	0	101	Ibrahim Cardiac Hospital & Research Institute.	Renal Dysfunction
18	J Alam et. al[28]	2018	Non-randomized Clinical Trail	60	0	60	National Institute of Cardiovascular Diseases	Body Mass Index
19	Rahman et. al[29]	2019	Cross sectional Study	70	0	70	National Institute of Cardiovascular Diseases	High Sensitive CRP
20	Ahsan et. al[30]	2019	Prospective Observational Study	60	0	60	National Institute of Cardiovascular Diseases	Diabetes Mellitus
21	Shahidullah et. al[31]	2019	Prospective Interventional Study	70	0	70	National Institute of Cardiovascular Diseases	Tranexamic Acid
Unspecified Group								
22	Alam et. al[32]	2017	Randomized Controlled Trail	200*	-	-	NICVD and Al-Helal Specialized Hospital	Radial Artery
23	Ranjan et. al[33]	2018	Retrospective Study	2647*	-	-	Bangabandhu Sheikh Mujib Medical University	Coronary Endarterectomy
24	Islam et. al[34]	2019	Non-randomized Clinical Trail	60*	-	-	National Institute of Cardiovascular Diseases	Diabetes Mellitus
25	Ranjan et. al[35]	2019	Prospective Observational Study	1100*	-	-	Bangabandhu Sheikh Mujib Medical University	Syntax Score
			Total (Group/Total)	**3190/7197**	**2518**	**672**		

** Unspecified grouping as per study requirement.* ***IMA:*** *Internal Mammary Artery,* ***NICVD:*** *National Institute of Cardiovascular Diseases,* ***BSMMU:*** *Bangabandhu Sheikh Mujib Medical University*

The risk of bias for each individual study[11-35] was mostly serious to critical. We believe that the retrospective and non-randomised nature of the included studies is responsible for these results. Since most of the studies used in the meta-analysis were observational studies, it has contributed to significant confounding and selection bias. The scientific journals reported that the surgeon's decision to proceed with BECAB or CCAB was heavily influenced by institutional practice and the expertise of the individual surgeon, which would somewhat explain the bias present in the studies. Moreover, a number of the included studies had missing data for the BECAB and/or CCAB groups, further contributing to the overall bias.

Data abstraction and outcomes of interest

Three authors (F.S, A.L, M.K) independently abstracted details of the study population. Data extracted included: Title, first author, year of publication, study type, number of patients. The primary outcome measures were operative outcome: operation time, number of grafts and in-hospital mortality. The secondary outcome measures were postoperative atrial fibrillation, ventilation time, length of ICU stay and duration of hospital stay.

Statistical analyses

All forest plots were generated using RevMan 5.3[36]. All meta-analyses were carried out using random-effects models to account for statistical variability across all studies that provided data of the clinical outcomes of coronary revascularization surgery. Pooled analyses of our results were carried out using the OpenMetaAnalyst Software[37]. We reported all the pooled results with 95% confidence intervals (95% CIs).

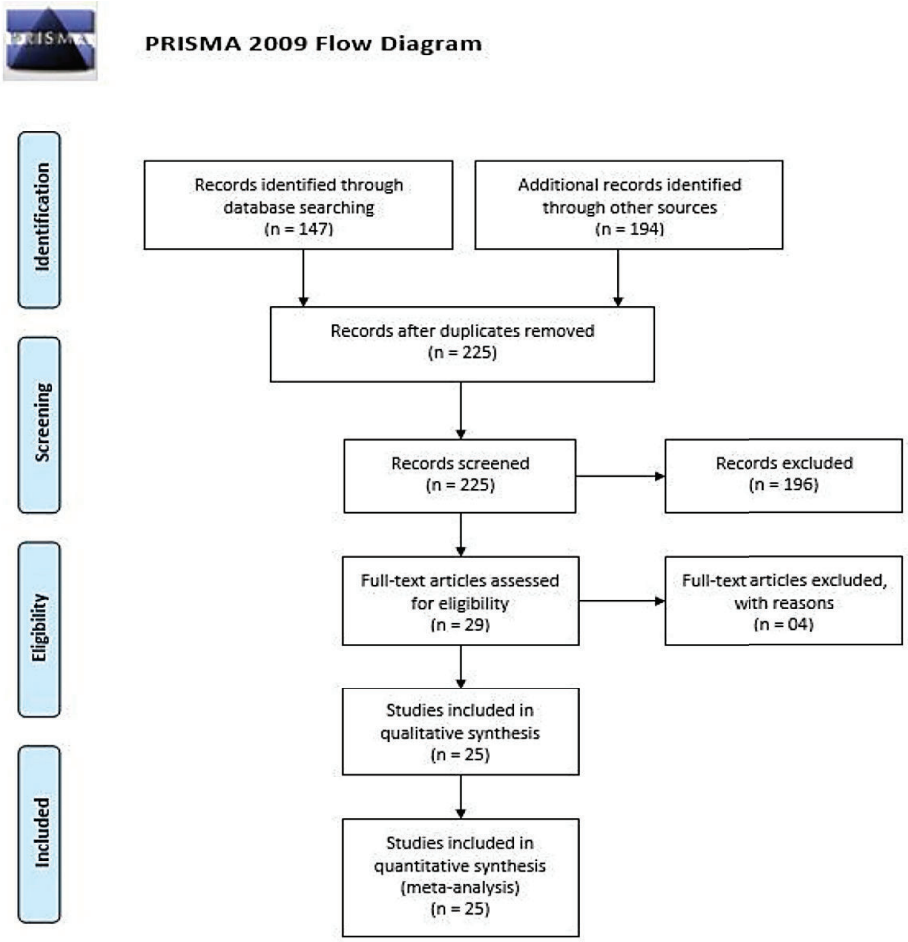


Fig.-1: *The systematic search revealed a total of 341 papers, of which 225 remained for review after duplicates were removed. After implementation of inclusion and exclusion criteria 29 articles were selected for full-text review. Following the full-text assessment of these articles, 25 studies remained for inclusion into the present study.*

Results

A total of 341 potential articles were identified from all databases (Figure 1). 25 studies included 7197 patients (2518 from BECAB, 672 for CCAB and 4007 with no assigned group) were selected following standard inclusion criteria for further analysis.

Quantity of evidence

The initial systematic search using our search strategy revealed a total of 147 published papers. An alternative search on The Ubiquity Partner Network (UPN) via Bangladesh Journal Online (BanglaJOL)[7] for published papers from Bangladesh revealed an additional 194 papers. After duplicates were excluded using Endnote X9 reference management software, 225 papers remained for further review.

Based on screening of titles and abstracts, irrelevant studies that did not satisfy our inclusion criteria were excluded, leaving 29 articles for full-text review. Following the full-text assessment of these articles, studies that lacked data on coronary revascularization surgery (n=4) were excluded, leaving 25 papers[11-35] for inclusion into the present study.

The PRISMA statement flow diagram shown in Figure 1 highlights the aforementioned screening process. We were aware that 4 studies from Ranjan et. al[20,24,33,35] and 2 studies each from Alam et. al[22,32] and Sazzad et. al,[18,27] all published in different years had been included in our meta-analysis as seen in Table 1. Assessment of the full texts verified that these studies were performed on completely different study populations, and were therefore included separately in our meta-analysis. To aid the identification of these papers, we made use of superscripted referencing throughout the present manuscript to properly distinguish the different publications.

Quality of evidence

From our risk of bias assessment of the included studies, we determined that 2 randomized controlled trials were associated with high risk of performance bias due to the outcome assessors not being blinded to the type of intervention[12,32] (Table-2). For the 14 prospective observational studies, [15,18-27,30,31,35] there was high risk of bias in confounding factors. The non-ramdomized clinical trials[11,14,16,28,34] were also significantly biased due to absence of randomization. Additionally, the bias in selection of patients was observed in retrospective studies[17,33] which is typical of studies that are retrospective nature. The included cross-sectional[13,29] studies were also devoid of comparative groups and thus had low significance to our study due to their small sample sizes. We determined that the evidence provided by these studies (and the included studies overall) was still of an acceptable quality (Table 1).

Of the 25 included studies, 5 were non-randomized clinical trail, 2 were retrospective cohort studies, 2 were randomized controlled trials, 2 were cross-sectional studies and 14 were prospective observational studies (Table 2). All studies were single-centre studies (Table 2).

Basic demographics and Preoperative characteristics

A majority of the CABG patients were male and 55 years old on average. The preoperative demographics analysis showed overall 62.48% patient had hypertension, 64.21% were smokers and 44.72% patients were diabetic. More diabetic and hypertensive patients were found in the BECAB group, while more smoker patients were in present in the CCAB group. However, these differences were statistically insignificant (Supplementary Table 2). Both groups were homogenous in terms of preoperative ejection fraction (EF), the number of NYHA –II/III patients and the number of patients with double vessel, triple vessel or left main coronary artery disease. The difference in incidence of preoperative stroke/ transient ischaemic attack (TIA) and MI between the 2 groups within 3 months of surgery was also insignificant.

Primary Outcomes

With the data from 5 studies and a total of 360 patients, we observed significantly lower operative times associated with BECAB as compared to CCAB (MD: -52.30, CI: -67.73 to -36.86, p<0.0001) (Figure 2A). There was no significant difference in the number of grafts used from 3 studies and 240 patients (MD: 0.15, CI: -0,54 to 0.84, p=0.67) (Figure 2B). There was also no significant difference in in-hospital mortality when data from 3 studies and 240 patients were compared (RR: 0.70, CI:0.22 to 2.25, p=0.55) (Figure 2C).

Secondary Outcomes

Comparing data from 3 studies and 180 patients, there was no significant difference in the rates of postoperative atrial fibrillation between the BECAB and CCAB groups (RR: 0.80, CI: 0.21 to 3.08, p=0.75) (Figure 2D). We observed shorter ventilation times associated with the BECAB group (MD: -8.64, CI: -9.47 to -7.82, p<0.0001) in

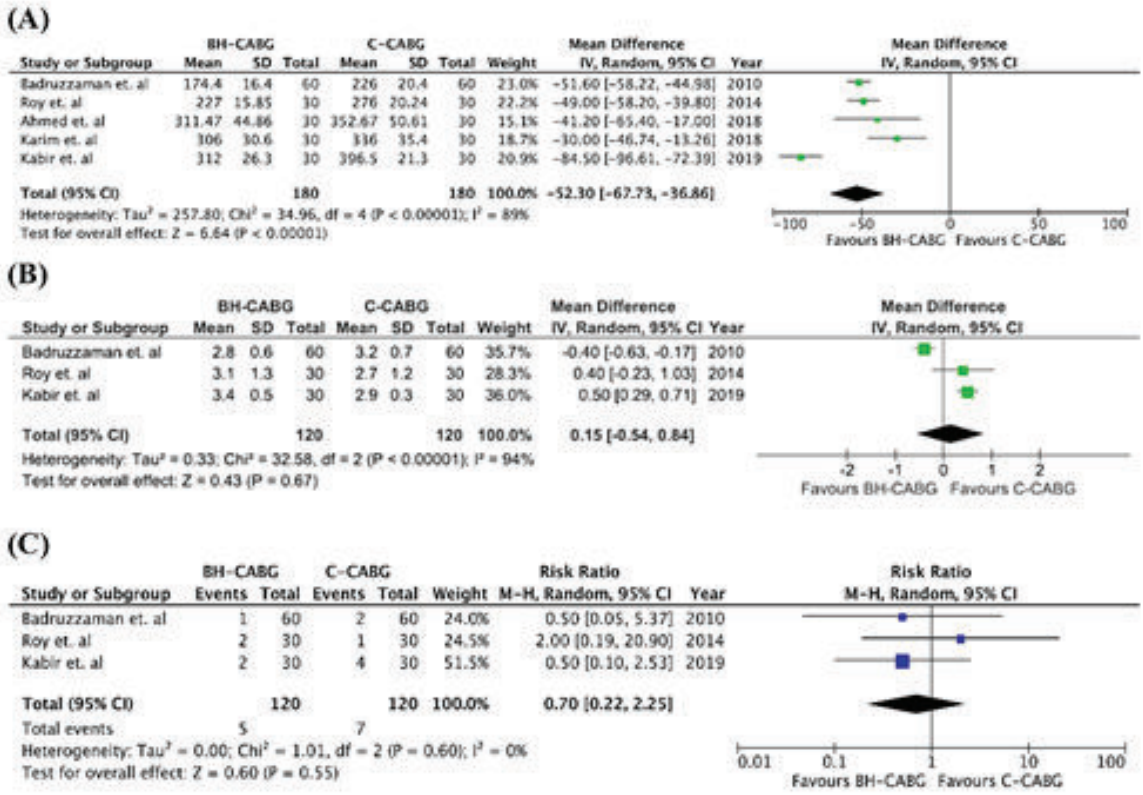


Fig.-2: *Forest plots showing (A) less operation time associated with BECAB, (B) no significant difference in the number of grafts used and (C) no significant in-hospital mortality.*

a pooled analysis of 5 studies and 360 patients (Figure 3E). With data from 5 studies and 400 patients, we also observed shorter ICU stays in the BECAB group as compared to the CCAB group (MD: -17.47, CI: -33.57 to -1.38, p=0.03) (Figure 3F). Finally, there were no significant differences in hospital stay between the groups when data from 3 studies and 180 patients were compared (MD: -0.41, CI: -2.79 to 1.98, p=0.74) (Figure 3G).

Analysis of Pooled Data

Our pooled analysis of 4 studies showed that the average blood loss for BECAB patients was 500.303 [352.099, 648.507] ml (I^2=99.62%, p<0.001). This was lower than the average blood loss for CCAB patients from 3 studies, which was 656.513 [453.537, 859.490] ml (I^2=99.68%, p<0.001). With data from 7 studies, the average incidence rate of perioperative MI for the BECAB group was 0.020 [0.002, 0.049] (I^2=80.00%, p<0.001), which was lower than that of the CCAB group at an average rate of 0.049 [0.015. 0.096] (I^2=42.56%, p=0.156). The pooled average rate of stroke or TIA for the BECAB group was 0.015 [0.000, 0.042] (I^2=63.84%, p=0.011), which was lower than that of CCAB group at an average rate of 0.081 [0.038, 0.136] (I^2=34.51%, p=0.191). The pooled average incidence rate of AKI with or without the need for dialysis was 0.006 [0.002, 0.012] (I^2=0.00%, p=0.543) for the BECAB group, which was lower than that of the CCAB group, with an average rate of 0.087 [0.055, 0.124] (I^2=0.00%, p=0.896). Pooled analysis of 6 studies showed that the average rate of respiratory complications in the BECAB group was 0.020 [0.000, 0.058] (I^2=70.65%, p=0.004), which was also lower than that of our pooled analysis of the CCAB group at a rate of 0.090 [0.043, 0.151] (I^2=18.41%, p=0.294). The rate of low output syndrome pooled from 2 studies was 0.123 [0.106, 0.141] (I^2=0.00%, p=0.369) for the BECAB group, while the pooled analysis of the CCAB group from 2 studies was 0.179 [0.108, 0.262] (I^2=0.00%, p=0.877). Finally, the average follow-up EF pooled from 5 studies for BECAB patients was 52.324 [48.200, 56.448] (I^2=98.64%, p<0.001), while pooled analysis of average EF of 3 studies for CCAB patients was 52.443 [42.097, 62.788] (I^2=99.68%, p<0.001) (Table 3).

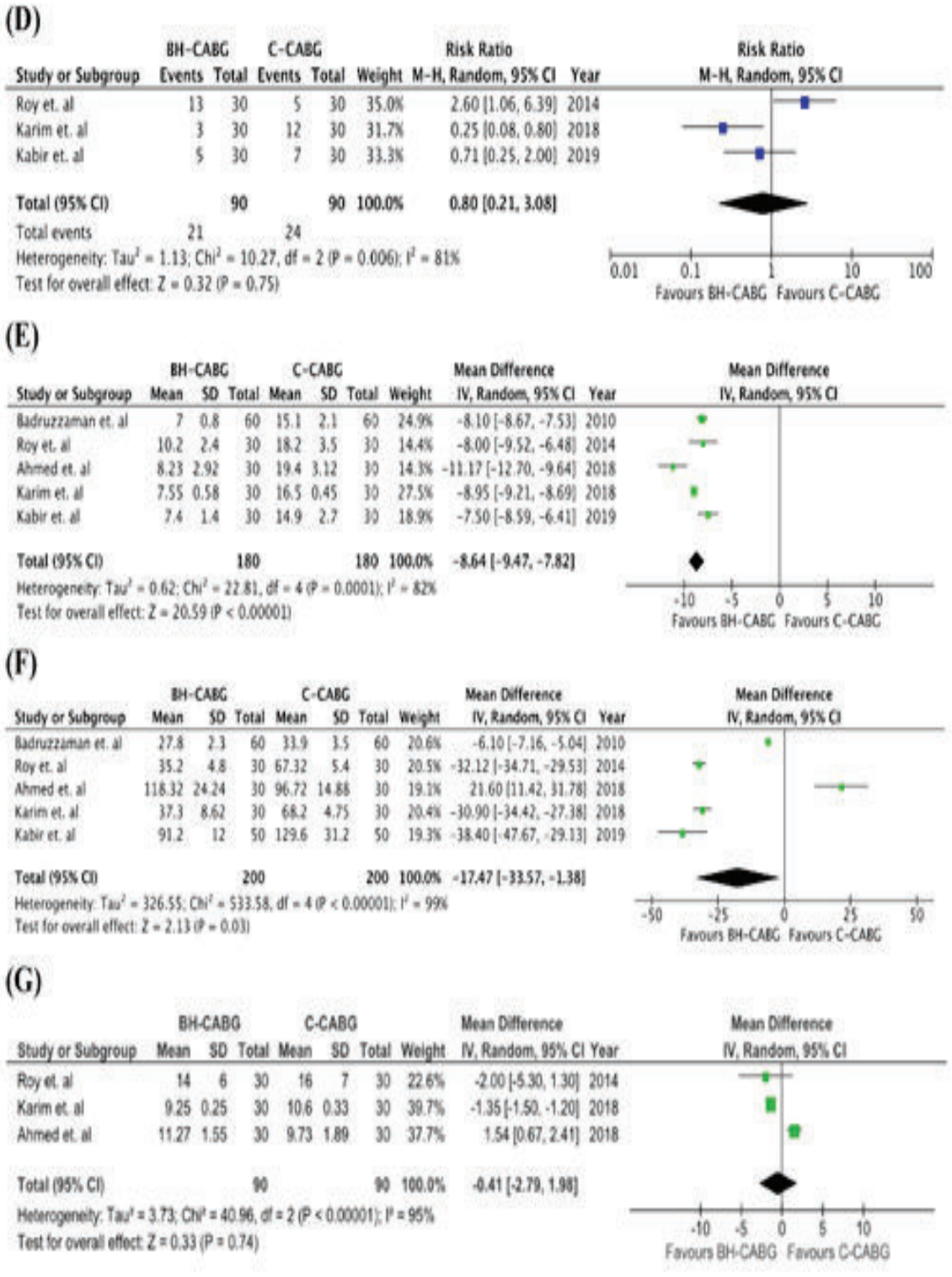


Fig.-3: *Forest plots showing (D) no significant difference in postoperative atrial fibrillation, (E) less ventilation time associated with BECAB, (F) shorter ICU stay associated with BECAB and (G) no significant difference in hospital stay.*

Table-III
Analysis of Pooled Data

Sl	Interest Variable	Study	BECAB	CCAB	Pooled Data
1	**Blood loss (ml)**	Roy et. al[12]	630.4±8.7	625.54 ±10.42	627.97 ±9.56
		Kabir et. al[16]	524.1±135.3	935.2±95.7	729.65±115.5
		Sazzad et. al[18]	475.92 ± 252.85	NA	475.92 ± 252.85
		R Karim et. al[21]	370.67±71.15	NA	370.67±71.15
		Hasan et. al[26]	NA	410.29±109.76	410.29±109.76
		Overall pooled	**500.303 [352.099, 648.507] I^2=99.62%, p<0.001**	**656.513 [453.537, 859.490] I^2=99.68%, p<0.001**	
2	**Perioperative MI (%)**	Roy et. al[12]	1.66	5	6.66
		Saydur el al[17]	3	NA	3
		M Begum et. al[19]	0	NA	0
		Ranjan et. al[20]	6.66	NA	6.66
		R Karim et. al[21]	6.25	NA	6.25
		Ranjan et. al[24]	3.35	NA	3.35
		Biswas et. al[25]	0	NA	0
		Hasan et. al[26]	NA	1.35	1.35
		J Alam et. al[28]	NA	6.35	6.35
		Ahsan et. al[30]	NA	8.33	8.33
		Overall pooled	**0.020 [0.002, 0.049] I^2=80.00%, p<0.001**	**0.049 [0.015. 0.096] I^2=42.56%, p=0.156**	
3	**Stroke/TIA (%)**	Roy et. al[12]	3.33	15	18.33
		Ahmed et. al[13]	6.7	0	6.7
		Kabir et. al[16]	0	8.7	8.7
		Saydur el al[17]	0	NA	0
		Ranjan et. al[20]	19.99	NA	20
		Salekin et. al[23]	0	NA	0
		Ranjan et. al[24]	0.81	NA	0.81
		J Alam et. al[28]	NA	11	11
		Ahsan et. al[30]	NA	5	5
		Overall pooled	**0.015 [0.000, 0.042] I^2=63.84%, p=0.011**	**0.081 [0.038, 0.136] I^2=34.51%, p=0.191**	
4	**Acute Kidney Injury with or without need for dialysis (%)**	Roy et. al[12]	3.33	6.66	10
		Kabir et. al[16]	3.7	13	8.35
		Saydur el al[17]	0.7	NA	0.7
		M Begum et. al[19]	2.5	NA	2.5
		Ranjan et. al[20]	6.66	NA	6.66
		Salekin et. al[23]	0	NA	0
		Ranjan et. al[24]	1.5	NA	1.5
		Sazzad et. al[27]	NA	7.92	7.92
		J Alam et. al[28]	NA	8.6	8.6
		Ahsan et. al[30]	NA	10	10
		Overall pooled	**0.006 [0.002, 0.012] I^2=0.00%, p=0.543**	**0.087 [0.055, 0.124] I^2=0.00%, p=0.896**	
5	**Respiratory complications (%)**	Roy et. al[12]	10	11.66	21.66
		Saydur el al[17]	0.7	NA	0.7
		M Begum et. al[19]	5	NA	5
		Ranjan et. al[20]	13.33	NA	13.33
		Salekin et. al[23]	0	NA	0
		Biswas et. al[25]	0.5	NA	0.5
		J Alam et. al[28]	NA	4.95	4.95
		Ahsan et. al[30]	NA	11.67	11.67
		Overall pooled	**0.020 [0.000, 0.058] I^2=70.65%, p=0.004**	**0.090 [0.043, 0.151] I^2=18.41%, p=0.294**	
6	**Low Output Syndrome (%)**	Roy et. al[12]	5	15	20
		Ranjan et. al[24]	12.95	NA	12.95
		Rahman et. al[29]	NA	18.57	18.57
		Overall pooled	0.123 [0.106, 0.141] I^2=0.00%, p=0.369	0.179 [0.108, 0.262] I^2=0.00%, p=0.877	
7	**Follow-up EF**	Badruzzaman et. al[11]	58.10±6.40	63.10±6.40	60.6±6.40
		Roy et. al[12]	46.26±2.01	42.9±1.7	44.58±1.85
		Kabir et. al[16]	51.6±2.8	51.4±2.9	51.5±2.85
		R Karim et. al[21]	55.34±3.97	NA	NA
		Salekin et. al[23]	50.46±5.06	NA	50.46±5.06
		Overall pooled	**52.324 [48.200, 56.448] I^2=98.64%, p<0.001**	**52.443 [42.097, 62.788] I^2=99.68%, p<0.001**	

Discussion:

BECAB is performed without the use of a heart-lung machine, thereby eliminating the need for placement of tubes, alternative artificial circulation and excessive manipulation of the aorta.[38] Despite these benefits, BECAB has its own set of challenges, particularly the difficulty that comes with operating on a constantly moving, blood-filled heart.[38] This has led to much discussion over the consequences of BECAB on patient outcomes and graft quality. Therefore, in our present study, we sought to perform a statistical evaluation of current literature reporting outcomes on BECAB, in order to discuss such concerns in an adult Bangladeshi CABG patient population.

From the results of our meta-analysis, we observed that there were significantly lower rates of operation time associated with BECAB as compared to CCAB. We speculate that this may present as a potential benefit of BECAB as evidence from previous studies have reported an association between longer operation times and higher risks of multiple organ dysfunction syndrome.[39] Longer operation times have also been shown to be significant predictors of mortality and morbidity.[40,41] Apart from shorter operation times, BECAB was also associated with shorter postoperative ventilation times and ICU stay. There were no significant differences in the number of grafts used, postoperative atrial fibrillation and hospital stay. This may suggest that the clinical outcomes of BECAB are non-inferior to, if not better than that of CCAB. Although, given the scarcity of papers that could be included in our meta-analysis, more research will be needed for any decisive conclusion to be made.

From our pooled analyses of patients in the BECAB cohort, we observed that the average blood loss was 500.303 [352.099, 648.507] ml, which was lower than that of the CCAB cohort. In addition, the average rates of perioperative MI (0.020 [0.002, 0.049]), stroke/TIA (0.015 [0.000, 0.042]), AKI (0.006 [0.002, 0.012]), respiratory complications (0.020 [0.000, 0.058]) and low output syndrome (0.123 [0.106, 0.141]) were all lower than the averages observed in the CCAB cohort. Once again, this may indicate that the clinical outcomes of BECAB may prove to be better than that of CCAB. However, once again we hesitate to conclude this with certainty due to the significant heterogeneity across the studies and between the groups, which made a direct statistical comparison between the average AEs of the BECAB and CCAB cohorts difficult.

In our meta-analysis, we observed high heterogeneity present in our comparisons of operation time, number of grafts, postoperative incidence of AF, ventilation time, ICU stay and hospital stay, as well as in the pooling of average blood loss, perioperative MI and follow-up EF. We determined that this could largely be attributed to the aforementioned differences in study design, as well as the presence of confounding factors.

A previous meta-analysis performed (published in 2016) comparing the clinical outcomes of BECAB patients with that of CCAB patients on high-risk patients outside the Bangladeshi population reported that BECAB was associated with lower early morbidly and mortality than BECAB, with lower rates of myocardial infarction, renal failure and low output syndrome.[42] Interestingly, we observed similar results in a specifically adult Bangladeshi population in our present meta-analysis. Our results could thus provide further evidence in support of the use of BECAB.

Other studies in literature have also suggested potential benefits of BECAB in reducing the risk of stroke, neurocognitive dysfunction, organ dysfunction, and atrial fibrillation,[43] as well as a low risk of mortality and/or complications in low risk patients.[38] These results were evaluated in the ROOBY trial,[44] which was carried out on 2203 patients. The trial observed no significant difference in 30-day mortality between the groups but did find higher rates of graft patency associated with BECAB.[44] There were also no differences in cognitive function at one year.[44] Hence, it appears that there is a general consensus that the clinical outcomes of BECAB are at least comparable to that of CCAB, which are consistent with our own observations. However, given the lack of research on a specifically Bangladeshi CABG population, more randomised controlled trials for this particular patient cohort comparing the clinical outcomes of BECAB and CCAB are needed in future to validate the results found in the present systematic review.

Conclusion:

In an adult Bangladeshi CABG population, BECAB was associated with shorter operation times, ventilation times and ICU stay as compared to CCAB. Additionally, we observed lower pooled average rates of perioperative MI, stroke/TIA, AKI, respiratory complications and low output syndrome in the BECAB cohort. At the very least, these results may suggest that the clinical outcomes of BECAB are non-inferior to that of CCAB. However, whether these clinical outcomes can be judged to be better than CCAB is a matter that requires more evidence from further research and data from randomized controlled trials.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgements
None

Declaration of conflicting interests
The Authors declare that there is no conflict of interest.

Authors' contributions F.S.: Conceptualization, Data curation, Formal analysis, Methodology, Statistics, Software and Writing – original draft. A.L.: Data curation, Formal analysis, Methodology, Statistics, Software and Writing – original draft. G.G: Conceptualization, Methodology, Project administration. M.K: Methodology, Statistics, Software and review & editing. T.K: Conceptualization, Validation, Visualization and Writing – review & editing.

References:

1. Sazzad F, Ganesh G, Cheekoty P, Veerappan M and Kofidis T. Impact of avoiding cardioplegic arrest on clinical outcome in patients undergoing CABG in Bangladesh: a systematic review and meta-analysis. Indian Journal of Thoracic and Cardiovascular Surgery. September 2020; online ahead of print. Available from https://doi.org/10.1007/s12055-020-01054-4
2. Islam AM, Majumder A. Coronary artery disease in Bangladesh: A review. Indian heart journal. 2013;65(4):424-35.
3. Hoque A, Ahmed F, Hasan KM, Rahman R. Clinico-demographic Characteristics of Coronary Artery Bypass Surgery Patients: Experience of 60 Cases at Referral Cardiac Surgery Hospital in Bangladesh. Journal of Science Foundation. 2016;14(2):62-5.
4. Rahman A, Flora MS, Haider R, Jahan R, Zafreen F. Health Related Quality of Life of Patients after Cardiac Surgery. Journal of Armed Forces Medical College, Bangladesh. 2018;14(1):50-3.
5. Mahmood KNU, Mandal SC, Talukdar SH. Surgical Treatment of Left Main Coronary Artery Disease Off-Pump CABG is a Good Option. Bangladesh Heart Journal. 2015;30(2):61-7.
6. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8(5):336-41.
7. Bangladesh Journals Online (BanglaJOL). Database of journals published in Bangladesh, Established by INASP in 2007. Managed by *Bangladesh Academy of Sciences*. Available from https://www.banglajol.info/index.php/index/about
8. Schünemann HJ, Higgins JP, Vist GE, Glasziou P, Akl EA, Skoetz N, et al. Completing 'Summary of findings' tables and grading the certainty of the evidence. Cochrane Handbook for Systematic Reviews of Interventions. 2019:375-402.
9. Higgins J. Cochrane handbook for systematic reviews of interventions. Version 5.1. 0 [updated March 2011]. The Cochrane Collaboration. www cochrane-handbook org. 2011.
10. Sterne J, Higgins J, Reeves B. on behalf of the development group for ACROBAT-NRSI. A Cochrane Risk Of Bias Assessment Tool: for non-randomized studies of interventions (ACROBAT-NRSI), Version 1.0. 0, 24 September 2014. 2015.
11. Badruzzaman M, Hossain A, Adhikary AB, Quader SA, Kamal S, Saha SK. Evaluation of myocardial protection in off-pump vs on-pump coronary bypass surgery by troponin I estimation. Bangladesh Medical Research Council Bulletin. 2010;36(3):93-6.
12. Roy HR, Ahmed NU. On Pump Beating Heart CABG is Superior to Conventional CABG in Poor Left Ventricular Function. Journal of Surgical Sciences. 2014;18(1):20-7.
13. Ahmed T, Karim MR, Khan JH, Moinuddin S. Evaluation of neurocognitive dysfunction after coronary artery bypass surgery. Cardiovascular Journal. 2018;10(2):186-93.
14. Karim MR, Ahmed T, Moinuddin S, Chowdhury TA, Khan MR. Atrial fibrillation after Coronary Artery Bypass Surgery with and without Cardiopulmonary Bypass. Cardiovascular Journal. 2018;10(2):171-9.
15. Alauddin M, Hossain A, Hoque R, Adhikary AB. Off-pump versus on-pump coronary artery bypass grafting in patient of impaired renal function. Bangabandhu Sheikh Mujib Medical University Journal. 2019;12(1):15-8.
16. Kabir MM, Rahim AA, Hossain AI, Hossain N, Islam SM, Bari MS, et al. Early Outcome of on Pump Beating Heart CABG Surger. Cardiovascular Journal. 2019;12(1):13-9.

17. Khan SR, Kashem A, Mohiuddin MA, Kabir J. Short-term outcomes associated with bilateral internal thoracic artery grafting. Bangladesh Heart Journal. 2016;31(1):3-9.

18. Sazzad MF, Moniruzzaman M, Chanda PK, Ahmed MNU, Rasheed H, Gomez NC, et al. Short Term Clinical and Angiographic Outcome of Skeletonized Harvesting Technique of Left Internal Mammary Artery, Compared to Pedicled Harvesting for Coronary Revascularization. University Heart Journal. 2016;12(2):82-7.

19. Begum M, Sarker R, Hasan MK, Zaman T, Jahan H, Hussain SS, et al. Association of Perioperative Whole Blood Transfusion with Troponin I Release after Off-Pump Coronary Artery Bypass Surgery. University Heart Journal. 2017;13(2):55-8.

20. Ranjan R, Adhikary D, Saha H, Mandal S, Saha SK, Adhikary AB. Concurrent Carotid Endarterectomy and off-Pump Coronary Artery Bypass Graft Surgery in Bangladesh: a Prospective Cohort Study. Faridpur Medical College Journal. 2018;13(1):2-7.

21. Karim MR, Ahmed T, Khurshid R, Moinuddin S, Hasan MK. Preoperative Aspirin Use and Outcomes in Off-pump Coronary Artery Bypass Grafting Surgery. Bangladesh Heart Journal. 2018;33(1): 16-21.

22. Alam AM, Ahmed I, Ahmad M, Hossain AAM, Reza MM, Rahman M, et al. Effect of Pre-operative Amiodarone on Atrial Fibrillation after Off-Pump Coronary Artery Bypass Surgery. Bangladesh Heart Journal. 2018;33(1):67-73.

23. Salekin MS, Sazzad MF, Al Nahian S, Musa SAM, Alam MR, Choudhury DIR, et al. Short Term Outcome of Off Pump Coronary Artery Bypass Grafting in Patients with Low Ejection Fraction. University Heart Journal. 2018;14(2):53-61.

24. Ranjan R, Adhikary D, Mandal S, Saha SK, Hasan K, Adhikary AB. Performance of EuroSCORE II and logistic EuroSCORE in Bangladeshi population undergoing off-pump coronary artery bypass surgery: A prospective cohort study. JRSM Cardiovascular Disease. 2019; 8:204800 4019862125.

25. Biswas P, Gomez N, Biswas S, Gupta S, Howlader S, Chanda P, et al. Significant Left Main Coronary Artery Disease Does Not Incur Any Additional Risk to the Short Term Outcome of Off Pump Coronary Artery Bypass Grafting Surgery. Mymensingh Med J. 2020;29(1).

26. Hasan MA, Milon MKH, Kashem MA, Karim MR. Effects of Preoperative Mean Platelet Volume on Early Outcomes of Patients After Conventional Coronary Artery Bypass Graft Surgery. University Heart Journal. 2018;14(1):24-7.

27. Sazzad MF, Yasmin F, Salekin MS, Musa SAM, Saklayen S, Hoque A, et al. Does Mild to Moderate Renal Dysfunction in Non-Dialysis Dependent Patients. Journal of Surgical Sciences. 2018;22(2):104-9.

28. Alam MJ, Ahmed I, Begum R, Jamil KAH, Moinuddin S. Evaluation of Body Mass Index as a Factor of Outcome in Coronary Artery Bypass Surgery. Cardiovascular Journal. 2018;10(2):150-7.

29. Rahman MA, Islam AS, Saha JK, Rahman ML, Rahman M, Quashem MA. Preoperative High Sensitivity C-reactive Protein Level Predicts Early Outcome After Coronary Artery By-pass Surgery. KYAMC Journal. 2019;9(4):153-8.

30. Ahsan SI, Sabur S. Early Outcome of Conventional Coronary Artery Bypass Grafting with Peri-operative Hyperglycaemia in Diabetic and Non-Diabetic Patients in NICVD, Dhaka. Journal of Shaheed Suhrawardy Medical College. 2019;11(1):39-42.

31. Shahidullah A, Rahim AA, Hossain AI, Islam SM, Bari MS, Hosain N. Effect of Perioperative Administration of Tranexamic Acid on Postoperative Bleeding Following on Pump CABG. Cardiovascular Journal. 2019;12(1):20-3.

32. Alam AM, Ahmed I, Ahmad M, Mohashinreza M, Hossain M, Rahman M, et al. Clinical Outcomes for Radial Artery Versus Saphenous Vein in Coronary Artery Bypass Graft Surgery. University Heart Journal. 2017;13(1):21-5.

33. Ranjan R, Adhikary A. Outcome of Coronary Artery Bypass Graft Surgery with Coronary Endarterectomy. Bangladesh Medical Research Council Bulletin. 2018;44(3):124-31.

34. Islam SM, Quashem MA, Hossain AI, Pervin R, Shahidullah A, Ahmed T, et al. Early Outcome of Coronary Artery Bypass Graft Surgery in Patients with Preoperative Elevated Level of HbA1c with Diabetes Mellitus. Bangladesh Heart Journal. 2019;34(2):92-9.

35. Ranjan R, Adhikary AB. SYNTAX score and coronary artery bypass graft surgery in Bangladesh. Asian

Cardiovascular and Thoracic Annals. 2019;27(7):542-7.

36. RevMan R. The nordic cochrane centre, the cochrane collaboration. Available from https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman/revman-5

37. OpenMetaAnalyst: Wallace BC, Dahabreh IJ, Trikalinos TA, Lau J, Trow P, Schmid CH. Closing the gap between methodologists and end-users: R as a computational back-end. J Stat Softw. 2012;49(5):1-15.

38. Shekar PS. On-pump and off-pump coronary artery bypass grafting. Circulation. 2006;113(4):e51-e2.

39. Sablotzki A, Friedrich I, Mühling J, Dehne MG, Spillner J, Silber RE, et al. The systemic inflammatory response syndrome following cardiac surgery: different expression of proinflammatory cytokines and procalcitonin in patients with and without multiorgan dysfunctions. Perfusion. 2002;17(2):103-9.

40. Salsano A, Giacobbe DR, Sportelli E, Olivieri GM, Natali R, Prevosto M, et al. Aortic cross-clamp time and cardiopulmonary bypass time: prognostic implications in patients operated on for infective endocarditis. Interactive cardiovascular and thoracic surgery. 2018;27(3):328-35.

41. Al-Sarraf N, Thalib L, Hughes A, Houlihan M, Tolan M, Young V, et al. Cross-clamp time is an independent predictor of mortality and morbidity in low-and high-risk cardiac patients. International Journal of Surgery. 2011;9(1):104-9.

42. Ueki C, Sakaguchi G, Akimoto T, Ohashi Y, Sato H. On-pump beating-heart technique is associated with lower morbidity and mortality following coronary artery bypass grafting: a meta-analysis. European Journal of Cardio-Thoracic Surgery. 2016;50(5):813-21.

43. Ehsan A, Shekar P, Aranki S. Innovative surgical strategies: minimally invasive CABG and off-pump CABG. Current Treatment Options in Cardiovascular Medicine. 2004;6(1):43-51.

44. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, et al. On-pump versus off-pump coronary-artery bypass surgery. New England Journal of Medicine. 2009;361(19):1827-37.

Original Article

Arteriovenous Fistula Creation for Hemodialysis: Evaluation of Complications

Motiur Rahman Sarkar[1], Nazmul Hosain[2], Moynul Islam[3], Saffait Jamil[4], Muhammad Mahmudul Hoque[3]

Abstract:

Background: Vascular access care is a classic example of multidisciplinary team work among nephrologists, vascular surgeons, duplex specialists, dialysis nurses and dialysis staff. The objectives of this study were to determine the complication of arteriovenous fistula (AVF) for hemodialysis (HD) and to find out the role of duplex study for the management of fistula complications.

Methods: This was a prospective type of study done on 121 arteriovenous fistulas. All operations were done in different hospitals in Dhaka city. After duplex study of upper limb vessels, the site of fistula creation was determined. All Radio-cephalic, ulnar-basilic and brachio-cephalic fistulas were done under local anesthesia. Other fistula of the series was done under brachial block. Immediate postoperative bruit, thrill and distal pulses were monitored. Fistulas were considered mature after at least 6 weeks of fistula creation with good visualization of arterialized vein and good thrill. Patients were advised to report if any complication arises.

Results: The most common fistula was Radio-cephalic fistulas (72.73%) and then Brachio-cephalic fistulas (19.84%). The left upper limb was the first choice for fistula creation as a non-dominant limb. Most fistula was created in left upper limb (76.86%). The most common complication was stenosis of arterialized veins (4.13%) and another type of stenosis was found at anastomotic site (2.48%). Second most common complication was cannulation site infections (3.31%). Another common type of infection was found at the site of fistula creation (2.48%). Thrombosis, aneurysm and pseudoaneurysm were identified as the most detrimental complications.

Conclusion: Arteriovenous fistula is an important issue for hemodialysis patient as the life line. Dialysis nurses and technician should have knowledge about antisepsis and potential complication of AVFs. Early diagnosis and early treatment prevent loss of vascular access and reduce serious morbidity and mortality. Both the patients and dialysis staffs should give highest care for the AVF to reduce the complications.

Key Wards: *Arteriovenous fistula, Haemodialysis, Duplex study, Complications.*

(Bangladesh Heart Journal 2020; 32(2): 100-105)

Introduction:

As the population ages and the incidence of diabetes rises, chronic kidney disease (CKD) and end-stage renal disease (ESRD) are increasingly common diagnoses all over the world. In 2015, data from the United States Renal Data System (USRDS) showed that 117,162 new patients began therapy for ESRD, whereas the prevalence of dialysis population reached 661,648[1]. The main treatment of ESRD is hemodialysis. The high prevalence of CKD necessitates adequate vascular access for hemodialysis and hence creation of arterio-venous fistulas for these ESRD patients. Creating long standing good quality AV fistula is thus a challenging job for the surgeons.

1. Assistant Professor, Department of Vascular Surgery, National Institute of Traumatology and Orthopedic Rehabilitation, NITOR.
2. Head of the Department of Cardiac Surgery, Chittagong Medical College, Chattogram.
3. Registrar, Department of Vascular Surgery, National Institute of Cardiovascular Diseases, NICVD, Dhaka.
4. Assistant Registrar, Department of Vascular Surgery, National Institute of Cardiovascular Diseases, NICVD, Dhaka.

Address for Correspondence: Dr. Md. Motiur Rahman Sarkar, Assistant Professor, Vascular Surgery, National Institute of Traumatology and Orthopedic Rehabilitation, NITOR. Email: drmotiurvs@gmail.com

DOI: https://doi.org/10.3329/bhj.v35i2.52895

The National Kidney Foundation of USA began the Dialysis Outcomes and Quality Initiative (DOQI) in 1995, now referred to as the Kidney Disease Outcomes and Quality Initiative (KDOQI), which published a large evidence-based set of clinical guidelines to help improve healthcare outcomes among patients with end stage renal disease. One major focus of KDOQI is optimal arteriovenous access management, which has led to the creation of the National Vascular Access Improvement Initiative (NAVII) and its Fistula First campaign. KDOQI makes it clear that all patients with stage IV or stage V chronic kidney disease who opt for hemodialysis should undergo autologous fistula creation[2].

In order to preserve viable access sites, they recommend a radio-cephalic arteriovenous fistula (RCAVF) as the first and best option. If not feasible, then a brachiocephalic arteriovenous fistula, followed by a basilic vein transposition should be created in the non-dominant arm. Prosthetic arteriovenous bridge grafts and tunneled dialysis catheters are mentioned as last resorts in patients with no autologous options. These recommendations are based upon available data that suggests that AVF have superior patency, fewer complications, require fewer reinterventions, and ultimately improve patient survival[2].

The quality of vascular access for hemodialysis should be suitable for repeated puncture and allow a fast blood flow rate for high-efficiency dialysis with minimal complications. Therefore, long-term functioning AVF needs a well-trained surgeon to create it and enough time allowed for maturation. The dialysis staff must be well versed in cannulation of the AVF, and there should be a minimal need for corrective interventions. Yet it must be recognized that, under the present circumstances, an ideal approach really does not exist[3,4]. Current literature suggests the arteriovenous fistula to be the preferred type of vascular access for hemodialysis. Once established, fistulas have longer patency and lower rates of complications compared with arteriovenous grafts and catheters. Fistula complications are associated with morbidity, mortality, and a high economic burden[5].

Objectives of our study were to understand the complications after fistula creation, long term follow up during dialysis and also to figure out the management techniques of these complications. The objectives also include understanding the role and importance of Duplex study for fistula creation and for evaluation of complications. We present our experience on facing complications and management technique of AVF.

Methods:

This was a prospective type of study done from January,2013 to December,2019. The total number of arteriovenous fistulas created was 121. All AV fistulas were created in different Hospitals of Dhaka city. Patient details were recorded for data collection with personal address and phone number. All patients were personally worked up and followed up. After taking detailed history and clinical examination, all patients had undergone duplex study of upper limb vessels (arteries and veins) for the site of fistula creation.

Technique

Complete informed written consent was taken before beginning of each procedure. All radio-cephalic, brachio-cephalic and ulnar-basilic fistula were created under local anesthesia. All brachio-basilic transposition fistula and brachio-basilic straight graft fistula with PTFE graft was done under brachial block. Arteriovenous anastomosis was done using either 6·0 or 7·o prolene double ended round body needle. Immediate postoperative bruit, thrill and distal pulses were monitored. Every patient was followed up at 1st, 5th and 10th (postoperative day) POD for bruit, thrill and wound examination. Fistula was considered matured after at least 6 weeks of fistula creation with good visualization of arterialized veins and good thrill. Patient was advised to attend if any complication arise.

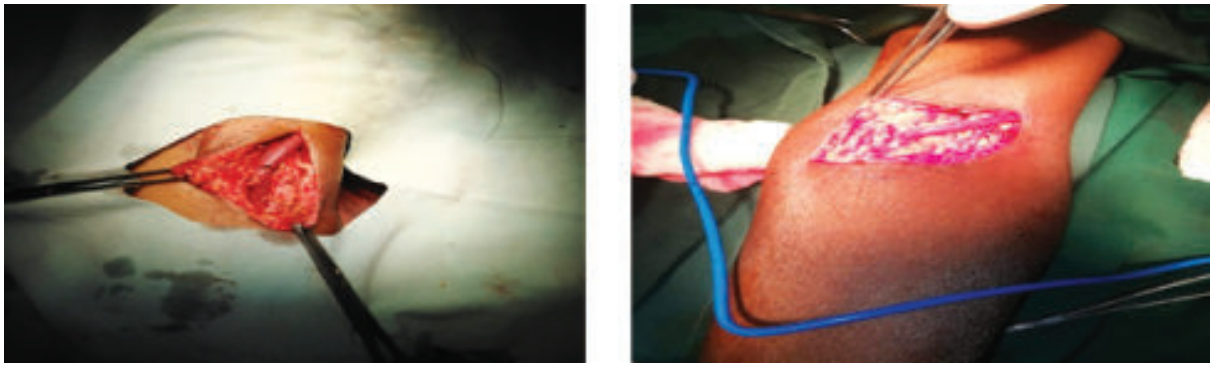


Fig.-1 A & B: *Distal Radio-Cephalic Fistula & Brachio-Cephalic Fistula.*

Inclusion criteria

a. Chronic renal failure patient who need permanent hemodialysis access.

b. Patient on hemodialysis with temporary dialysis catheter.

c. Failed arteriovenous fistula.

Exclusion Criteria

a. Moderate to severe atherosclerotic artery (exclusion was done by duplex study)

b. Inadequate caliber of upper limb veins that will be used for fistula creation(exclusion was done by duplex study)

c. Fistula creation for renal transplantation

Results:

A total of 121 arteriovenous fistula were created from the period of January 2013 to December 2019 all by a single vascular surgeon in different hospitals of Dhaka city.

Table-I

Type of arteriovenous fistula (n=121)

Type of fistula	Number	Percentage
Radio-cephalic	88	72.73%
Brachio-cephalic	24	19.84%
Brachio-basilic	07	5.77%
Ulnar-basilic	01	0.83%
Brachio-axillary straight graft fistula	01	0.83%
Total	121	100%

The most common type of arteriovenous fistula was Radio-cephalic fistula (72.73%) and the next common type of fistula was Brachio-cephalic fistula (19.84%). Brachio-basilic transposition fistulas (5.77%) were created when there was no option for creation of Radio-cephalic, Brachio-cephalic and ulnar-basilic fistula. In this study one Brachio-axillary straight graft fistula was created with 5 mm diameter PTFE graft.

Table-II

Choice of Upper Limb for Fistula Creation(n=121)

Choice of Upper limb	Number	Percentage
Left Upper Limb	93	76.86%
Right Upper Limb	28	23.14%
Total	121	100%

Left Upper Limb was first choice for fistula creation in right-handed patients as a non-dominant limb. When there was no good quality vessel or repeatedly failed fistula creation in left side than right upper limb was chosen for fistula creation. In our series left upper limb was used in 93 cases (76.86%). In case of CVD patients paralyzed upper limb was used as a first choice for fistula creation.

Table-III

Causes of Renal Failure(n=121)

Diagnosis	Number	Percentage
CKD	118	97.52%
Obstructive Uropathy	2	1.65%
Polycystic Kidney disease	1	0.83%
Total	121	100%

Almost all the patients were referred by Nephrologist for fistula creation with confirmed diagnosis. Most of the patients (97.52%) were suffering from Chronic Kidney Disease.

Table-IV

Complications of Arteriovenous fistula(n=121)

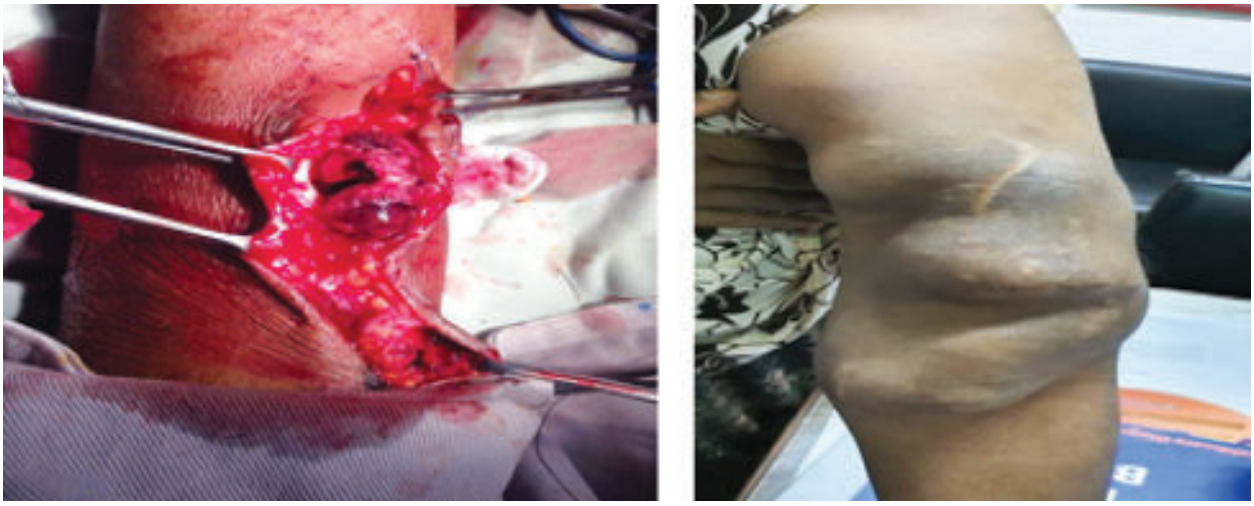
Complicaion	Number	Percentage
Haematoma	02	1.63%
Bleeding	02	1.63%
Seroma	02	1.63%
Infection	03	2.48%
Ischaemic Steal Syndrome	00	0%
Thrombosis	04	3.31%
Pseudoaneurysm	02	1.63%
Aneurysm	03	2.48%
Anastomotic Rupture	00	0%
Anastomotic stenosis	03	2.48%
Arterialized vein stenosis	05	4.13%
Canulation site infection	04	3.31%
Venous Hypertension	01	0.83%

In this study, the most common complication was stenosis of arterialized vein (4.13%). Repeated use of cannulation for dialysis followed by inflammation and fibrosis was the leading cause of stenosis. Stenosis was also commonly found at the anastomotic site (2.48%). Probably anastomotic stenosis occurred due to venous intimal hyperplasia. All stenoses was managed successfully by endovascular intervention with balloon angioplasty. The

second most common complication was infection. Cannulation site infection (3.31%) was followed by infection at the site of fistula creation (2.48%). These were managed successfully by regular careful dressing and proper use of antibiotics after culture sensitivity test.

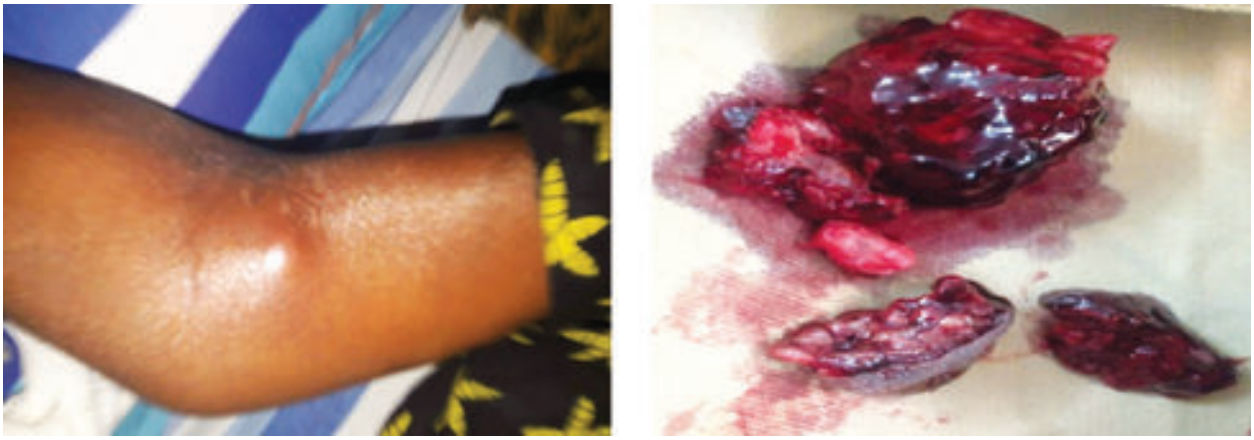
Thrombosis was found in 4 cases and fistula was found non-functioning at the time of presentation. Two of them were thrombosed at the anastomotic sites. Thrombectomy was done and fistula became functioning. Two other thrombosed fistulae were abandoned from dialysis due to multiple site aneurysm with thrombus.

Two cases of hematomas were found. One was in brachio-basilic transposition fistula wound. Exploration was done on the 1st post-operative day and bleeding tributaries from skeletonized basilic vein were identified and ligated, the fistula became functioning. Another hematoma was found in Radio-cephalic fistula wound, which was conservatively managed. Pseudoaneurysm was an important complication of arteriovenous fistula. Two pseudoaneurysms were about to burst, but functioning. It was managed by excision of aneurismal sac and ligation of both arterial and venous end. A true aneurysm in arterialized vein was managed by interposition saphenous vein graft. One venous hypertension was found in our series. This occurred due to central vein stenosis and managed by stenting in central vein.



A B

Fig.-2 A & B: *Thrombosis of AVF & Aneurysm of brachio-cephalic AVF*



A B

Fig.-3 A & B: *Pseudoaneurym of Brachio-Cephalic Fistula & Thrombus & wall of Pseudoaneurysm.*

Discussion:

Creation of Arteriovenous fistula is an important surgery for the vascular surgeons. Almost all AV fistulas were done with local anesthesia, but Brachio-basilic transposition fistula and one graft fistula (PTFE) was done under brachial block . Distal radio-cephalic fistula gives more length and more patency rate than others, so surgeons as well as patients first choice was distal radio-cephalic fistula. In a study done in Brazil, 52.5% of the study population was Distal Radio-cephalic fistulae, 16% was Proximal Radio-cephalic, 15% was Brachio-basilic fistulae[6].

Most of the arteriovenous fistula (97.52%) in our series were made for Chronic Kidney Diseases'[. Other causes of End Stage Renal Disease were obstructed uropathy (1.65%) and polycystic kidney disease (0.83%).

The most common complication was arterialized vein stenosis (4.13%). The risk of thrombosis increases with the degree of stenosis. The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF/KDOQI) guide lines defines significant stenosis of the vessel lumen as a reduction by more than 50%[7].Clinical suspicion of stenosis is confirmed by the presence of several factors: Reduced flow to dialysis machine, problems with puncture, such as prolonged bleeding after AVF puncture, pain in the area of the fistula or increased venous pressure. Recirculation is an important issue since it appears to be a significant cause of inadequate hemodialysis. The most common cause is the presence of the high-grade venous stenosis, which obstruct venous outflow, leading to back flow into the arterial needle. Recirculation is diagnosed when the dialyzed blood returning through the venous side reenters the dialyzer through the arterial needle rather than returning to the systemic circulation, and as a result, the efficiency dialysis is reduced[7].

The etiology of arterialized vein stenosis is not clearly known but repeated cannulation for long time during dialysis period may be the cause. Continuous inflammation and fibrosis were the cause for stenosis. Another type of outflow stenosis was found in these series was anastomotic stenosis (2.48%). Intimal hyperplasia was the cause for anastomotic stenosis. All causes preoperatively diagnosed as stenosis by duplex study and successfully managed endovascularly by balloon angioplasty.

In a prospective hospital based study conducted in Taif city, Saudi Arabia with the total number of 196 patients infections were found as about 20% of all AVF complications. The most common infections include perivascular cellulitis, which manifests as localized erythema and edema and is easily treated. Much more serious is an infection associated with anatomical abnormalities, such as aneurysms, hematomas or abscesses, which require surgical excision and drainage[8].

Thrombosis was leading cause of non-functioning arteriovenous fistula. Severe pain feels at the site of thrombus formation of AVF and patient can feel the thrombus . By duplex study all thrombosed AVF was diagnosed as fistula was not working. Two anastomotic site thrombosed fistulas were reverted as working fistulas after thrombectomy, but two others had multiple site thrombosis with aneurysm. They were abandoned from dialysis. The most common cause of vascular access thrombosis is venous neointimal proliferation that causes vascular stenosis, leading to fistula thrombosis[9].

We found aneurysm (2.48%) and pseudoaneurysm (1.63%) of AVF as a complication during this study period. They were the most devastating complications of AVF fistula. An aneurysm is a pathological enlargement of the blood vessel wall resulting from repetitive puncture[10]. Diffuse and progressive degeneration of the vascular access site occurs. Patient may present with signs of bleeding, infection or ulceration[7,11]. False aneurysms are hematomas located outside the vessel wall, formed due to a leaking hole in the artery or vein, most often due to iatrogenic trauma – primarily repeated needle punctures[12] . Color Doppler ultrasound can differentiate false-aneurysm expansion from a hematoma, the presence of a thrombotic mass swirling of blood within cavity which enables a decision to be made on possible surgical correction. Surgical intervention is recommended when there is a risk of perforation and ulceration if there are elements of bleeding or if there is a limited place for puncture because of the size of the aneurysm[13]. Both the aneurysms of AVF were managed by excision and interposition graft by saphenous vein and fistula was working after reconstruction. Two pseudoaneurysm presenting fistulas were managed by excision of sac with ligation of both arterial and venous ends.

Two bleeding fistulas were found in immediate postoperative period within one and half hours of Brachio-cephalic fistula creation. Re exploration was done. Bleeding point was identified and proper hemostasis was done. There was no ischemic steal syndrome and anastomotic ruptured AVF in our series, but there was found a case of venous hypertension. Diagnosed

clinically by the signs of upper limb swelling and edema and was confirmed by venography. This venous hypertension of AVF complication was managed by stenting in central venous stenotic site.

Conclusion:

Arteriovenous fistula is an important issue for the hemodialysis patients. It gives more length and easy to cannulation, easy to hemostasis after completion of dialysis. Any complication during dialysis like low flow in machine, abnormal dilatation of access that is aneurysm, pseudoaneurysm or color changes around puncture site called extravasation of blood etc should be addressed and consulted with vascular surgeons immediately. Because early diagnosis and early treatment prevent loss of vascular access as well as avoid serious morbidity and mortality. Both the patient and dialysis staff should give highest care for the AVF to reduce the complications. A good quality vascular access provides good length for repeated puncture and allow a high blood flow rate to dialysis machine with minimal complication.

References:

1. Macsata RA and Sidawy AN. Hemodialysis Access: General Considerations and Strategies to Optimize Access Placement. Rutherford›s Vascular Surgery and Endovascular Therapy. 9th Edition, Elsevier, Philadelphia;2019: 2288-2299.
2. Biuckians A, Scott EC, Meier GH, Panneton JM, Glickman MH. The natural history of autologous fistulas as first-time dialysis access in the KDOQI era. J Vasc Surg. 2008;47:415-21.
3. Allon M, Robbin M: Increasing arteriovenous fistulas in hemodialysis patients: problems and solutions. Kidney Int 2002; 62: 1109–1124.
4. Ethier J, Mendelssohn DC, Elder SJ, Hasegawa T, Akizawa T, Akiba T, Canaud BJ, Pi soni RL: Vascular access use and outcomes: an international perspective from the dialysis outcomes and practice patterns study. Nephrol Dial Transplant 2008; 23: 3219–3226.
5. Al-jaishi AA, Liu AR, Lok CE, Zhang JC and Moist LM. Complications of the Arteriovenous Fistula: A Systematic Review. J Am Soc Nephrol 2017; 28:1839-1850.
6. Johny S,Pawar B. Complications of arteriovenous fistula for haemodialysis access.Int Surg J.2018 Feb;5(2):439-444.
7. Stolic R. Most Important Chronic Complications of Arteriovenous Fistulas for Hemodialysis. Med Princ Pract 2013;22: 220–228
8. Aljuid MM, Alzahrani NN, Alshehri AA, Alkhaldi LH, Alosaimi FS, Aljuaid NW, Asiri OA, Atalla AA. Complications of arteriovenous fistula in dialysis patients: Incidence and risk factors in Taif city, KSA. Journal of Family Medicine and Primary Care 2020 january;9(1):407-411
9. Bonatti J, Oberhuber A, Schachner T, Zou Y, Hammerer-Lercher A, Mittermair R, Laufer G: Neointimal hyperplasia in coronary vein grafts: pathophysiology and prevention of a significant clinical problem. Heart Surg Forum 2004; 7: 72–77.
10. K/DOQI Workgroup Clinical practice guidelines for vascular access. Am J Kidney Dis 2006; 48(suppl 1) :S176–S247.
11. Tordoir JH,Mickley V: European guidelines for vascular access: Clinical algorithms on vascular access for haemodialysis. EDTNA ERCA J 2003; 29: 131–136
12. Saeed F, Kousar N, Sinnakirouchenan R, Ramalingam VS, Johnson PB, Holley JL: Blood loss through AV fistula: a case report and literature review. Int J Nephrol. 2011;2011: 350870.
13. Wiese P, Nonnast-Daniel B: Colour Doppler ultrasound in dialysis access. Nephrol Dial Transplant 2004; 19: 1956–1963.

Original Article

Association between Circulating Fibrinogen Level and Severity of Coronary Artery Disease in Type 2 Diabetic Patients with Chronic Stable Angina

Md. Sadaqul Islam Sikdar[1], Md Mamunur Rashid[2], Md Khalekuzzaman[3], Iftekhar Alam[1], Mst. Nazmun Nahar[4], Md. Shariful Islam[5], Lipi Debnath[6], Abdullah Al Masud[7]

Abstract:

Background: Prevalence of coronary artery disease (CAD) among Bangladeshi population is higher in urban than rural population. Among the conventional risk factors diabetes mellitus is a major concern for Bangladeshi population. Fibrinogen (Fg) in plasma is associated with severity of CAD in some populations with acute coronary syndrome.

Objective: The aim of the study was to find out the correlation between circulating fibrinogen level and severity of coronary artery disease in patients with type 2 diabetes mellitus with chronic stable angina (CSA).

Methods: The study was carried out in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka from October 2015 to March 2016.Total 132 patients with chronic stable angina (CSA) and type 2 diabetes mellitus who got admitted for coronary angiogram were included in the study and they were divided into 2 groups according to the on admission level of fibrinogen. Coronary angiogram (CAG) was performed in all patients. The severity of the CAD was assessed by angiographic vessel score and Gensini score.

Results: Mean Gensini score was 27.0±22.3 vs 22.2±16.4 and mean vessel score 1.6±0.9 vs 1.2±1.0 in group I and group II respectively (p=0.03 and 0.04, respectively). There was positive correlation between Fg and CAD severity in term of vessel score (r=0.19) and Gensini score (r=0.15). Univariate and multivariate analysis revealed that dyslipidemia, smoking and elevated fibrinogen were the independently significant predictors of severe CAD in type 2 diabetic patients with CSA.

Conclusion: Elevated plasma fibrinogen positively correlates with the severity of CAD in patients with diabetes mellitus having chronic stable angina.

Key Words: *Fibrinogen (Fg), Coronary artery disease (CAD), Vessel score, Gensini score*

(Bangladesh Heart Journal 2020; 32(2): 106-113)

Introduction:

Cardiovascular diseases account for more than 17 million deaths globally each year. It contributes 30% of all deaths. 80% of those occur in low-income and middle-income countries. This figure is expected to grow to 23.6

1. Assistant Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
2. Professor, Department of Cardiology, National Institute of cardiovascular Diseases, Dhaka, Bangladesh.
3 Professor, Department of Cardiology, Dhaka Medical College Hospital, Dhaka, Bangladesh.
4. Associate Professor, Department of Radiology and Imaging, National Institute of Neuro Science, Dhaka, Bangladesh.
5. Assistant Registrar, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh
6. Junior Consultant, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
7. Assistant professor, Department of Cardiology, Kushtia Medical College, Kushtia, Bangladesh.

Address of Correspondence: Dr. Md. Sadaqul Islam Sikder, Assistant Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.

DOI: https://doi.org/10.3329/bhj.v35i2.52896

million by the year 2030. Coronary artery disease alone caused 7 million deaths worldwide in 2010[1]. Estimates from the Global Burden of Disease Study suggests that by the year 2020 the South Asian part of the world (India, Pakistan, Bangladesh, Nepal) will have more individuals with atherothroembolic cardiovascular disease than any other regions[2].

The exact prevalence of coronary artery disease in Bangladesh is not known. The prevalence of coronary artery disease was first reported in 1976, which was 0.33%. More recent data indicates the coronary artery disease prevalence is 1.85% to 3.4% in rural population and it is 19.6% in an urban population[3]. Three small scale population based studies showed average prevalence of ischemic heart disease (IHD) 6.5 per thousand population of Bangladesh[4]. According to Bangladesh bureau of statistics, 2006 it is the fourth leading cause of death[5].

It is well-recognized that, diabetes mellitus is a powerful independent risk factor for increased cardiovascular mortality associated with coronary artery disease[6,7]. A spectrum of researches attribute coronary atherosclerotic process in a diabetic setting, at least partly due to an imbalance of thrombotic and fibrinolytic system as well as augmented inflammation[8,9].

Fibrinogen (Fg) is a marker of activation of thrombotic system and its plasma level; has been shown to correlate to a certain extent with the development of coronary atherosclerotic lesions, risk of myocardial injury after percutaneous coronary intervention and cardiovascular events in diabetic patients, regardless of platelet aggregation[10,11]. Ridker et al. indicated that elevated serum levels of D-dimer, induced by cleavage of plasmin at the fragment D site of fibrin polymers were related to coronary artery occlusion[12]. Taken together, these observations support a notion that plasma fibrinogen may serve as a mediator linking to thrombotic disease and clinical outcomes.

In a study of Xiong et al. revealed that elevated fibrinogen was independently associated with the presence of significant coronary artery disease[13]. Furthermore, it has been frequently reported that diabetic patients may be clinically asymptomatic even with severe coronary artery disease because of silent myocardial ischemia[14]. The methods for early detection of significant coronary artery disease in diabetic patients have been proven to be elusive, and as a result, prognostic improvement of these patients has not been successfully achieved[15,16]. Therefore, it is necessary to identify early diagnostic biomarkers to improve the clinical outcomes of diabetic patients with coronary artery disease.

There is growing evidence that, elevated plasma fibrinogen is associated with the presence of significant CAD in patients with type 2 diabetes mellitus with chronic stable angina. Plasma fibrinogen as a diagnostic marker of severity of coronary artery disease may have important clinical implications in improving the management strategy and outcome of patients with CSA.

Methods:

This prospective observational study was carried out in the department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka from October 2015 to March 2016. Total 132 consecutive patients with type 2 diabetes mellitus and chronic stable angina (CSA) full filling the inclusion and exclusion criteria, those admitted for coronary angiogram (CAG) at NICVD were included in the study. Study population was divided into two groups on the basis of serum fibrinogen level, in group I 87 patients with Fg>3.3g/L and in group II 45 patients with Fg<3.3g/L were enlisted.

Patients with Type 1 diabetes, acute coronary syndrome, previous CABG or PCI, chronic heart failure, valvular heart disease, congenital heart disease, hepatic dysfunction, CKD and malignancy were excluded.

Informed written consent was taken from each patient before enrollment. Meticulous history was taken and detailed clinical examination was performed. Risk factors profile including smoking, hypertension, dyslipidaemia and family history of premature coronary artery disease (CAD) were noted. All necessary screening tests for coronary angiogram were done. Resting ECG of all patients was done at a paper speed of 25 mm/s and 10mm standardization at admission using Fukuda ECG machine (Model: FX -2111) Denshi Co Ltd. Japan. Trans-thoracic echocardiography was done by 2D & M-mode and Doppler echocardiography modalities by Accuson X700 ultrasound system, Siemens, Germany. Left ventricular ejection fraction (LVEF) was measured by Tichoitz's method. Blood Sample was taken for fibrinogen before the day of CAG. Fibrinogen measured by automatic system by Stago-Compact Max using STA: Fib-2 reagent using clot based method.

Coronary angiogram was done either by right femoral or right redial route by Trinias C12 unity system, Shimadzu, Japan. All angiography views were evaluated by two experienced cardiologists who were blinded to the study. The severity of the CAD was assessed by Vessel score and Gensini score [17, 18].

From the categorical viewpoint, significant coronary artery disease was defined as > 70% stenosis in any of the three major coronary artery, stenosis <70% in major epicardial coronary arteries were termed non-obstructive CAD. Extent of CAD was defined as insignificant, single, two or three vessel CAD[19]. Score ranges from 0 to 3 were assigned depending on the number of vessels involved. Left main coronary artery was scored as single vessel disease[20].

For severity of CAD the Gensini score system was used. The reduction in the lumen diameter and the roentgen graphic appearance of concentric lesions and eccentric plaques were evaluated (reductions of 25%, 50%, 75%, 90%, 99%, and complete occlusion are given Gensini scores of 1, 2, 4, 8, 16, and 32, respectively). Each principal vascular segment was assigned a multiplier in accordance with the functional significance of the myocardial area supplied by that segment: the left main coronary artery, X5; the proximal segment of left anterior descending coronary artery (LAD), X2.5; proximal segment of the circumflex artery, X2.5; the mid-segment of the LAD, XI.5; the right coronary artery, the distal segment of the LAD, the posterolateral artery and the obtuse marginal artery X1.0 and others XO.5. This score therefore, places emphasis on the severity of stenosis, while including some of the extent of CAD[21].

Data was analyzed by using SPSS version 21. (Statistical package for social science). Continuous variables were expressed as median or mean ± SD. Categorical variables were expressed as percentage. To test association between Fibrinogen with coronary artery disease severity was done by Pearson's and Spearman's rank order correlation. Univariate and multivariate logistic regression analysis were done to evaluate the independent predictors of severe CAD. The odds ratio (OR) and 95% confidence interval were calculated. Level of significance was p d" 0.05. The study protocol was approved by Bangladesh College of physicians and surgeons. Confidentiality regarding all information's and records was maintained strictly and the patients had the right to withdraw him/her self from the study at any time during the study period.

Results:

The mean age of the study population was 51.9±8.8 years and majority of the study population belonged to 41-50 years age range in both groups (Table I).

Male patients were predominant in both groups. No significance (p=0.22) was found between two groups in terms of sex distribution (Figure 1).

Hypertension, dyslipidaemia and smoking were significant risk factors among the groups, prevalent more in group I patients (Table II).

Table-I

Age distribution of the patient groups

Age Group	Group I (n=87)		Group II (n=45)		Total (N=132)		p value
	Number	%	Number	%	Number	%	
31 – 40	04	4.6	07	15.6	11	8.3	
41 – 50	47	54.0	19	42.2	66	50.0	
51 – 60	22	25.3	13	28.9	35	26.5	
>60	14	16.1	06	13.3	20	15.2	
Mean ± SD	52.7±8.7		50.4±8.7		51.9±8.8		0.14^{NS}

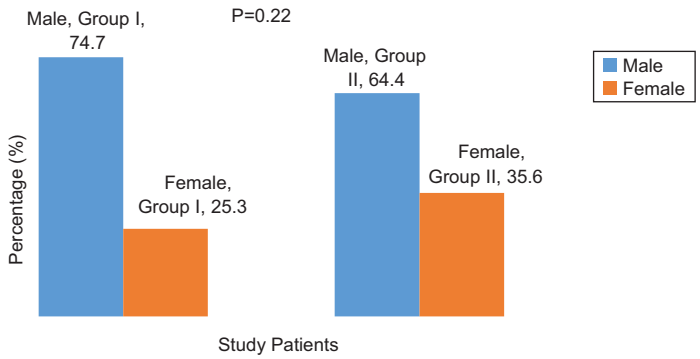


Fig.-1: *Sex distribution among the study groups*

Table-II

Distribution of risk factors in between the study groups

Risk Factors	Group I (n=87)		Group II (n= 45)		p value
	Number	%	Number	%	
Hypertension	58	66.7	21	46.7	0.03^{S}
Dyslipidaemia	42	48.3	11	24.4	0.008^{S}
Smoking	49	56.3	17	37.8	0.04^{S}
Family H/O of CAD	35	40.2	16	35.6	0.60^{NS}

It was found that vessel score 0 was significantly higher in group II than group I (p=0.009). The remaining vessel scores was more in group I than group II (Table III).

Table-III

Distribution of vessel score in between the patient groups.

Vessel Score	Group I (n=87)		Group II (n=45)		p Value
	Number	%	Number	%	
Score - 0	10	11.5	16	35.6	0.009^{S}
Score - 1	34	39.1	11	24.4	0.09^{NS}
Score - 2	29	33.3	12	26.7	0.43^{NS}
Score - 3	14	16.1	06	13.3	0.67^{NS}

There was significant association between Fg (gm/L) and vessel involvement of the study patients (p=0.04). Table IV shows the high sequence of mean Fg (gm/L) of study patients according to the number of vessel involvement.

Table-IV

Association between Fg gm/L and number of vessels involved.

Vessel involvement		Fibrinogen (Fg) gm/L		p value
Type	Number(N=132)	Mean	SD	
No Vessel	26	3.39	0.91	
SVD	45	4.01	0.81	0.04^{S}
DVD	41	4.29	0.65	
TVD	20	4.36	0.82	

Severity of CAD assessed by Gensini score was predominantly higher in group I patients then group II (Table V)..

Table-V

Distribution of Gensini score in between the patient groups.

Gensini Score	Group I (n=87)		Group II (n-45)		p value
	Number	%	Number	%	
Mild (1-10)	16	18.4	05	11.1	0.27^{NS}
Moderate (11-50)	44	50.6	16	35.6	0.03^{S}
Severe (> 50)	17	19.5	08	17.8	0.61^{NS}

The table VI displays the severity of CAD among the study patients. The mean vessel score and Gensini score was statistically significantly higher in group I.

Table-VI
Severity of CAD among the study groups

Severity of CAD	Group I (n=87) Mean ± SD	Group II (n=45) Mean ± SD	p Value
Vessel Score	1.6 ± 0.9	1.2 ± 1.0	0.04[S]
Gensini Score	27.0 ± 22.3	22.2 ±16.4	0.03[S]

There is a positive correlation between Fg and coronary artery disease severity in terms of vessel score (r=0.19). It was observed that the Spearman's correlation statistically significant (p=0.03) by correlation t test (Figure 2).

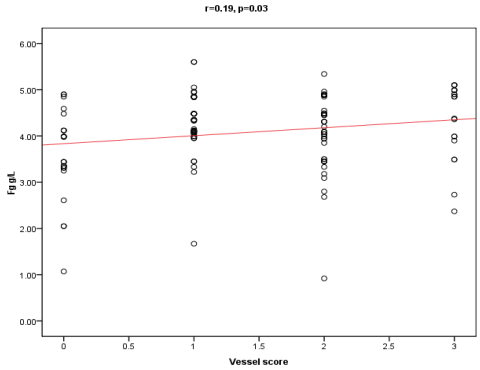


Fig.-2: *Correlation between Fg and vessel score by Spearman's correlation*

There is a positive correlation between Fg and coronary artery disease severity in terms of Gensini score (r=0.15). It was observed that the Pearson's correlation statistically significant (p=0.04) by correlation t test (Figure 3).

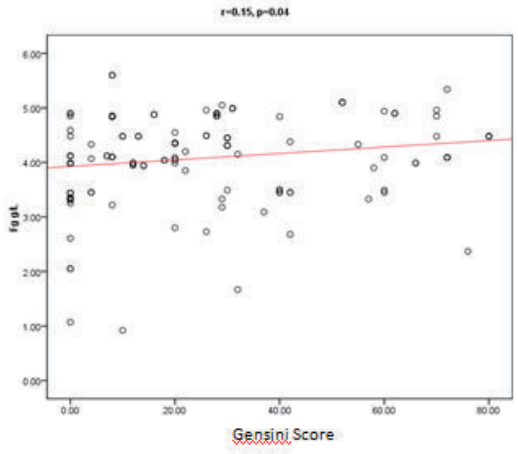


Fig.-3: *Correlation between Fg and Gensini score by Pearson's correlation t-test.*

Univariate and multivariate analysis revealed that out of the 6 variables dyslipidemia, smoking, elevated fibrinogen (Fg) were found to be the independently significant predictors of severe CAD with type 2 diabetic patients (Table VII).

Table-VII
Univariate and multivariate logistic regression analysis of determinants of coronary artery disease.

Variables	Univariate		Multivariate	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Age >50	1.89(0.62-4.69)	0.15[NS]	1.37(0.46-3.81)	0.26[NS]
Hypertension	0.81(0.25-2.54)	0.60[NS]	0.70(0.24-2.40)	0.71[NS]
Dyslipidaemia	2.94(1.20-3.79)	0.02[S]	2.54(1.19-3.20)	0.03[S]
Smoking	3.17(1.30-6.15)	0.01[S]	2.70(1.22-5.11)	0.03[S]
Elevated Fibrinogen	1.88(1.30-2.66)	0.001[S]	1.54(1.20-2.46)	0.002[S]

Discussion:

General considerations: This study intended to evaluate fibrinogen (Fg) and its association with severity of coronary artery disease in type 2 diabetes mellitus patients with chronic stable angina. After analyzing the collected clinical and angiographic data and results, it is found that; elevated fibrinogen is associated with presence of significant coronary artery disease.

Coronary artery disease is premature in onset, clinically aggressive and angiographically extensive in South Asians. The underlying etiology and pathophysiology of high prevalence of CAD in Bangladeshis are incompletely understood. Genetic predisposition, high prevalence of central obesity and metabolic syndrome along with conventional risk factors may play important role. Lifestyle related factors, including poor dietary habits, excess saturated and trans-fat, high salt intake and low-level of physical activity may be important as well. Some novel risk factors including hypovitaminosis D, arsenic contamination in water and food-stuff, particulate matter air pollution may also play unique role[3].

Fibrinogen contributes to blood viscosity, platelet aggregation, fibrin formation, and modulates subsequent coagulation activation and fibrinolysis[22,23,24]. Furthermore, fibrinogen participates directly in atherogenesis. Plasma fibrinogen appears to be not only an inflammatory marker linking to thrombotic disease but also a predictor connecting with the cardiovascular events[11].

Thompson et al. found fibrinogen to be a strong predictor of coronary events in patients with angina pectoris[25]. In

those subjects with high total cholesterol, a high fibrinogen level conferred added risk compared with those with low fibrinogen. Patients in the highest fibrinogen quintile had three times the risk of a coronary event than those in the lowest quintile[26].

Subjects with diabetes mellitus have been found to have hyper-reactive platelets. This platelet hyper-reactivity may result in part from increased fibrinogen levels associated with diabetes because fibrinogen acts as a cross bridge between platelets. Poor diabetic control has also been particularly associated with higher levels of fibrinogen and other haemostatic variables[26].

Discussion on the results of the present study:

There was no significant difference of age and sex distribution among the group I and group II. Zaher et al. found the mean age of CAD patients 49.85±9.89 years in Bangladeshi population, which support the finding of the present study[27]. Male patients were predominant in both groups. In a study by Retterstol et al. there was 78.1% male and 21.9% female patients with CAD[28]. Similar result was found by Xiong et al., Hong et al. and Cersit et al. regarding age and gender distribution [28,13,29].

In this study hypertension, dyslipidaemia and smoking had higher statistically significant association in group I patients. Family history of coronary artery disease had similar prevalence in both groups. Previous work in young adults has shown that fibrinogen concentrations are positively associated with BMI, hypertension and cigarette smoking and negatively associated with physical activity and HDL cholesterol[30].

Mean fibrinogen level of study patients according to the number of vessels involvement in none, single, double and triple vessel disease are being 3.39, 4.01, 4.29 and 4.36 respectively. There was significant association between fibrinogen and vessel involvement of the study patients. The no score was significantly higher in group II than group I (p=0.009). The remaining vessel scores were more in group I than group II (p>0.05). So the more vessel involvement was demonstrated in group I than group II and this association was statistically significant (p=0.009). In study by Cersit et al. there was a significant elevation in fibrinogen levels with an increasing number of vessel involvement[29].

According to Gensini scoring system coronary artery disease severity was more in group I than group II. The mean Gensini score was 27.0±22.3 in group I and 22.2±16.4 in group II patients. The difference was statistically significant (p=0.03). The mean vessel score was greater in group I than group II (1.6±0.9 vs. 1.2±1.0) which was statistically significant (p=0.04). In the study by Zhang et al. indicated that patients with high Gensini score had significantly elevated fibrinogen level[32]. Xiong et al. also found that elevated fibrinogen level associated with high Gensini score[13].

In this study there was positive correlation between fibrinogen and coronary artery disease severity in terms of vessel score (r=0.19) and Gensini score (r=0.15) as evidenced by the Spearman's correlation and Pearson's correlation t-test and both are statistically significant. Cersit et al. in their study showed plasma fibrinogen level was significantly higher in patients with stenosis than in patients without stenosis[29]. In the study of Zhang et al. spearman correlation analysis revealed a positive association between fibrinogen level and Gensini score[32]. Xiong et al. also found that elevated fibrinogen level positively associated with higher level of Gensini score[13].

In this study univariate logistic regression analysis of variables likely to cause severe CAD revealed that dyslipidaemia, smoking, elevated fibrinogen were independent predictor of severe coronary artery disease. However, age and hypertension were not independent predictor of severe CAD. In multivariate logistic regression analysis, after adjustment of factors, dyslipidemia, smoking, elevated fibrinogen were found to be the independent predictors of severe CAD. In the study of Zhang et al. multivariate logistic regression analysis demonstrated that plasma fibrinogen level was independently associated with high Gensini score[32]. Hong et al. by multivariate logistic regression analysis found that plasma fibrinogen was an independent predictor of a high Gensini score for diabetic patients[11]. The findings are quite similar and support the results of this study. So, elevated level of plasma fibrinogen is an independent marker of severity of CAD in type II diabetic patients with CSA.

Limitations of the study

This was a single center study that was not representative of the whole country. Measurement of Fg in plasma mainly reflects atherosclerotic process of whole-body vasculature, not specific for coronary arteries. Coronary angiography was evaluated by visual estimation, so there was chance of inter observer and intra observer variation of interpretation of severity of the stenosis.

Conclusion:

The present study demonstrates that elevated plasma fibrinogen is associated with more severe CAD in type 2 diabetes mellitus patients with chronic stable angina.

There is a positive correlation between the plasma levels of fibrinogen and severity of CAD. High fibrinogen level as an early diagnostic marker of coronary artery disease may have important clinical implications in improving the management strategy and outcome of these patients.

Reference:

1. Wong N.D. (2014) Epidemiological studies of CHD and the evolution of preventive cardiology. Nature Reviews Cardiology. 11, 276–289.
2. Chakraborty B., Zaman F. and Sharma A.K. (2009) Combating Coronary Artery Disease in South Asia-What is special. Bangladesh Journal of Cardiology, 1(2), 088-090.
3. Islam A. M. and Majumder, A. (2013) Coronary artery disease in Bangladesh. A review. Indian Heart Journal, 65(4), 424–435.
4. Islam M.N., Ali M.A. & Ali M. (2004) Spectrum of cardiovascular disease: The current scenario in Bangladesh. Bangladesh Heart Journal. 19, 1-7.
5. Bangladesh Bureau of Statistics: Health, Family planning and social statistics, cat no 13:20, BBS, Dhaka, 2007.
6. Mellbin L.G., Malmberg K., Ryden L., Wedel H., Vestberg D. &Lmd M. (2013) The relationship between glycaemic variability and cardiovascular complications in patients with acute myocardial infarction and type 2 diabetes: A report from the DIGAMI2 trial. European Heart Journal. 34, 374-9.
7. Muhlestein J.B., Lappe D.L., Lima J.A., Rosen B.D., May H.T., Knight S. et al. (2014) Effect of screening for coronary artery disease using CT angiography on mortality and cardiac events in high-risk patients with diabetes: The FACTOR-64 randomized clinical trial. Journal of American Medical Association. 312, 2234-43.
8. Folsom A.R., Aleksic N., Park E., Salomaa V., Juneja H. & Wu K.K. (2001) Prospective study of fibrinolytic factors and incident coronary heart disease: The Atherosclerosis Risk in Communities (ARIC) Study. Arteriosclerosis, Thrombosis, and Vascular Biology. 21, 611-7.
9. Morange P.E., Bickel C., Nicaud V., Schnabel R., Rupprecht H.J., Peetz D. et al. (2006). Haemostatic factors and the risk of cardiovascular death in patients with coronary artery disease:The Athero Gene study.Arteriosclerosis, Thrombosis, and Vascular Biology. 26, 2793-9.
10. Zhou B.R., Pan Y. &Zhai Z.M. (2011) Fibrinogen and P-selectin expression in atherosclerosis model of Sprague Dawley rat. Chinese Medical Journal. 124, 3768-72.
11. Hong L.F., Li X.L., Luo S.H., Guo Y.L., Zhu C.G. & Qing P. (2014) Association of Fibrinogen with Severity of Stable Coronary Artery Disease in Patients with Type 2 Diabetic Mellitus.Hindawi Publishing Corporation, Disease Markers, Article ID 485687, 8 pages.
12. Ridker P.M., Hennekens C.H., Cerskus A. &Stampfer M.J. (1994) Plasma concentration of cross-linked fibrin degradation product (D-dimer) and the risk of future myocardial infarction among apparently healthy men. Circulation 90, 2236-40.
13. Xiong W.X., Shen Y., Dai D.P., Lu L., Zhang Q., Zhang R.Y. et al. (2015) Clinical Utility of the Ratio Between Circulating Fibrinogen and Fibrin (ogen) Degradation Products for Evaluating Coronary Artery Disease in Type 2 Diabetic Patients.Chinese Medical Journal)128(6), 727–732.
14. Papageorgiou N., Tousouhs D., Siasos G. &Stefanadis C. (2010) Is fibrinogen a marker of inflammation in coronary artery disease? Hellenic Journal of Cardiology. 51, 1-9.
15. Dou K.F., Xu B., Yang Y.J., Chen J.L., Qiao S.B., Li J.J. et al. (2009) Two-year clinical outcome after successful implantation of drug-eluting and bare metal stents in diabetic patients: Results from a real-world single center registry. Chinese Medical Journal. 122, 612-6.
16. Shen W.F. (2007) Screening for coronary artery disease in asymptomatic patients with type 2 diabetes mellitus. Chinese Medical Journal. 120, 1859-61.
17. Huang G., Zhao J.L., Du H., Lan X.B. & Yin Y.H. (2010) Coronary Score Adds Prognostic Information for Patients With Acute Coronary Syndrome. Circulation, 74(3), 490 – 495.
18. Montorsi P., Ravagnani P.M. &Galli S. (2006) Association between erectile dysfunction and coronary artery disease. Role of coronary clinical presentation and extent of coronary vessels involvement: the COBRA trial. European Heart Journal, 27, 2632-2639.
19. Chaitman B.R., Bourassa M.G., Davis K., Rogers W.J., Tyars D.H. & Berger R. (1981) Angiographic

prevalence of high-risk coronary artery disease in patient subsets. Circulation 64, 360-367.

20. Sullivan D.R., Thomas, H., Marwick S. & Ben, Freedman (1990) A new method of scroing coronary angiograms to reflect extent of coronary atherosclerosis and improve correlation with major risk factors. American Heart Journal. 19(6), 1262-7.

21. Gensini G.G. (1983) A more meaningful scoring system for determining the severity of coronary heart disease. American Journal of Cardiology. 51, 606.

22. Danesh J., Collins R., Peto R. & Lowe G.D.O. (2000) Haematocrit, viscosity, erythrocyte sedimentation rate: meta-anlyses of prospective studies of coronary heart disease. European Heart Journal. 21, 515–520.

23. Sinzinger H. & Pirich C. (1992) Platelet function and fibrinogen. In: Ernst, E.; Koenig, W.; Lowe, GDO.; Meade, TW., editors. Fibrinogen: A "New" Cardiovascular Risk Factor. Vienna, Austria: BlackwellMZV, 46-50.

24. Kim P.Y., Stewart R.J., Lipson S.M. &Nesheim M.E. (2007) The relative kinetics of clotting and lysis provide a biochemical rationale for the correlation between elevated fibrinogen and cardiovascular disease. Journal of Thrombosis and Haemostasis. 5: 1250–1256.

25. Thompson S.G., Kienast J., Pyke S.D., Haverkate F. and van de Loo J.C. (1995) Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study Group. The New England Journal of Medicine, 332(10), 635–641.

26. Stec J.J., Silbershatz H., Tofler G.H., Matheney, T.H., Sutherland P., Lipinska I. et al. (2000) Association of Fibrinogen With Cardiovascular Risk Factors and Cardiovascular Disease in the Framingham Offspring Population. Circulation, 102(14), 1634–1638.

27. Zaher A., Majumder A.A.S., Mohibullah A.K.M. (2003) Homocysteine as a risk factor for coronary artery disease in Bangladeshi population. Bangladesh Heart Journal. 18, 3–7.

28. Retterstol L., Kierulf P., Pedersen J.C., Bohn M., Bakken A., Erikssen J. & Berg K. (2001) Plasma fibrinogen level and long-term prognosis in Norwegian middle-aged patients with previous myocardial infarction. A 10 year follow-up study. Journal of Internal Medicine 249, 511-518.

29. Cersit S., Cay S., Koza Y., Acikgoz S.K., Cabuk G., Senturk B. and Dogan P. (2014) Association between Plasma Fibrinogen Level and Saphenous Vein Graft Patency. Zhonghua Minguo Xin Zang Xue Hui Za Zhi. 2014 May; 30(3): 223–228.

30. Folsom A.R., Qamhieh H.T., Flack J.M., Hilner J.E., Liu K., Howard B.V. et al. (1993) Plasma fibrinogen: levels and correlates in young adults. The Coronary Artery Risk Development in Young Adults (CARDIA) Study. American Journal of Epidemiology. 138(12), 1023-36.

31. Corban M.T., Hung O.Y., Mekonnen G., Eshtehardi P., Eapen D.J., Rasoul-Arzrumly E. (2016) Elevated Levels of Serum Fibrin and Fibrinogen Degradation Products Are Independent Predictors of Larger Coronary Plaques and Greater Plaque Necrotic Core. Circulation. 80(4), 931–937.

32. Zhang Y., Zhu C.G., Guo Y.L., Xu R.X., Li S., Dong Q. et al. (2014) Higher Fibrinogen Level is Independently Linked with the Presence and Severity of New-Onset Coronary Atherosclerosis among Han Chinese Population. PLoS One, 9(11), e113460.

Original Article

Comparative Assessment of Serum Homocysteine and High Sensitivity C-reactive Protein in type 2 Diabetic and non Diabetic Patients with ACS

Lipi Debnath[1], Abdul Wadud Chowdhury[2], Iftekhar Alam[3], Md. Mamunur Rashid[4], Md. Sadaqul Islam Sikder[3]
Bijan Kumar Nath[5]

Abstract:

Background: Increased level of serum homocysteine (Hcy) and high sensitivity C-reactive protein (hs-CRP) have a proven implication with epithelial injury leading to coronary artery disease ((CAD). These are strongly associated with different metabolic syndrome variables, although different studies have shown both positive and negative responses when correlated with type 2 diabetes malitus (T2DM). In this study we explored the role of these markers of CAD in type II diabetic and non diabetic patients with newly diagnosed acute coronary syndrome (ACS) at a tertiary care hospital among Bangladeshi population.

Methods: We wanted to identify whether Hcy and hs-CRP link positively or negatively with type 2 diabetes in this cross sectional observentional study. A total of 260 patients with new onset ACS were included in the study, out of which 72 patients with T2DM and 188 patients without diabetes were considered as group I and group II respectively. Clinical and biochemical data were compared in between the groups.

Results: The mean age of the study population was 50.33±15.50 years and 45.86±18.76 years in group I and II respectivly. Male female ratio was 4:1 among the whole study subjects. There was significantly higher level of serum homocysteine in group II than group I 18.41±15.49 µmol/L vs. 14.11±6.48 µmol/L respectively (p <0.05). Similarly hs-CRP in group I was 26.84±30.30 mg/L and in group II 37.48±37.99mg/L, higher in group II (p<0.05). Both Hcy and hs-CRP were higher in male and female patients in group II. Dyslipidaemia was significant risk factor in group I and smoking in group II (p<0.05).

Conclusion: In patients with ACS serum Hcy and hs-CRP were significantly higher in non-daibetic patients then in patients with type 2 diabetes. This association may be population or ethenicity specific which provide further scope for future elaborate studies.

Keywords: *Homocysteine (Hcy), high sensitivity C reactive protein (hs-CRP), type 2 Diabetes mellitus (T2DM), acute coronary syndrome (ACS).*

(Bangladesh Heart Journal 2020; 32(2): 114-120)

Introduction:

Various studies have pointed out that South Asians have a higher prevalence of coronary artery disease (CAD) as compared with other ethnicities, with a higher rate at younger ages[1]. Traditionally there are some conventional risk factors like age, male sex, positive family history, hypertension, smoking, hyperlipidaemia, metabolic syndrome, diabetes, lack of exercise, obesity, and some emerging risk factors, like C- reactive protein, Homocysteine, Fibrinogen etc[2].

1. Junior Consultant, Department of Cardiology National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
2. Professor, Department of Cardiology, Dhaka Medical College and Hospital, Dhaka, angladesh..
3. Assistant Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh
4. Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
5. Senior Consultant, Department of Surgery, Sadar Hospital, Chottogram, Bangladesh.

Address of Correspondence: Dr. Iftekhar Alam, Assistant professor, Department of Cardiology, National Institute of cardiovascular Diseases, Dhaka, Bangladesh. Tel-8801720056180, e-mail:iftekhar1029@gmail.com.

DOI: https://doi.org/10.3329/bhj.v35i2.52897

DM is associated with a higher short-term risk for major adverse cardiovascular and cerebrovascular events and heart failure and a higher long-term risk for mortality in unselected patients with acute ischemic chest pain[3]. Studies demonstrated that, patients with type 2 diabetes mellitus (T2DM) without prior myocardial infarction (MI) have a risk of death from CAD as patients without diabetes with prior MI[4]. Diabetes is now considered to be a risk equivalent of coronary artery disease for future MI and cardiovascular death[5].

T2**DM** is a strong risk factor for coronary artery disease, which in turn is the leading cause of mortality and morbidity in diabetic patients[6]. Although this increased risk has been attributed primarily to hyperglycemia, dyslipidemia, and a prothrombotic state, recent observations have focused attention on low-grade inflammation in the pathogenesis of T2DM and its complications[7].

In recent years, a considerable numbers of studies have analyzed the prognostic role of different biomarkers in acute coronary syndromes (ACS)[8]. Moderate hyperhomocysteinemia defined as total homocysteine concentration between 12 to 30 µmol/L, occurs in about 30% of patients with clinical complications of atherosclerosis. Prospective and genetic studies have shown that moderate hyperhomocysteinemia in healthy persons is a weak predictor of cardiovascular disease[9]. Contrary to it, in patient with ischemic heart disease, renal failure or diabetes mellitus and in thromboembolic disease, hyperhomocysteinemia represents a strong predictor of vascular morbidity and mortality[10].

DM is associated with a higher short-term risk for MACCEs and HF and a higher long-term risk for mortality in unselected patients with AICP. DM should be included as a high-risk variable in national acute coronary syndrome guidelines. Top of Form

Bottom of Form

Atherosclerosis with thrombosis superimposed is by far the most frequent underlying cause[11]. Inflammation plays an important role in all stages of the atherosclerotic process, from the onset of initial lesions to plaque progression and complications[12]. Prognostic studies have shown that C-reactive protein (CRP) is a strong predictor of cardiovascular events[13]. In particular, in acute coronary syndrome, high concentrations of CRP are a marker of recurrent cardiac events for up to 5 years[14.] Both hyperhomocysteinemia and increased inflammatory activities are shown to be associated with atherosclerosis and coronary disease[9].

Over the past decade, atherosclerosis and inflammation have been closely linked and hs-CRP, as an acute phase reactant and non-specific marker of inflammation has been widely studied[9]. The analysis of biochemical markers particularly hs-CRP helps to better define the prognosis and may be helpful in stratifying patients at risks for major cardiac events[15]. Also chronic poor metabolic control of diabetes is characterized by elevated plasma homocysteine concentration[10]. In uncomplicated T2DM patients without nephropathy, Mazza et al., have shown that basal level of homocysteine was 35% lower in compared with healthy controls. They concluded that chronic hyperglycemia may affect its renal excretion, or accelerate hepatic trans-sulfuration secondary to insulin disorders[16].

In Bangladesh few studies to evaluate association of Hcy as a risk factor in ACS patient and correlations of hs-CRP with angiographic severity of coronary artery disease was done separately, but no study has been done to evaluate the relation between homocysteine and hs- CRP in acute coronary syndrome patient. The aim of this study is to ascertain the differences in the behavior of C-reactive protein and homocysteine concentrations as well as their impact in patient of acute coronary syndrome, with and without type 2 diabetes.

Methods:

This cross sectional observational study was carried out in the department of Cardiology of Dhaka Medical College Hospital (DMCH), from October 2010 to September 2011. 260 patients with acute coronary syndrome encompassing STEMI, NON STEMI and UA who were admitted at the CCU of DMCH were the study population. They were divided on the basis of presence of T2DM, group I patients with T2DM and group II patients without T2DM. All consecutive patients who were clinically diagnosed as ACS and undertook measurement of serum serum Homocysteine and high sensitive CRP were enrolled in the study on the basis of inclusion and exclusion criteria. Patients with history of previous UA, STEMI, NSTEMI, percutaneous coronary intervention, coronary artery bypass grafting, cardiomyopathy, Congenital heart disease, vulvular heart disease, severe co-morbid conditions and taking Folic acid, Vit.B-6,Vit.B-12 or statins were excluded from the study.

Informed consent was taken from all patients or from the legal guardians. Initial evaluation of the study population by history and clinical examination was performed and recorded accordingly in the preformed data collection sheet. Demographic variables e.g. Age, sex and personal information were recorded. Risk factors of ischemic heart

disease (IHD) e.g. hypertension, smoking, dyslipidaemia, diabetes mellitus, family history of premature CAD and obesity was noted. Necessary laboratory investigations RBS, fasting lipid profile, S. Creatinine, S. Troponin-I was done and recorded. 12 lead resting ECG was done at a paper speed of 25 mm/s and 10mm/mV standardization at admission. Trans-thoracic echocardiography was done by 2D & M-mode and Doppler echo modalities and left ventricular ejection fraction (LVEF) was measured by Tichoitz's method.

Blood was collected for fasting serum homocysteine assay and hs -CRP on the next morning following the admission day. Serum homocysteine level was measured by Fluorescence Polarization Immunoassay (FPIA) method and recorded in units of ¼mol/L. The serum Hs-CRP was performed by using DADE BEHRING BN 100, estimated by nephelometric system as per instructions of the manufacturer.

The research protocol was approved by the "Research Review Committee" & the "Ethical Committee" of DMCH, Dhaka. The numerical data obtained from the study were analyzed and significance of difference was estimated by using the statistical methods. Data were expressed in frequency, percentage, mean and standard deviation as applicable. Comparison between groups was done by unpaired student's test, chi-square test, and Fisher's exact test as applicable. Data were analyzed by using computer based SPSS program (version 16). Probability less than 0.05 was considered significant.

Results:

There was no significant age difference among the groups. The mean age of the study population in group I was 50.33±15.50 years and in group II the mean age was 45.86±18.76 years. (Table I)

Table I

Distribution of age of the patients

Age (in year)	Group I (n=72) N	%	Group II (n=188) N	%	P value
31 – 40	32	44.4	118	62.8	
41 – 50	12	16.7	24	12.8	
51 – 60	18	25.0	20	10.6	
61 – 70	10	13.9	24	12.8	
>70	0	0.0	2	1.1	
Mean ± SD	50.33±15.50		45.86±18.76		0.073^{ns}

In group I 75.0% was male and 25% female and in Group II 81.9% was male and 18.1% was female. Male female ratio was 4:1 among the whole study subjects. (Figure 1)

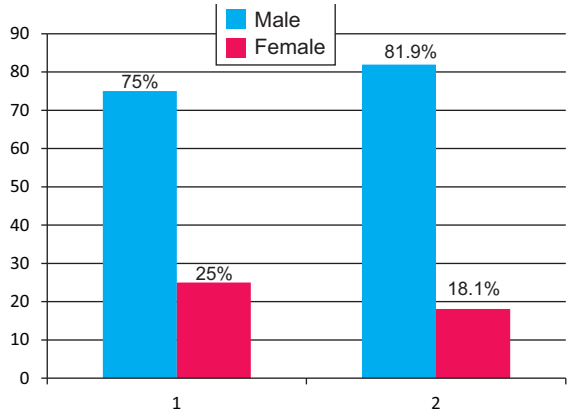


Fig.-1: *Sex distribution of the study subjects (N=260)*

There was similar presentation of ACS in between the groups, no statistically significant difference found in between the study groups regarding the clinical diagnosis. (Table II)

Table-II

Clinical presentation of subsets of ACS among the study groups

Clinical diagnosis	Group II(n=72) n	%	Group II (n=188) n	%	p Value
STEMI	52	72.2	132	70.2	0.460^{ns}
NSTEMI	8	11.1	24	12.8	0.928^{ns}
UA	12	16.7	32	17.0	0.253^{ns}

The table III shows the serum homocysteine level with clinical diagnosis in between the groups. The mean serum homocysteine level was higher in group II patients with diabetis malitus. The mean serum homocysteine level in STEMI, NSTEMI and UA were statistically significant ($p<0.05$) between the two groups.

The mean hs-CRP level in patients having acute STEMI, acute NSTEMI and UA were statistically significant ($p<0.05$) in group II. (Table IV)

Serum Homocysteine level was divided into two sub groups according to sex. The mean serum homocysteine level was statistically significant ($p<0.05$) between male and female patients within each group.(Table V)

The mean hs-CRP level difference in male and female was statistically significant ($p<0.05$) in group I but not significant ($p>0.05$) in group II. (Table VI)

Smoking and dyslipidemia were statistically significant ($p<0.05$) between two groups but others were not significant ($p>0.05$) in chi square test. (Table VII)

The mean serum Homocysteine differences were statistically significant and high in group II in HTN, smoker and dyslipidemia, but obesity and F/H of premature heart disese was not statistically significant. (Table VIII)

The mean serum Hs-CRP differences were statistically significantly high in group II for HTN, and F/H of premature CAD, but other risk factors were not statistically significant between the two groups. (Table IX)

Table-III

Distribution inbetween the groups of serum homocysteine level according to clinical diagnosis of ACS (N=260).

Clinical Diagnosis	Group I (n=72)	Group II (n=188)	p Value
	Serum homocysteine (µmol/L)		
	Mean±SD	Mean±SD	
STEMI	14.14±6.6	19.63±18.1	0.012[s]
NSTEMI	15.89±8.02	18.19±6.0	0. 012[s]
UA	12.75±4.88	15.21±5.19	0.001[s]
Group mean	14.11±6.48	18.41±15.49	0.024[s]

Table-IV

Distribution inbetween the groups of hs-CRP level according to clinical clinical diagnosis (N=260)

Clinical Diagnosis	Group I (n=72)	Group II (n=188)	p Value
	Hs CRP level (mg/L)		
	Mean±SD	Mean±SD	
STEMI	30.12±33.11	41.26±43.26	0.049[s]
NSTEMI	14.12±12.32	39.67±29.53	0. 001[s]
UA	8.12±7.77	28.51±27.61	0.001[s]
Group mean	26.84±30.30	37.48±37.99	0.034[s]

Table-V

Mean Serum Homocysteine level (mmol/L) of the study subjects according to sex (N=260)

S. Homocysteine (µmol/L)	Group I (n=72)		Group II (n=188)		P value
	N	%	n	%	
Male					
Mean ± SD	16.25	±5.81	19.48	±16.68	0.108[ns]
Female					
Mean ± SD	7.67	±3.45	13.69	±6.82	0.001[s]

Table-VI

hs-CRP level (mg/L) of the study subjects according to sex (N=260)

hs-CRP level (mg/L)	Group I (n=72) N %	Group II (n=188) n %	P value
Male			
Mean±SD	31.41±32.77	39.97±38.71	0.097[ns]
Female			
Mean±SD	13.13±14.87	26.24±32.75	0.012[s]

Table-VII

Distribution of risk factors among the study groups

Risk factors	Group I (n=72)		Group II (n=188)		P value
	N	%	n	%	
HTN	30	41.7	70	37.2	0.510^{ns}
Smoking	22	30.6	96	51.1	0.002^{s}
Obesity	12	16.7	38	20.2	0.516^{ns}
Dyslipidemia	54	75.0	112	59.6	0.020^{s}
Family history	6	8.3	30	16.0	0.111^{ns}

Table-VIII

Distribution of the study subjects according to mean serum homocysteine level and risk factors for ACS (N=260)

Risk factors for ACS	Group I (n=72)	Group II (n=188)	P Value
	Serum homocysteine (µmol/L)		
	Mean±SD	Mean	±SD
HTN	14.86±7.29	19.83±20.30	0.044^{s}
Smoker	15.81±7.12	19.09±11.82	0.028^{s}
Obesity	14.95±10.25	18.65±15.60	0.064^{ns}
Dyslipidemia	14.07±6.10	17.88±14.91	0.036^{s}
F/H Of Premature CAD	14.26±10.09	15.74±5.51	0.132^{ns}

Table-IX

Distribution of the study subjects according to mean Serum hs-CRP level and risk factors for ACS (N=260)

Risk factors for ACS	Group I (n=72)	Group II (n=188)	P value
	Hs CRP level (mg/L)		
	Mean±SD	Mean±SD	
HTN	10.89±35.33	37.93±38.95	0.001^{s}
Smoking	32.03±32.32	35.33±39.36	0.987^{ns}
Obesity	34.82±50.88	30.39±27.72	0.711^{ns}
Dyslipidemia	29.59±33.71	39.57±43.14	0.137^{ns}
F/H Of Premature Cad	13.35±6.91	30.41±21.63	0.001^{s}

Discussion:

This cross sectional study was carried out with an aim to evaluate the serum homocysteine and hs-CRP level in type 2 diabetic and non diabetic patients with recently diagnosed ACS.

In this study, mean age was 50.33±15.50 years ranging from 32 to 72 years in group I and 45.86±18.76 years ranging from 31 to 80 years in group II, difference was not significant (p>0.05). Similar age range was obtained by Ockene et al., observed the mean age of patients 49 years with range from 20-70 years[17]. Gonzalez-Porras et al., observed the mean age of patients 47 years with range from 26-54 years[11].

In the current study, 75.0% and 81.9% were male in group I and group II respectively, which indicates that ACS was more common in male subjects, which closely resembled with Gonzalez-Porras et al., where the authors found male female ratio was almost 6:1[11]. Similarly, Puri et al. observed ACS was more common in male subjects[18].

In this current study, STEMI was found 72.2% in group I and 70.2% in group II. NSTEMI was found in 11.1% and 12.8% in group I and group II respectively. UA was found in 16.7% in group I and 17.0% in group II. Gonzalez-Porras et al., have shown 57.0% STEMI, 23.0% NSTEMI and 20.0% UA[11]. Cusack et al., found that, stable angina with major adverse cardiac event (MACE) in 22.0% and no MACE in 35.0%. Unstable angina was in 24.0% and 35.0% respectively with MACE and no MACE[19].

Regarding the clinical association with serum homocysteine level it was observed that the mean serum

homocysteine level in patients with subsets of ACS were significantly (p<0.05) higher in patients without DM. The observed mean homocysteine was 14±6.48 µmol/L and 18.41±15.49 µmol/L in group I and II respectively. Kurowska et al., showed the mean(±SD) serum homocystieine level in patients having MI 14.7±6.7 µmol/L in patients with type 2 diabetes and 16.9±7.4 µmol/L in patients without diabetes. In UA the investigators showed the mean serum homocystieine level was 13.9±5.6 µmol/L in patients with type 2 diabetes and 13.8±4.2 µmol/L in patients without diabetes, which are similar with the current study[20].

Similarly, the mean hs-CRP level in patients with subsets of ACS was significantly (p<0.05) higher in group II. The mean hs-CRP level of group I and group II was 26.84±30.30 mg/L and 37.48±37.99 mg/L respectively. In the study by Kurowska et al., mean hs-CRP level in patients with MI was 24.3±36.6 mg/l in patients with type 2 diabetes and 29.7±40.8 mg/l in patients without diabetes[20]. In case of UA the hs-CRP level was 6.6±6.5 mg/l in patients with type 2 diabetes and 25.2±49.9 mg/l in patients without diabetes, which were significantly (p<0.05) higher in patients with out DM, which support the findings of current study. Facila et al., concluded that homocysteine over 10µmol/l was an independent prognostic factor increasing the long term risk of all cause mortality after acute coronary syndrome[21].

In this present series it was observed that the mean serum homocysteine level was higher in male and female ACS patients without DM. This finding is supported by Kurowska et al., who showed that the mean serum homocystieine level was 14.4±5.5 µmol/L in male patients with T2DM and 15.4±6.4 µmol/L in male patients without diabetes[20]. Kurowska et al., showed the mean(±SD) serum homocystieine level was 14.4±7.1 µmol/L in female patients with T2DM and 15.2±6.0 µmol/L in female patients without diabetes, which was statistically significant (p<0.05) and support the findings of the current study[20].

Similarly the mean hs-CRP level was higher in male and female ACS patients without DM in this syudy. Kurowska et al., showed lesser hs-CRP level in male patient, which was 17.0±19.8 mg/l in patients with type 2 diabetes and 31.0±50.1 mg/l in patients without diabetes, that was significantly (p<0.05) higher in ACS patients without DM[20]. Thus support the current study. Kurowska et al showed, the mean hs-CRP level was 17.0±38.3 mg/l in female patients with type 2 diabetes and 20.5±33.6 mg/l in female patients without diabetes, which was significantly (p<0.05) higher in ACS patients without DM, which is consistent with the current study[20]. On the other hand, Idzior-Walu[et al. CRP levels was significantly higher in women with diabetes than in men which was 4.7±3.2 mg/l vs 4.1±7.2 mg/l in female and male respectively[22].

Regarding the risk factors dyslipidaemia and smoking was statistically singnificant risk factor in group I and group II respectively. Puri et al. showed that hypertension, smoking, positive family history and dyslipidaemia were the most common risk factors in patients with ACS[18]. The mean serum Homocysteine differences were significantly (p<0.05) higher in HTN, smoker and dyslipidemia in patients without T2DM. But obesity and F/H of premature CAD was almost comparable in both groups. Puri et al. showed the mean homocysteine was 23.93±10.94 nmol/ml and 25.41±11.88 nmol/ml in hypertensive and smoker patients respectively. The mean serum hs-CRP differences was significantly (p<0.05) higher in HTN and F/H of premature CAD in patients without DM, but other risk factors was not significant (p>0.05) between the two groups[18].

This is consistent with the finding done by Akalin A et al., that show inflammatory activity and Hcy levels are increased in type 2 diabetic patients with atherosclerotic vascular diasease, but there was no correlation between Hcy and inflammatory markers except TNF±. Inflammation is not involved in the process by which Hcy leads atherosclerosis in type 2 diabetes[10]. Mazza et al. demonstrated that homocysteine levels poorly correlated with the severity of coronary artery disease, but had a strong predictor of acute coronary syndrome recurrence[16]. A study done by Kurowska et al. reported that the patients without previously diagnosed diabetes, the increased homocysteine level and the intensity of chronic and acute inflammatory reactions could be related to latent, long-term metabolic disturbances existing in the great percentage of these patients[20].

Conclusion:

This cross sectional observational study was done to compare the serum homocysteine and hs-CRP levels in ACS patients with and without T2DM. The result of the current study suggests that further studies are required for the assessment of relationship of plasma homocysteine to atherosclerotic vascular disease and inflammatory markers in T2DM patients and implication of lower blood Hcy and hs-CRP level on the prognosis of acute coronary syndrome patients to reach a conclusive decision.

References :

1. Raj B. What is the risk of coronary heart disease in South Asians? A review of UK research. J Pub Health Med 2000; 22: 375-385.
2. Maron DJ, Rider PM, Grundy SM, Prevention Strategies for Coronary Heart Disease. In: Fuster

V, Walsh RA, O'rourke RA, Wilson PP, editors, Hurst's, the heart, 12th edn, Mc Graw Hill, New York, USA, 2008; pp. 1235-1244.

3. Farkouh ME, Aneja A, Reeder GS et al, Usefulness of Diabetes Mellitus To Predict Long-Term Outcomes in Patients with Unstable Angina Pectoris, American Journal of Cardiology, 2009; 104(4):492-497.

4. Haffner SM, Lehto S, Ronnemaa T, PyorLa K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Eng J Med. 1998; 339 (4); 229 – 234.

5. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel 111). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel 111) final report. Circulation; 2002; 105 (25): 3143-3421

6. Nathan DM. Long-term complications of diabetes mellitus. N Engl J Med 1993; 328:1676-1685.

7. Pickup JC. Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. Diabetes Care 2004; 27:813-823.

8 Bodi V, Sanchis J, Llacer A. et al; Risk stratification in non- ST elevation acute coronary syndromes; predictive power of troponin I, C – reactive protein, fibrinogen and homocysteine. Int. J. Cardiol, 2006; 109, 248.

9 Zak A. ZemanM. ; Consequences of moderate hyperhomocysteinemia in internal medicine. Lek. Cesk.; 2004; 143, 367.

10 Akalin A. Alatas O, Colak o. :Relation of plasma homocysteine levels to atherosclerotic vascular disease and inflammation markers in type 2 diabetic patients. Eur. J. Endocrinol.; 2008; 158, 47.

11 Gonzalez-Porras JR, Martin-Herrero F, Garcia-Sanz R, et al. Hyper- homocysteinemia is a risk factor of recurrent coronary event in young patients irrespective to the MTHFR C677T polymorphism. Thrombosis Research 2007; 119: 691-698.

12 Ross R. Atherosclerosis: an inflammatory disease. N Engl J Med 1999; 340:115- 126.

13 Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, Aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997; 336:973- 979.

14 Mueller C, Buettner HJ, Hodgson JM, Marsch S, Perruchoud AP,Roskamm H, Neumann FJ. Inflammation and long-term mortality after Non-ST elevation acute coronary syndrome treated with a very early invasive strategy in 1042 consecutive patients. Circulation 2002; 105:1412-1415.

15 Brunetti N. D., T roccoli R, Correal M. et. Al.: C-reactive protein in patients with acute coronary syndrome : correlation with diagnosis, myocardial damage, ejection fraction and angiographic findings. Int. J. Cardiol. , 2006: 109, 248.

16 Mazza A., Bossone E., Mazza F. et. al.: Reduced serum homocysteine levels in type 2 diabetes. Nutr. Metab. Cardiovasc.Dis., 2005; 15, 118.

17 Ockene IS, Matthews CE, Rifai N, Ridker PM, Reed G, Stanek. E. Variability and classification accuracy of serial high- sensitivity C- reactive protein measurements in healthy adults. Clin Chem 2001; 47: 444-50.

18 Puri A, Gupta OK, Dwivedi RN, et al. Homocysteine and Lipid levels in young patients with coronary artery disease. JAPI. 2003; 51:681-685.

19 Cusack MR, Marber MS, Lampiase PD, Bucknall CA, Redwood SR. Systemic inflammation in unstable angina is the result of myocardial necrosis. J Am Coll Cardiol 2002; 39:1917-23.

20 Kuruowska M., Kaznowska- Bysetryk I., Dudzinska M., Tarach J., Malicka J. et al. Comparison of homocysteine and C - reactive protein levels determined at the moment of hospitalization in patients with acute coronary syndrome (ACS) with and without type 2 diabetes. ANNALES UNIVERSITATIS MARIAE CURIE- SKLODOSKA LUBLIN- POLONIA 2008; Vol. XXI, N1, 60.

21 Facila L., Nunez J. et al. :Early determination of homocysteine levels in acute coronary syndroms, is it an independent prognestic factor? In. J. Cardiol. 2005: 100, 275.

22 Idzior- Walus B, Cieslik G. et. al.: Homocysteine and C- reactive protein concentrations in serum of diabetic patients. Prazeg . Lek., 2003: 60, 778.51.

Original Article

Clinical, Electrocardiographic and Echocardiographic Profile of Ischemic Cardiomyopathy: An analysis of 100 cases .

Mainul Islam[1], M.Atahar Ali[2], Umme Habiba Ferdaushi[3], Shaila Nabi[4], Sayeedur Rahman Khan[5], Md. Shariful Islam[5], Hasan Mahmoud[3]

Abstract:

Background: Ischemic heart disease (IHD) is one of the leading cause of morbidity and mortality worldwide. Ischemic cardiomyopathy (ICM) is a delayed complication of IHD that arises as dilated cardiomyopathy with depressed ventricular function, which cannot be attributed entirely to coronary artery obstruction or ischemic injury.

Objectives: To evaluate the clinical, electrocardiographic and echocardiographic profile of patients presenting with ischemic cardiomyopathy.

Methods: In this cross sectional observational study 100 patients of ischemic cardiomyopathy admitted in hospital or visited OPD in NICVD, Dhaka from March'15 to Sept'15 were studied. Enrollment of the patients were done after fulfilling the inclusion and exclusion criteria. Clinical, electrocardiographic and echocardiographic data were collected then data analysis was done.

Results: Data analysis of 100 patients was showed age range was 40-80 years and mean age was 61.4±7.9 years. 79% subjects were male. Most common symptoms were dyspnea (93%), chest pain(73%), palpitation (39%) and edema (23%). Most patients were in NYHA functional class IV (43%). 64% cases had history of anterior myocardial infarction (MI), 22% had inferior MI, 25% had H/O PTCA and 7% had CABG. 71% subjects had tachycardia, 65% had lungs basal rales, 56% had systolic blood pressure below 100 mmhg and 25% had edema. ECG findings was as follows sinus rhythm (85%), Sinus tachycardia 71%, AF 15%, LBBB 34%, RBBB 12%, pathological Q in anterior surface 65% and inferior surface 21%, non specific ST-T changes 41% and PVCs was found in 17%.On echocardiography ,anterior wall hypokinesia was seen in 52% and global hypokinesia in 43%. Mean left ventricular ejection fraction (LVEF) was 31±5.9% and mean left ventricular internal diastolic diameter (LVIDd) was 6.5±0.4 cm. (59%) subjects had mitral regurgitation (MR) grade-I and 20% had MR grade-II.

Conclusion: The clinical presentation of ischemic cardiomyopathy varies from patient to patient. Severity of symptoms correlates with severity of left ventricular systolic dysfunction, left ventricular diameter and mitral regurgitation grade . Anterior Myocardial infarction has more chance to develop ischemic cardiomyopathy.

Key words: *Cardiomyopathy, Heart failure, Electrocardiogram, Echocardiography.*

(Bangladesh Heart Journal 2020; 32(2): 121-127)

Introduction:

Coronary artery disease (CAD) is the leading cause of mortality and morbidity in industrialized countries and it is emerging as public health problem in developing countries[1]. It is established that 30% of all deaths can be attributed to cardiovascular disease, of which more than half are caused by CAD. Globally, of those dying from cardiovascular diseases, 80% are in developing countries not in the western world [2]. By the year 2020, CAD will hold first place in the world health organization's list of leading cause of disability[3].

Bangladesh has undergone a remarkable demographic transition over last three decades. Striking changes have

1. Assistant Registrar, NICVD, Dhaka.
2. Senior Consultant of Cardiology, Evercare Hospitals, Dhaka
3. Junior Consultant of Cardiology, NICVD, Dhaka.
4. Associate Prof. of Cardiology, NICVD, Dhaka.
5. Medical Officer, NICVD, Dhaka

Address of Correspondence: Dr. Mainul Islam, Assistant Registrar, NICVD, Dhaka, Bangladesh. E-mail:mainulislam67@yahoo.com

DOI: https://doi.org/10.3329/bhj.v35i2.52898

also been observed in the lifestyle and food habit in our population[4].

While Bangladesh is turning from agro-based socioeconomic structure towards industry based setting, coronary artery disease in middle aged and young group is also appearing into scene[5]. The prevalence of CAD in Bangladesh was estimated as 3.3 per thousand in 1976 and 17.2 per thousand in 1986 indicating fivefold increase of the disease by 10 years[6].Three small scale studies showed average prevalence of ischemic heart disease (IHD) is 6.5 per thousand population of Bangladesh [7]. According to Bangladesh bureau of statistics, 2006. IHD is the fourth leading cause of death [8].

Complications of CAD are acute and chronic. The most common chronic complication of CAD is chronic ischemic heart failure wherein the heart becomes dilated, myocardium become thinned, scarred and fibrosed ; as a result systolic LV dysfunction develops, leading to congestive heart failure. In a word this condition known as ischemic cardiomyopathy[9]. Burch and Colleagues in 1970 first used the term Ischemic Cardiomyopathy to describe the condition in which Coronary Artery Disease results in severe myocardial dysfunction[10]. In the United States, the most common form of dilated Cardiomyopathy is ischemic Cardiomyopathy or the Cardiomyopathy that follows myocardial infarction[11].

Dilation of LV and a decrease of ejection fraction occurs in 15-40% of subjects within 12-24 months after anterior MI[12,13] and in a smaller percentage of subjects after an inferior MI[12]. Based on limited data[14], it is tempting to speculate that subjects who undergo the remodeling process and develop an ischemic cardiomyopathy are those with particularly heightened compensatory mechanisms, perhaps as result in polymorphic variation in this system[15]. The remodeling process is an attempt of the compromised ventricle to increase its performance by increasing stroke volume, but ultimately, it correlates with an adverse outcome in the long run[16].

The gross pathology of ischemic cardiomyopathy includes transmural or sub endocardial scarring representing old MIs that may compromise up to 50% of LV chamber. The histopathology of the non-infarcted is similar to changes which occur in dilated cardiomyopathy[17].

The prognosis of idiopathic dilated Cardiomyopathy is considered to be better than that of Ischemic cardiomyopathy[18,19] and prior to the use of ACE inhibitors; the survival was approximately 50% at 5 year[20].

This study was conducted to evaluate the demographic variations, clinical findings, electrocardiographic and echocardiographic findings in patients of Ischemic Cardiomyopathy.

Methods:

A total 100 patients with history of ischemic heart disease with left ventricular dilatation and systolic dysfunction admitted in or visited at OPD of NICVD for a period of six months from March'15 to Sept'15 were studied. It was a cross sectional observational study. Enrollment of the patients were done after fulfilling the inclusion and exclusion criteria. Patients were included in this study by consecutive purposive sampling. All patients gave written informed consent for the study. After enrollment clinical evaluation was done by detailed history taking and proper clinical examination. Then electrocardiogram and echocardiogram were done. All data were collected in a pre-formed data sheet. Statistical analysis was performed using SPSS version 16 (statistical Package for Social Science). Results were expressed as mean ± SD.

Inclusion criteria:

Chronic heart failure patients with dilated Left ventricle with one of the followings[10]:-

1. History of myocardial infarction.
2. H/O revascularization (CABG/PCI)
3. In coronary angiography (CAG) ³ 70% stenosis of major epicardial artery.

Exclusion criteria:

1. Idiopathic Dilated cardiomyopathy.
2. Valvular heart disease i.e. Valvular cardiomyopathy.
3. Hypertrophic cardiomyopathy.
4. Restrictive cardiomyopathy.
5. Post-partum dilated cardiomyopathy
6. Ischemic cardiomyopathy with device therapy (CRT/ICD).

Results and Observations:

A total 100 patients of ischemic cardiomyopathy were included in this study.The data analysis of these patients showed mean age was 61.4±7.9 years ranges from 40 years to 80 years and 79 (79%) were male.

Table-I

Distribution of the study patients according to clinical presentations(n-100)

Sign and symptoms	Number	Percent
Dyspnea	92	92.0
Chest pain	73	73.0
Palpitation	39	39.0
Edema	23	23.0
Paroxysmal Nocturnal Dyspnea (PND)	52	52.0
Orthopnea	46	46.0
Cardiogenic shock	21	21.0
Syncope	5	5.0
Cardiac arrest	5	5.0

Table I displays the clinical symptoms of the studied ischemic cardiomyopathy patients. The remarkable symptoms presented were dyspnea (92%), chest pain (73%),Paroxysmal nocturnal dyspnea (52%), orthopnea (46%), palpitation (39%), edema (23%) and cardiogenic shock (21%). The rest of the symptoms such as syncope and cardiac arrest were present in 5% patients.

Table-II

Distribution of the study patients according to NYHA class (n=100).

NYHA class	Number	Percent
Class I	0	0
Class II	25	25.0
Class III	32	32.0
Class IV	43	43.0

Table II showes NYHA class II, III and IV were observed 25%, 32% and 43% in study population respectively. Majority of the patients were in NYHA functional class IV.

Risk factor evaluation shows 40% patients had diabetes, 40% patients had hypertension, 47% were smokers, 25% had family history of coronary artery diseases and 25% patient had chronic kidney diseases.

Table-III

Distribution of the study patients according to past history of MI and intervention (n=100).

Myocardial Infarction (MI)	Number	Percent
Anterior	64	64.0
Inferior	22	22.0
Interventional procedure		
PTCA	25	25.0
CABG	7	7.0

Table III demonstrates MI and interventional status of the study patients. 64% and 22% patients were diagnosed as anterior MI and inferior MI respectively. 25% and 7% patients had undergone interventional treatment as PTCA and CABG respectively.

The physical examinations demonstrated the presence of tachycardia and pulmonary rales were more common in patients 71% and 65% respectively. Patients with systolic BP <100 mmHg in 35%, pallor in 26%, raised JVP in 18%, hepatomegaly in 20%, pedal edema in 25%, ascites in 17%, gallop in 41% and systolic murmur in 18% patients.

Table-IV

Distribution of the study patients according to ECG findings (n=100).

ECG findings	Number	Percent
Sinus	80	80.0
Atrial fibrillation	15	15.0
Ventricular		
Tachycardia/Ventricular		
Fibrillation	5	5
Sinus tachycardia		
QRS morphology	71	71.0
-Normal narrow		
-LBBB	54	54.0
-RBBB	34	34.0
Pathological- Q	12	12.0
-Anterior surface		
-Inferior surface	65	65.0
ST-T changes	21	21.0
PVCs	41	41.0
	17	17.0

Table IV showes majority of the ECG is in sinus rhythm (80%), atrial fibrillation (15%) and ventricular tachycardia / ventricular fibrillation (5%). The sinus tachycardia (71%) was more frequently seen in patients with ischemic cardiomyopathy followed by LBBB (34%), and RBBB (12%). Anterior and inferior surface in pathological Q were found in 65% and 21% respectively. ST-T changes had in 41% patients. PVCs was found in 17% patients of the study population.

Table-V

Echocardiographic structural and functional parameters of the study patients (n=100).

Characteristics		Number	Percent (%)	Mean ± SD Range (min-max)
Regional wall motion abnormality (RWMA)				
	Anterior wall	52	52.0	
	Inferior wall	12	12.0	
	Global	43	43.0	
LVEF in %				31.9±5.9(20 – 45)
	Severe impairment (<30)	30	30.0	
	Moderate impairment (30 -44)	68	68.0	
	Mild impairment (45-54)	2	2.0	
LVIDd in cm				6.5±0.4(5.6 – 8.2)
	Severely enlarge (Male>6.9 cm, Female>6.2 cm)	31	31.0	
	Moderate enlarge (Male 6.4-6.8 cm, Female 5.8-6.1 cm)	35	35.0	
	Mildly enlarge (Male 6.0-6.3 cm, Female 5.4-5.7 cm)	34	34.0	
LVIDs in cm				5.2±0.5(4.0 – 6.2)
	Enlarge (> 4.1 cm)	100	100.0	
MR grading				
	Grade I	59	59.0	
	Grade II	20	20.0	
	Grade III	14	14.0	
	None	7	7.0	

Table: V demonstrates anterior wall hypokinesia in 52%, inferior wall hypokinesia in 12% and global hypokinesia in 43% ischemic cardiomyopathy patients. Left ventricular systolic dysfunction was moderately impaired in 68% patients, severely impaired in 30% and mildly impaired in 2% patients. Mean Left ventricular ejection fraction (LVEF) was observed 31.9±5.9% with range of 20-45%. Moderately enlarge LVIDd in 35% patients, mildly enlarge in 34% patients and severely enlarge in 31% patients. Mean LVIDd was found 6.5±0.4cm with a range of 5.6-8.2cm. Enlarge LVIDs had in 100% patients. Mean LVIDs was found 5.2±0.5cm with a range of 4.0-6.2 cm. Mitral Regurgitation (MR) with grade I was the most common (59%) patients followed by grade II in 20% and grade III in 14% patients. 7% patients had no MR.

Discussion:

This study intended to evaluate the clinical profile of patient presenting with Ischemic cardiomyopathy. After analyzing the collected data and results it is found that ischemic cardiomyopathy is a delayed complication of ischemic insult to heart and one of the leading cause of hospital admission of heart failure patients.

Ischemic cardiomyopathy caused by coronary artery disease is far more common than are the other clinicophysiological syndromes caused by coronary artery

disease that are associated with chronic heart failure [21, 22]. The other syndromes of coronary artery disease causing heart failure, are almost always considered as diagnostic possibilities in an individual patient with heart failure because of an accompanying history of chest pain, detection of cardiac murmur, and electrocardiographic evidence of myocardial infarction. By contrast, Cardiomyopathy caused by coronary artery disease is known to occur, without accompanying clinical clues to the presence of coronary artery disease[23]. Coronary artery disease becomes more severe and more symptomatic with aging [24,25] and advanced age adversely affects the survival of patients with acute ischemic syndrome [26,27].

In this study, the mean age was found 61.4±7.9 years. Similar age incidences were reported in the previous studies [30].

In our study, presenting symptoms were dyspnea 92 (92%), chest pain 73 (73%), palpitation 39 (39%), edema 23 (23%), paroxysmal nocturnal dyspnea (PND) 52 (52%), orthopnea 46 (46%), shock 21 (21%), syncope and cardiac arrest were 5(5%).Most of the symptoms were consistent with previous study[1,5] except chest pain which was more frequent (92%) in previous study[28].

Out of these patients- 25% patients were in New York Heart Association (NYHA) class II, 32% were in class III and 43% patients class IV. In previous study[28] maximum patients were in NYHA class III 46% but in our study maximum patients were in class IV 43%. It may be due to our majority of the patients were hospital admitted patients.

Among our population 40% were hypertensive and 40% were diabetic, 47% were smoker, 25% had family history of CAD and 23% patients were suffering from chronic kidney disease. These statistics are consistent with previous study[29] except smoking which were more frequent in our study.

In our study patients 71% had tachycardia, 35% blood pressure (BP) <100mmhg, 26% pallor,18% raised JVP, 20% hepatomegaly, 25% pedal edema , 17% ascites, 65% basal rales,41% gallop and 18% had apical systolic murmur which were not consistent with previous study[28] except tachycardia. In previous study all parameters were in higher percentages.

Electrocardiography (ECG) findings in this study were similar to previous study[29].

In echocardiography anterior wall hypokinetic (left anterior descending artery territory) was 52%, inferior wall hypokinetic (right coronary artery territory) was 12% and overlapping or global hypokinetic was 43%. There were similae findings with previous study[36]. Maximum patients left ventricular ejection fraction (LVEF) were moderately impaired i.e. LVEF-(30-44%) and the no. of the patients were 62%. The mean left ventricular ejection fraction (LVEF) was found 31.9±5.9 %. In previous studies it was 26.6±7.8 %[36], 27.8±5.7 %[37], and 26±9.5%[31]. The mean LVIDd and LVIDs were found 6.5 ±0.5 and 5.2±0.5 respectively which were similar to previous study[29].On echo-color Doppler study 59% patients had mitral regurgitation (MR) grade-I, 20% MR grade-II, 14% MR grade-III and 7% had no MR. Previous study[29,32] related to ischemic cardiomyopathy and dilated cardiomyopathy also showed similar pictures. We, the physicians have to take challenge to manage these patients daily. Most of the patients are not able to take proper treatment due to economic constrain. Some of these patients have the criteria for modern treatment of heart failure i.e. device therapy alongside to medical management, so that morbidity and mortality can be reduced.

Limitations of the study:

1. As the sample size was small and the study period was short, it is difficult to generalize all the findings to a reference population.
2. It was not possible to perform CAG to all study population. So angiographic diagnosis was not made in all cases.
3. Most of the patients were hospital admitted. So the community prevalence is difficult to assess.
4. Number of hospitalizations since diagnosis was not shown in this study.
5. As it is single population observational study there was no comparison with other cardiomyopathy.

Conclusion:

Ischemic cardiomyopathy is a one of the commonest causes of congestive heart failure causing repetitive hospital admissions. The clinical presentation of ischemic cardiomyopathy varies from patient to patient, and most patients present with delayed symptoms. Severity of symptoms correlate with severity of left ventricular systolic dysfunction, left ventricular diameter and mitral regurgitation grade . Anterior Myocardial infarction has more chance to develop ischemic cardiomyopathy.

References:

1. The world Health report, 2003. Neglected global epidemic three growing threat shaping the future World Health Organization,Geneva,2003;85-99

2. Anderson RN United States life tables: Eliminating certain causes of death Hyattsville MD: National center for health statistics, 1999.

3. Murry CJ, Lopez AD, KJauder E, Mortality by cause for eight regions of the world : burden of disease study Lancet 1997,349: 1269-1276.

4. Mitra SN, Sabir A , Cross AR et al. Bangladesh demographic and health survey 1996-97,National Institute of Population Research and Training (NIPORT),Dhaka ,Bangladesh.

5. Bhopal CN, Whitic M, Yalllop H et al. Heterogenecity of coronary heart disease, risk factors in India, Pakistan ,Bangladesh and European origin population. BMJ 1999, 319:215-20.

6. Acute Coronary Syndrome: Guidelines for management, Bangladesh Cardiac society, Dhaka, Bangladesh 2004

7. Islam MN, Ali MA, Ali M. Spectrum of cardiovascular disease: The current scenario in Bangladesh, Bangladesh Heart Journal 2004, 19:1-7.

8. Bangladesh bureau of statistics : Health, Family planning and Social statistics ,cat.no 13:20, BBS , Dhaka ,2007

9. Mihai G. George S. Jhon DP et al. Navigating the crossroad of coronary artery disease and heart failure. Circulation. 2006; 114:1202-1213.

10. Burch GE, Giles TD et al. Ischemic cardiomyopathy. American Heart Journal. 1970; 79: 291 - 292.

11. Hokki, Anderson KM, Kannel WB, Grossman W, Levy D. Survival after the onset of congestive heart failure in Framingham heart study subjects. Circulation.1993;88:107-115

12. McKay RG,Pfeffer MA,Pasternak RC,et al. left ventricular remodeling after myocardial infarction : a corollary to infarct expansion. Circulation. 1986;74:693-702.

13. Mitchell GF, Lamas GA, Vaughan DE, et al.left ventricular remodeling in the year after myocardial infarction: a quantitative analysis of contractile segment lengths and ventricular shape. J Am Coll Cardiol .1992;19:1136-1144.

14. Pinto YM, van Gilst WH , Kingma JH, Schunkert H, for the captropril thrombolysis study investigators.Deletion type allele of the angiotensin converting enzyme gene is associated with progressive ventricular dilatation after anterior myocardial infarction. J Am Coll Cardiol. 1995; 25: 1622-1626.

15. Raynolds MV,Bristow MR, Bush EW,et al. angiotensin-converting enzyme DD genotype in patients with ischemic or idiopathic cardiomyopathy .Lancet.1993;342:1073-1075.

16. Mann DL, Bristow MR. Mechanisms and models in heart failure: the biomedical model and beyond. Circulation .205;111:2837-2849.

17. Gerdes AM, Kellerman SE, Moore JA, et al. structural remodeling of cardiac myocytes from patients with chronic ischemic heart disease. Circulation .1992;86:426-430.

18. Fransciosa JA, Wilen M. Ziesche S, Cohn JN. Survival in men with severe chronic left ventricular failure due to either,coronary heart disease or idiopathic dilated cardiomyopathy. American Jour of Cardiology. 1983; 51: 831 – 836.

19. Likoff M, Chandler S, Kay H. Clinical determinants of mortality in chronic congestive heart failure secondary to idiopathic or ischemic cardiomyopathy. American Jour of Cardiology. 1987; 59: 634 – 638.

20. Fuster V, Gersh BJ et al. The natural history of idiopathic dilated cardiomyopathy. American Jour of Cardiology. 1981; 47: 497 – 508 .

21. Brody W and Criley JM. Intermittent severe mitral regurgitation. Hemodynamic studies in a patient with recurrent acute left sided heart failure. New England Journal of Medicine. 1970; 283: 673 – 676.

22. Baxely WA, Jones WB and Dodge HT. Left ventricular anatomical and functional abnormalities in chronic post infarction heart failure. Journals of Internal Medicine. 1971; 74: 499 – 508.

23. Raftery EB, Banks DC, Oram S: Occlusive disease of the coronary arteries presenting as primary congestive cardiomyopathy .Lancet. 1969; 2: 1147-1150.

24. Fisher LD, Maynard C, Rademark AW, Alderman EL, Mock M: Age variation in association between angiographic coronary artery disease and angina from the coronary artery surgery study (CASS). International Jour of Cardiology. 1989; 24: 317-326.

25. Chaitmann BR, Bourassa MG, Davis K, Rogers WJ, Tyraas DH, Berger R, Kennedy JW, Fisher L, Judkins MP, Mork M, Kitrip T. Angiographic prevalence of high

risk coronary artery disease in patients subjects (CASS) Circulation. 1981; 64: 360 –367.

26. R Lapu-Bula, Robert A, Kock M De et al. Risk stratification in patients with dilated cardiomyopathy: contribution of Doppler derived left ventricular filling. American Jour of Cardiology. 1998 (82); 779-785.

27. European Coronary Surgery group: Long term results of prospective randomized study of coronary 295: 731 – 739 artery bypass surgery in stable angina pectoris . Lancet. 1982; 2: 1174-1180.

28. Shoaib AZ, Rabbani MU, Parvez A. 2-D Echo and doppler evaluation in ischemic cardiomyopathy. JK-Practitioner 2012; 17(1-7):5-9.

29. Mantzian L,Ziakas A, Ventoulis I,Kemperidis Differences in Clinical Presentation and Findings between Idiopathic Dilated and Ischemic Cardiomyopathy in an Unselected Population of Heart Failure Patients. The open cardiovascular medicine Journal, 2012; 6, 98-105.

30. The comparative analysis of of ECG between ischemic cardiopathy and dilated cardiomyopathy. http://heart.bmj.com/content/98/Suppl_2/E167.3

31. Virendra CP,Neeraj D,Chetan G.Clinical and echocardiogram profile of cardiomyopathy at tertiary care Centre.Journal of cardiovascular disease research,2014;5(1):34-43.

32. Banerjee SK, Rahman F, Salman M, Siddique MA. Idiopathic dilated cardiomyopathy: clinical profile of 100 patients. University Heart Journal. 2010; 6(1):9-12.

Original Article

Serum Potassium and Angiographic Severity of Coronary Artery Disease in Non-ST Elevation Myocardial Infarction

Maimuna Sultana[1], Afzalur Rahman[2], Pradip Kumar Karmakar[3], AKM Monwarul Islam[3], Al-Mamun[4], Khondaker Aisha Siddika[4], Kazi Md. Rubayet Anwar[5], Gokul Chandra Datta[5], Deb Dulal Debnath[5], Shaikat Chowdhury[5], Md. Nazmul Islam[6]

Abstract:

Background: Non-ST elevation myocardial infarction (NSTEMI) patients like other patients with acute coronary syndrome (ACS) need assessment of severity of coronary artery disease (CAD) for prognostication and management. The available scoring systems are complex and include invasive parameters. On the other hand, potassium is a key element and its blood level has been shown to reflect health and disease of vasculature including in some ACS. Objective: The study was conducted to find out the relationship between serum potassium level and angiographic severity of CAD in NSTEMI.

Method: A total of 200 cases of NSTEMI patients undergoing coronary angiography (CAG) were included. Patients getting medications that alter potassium homeostasis (e.g., diuretics, glucocorticoids, intravenous insulin), having renal impairment, haematological or liver disease, congenital or valvular heart disease, cardiomyopathy, prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were excluded. Serum potassium was measured soon after admission with NSTEMI, and the patients were divided: mid to high normal (4 to 5.5 mmol/L) constituted the group I and low normal (3.5-3.9 mmol/L) constituted the group II. CAG was done during index admission, SYNTAX score calculated and compared between 2 groups.

Results: High SYNTAX score was significantly more commonly found in group I than in group II (62.1% vs. 14.7%, p<0.001). Mean SYNTAX score was higher in group I than in group II (24.3±8.2 vs. 15.3±7.8, p<0.001). There was a linear relationship between serum potassium level and SYNTAX score. Mid to high normal serum potassium, hypertension and dyslipidemia were found to be significantly related to higher SYNTAX score with odds ratio being 10.44, 4.37 and 2.12 respectively.

Conclusions: Within physiological limits, higher serum potassium level correlates with severe coronary artery disease in NSTEMI patients. It may be used as an additional tool in conjunction with other scoring systems to assess the severity of CAD in this subset of ACS patients.

Key words: *Potassium, Coronary Artery Disease, Non-ST Elevated Myocardial Infarction, Coronary Angiography*

(Bangladesh Heart Journal 2020; 32(2): 128-133)

Introduction:

Cardiovascular diseases (CVDs) are the leading cause of death in the world and a major barrier to sustainable human development.[1] The 2013 Global Burden of Disease (GBD) study estimates that CVD caused 17.3

1. Junior Consultant (Medicine), Kurmitola General Hospital, Dhaka, Bangladesh.
2. Professor of Cardiology & Senior Consultant, Lab Aid Cardiac Hospital, Dhaka, Bangladesh.
3. Associate Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
4. Junior Consultant, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
5. Medical Officer, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
6. Post Graduate Fellow, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
Address of Correspondance: Dr. Maimuna Sultana, Junior Consultant (Medicine), Kurmitola General Hospital, Dhaka, Bangladesh. Telephone: +8801712856496 (cell phone), Email: the.maimuna@gmail.com

DOI: https://doi.org/10.3329/bhj.v35i2.52899

million deaths globally.[2] Eighty percent of deaths occur in low- and middle-income countries. Among the CVDs, ischemic heart disease (IHD), or the coronary artery disease (CAD) accounts for almost 1.8 million deaths annually and 20% of all deaths in Europe.[3] Estimates from the GBG suggests that by the year 2020, the South Asian region will have more individuals with atherothrombotic CVD than any other region.[4] The exact prevalence of CAD in Bangladesh is not known. Only a limited number of small-scale epidemiological studies are available. A recent review has estimated the prevalence of CAD in Bangladesh to be 4-6%.[5]

Risk evaluation is important for the management of patients with CAD. Clinicians need simple, reliable, reproducible, and quantitative tools to identify patients' risks and recommend prevention strategies. The Thrombolysis in Myocardial Infarction (TIMI) score and the Global Registry of Acute Coronary Events (GRACE) score used for the risk stratification of acute coronary syndrome (ACS) patients are primarily based on multivariable models that include components of the medical history, admission electrocardiogram (ECG), and cardiac biomarkers.[6]

Potassium is a key mineral that is crucial for life. The normal range for serum potassium is narrow (3.5 to 5.5 mmol/L) and minor deviation from this range (by less than 1.0 mmol/L) is associated with significant morbidity and mortality. Also, measurement of serum potassium is rapid, simple and reproducible. However, potassium level in serum may be raised erroneously due to tight tourniquet, vigorous exercise, hemolysis, thrombocytosis or leukocytosis.[7] It is well-known that changes in serum potassium ion concentration result in changes in the heart rate and myocardial contractility. Beyond this, there are some evidence that serum potassium significantly affects vasodilatation, and atherosclerosis for-mation.[8] These effects on vasculature may be due to a compensatory mechanism medi-ated by the renin-angiotensin system or may result from the pathophysiologic process of myocar-dial ischaemia.[8] Besides the established risk factors of CAD, i.e., age, diabetes mellitus, male gender, hyperlipidaemia, smoking, family history of CAD, and peripheral artery disease[9], serum potassium level tends to correlate with the severity of coronary artery lesions as assessed by Gensini score[8], and serum potassium level on admission was found to be an independent risk factor for target lesion revascularization.[10]

The importance of these findings lies in the possibility that serum potassium level may be useful for stratification of risks in patients with ACS. To date, for risk stratification and to identify the severity of coronary artery lesion, several validated scoring systems are available for use in clinical practice, the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score (SX) is a favoured one in this regard.[11] Although these scoring systems have many advantages, they require an invasive method such as coronary angiography to perform the scoring. Therefore, the clinicians are still in search of an easily accessible, cost-effective and noninvasive method to carry out risk stratification to determine the extent and severity of CAD in ACS patients.[12] The present study was planned to find out the relationship between serum potassium level and the severity of CAD in patients with non-ST elevation myocardial infarction (NSTEMI).

Materials and Methods:

This cross-sectional observational study was done in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh during September, 2018 to August, 2019. A total of 200 patients with NSTEMI who were admitted into NICVD and underwent coronary angiography (CAG), were included for this study. Those getting medications that alter potassium homeostasis (e.g., diuretics, glucocorticoids, intravenous insulin), having renal impairment, haematological or liver disease, congenital or valvular heart disease, cardiomyopathy, prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were excluded. For each patient, relevant history was taken and clinical examination was done and recorded in predesigned structured data collection sheet. For measurement of serum potassium, 2.5 ml of blood was drawn before the day of CAG under aseptic technique from peripheral veins. The collected blood was then directly put into an automated hematology analyzer (Beckman Coulter AU480/ Siemens Dimension EXL LM) to get the values of serum electrolytes including potassium. Other investigations e.g., complete blood count, serum creatinine, lipid profile, blood sugar, were done as per standard protocol. The study patients were divided into 2 groups on the basis of serum potassium level: mid to high normal (4 to 5.5 mmol/L) constituted the group I and low normal (3.5-3.9 mmol/L) constituted the group II. Echocardiography was done before sending the patient to cath lab. CAG was done by conventional method. From the baseline diagnostic CAG, angiographic severity assessment was done by the SYNTAX scoring system by 2 independent experienced interventional

cardiologists blinded to the identities and clinical information of the patients. All coronary lesions with a diameter stenosis e"50% in vessels e"1.5 mm were scored, using the SYNTAX algorithm, which is available on the website www.syntaxscore.com. Patients with SYNTAX scores ≥23 were considered to have moderate to severe CAD according to this definition. For the present study, the patients were divided into 2 groups, those with low SYNTAX scores (≤22) and those with intermediate to high SYNTAX scores (e"23). Comparison of SYNTAX scores between group I (low normal serum potassium) and group II (mid to high normal serum potassium) NSTEMI patients was done.

Data were analyzed by SPSS (Statistical Package for Social Sciences) version 22.0. Continuous data were presented as mean ± SD. Between group comparisons were performed using t-test. Categorical data were presented as percentages and analyzed using chi square test. The correlation between serum potassium level and SYNTAX score was examined by Pearson's correlation analysis. Differences with p values <0.05 were considered statistically significant.

Ethical approval was taken from the Ethical Review Committee of NICVD prior to the commencement of the study. Informed written consent was taken from the participants accordingly.

Results:

The study involved 200 NSTEMI patients undergoing CAG: Group I had 132 NSTEMI patients with mid to high normal serum potassium level (4-5.5 mmol/L), and group II had 68 NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L). The mean age of the studied patients was 52.7±8.9 years in group I and 50.9±9.7 years in group II. Out of 200 patients, 172 (86%) were male and 28 (14%) were female. No statistically significant differences were found in age and sex distribution between the groups (p>0.05). Among the CAD risk factors, diabetes mellitus and dyslipidaemia were significantly more in group I than in group II (p<0.05). (Table 1).

The biochemical parameters, including haemoglobin (Hb), RBS, serum creatinine, total cholesterol, LDL cholesterol and HDL cholesterol were almost similar in both the groups, however, TG was found significantly higher in group I than in group II (203.03±63.3 vs. 173.7±52.7 mg/dl, p=0.001). (Table 2) The mean percent of ejection fraction was 52.5±8.2% in group I and 54.4±8.4% in group II, the difference between the two groups was statistically insignificant (p=0.12).

High SYNTAX score was more commonly found in group I than in group II (62.1% vs 14.7%), and the difference between the 2 groups was statistically highly significant (p<0.001). On the other hand, low SYNTAX score was more common in group II than in group I (37.9% vs 85.3%), and the difference was statistically highly significant. Mean SYNTAX score was higher in group I than in group II (24.3±8.2 vs. 15.3±7.8), the difference between the groups was highly significant (p<0.001). (Table 3). Other statistics of SYNTAX score including the 25th and 75th percentile levels, the median, the maximum and minimum values and the inter-quartile ranges of SYNTAX score were higher in group I patients with high serum potassium level than in group II patients with low normal potassium. (Figure I)

Table-I

Distribution of study subjects by coronary artery disease risk factors (N=200)

Risk Factors	Group I (n=132)		Group II (n= 68)		p value
	Number	%	Number	%	
Smoking	78	59.1	36	52.9	0.40^{NS}
Hypertension	80	60.6	48	70.6	0.16^{NS}
Diabetes mellitus	76	57.6	28	41.2	0.03^{S}
Dyslipidaemia	62	47.0	20	29.4	0.02^{S}
Family H/o premature CAD	32	24.2	12	17.6	0.28^{NS}

Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)
Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)
p value was reached from chi square test. S= Significant (p<0.05), NS = Not significant (p>0.05). CAD = Coronary artery disease

Table-II

Distribution of the study patients by biochemical status (N=200)

Biochemical parameters	Group I (n=132) Mean ± SD	Group II (n= 68) Mean ± SD	p value
Hb (gm/dL)	11.7±1.3	12.0±0.9	0.09^{NS}
RBS (mmol/L)	9.8±4.0	8.9±3.5	0.93^{NS}
Serum creatinine (mg/dl)	1.12±0.25	1.07±0.20	0.21^{NS}
Total cholesterol (mg/dl)	210.2±27.9	202.5±23.5	0.05^{NS}
LDL cholesterol (mg/dl)	87.7±23.5	83.3±18.6	0.18^{NS}
HDL cholesterol (mg/dl)	40.3±4.5	39.3±4.7	0.16^{NS}
TG (mg/dl)	203.03±63.3	173.7±52.7	0.001^{S}

Here, Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)
Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)
p value was reached from unpaired Student's t test
S= Significant (p<0.05), NS = Not significant (p>0.05), Hb = Haemoglobin, RBS = Random blood sugar, LDL = Low density lipoprotein, HDL = High density lipoprotein, TG = Triglyceride

Table-III

Distribution of the study patients by SYNTAX score (N=200)

SYNTAX Score	Group I (n=132)		Group II (n= 68)		p value
	Number	%	Number	%	
High (e"23)	82	62.1	10	14.7	<0.001^{S}
Low (d"22)	50	37.9	58	85.3	<0.001^{S}
Mean ± SD	24.3±8.2	15.3±7.8	<0.001^{S}		

Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)
Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)
p value was reached from chi square test and unpaired t test
S= Significant (p<0.05), NS = Not significant (p>0.05)

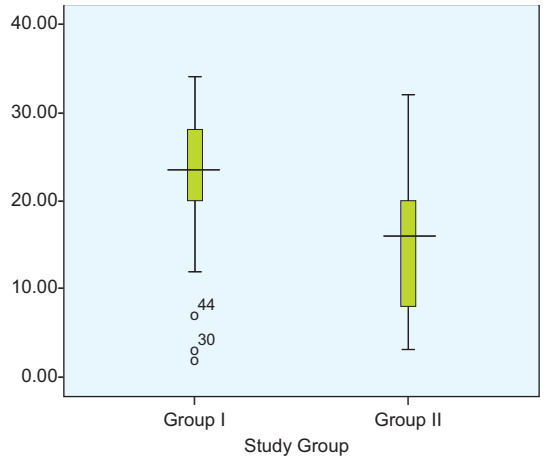


Fig.-1: *Relationship between serum potassium level and SYNTAX score by box plot diagram*

Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)

Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)

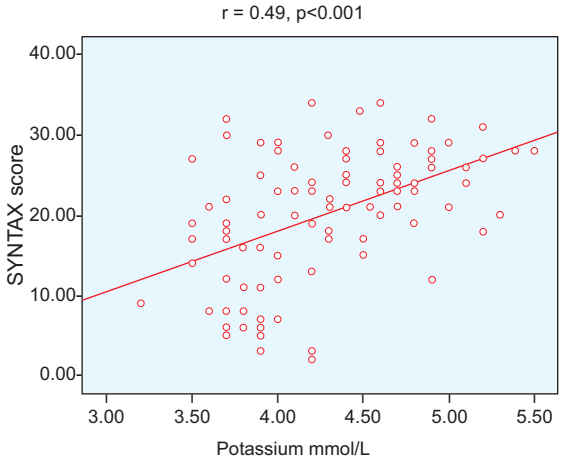


Fig.-2: *Scatter diagram showing correlation between serum potassium level and SYNTAX score*

Also, a positive correlation was found between serum potassium level and SYNTAX score with correlation coefficient, r=0.49, p<0.001. As serum potassium level increases, SYNTAX score also increases. (Figure II)

Table-IV

Multivariate logistic regression for determinants of severity of coronary artery disease as assessed by high SYNTAX score

Variables of interest	Regression coefficient (β)	p value	OR	95% CI
Agee"50 years	0.437	0.27^{NS}	1.54	0.714 – 3.354
Smoking	0.575	0.12 ^{NS}	1.77	0.856 – 3.691
Diabetes mellitus	0.420	0.25^{NS}	1.52	0.739 – 3.135
Hypertension	1.477	<0.001^{S}	4.37	2.024 – 9.474
Dyslipidemia	10.755	0.03^{S}	2.12	1.062 – 4.260
Family history of CAD	0.634	0.13^{NS}	1.88	0.817 – 4.351
Mid to high serum potassium level	2.346	<0.001^{S}	10.44	4.547 – 23.993

Dependent variable: high SYNTAX Score;
Independent variables: age e"50 years, smoking, diabetes mellitus, hypertension, dyslipidemia, family history of CAD and mid to high normal serum potassium level (4-5.5 mmol/L)
S = Significant, NS = Not significant

Variables associated with high SYNTAX score were further analyzed by logistic regression analysis to find out the determinants of severity of CAD as assessed by high SYNTAX score. Hypertension, dyslipidemia and mid to high serum potassium level were found to be the significant predictors of high SYNTAX score with ORs being 4.37, 2.12 and 10.44 respectively. (Table 4)

Discussion:

In present study, baseline demographics, i.e., age and sex were statistically similar between patients with low and mid to high normal serum potassium levels. The mean age of patients in group I and II was 52.7±8.9 and 50.9±9.7 years respectively. In a study conducted at Dhaka Medical College by Zahid et al[13] the mean age of NSTEMI patients was 55.9±9.1 years. The majority of the patients of the present study were male (84.8% and 88.2% in group I and group II respectively), such male predominance was also reported by other researchers.[13] The gender disparity in the present study may be multifactorial e.g., lower prevalence of CAD in women, less health-care seeking attitude of females and relative unwillingness for invasive procedures. Regarding CAD risk factors, smoking, hypertension and family history of CAD did not differ significantly between the groups. Diabetes mellitus and dyslipidaemia were found significantly more commonly in group I than in group II (p=0.03 and 0.02, respectively).

In this present study, the SYNTAX score of NSTEMI patients differed between group I and group II. The patients in group II with low normal serum potassium had mean SYNTAX score 15.3±7.8 while, patients in group I with mid to high normal serum potassium had mean SYNTAX score 22.6±7.1. Statistically, this difference was highly significant (p<0.001). Zhao et al[8] demonstrated that serum potassium levels were significantly increased in patients with lower (d" 39 points; 3.90 ±0.02 mmol/L, n=453) and higher (>39 points; 3.9± 0.02, n=194) Gensini scores compared with normal patients (3.82±0.03 mmol/L) (p value<0.05). Furthermore, serum potassium level of the high score group was also significantly higher than that of low score group (p<0.05). In another study[10], Honda et al found serum potassium level on admission as an independent risk factor for target lesion revascularization. Both of the studies had similar findings like the present study in terms of having increased CAD severity with increased serum potassium within normal range. Apart from this, in the USA, serum potassium level was found marginally associated with risk of CVD (hazard ratio per 1mg/dL increment, 1.03; 95% confidence interval, 1.00-1.05; p=.02a multicenter study.[14]

In this study significantly positive correlation was found between serum potassium level within normal range and SYNTAX score (r = 0.49, p value < 0.001). Within normal range as serum potassium level increases, SYNTAX score also increases. Most of the patients with low normal serum potassium had low SYNTAX score, while most of the patients with mid to high serum potassium had high SYNTAX score. Statistically, this correlation was highly significant (p<0.001). Similar significant positive correlation was found by Zhao et al between serum potassium and the severity of CAD assessed by Gensini score (p <0 .05).[8]

In this study, multivariate logistic regression analysis was done to find out the determinants of severe CAD. The analysis revealed that mid to high normal serum

potassium i.e., 4-5.5 mmol/L (odds ratio: 10.44; 95% CI is 4.547-23.993, p<0.001) and hypertension and dyslipidaemia were the independent determinants of increased angiographic severity of CAD (SYNTAX score e" 22). In the study by Zhao et al[8] and Honda et al[10] higher serum potassium level within normal range was demonstrated as independent predictor for severe CAD.

The study has got some limitations. The sample size was relatively small. Also, the sampling method was purposive, so there is risk of selection bias. The study was conducted in a single center, and involved multiple operators. Moreover, coronary artery lesion severity was assessed by visual method, so there was every chance of inter-observer variation.

Conclusion:

Serum potassium within normal range positively correlates with the severity of CAD as assessed by the SYNTAX score in NSTEMI patients. Mid to high normal serum potassium level, along with hypertension and dyslipidaemia, is a significant predictor of high SYNTAX score in patients with NSTEMI. If these findings are validated by larger, multicentric studies, serum potassium level may be added to the existing armamentarium to assess the severity of CAD in NSTEMI patients.

References:

1. Clark H. NCDs: a challenge to sustainable human development. *Lancet*. 2013 Feb 16;381(9866):510-1. doi: 10.1016/S0140-6736(13)60058-6.
2. Townsend N, Wilson L, Bhatnagar P, Wickramasinghe K, Rayner M, Nichols M. Cardiovascular disease in Europe: epidemiological update 2016. *Eur Heart J*. 2016 Nov 7;37(42):3232-3245. doi: 10.1093/eurheartj/ehw334.
3. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al.; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018 Jan 7;39(2):119-177. doi: 10.1093/eurheartj/ehx393.
4. Chakraborty B. Zaman F. Sharma AK. Combating Coronary Artery Disease in South Asia-What is Special? *Bangladesh Journal of Cardiology*. 2009; 1(2): 88–90.
5. Islam AKMM. Mohibullah M. Paul T. Cardiovascular Disease in Bangladesh: A Review. *Bangladesh Heart Journal*. 2017; 31(2): 80–99.
6. Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. *JAMA*. 2000 Aug 16;284(7):835-42. doi: 10.1001/jama.284.7.835.
7. Sica DA, Struthers AD, Cushman WC, Wood M, Banas JS Jr, Epstein M. Importance of potassium in cardiovascular disease. *J Clin Hypertens (Greenwich)*. 2002 May-Jun;4(3):198-206. doi: 10.1111/j.1524-6175.2002.01728.x.
8. Zhao GX. Jin XL. Kang JL. Jin CZ. Serum potassium levels are associated with coronary artery lesion severity in coronary artery disease. *International Journal of Clinical and Experimental Medicine*. 2016; 9(2): 3705-10.
9. Korkmaz L, Adar A, Erkan H, Aaç MT, Acar Z, Kurt IH, et al. Ankle-brachial index and coronary artery lesion complexity in patients with acute coronary syndromes. *Angiology*. 2012 Oct;63(7):495-9. doi: 10.1177/0003319711429561.
10. Honda T, Fujimoto K, Miyao Y, Koga H, Ishii M. Potassium concentration on admission is an independent risk factor for target lesion revascularization in acute myocardial infarction. *ScientificWorldJournal*. 2014 Jan 12;2014:946803. doi: 10.1155/2014/946803.
11. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention*. 2005 Aug;1(2):219-27.
12. Acet H, Erta_ F, Bilik MZ, Ayd1n M, Yüksel M, Polat N, et al. The relationship of TIMI risk index with SYNTAX and Gensini risk scores in predicting the extent and severity of coronary artery disease in patients with STEMI undergoing primary percutaneous coronary intervention. *Ther Adv Cardiovasc Dis*. 2015 Oct;9(5):257-66. doi: 10.1177/1753944715574814.
13. Zahid MA, Khan HL, Chowdhury AW, Sabah K, Kabir SE, Rahman MH, et al. Demographic Profile of NSTEMI (Non ST Elevation Myocardial Infarction) Patients & Association of ST-Segment Depression and Level of Troponin I with NSTEMI Patient's In-Hospital Outcome. *Medicine Today* 2016;27(2):14-9. Available at: https://doi.org/10.3329/medtoday.v27i2.30038.
14. Walsh CR, Larson MG, Leip EP, Vasan RS, Levy D. Serum potassium and risk of cardiovascular disease: the Framingham heart study. *Arch Intern Med*. 2002 May 13;162(9):1007-12. doi: 10.1001/archinte.162.9.1007.

Original Article

Association of Haemoglobin A1c Level with the Severity of Coronary Artery Disease in Non-diabetic Patients with Non-ST-Segment Elevation Myocardial Infarction

Md. Mamunuzzaman[1], Mahboob Ali[2], Mir Jamal Uddin[3], Shaila Nabi[4], Kajal Kumar Karmoker[5], Muhammed Aminur Razzaque[6], Pinaki Ranjan Das[6], Md. Sazzad Masum[7], Mohammad Bazlur Rashid[6], Syed Mohammad Ali Romel[8]

Abstract:

Background: In nondiabetic patients with non-ST-segment–elevation myocardial infarction, hyperglycemia may be associated with adverse outcome.

Objective: To find out the association between HbA1c levels and the severity of coronary artery disease in non-diabetic patients with non-ST-segment elevation myocardial infarction

Methods: This cross sectional analytical study was carried out at the National Institute of Cardiovascular Diseases (NICVD), Dhaka, during the period from July, 2012 to May, 2013. This study was done with an aim to find out the association between the HbA1c level and the angiographic severity of coronary artery disease in patients with non-ST- elevation myocardial infarction without diabetes mellitus. A total of 170 patients with NSTEMI without diabetes mellitus who agreed to undergo coronary angiography were included in the study. Eighty five patients were selected having HbA1c <5.7% (Group I) and 85 patients were selected having HbA1c ranging from 5.7% to 6.4% (Group II). Severity of the Coronary Artery Disease (CAD) was assessed by angiographic vessel score, and Gensini score.

Results: The mean age of the studied patients was 51.0±9.0 years ranging from 30 to 80 years and male to female ratio was 4.5:1. The incidence of hypertension and level of RBS were significantly higher in group II than group I. The HbA1c level increased in accordance with the vessel score increment. There was a significant difference of the mean value of HbA1c among the vessel involvement groups. In this study mild CAD (scored"36) was significantly higher in group I and moderate to severe CAD (score>36) was significantly higher in group II according to Gensini score. This study showed a positive correlation between HbA1c and vessel score (r=0.47, p=0.01) and also between HbA1c and Gensini score (r=0.41, p=0.01).

Conclusion: Elevated HbA1c levels in non-diabetic non-ST- elevation myocardial infarction patients are associated with the severity of coronary artery disease.

Keywords: *Haemoglobin A1c, non-ST-segment elevation myocardial infarction and non-diabetic*

(Bangladesh Heart Journal 2020; 32(2): 134-139)

1. Assistant Professor, Dept. of Cardiology, Shaheed M. Monsur Ali Medical College, Sirajganj, Bangladesh.
2. Former Professor of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh.
3. Director and Professor of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh.
4. Associate Professor of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh.
5. Associate Professor of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh.
6. Assistant Professor of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh.
7. Junior Consultant, Cardiology, 250 Beded Bangamata Sheikh Fazilatun Nesa Mujib General Hospital, Sirajganj, Bangladesh.
8. Assistant Professor of Cardiology, Kurmitola General Hospital, Dhaka, Bangladesh.

Address of Correspondence: Dr. Md. Mamunuzzaman, Assistant Professor, Dept. of Cardiology, Shaheed M. Monsur Ali Medical College, Sirajganj, Bangladesh.

DOI: https://doi.org/10.3329/bhj.v35i2.52900

Introduction:

At the beginning of the 20th century, cardiovascular disease (CVD) accounted for less than 10.0% of all deaths worldwide[1]. At the beginning of the 21th century, CVD accounts for nearly half of all deaths in the developed world and 25.0% in the developing world.[1]

In 2008, age standardized all cause mortality rate in Bangladesh was 1210 per 100,000 population, among them mortality due to non-communicable disease was 702 per 100,000 population. Mortality rate due to cardiovascular and respiratory disease were 421 and 97 per 100,000 population respectively.[2]

Diabetes is an independent risk factor of developing coronary artery disease. Much published data support the conclusion that diabetes puts people at very high risk of coronary artery disease. Diabetic patients face an 11% increased risk of mortality from ischemic heart disease.[3]

According to American Diabetic Association[4], it is reasonable to consider an individuals with an HbA1c level, ranges from 5.7 to 6.4% having high risk of future diabetes and it may be referred to as pre-diabetes. This pre-diabetic group should be informed of their increased risk for diabetes as well as CAD.[4]

O'Sullivan et al.[5] found that the HbA1c was associated with CVD and mortality. This association has also recently been extended to non-diabetic subjects as the relationship of CVD with glycaemia is believed to be a continuum without a threshold effect.

Selvin et al.[6] stated that classical cardiovascular risk factors such as smoking, hypertension, and hypercholesterolemia do not account for the excess risk of cardiovascular morbidity and mortality in patients with elevated HbA1c levels. In non-diabetic patients whose HbA1c level exceeded 4.6%; an increase in HbA1c of 1.0% point increased the relative risk of coronary artery disease to 2.36%. However, if the HbA1c level was not greater than 4.6%; an increase of HbA1c level was not associated with CAD risk.

In a study by Selvin et al.[7] after 15 years follow-up of more than 11000 participants, suggested that HbA1c values in normal range without diabetes can identify people at higher risk of CAD, stroke and death.

Sherif, et al.[8] found a statistically significant positive correlation between HbA1c levels and Gensini scores. Garg et al.[9] and Ikeda et al.[10] also showed that higher HbA1c levels are significantly associated with coronary artery disease. Elevated HbA1c level is also strongly correlated with disease severity and higher SYNTAX score[10]. The aim of this study was to see the association of HbA1c with the severity of coronary artery disease in non-diabetic patients with non-ST-segment elevation myocardial infarction.

Method:

This cross-sectional study was conducted in the Department of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka from July 2012 to June 2013 over a period of one year. A total of 170 patients with NSTEMI without diabetes mellitus underwent coronary angiography in NICVD were selected as study population. Eighty five patients were selected having HbA1c <5.7% (Group I) and 85 patients were selected having HbA1c ranging from 5.7% to 6.4% (Group II)[4]. Patients with acute ST elevation myocardial infarction, valvular congenital heart disease, prior PCI or CABG were excluded from this study.

Informed written consent was taken from each patient before enrollment. Non- ST-elevation MI was confirmed by ESC guideline 2011. Meticulous history and detailed clinical examination were carried out and recorded in patient's data collection sheet. Demographic data, such as, age, sex, height, weight, waist hip ratio were noted. Troponin I, lipid profile, random blood sugar, and echocardiographic ejection fraction were recorded. 12 lead resting ECG will be done. Two to three milliliters of whole blood in EDTA tube was collected from the patient and transferred to the laboratory in ice box. Samples are kept for one week in refrigerator at 2-8^0 C. Haemoglobin A1c measurement was done by non-porous ion-exchange high performance liquid chromatography (HPLC) performed on Tosoh G7 HPLC Glycohaemoglobin Analyzer. Angiographic severity of CAD was assessed by Vessel score and Gensini score. Interpretation of coronary angiogram was reviewed by at least two cardiologists who were unaware about this study. All the information was noted in the preformed data sheet. Data were presented as frequency with percentage for categorical variables and as mean with standard deviation for quantitative variables. Categorical variables were analyzed by Chi-Square test. Quantitative variables were analyzed by unpaired t-test or ANOVA. Correlation between HbA1c level and angiographic severity was measured by Pearson's and Spearman's correlation test. P value less than 0.05 was considered as statistically significant. Statistical analyses were performed with SPSS, version 12.0 (SPSS Inc).

Results:

In this study, 85 patients of NSTEMI with HbA1c level < 5.7% were considered as group I and 85 patients of NSTEMI with elevated HbA1c level (e" 5.7% - 6.4%) were considered as group II.

Table-I
Demographic profile of the study population (N =170)

Age (year)	Group I n (%)	Group II n (%)	Total n (%)	p value
≤40	13 (15.3)	14 (16.5)	27 (15.9)	
41 – 50	34 (40.0)	26 (30.6)	60 (35.3)	
51 – 60	27 (31.8)	36 (42.4)	63 (37.1)	
> 60	11 (12.9)	9 (10.6)	20 (11.8)	
Mean ± SD	50.8±9.0	51.1±9.0	51.0±9.0	0.810^{ns}
Gender				
Male	68 (80.0%)	71 (83.5%)	139 (81.8)	
Female	17 (20.0%)	14 (16.5%)	31 (18.2)	

The mean age of the studied patients was 51.0±9.0 years ranging from 30 to 80 years and male to female ratio was 4.5:1. No significant difference was found between two groups in terms of age and sex distribution.

Table-II
Comparison of the study patients according to cardiovascular risk factors (N=170)

Risk factors	Group In (%)	Group IIn (%)	p value
Smoking	66 (77.6)	68 (80.0)	0.700
Chewing tobacco	34 (40.0)	37 (43.5)	0.640
Hypertension	43 (50.6)	57 (67.1)	0.062
Dyslipidaemia	48 (56.5)	50 (58.8)	0.750
Family history of CAD	22 (25.9)	24 (28.2)	

Smoking, chewing tobacco, hypertension, dyslipidaemia and family history of the patients were higher in the group II than the group I. But there was no significant difference between two groups except hypertension.

Table-III
Comparison of the study patients according to biochemical parameters (N=170)

Biochemical parameters	Group I Mean ± SD	Group II Mean ± SD	P value
Total Cholesterol (mg/dl)	197.8±35.9	209.2±43.5	0.100
Triglyceride (mg/dl)	145.1±34.7	151.9±37.5	0.080
LDL cholesterol (mg/dl)	116.7±23.0	121.0±26.5	0.110
HDL cholesterol (mg/dl)	40.0±4.8	37.9±5.2	0.070
Creatinine (mg/dl)	1.04±0.20	1.24±0.33	0.090
RBS (mmol/L)	6.2±1.2	7.1±1.4	0.010
Troponin I (ng/ml)	13.0±9.3	14.2±10.2	0.240

All components of lipid profile, serum cratinine and troponin I were found higher in group II than group I but not statistically significant (p>0.05). RBS was found significantly higher in group II than group I (p<0.05).

Table-IV
Comparision of the study patients according to vessel score (N=170)

Vessel score	Group I n (%)	Group II n (%)	P value
Score- 0	17(20.0)	6(7.1)	0.01^{s}
Score- 1	42(49.4%)	22(25.9%)	0.001^{s}
Score- 2	19(22.4%)	28(32.9%)	0.04^{s}
Score- 3	7(8.2%)	29(34.1%)	0.001^{s}

According to vessel score, zero (0)- vessel score and 1- vessel score were significantly higher in group I, whereas 2-vessel score and 3- vessel score were significantly higher in group II.

Table-V

Association between HbA1c and number of vessels involved (N=170)

Vessel score	HbA1c in %		P value
	Mean	SD	
No vessel involvement (n=23)	5.27	0.59	
Single (n=64)	5.47	0.54	0.001[s]
Double (n=47)	5.81	0.47	
Triple (n=36)	6.05	0.57	

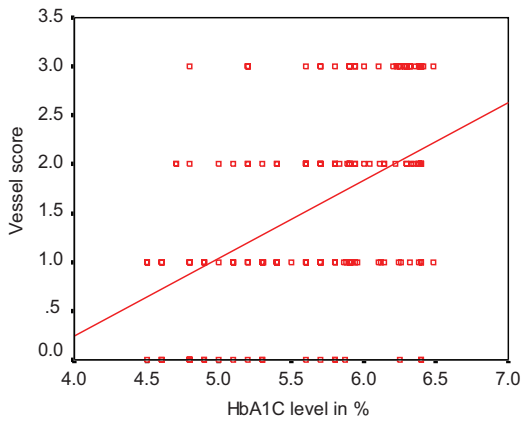
The mean HbA1c level was increased in proportion with the number of vessel involved which reflect the significant association between HbA1c % and vessel score of the study patients (p=0.001).

Table-VI

Distribution of the study patients according to Gensini score (N=170)

Gensini Score	Group I n (%)	Group II n (%)	P value
Mild (CAD d+36)	66 (77.6)	39 (45.9)	0.001
Moderate to severe (CAD >36)	19 (22.4)	45 (54.1)	

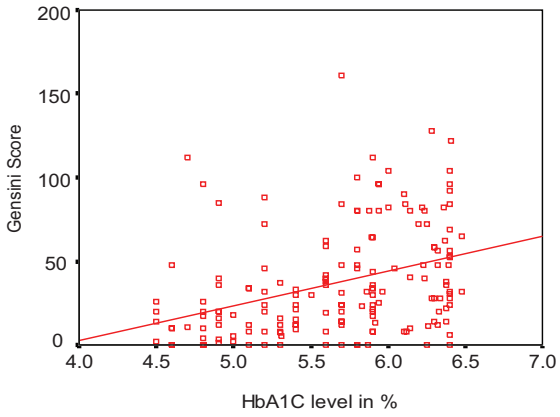
Moderate to severe Gensini score was significantly higher in group II (p=0.001).



Spearman's correlation r (rho)= 0.47 p= 0.01

Fig.-1: *Correlation between HbA1c level (in percentage) and severity of coronary artery disease according to vessel score*

The figure shows that there is a positive correlation between HbA1c and coronary artery disease severity in terms of vessel score (r=0.47; p=0.01).



Pearson's correlation r (rho)=0.41 p=0.01

Fig.-2: *Corellation between HbA1c level (in percentage) and severity of coronary artery disease according to Gensini score*

The figure shows that there is a positive correlation between HbA1c and coronary artery disease severity in terms of Gensini score (r=0.41; p=0.01).

Discussion:

The mean age of the studied patients was 51.0±9.0 years ranging from 30 to 80 years. Hung et al.[11], showed that the mean age of their study population was 51.5 ±13.2 years which was similar to the present study. Sherif, et al.[8] found the mean age of his study subjects was 55.2±7.6 years. Male female ratio was 4.5:1. Male female ratio was found 5.9:1 and 4.95:1 in study done by Khan[12] and Uddin[13] respectively.

The distribution of common risk factors for coronary artery disease in the present study revealed that the most common risk factor was smoking which was present in 66 patients (77.6 %) in group I and 68 patients (80.0 %) in group II but the difference between the two groups was not statistically significant (p=0.70) whereas hypertension was found 43(50.6%) and 57(67.1%) and respectively having statistically significant differnce between two group (p=0.02). Among other risk factors, tobacco use, dyslipidaemia and family history of premature CAD were 40.0%, 56.5% and 25.9% patients in group I and 43.5%, 58.8%, and 28.2% patients in group II respectively with no significant (p>0.05) difference between the study groups. Khan, et al.[12] found that smoking was the highest prevalent risk factor. Rivera, et al.[14], found that individuals with higher HbA1c level were more likely to have a higher prevalence of hypertension and smoking. He found that hypertension was present 47% in patients with HbA1c level 5.5-5.8% and 71% in patients with HbA1c level e”5.9% which was reached a significant difference (p <0.0 So these findings of the present study are similar to the findings of the study done by Rivera, et al[14].

The mean HbA1c level with normal angiographic findings was 5.27±0.59%, with single vessel was 5.47±0.54%, with double vessel was 5.81±0.47% and with triple vessel disease was 6.05±0.57%. So the HbA1c level was increased in proportion with the number of vessel involved by CAD and the differences were statistically significant (p=0.001). Timmer et al.[15] found association of higher HbA1c level with multivessel coronary disease (e”2 vessel involvement). Ravipati et al.[16] found that the mean HbA1c level was 6.66±0.58% in patients with 0-vessel coronary artery disease (CAD), 8.00 ± 0.84% in patients with 1-vessel CAD, 8.83 ±1.45% in patients with 2-vessel CAD, and 10.40±2.28% in patients with 3- 4-vessel CAD. There was significant increasing trend of hemoglobin A1c levels over the increasing number of vessels with CAD (p <0.0001). Results differ as because only diabetic patients were enrolled in their study. Konstantinou et al.[17] also found association of HbA1c with number of vessel involved.

In this study, the mild Gensini score (d”36) was found in 77.6% and in 45.9% patients in group I and group II respectively whereas moderate to severe (>36) was found in 22.4% patients in group I and 54.1% patients in group II respectively. Moderate to severe Gensini score was significantly higher in group II which was statistically significant (p= 0.001).

Ayhan, et al.[18] found significantly higher level of HbA1c in severe CAD than mild CAD in terms of Gensini score (4.7±1.2% vs 6.0±1.4%, p<0.001). This finding is consistent with this study but differ in value as because this study only includes premature CAD patients and no history of CAD. Sherif et al.[8] found that increased HbA1c level was significantly associated with increased Gensini score. Kataoka et al.[19] found that HbAc level of preclinical DM patient was 6.1±0.9% and impaired glucose tolerant patients was 5.5±0.4%. Gensini score was significantly higher (>36) in preclinical group of patient than IGT group. This result also supports present study.

In this study there was a positive correlation between HbA1c and coronary artery disease severity in terms of vessel score and Gensini score (r=0.47 and r=0.41 respectively, p= 0.01 and 0.01). Konstantinou, et al.[16] found in their study that the stenosis score were independently associated with HbA1c level (r=0.58, p<0.001). Ayhan et al.[17] found that HbA1c levels positively correlated with the Gensini score in coronary atherosclerotic patients (r=0.662; p=0.001). In subgroup analyses of CAD patients, HbA1c levels positively correlated with the Gensini score in mild and severe CAD patients also (r=0.347, p=0.002, r=0.337, p<0.001, respectively). Shu-hua, et al.[20] revealed that Gensini score was closely related to HbA1c level (r=0.201, p=0.001). Statistically significant positive correlation (p<0.001) was also found in study done by Sherif, et al.[8].

Conclusion:

The present study concluded that the elevated HbA1c levels in non-diabetic individuals with non-ST- elevation myocardial infarction patients are associated with the severity of coronary artery disease. This simple HbA1c level measurement could be utilized as an independent predictor of coronary artery disease and its severity in non-diabetic subjects. Early screening may help to maintain an optimal HbA1c level, therefore aggressive treatment in early stage glycometabolic disorder may prevent more severe coronary artery disease.

References:

1. Gaziano JM, Ridker PM, and Libby P. Primary and secondary prevention of coronary heart disease. In: Bonow RO, Mann DL, Zipes DP, Libby P,eds.

Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 9th ed. 2011. Philadelphia, Pa: Saunders Elsevier; chap 49.

2. WHO/ Cardiovascular Disease 2011.Factsheet No 317, World Health Organization, August 11, 2011.
3. Saydah S, Tao M, Imperatore G, Gregg E. GHb level and subsequent mortality among adults in the US. Diabetes Care. 2009 Aug 1;32(8):1440-6.
4. American Diabetes Association. Standards of medical care in diabetes—2012. Diabetes care. 2012 Jan 1;35(Supplement 1):S11-63.
5. O'sullivan CJ, Hynes N, Mahendran B, Andrews EJ, Avalos G, Tawfik S, Lowery A, Sultan S. Haemoglobin A1c (HbA1C) in non-diabetic and diabetic vascular patients. Is HbA1c an independent risk factor and predictor of adverse outcome?. European journal of vascular and endovascular surgery. 2006 Aug 1;32(2):188-97.
6. Selvin E, Coresh J, Golden SH, Brancati FL, Folsom AR, Steffes MW. Glycemic control and coronary heart disease risk in persons with and without diabetes: the atherosclerosis risk in communities study. Archives of internal medicine. 2005 Sep 12;165(16):1910-6.
7. Selvin E, Steffes MW, Zhu H, Matsushita K, Wagenknecht L, Pankow J, Coresh J, Brancati FL. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. New England Journal of Medicine. 2010 Mar 4;362(9):800-11.
8. Sherif AE, Khaled M, Ibrahim A, Elhattab MM. Association of glycosylated hemoglobin level and microalbuminuria with the severity of coronary artery disease. Journal of American Science. 2011;7:12.
9. Garg N, Moorthy N, Kapoor A, Tewari S, Kumar S, Sinha A, Shrivastava A, Goel PK. Hemoglobin A1c in nondiabetic patients: an independent predictor of coronary artery disease and its severity. InMayo Clinic Proceedings 2014 Jul 1 (Vol. 89, No. 7, pp. 908-916). Elsevier.
10. Ikeda N, Iijima R, Hara H, Moroi M, Nakamura M, Sugi K. Glycated hemoglobin is associated with the complexity of coronary artery disease, even in non-diabetic adults. Journal of atherosclerosis and thrombosis. 2012;19(12):1066-72.
11. Hung CS, Lee PC, Li HY, Ma WY, Lin MS, Wei JN, Shih SR, Hua CH, Chuang LM, Chen MF. Haemoglobin A1c is associated with carotid intima–media thickness in a Chinese population. Clinical endocrinology. 2011 Dec;75(6):780-5.
12. Khan AR, Islam AE, Au M. Study of risk factors and coronary angiographic pattern in younger patients with acute coronary syndrome. Bangladesh Heart Journal. 2004;19(2):109-19.
13. Uddin SN, Begum F, Malik F, Rahman S. Coronary artery disease in young patients: clinical review and risk factor analysis. Mymensingh medical journal: MMJ. 2003 Jan;12(1):3-7.
14. Rivera JJ , Eue-Keun Choi, E, Yoon YE, Chun E , Sang-il Choi S , Khurram Nasir K , Frederick L. Brancati FL, Roger S Blumenthal RS, and Chang H . Association between increasing levels of hemoglobin A1c and coronary atherosclerosis in asymptomatic individuals without diabetes mellitus. *Coronary Artery Disease*, 2010 May;21 (3):157-163.
15. Timmer JR, Hoekstra M, Nijsten MW, et al. Prognostic value of admission glycosylated hemoglobin and glucose in nondiabetic patients with ST-segment-elevation myocardial infarction treated with percutaneous coronary intervention. Circulation. 2011;124:704–11.
16. Ravipati G, Aronow WS, Ahn C, Sujata K, Saulle LN, Weiss MB. Association of hemoglobin A1c level with the severity of coronary artery disease in patients with diabetes mellitus. The American journal of cardiology. 2006 Apr 1;97(7):968-9.
17. Konstantinou DM, Chatzizisis YS, Louridas GE, Parcharidis GE, Giannoglou GD. Non-diabetic hyperglycaemia correlates with angiographic coronary artery disease prevalence and severity. Diabetes & metabolism. 2010 Nov 1;36(5):402-8.
18. Ayhan SS, Tosun M, Ozturk S, Alcelik A, Ozlu MF, Erdem A, Erdem K, Erdem FH, Yazici M. Glycated haemoglobin is correlated with the severity of coronary artery disease independently of traditional risk factors in young patients. Endokrynologia Polska. 2012;63(5):367-71.
19. Kataoka Y, Yasuda S, Morii I, Otsuka Y, Kawamura A, Miyazaki S. Quantitative coronary angiographic studies of patients with angina pectoris and impaired glucose tolerance. Diabetes care. 2005 Sep 1;28(9):2217-22.
20. Shu-hua, MI, Gong SU, Zhao LI, Yang HX, Zheng H, Hong TA, Yun ZH, Lei TI. Comparison of glycemic variability and glycated hemoglobin as risk factors of coronary artery disease in patients with undiagnosed diabetes. Chinese medical journal. 2012 Jan 1;125(1):38-43.

Original Article

Short and Long Term Outcome In Patients with Calcified Lesions Requiring Rotational Artherectomy

Lima Asrin Sayami[1], Al-Fazir Omar[2], Sheikh Ziarat Islam[3], Subasni Govindan[4], Zulaikha Zainal[5], Rosli Mohd Ali[6]

Abstract:

Objective: Despite the evolution of interventional techniques and operator experience, percutaneous revascularization of complex coronary lesions especially calcified lesions remains challenging because of lower procedural success and higher restenosis rates. Limited data are available on the effect of rotational atherectomy (RA) plus stenting in the treatment of complex calcified lesions of coronary artery disease. This study was aimed to investigate the characteristics, short and long term outcomes in patients undergoing RA.

Material and Methods:A database search was performed from the year 2008 to 2013 in National Heart institute, Malaysia. A total of 16009 patients who underwent PCIs were enrolled in 2 groups, RA group (258 patients) and non RA group (15751 patients). The Chi square test and Kaplan - Meier analysis were used.

Results:Male patients (73.6%) and elderly population (63.2%) were predominant in this study.The RA group had more co-morbidities such as diabetic on insulin (34%) and chronic kidney disease (57%). The lesions in RA group were more complex with higher Type C lesion (68.8%) and longer lesion (20.6%) compared to non RA group. Despite higher patient risk profile, the success rate of revascularization remains high in RA group (99.3%) as in non RA group (97%) (p value 0.89%).

More importantly there were no significant difference in in-hospital mortality, myocardial infarction and stent thrombosis in both group (p value 0.1). In 1 year Kaplan - Meier survival graph, there were better survival noted in non RA group (97.7%) compare to RA (89.6%) (p value <0.005),

Conclusion: The use of RA allows debulking of a calcified lesion and possibly explains the higher acute procedural success rates. However, the lower 1-yearsurvival in the RA group highlights the higher associated baseline co-morbitidity in this group. Therefore, besides coronary intervention, this RA group requires aggressive medical therapy through a multi-disciplinary approach.

Keywords:

(Bangladesh Heart Journal 2020; 32(2): 140-146)

Introduction:

Percutaneous coronary intervention is currently the most frequent form of revascularization for obstructive coronary artery disease. One challenge to successful revascularization is the calcified obstructed coronary

1. Assistant Professor, Cardiology Department, National Institute of Cardiovascular Disease, Dhaka, Bangladesh, Dhaka, Bangladesh.
2. Consultant, Institut Jantung Negara, National Heart Institute, Kuala Lumpur, Malaysia
3. Associate Professor, Cardiology Department, National Institute of Cardiovascular Disease, Dhaka, Bangladesh, Dhaka, Bangladesh.
4. Cath labTechnician, Institut Jantung Negara, National Heart Institute, Kuala Lumpur, Malaysia
5. Data Analyst, Institut Jantung Negara, National Heart Institute, Kuala Lumpur, Malaysia
6. Consultant, CVSKL, Kuala Lumpur, Malaysia

Address of Correspondence: Dr Lima Asrin Sayami, Assistant Professor, Department of Cardiology, NICVD, Dhaka, Bangladesh. Mobile: +8801818179708. E-mail: sayamllima@gmail.com

DOI: https://doi.org/10.3329/bhj.v35i2.52901

vessel. Prevalence of calcified coronary lesion is high in elderly, diabetic and renal patients. Rotational atherectomy (RA) can be useful in the treatment of these lesions.

First used in 1989, rotational atherectomy is based on the differential removal of plaque by a rotating diamond covered burr (1). Since introduction of RA, data have not shown long-term benefit and target lesion revascularization rates remained unacceptably high, ranging from 15–36% at 6–9 months(2-9). However, it has found a niche in improving procedural success rates in complex, heavily calcified lesions in which balloon angioplasty and stenting alone often result in failure or suboptimal stent expansion(10-15). Once, RA was involved in up to 10% of percutaneous coronary interventions (PCI) (16). Currently, RA use has fallen to 3% to 5% in select high-volume centers and <1% in others (17) because it is technically demanding procedure reliant on operator experience.

Since the advent of drug-eluting stent (DES) technology, there has been a resurgence in rotational atherectomy(8-9). DES are associated with improved outcomes after RA. In patients treated with RA, rates of MACE are lower with DES compared with BMS in 3 recent series(8,18-19). Therefore, we sought to analyze patient characteristics, long and short clinical outcomes of patients who underwent RA between January 1, 2008 and December 31, 2013 in National Heart Institute, Malaysia .

Methods:

This was a retrospective analysis at National Heart Institute, Malaysia . The cardiac catheterization database was searched to identify all cases involving RA between the year 2008 to 2013. A total of 16009 patients who underwent PCIs were enrolled in 2 groups. RA group consist of 258 patients while in non RA group there were 15751 patients. The use of RA and all other clinical decisions were at the discretion of the interventionalist. DES were routinely implanted during coronary interventions. Patient demographics, medical history, procedural characteristics, short and long term outcomes were recorded through a comprehensive chart review. Procedural and lesion characteristics were further defined using quantitative coronary angiography.

All patients had objective evidence of myocardial ischemia and > 70% angiographic diameter stenosis by visual estimate. Informed written consent was obtained from each patient. Rotational atherectomy was performed using the standard femoral/radial approach and usually use of a single burr with burr-to-artery ratio of 0.7 to 0.8. But a step-up burr technique, generally beginning with 1.25 mm or 1.5 mm burrs also used if required. The rotational burr was slowly advanced with a high-speed rotation (> 160,000 rpm). Adjunctive balloon angioplasty was performed using balloons sized with balloon-to-artery ratios of 1.1:1. Stents were deployed by inflating the stent delivery balloon with a nominal pressure and, if necessary, adjunctive high-pressure balloon dilatation was performed to achieve angiographic optimization (residual diameter stenosis < 10% by visual estimate). During the procedure, patients received 100units/kg bolus heparin with repeated boluses to maintain the activated clotting time > 250 seconds.

Lesions were classified according to American College of Cardiology/American Heart Association criteria(20). Lesion length was measured as the distance from the proximal to the distal shoulder of the lesion in the least foreshortened projection. Complex lesions were defined as type B2 and type C lesions according to American Heart Association/American College of Cardiology classification(20). Long lesions were defined as e" 20 mm. A lesion was defined as bifurcating if a branch > 1.5 mm with ostial disease originated within the stenosis and the branch was completely surrounded by stenotic portions of the parent vesse(21). A lesion that originated within 3 mm of the vessel origin was defined as ostial (21). Lesion calcification was defined prior to contrast injection as: severe if radiopacities were readily apparent without cardiac motion; moderate if radiopacities were apparent only with cardiac motion; mild if faint radiopacities were seen only with cardiac motion; and none if no radiopacities were seen (21).

Clinical outcomes were determined during the index hospitalization, at six month and twelve month follow up. Complications were defined as death, periprocedural MI(new creatine kinase elevation above two times the upper limit of normal), stent thrombosis, perforation, worsening of renal function. Angiographic success was defined as < 20% residual stenosis and thrombolysis in myocardial infarction (TIMI) grade 3 flow at the conclusion of the procedure. Procedural success was defined as angiographic success in the absence of MACE. All patients were requested to visit the outpatient clinics at regular intervals (at 6month and one year after intervention). Follow-up information was obtained by hospital chart. One year survival was plotted in Kaplan – Meier graph.

Results are reported as median or percentages of the total. For statistical comparison, cases were devided into

two groups based on whether or not undergone RA. Chi square test and Kaplan –Meier analysis were used. Statistical significance was considered a p-value < 0.05.

Results:

A total of 258 cases involving RA were identified between January 1, 2008 and December 31, 2013. RA was indicated for plaque modification in the setting of moderate to severe calcification in 1.6% of population. In 248 patients single vessel was rotablated while 16 patients required double vessel rotablation. There were no significant differences in the baseline clinical characteristics between the two groups (Table 1). Majority of the patients were male patients (73.6%) and elderly population (63.2%).

Although the patients in RA group had more comorbidities such as diabetic on insulin (34%) and chronic kidney disease(57%) in comparison to non RA group, the difference was not statistically significant (figure1).

Table-I

Baseline Characterstics

	RA Group		Non RA group		p-value	TOTAL
	TOTAL	%	TOTAL	%		
No of cases	258	1.6	15751	98.4		16009
Gender, N (%)						
Male	190	73.6%	12987	82.50%	0.473	
Female	68	26.4%	2764	17.50%	0.228	
Age, Median (IQR1,IQR3)	65.6 (58.1,71)	57.8 (51.1,64.9)				
Age range, N (%)						
Below than 40 yr	3	1.1%	640	4.1%	0.18	
40 – 50 yr	15	5.8%	2770	17.6%	0.014	
50 – 60 yr	59	22.9%	5691	36.1%	0.091	
60 – 70 yr	103	40.0%	4658	29.6%	0.232	
More than 70 yr	78	30.2%	1992	12.6%	0.01	
BMI, Median (IQR1,IQR3)	25.5 (23.3,28.8)	26.5 (24,29.4)				
BMI range, N (%)						
Below than 18.5	8	3.1%	192	1.2%	0.317	
18.5 – 24.9	93	36.0%	4743	30.1%	0.46	
25 -29.9	88	34.1%	6063	38.5%	0.558	
More than 30	43	16.7%	3037	19.3%	0.739	
Not available	26	10.1%	1716	10.9%	0.827	

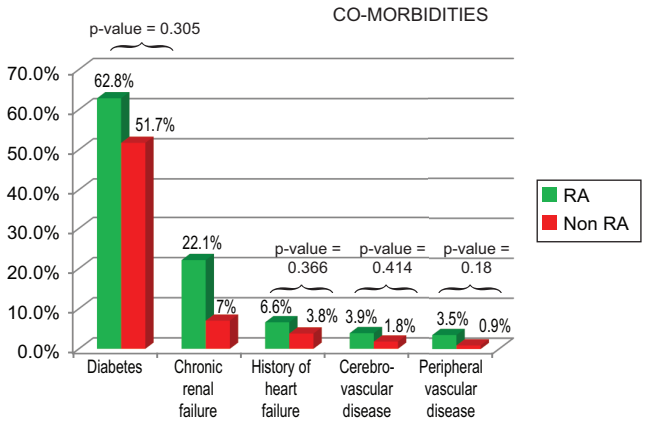


Fig.-1: *Patient's comorbidities*

Table-II

Lesion Characterstics

	RA Group		Non RA group		p-value	TOTAL
	Total	%	Total	%		
No of lesions treated	292	1.3	22400	98.7	22692	
Coronary lesion, N (%)						
De Novo	280	95.9	20989	93.7	0.885	
In Stent Restenosis	10	3.4	1273	5.7	0.317	
Stent thrombosis	1	0.3	72	0.3	NIL	
Lesion types, N (%)						
TypeA	4	1.4	1863	8.3	0.02	
Type B1	25	8.6	5553	24.8	0.006	
Type B2	62	21.2	5773	25.8	0.466	
Type C	201	68.8	8894	39.7	0.005	
Not available			317	1.4	NIL	
Lesion description, N (%)						
Bifurcation	45	15.4	2391	10.7	0.433	
Total occlusion	9	3.1	1243	5.5	0.317	
CTO (>3 months)	27	9.2	1814	8.1	0.808	
Estimated lesion length, mm						
Mean (SD)	35.8 (20.6)	24.6 (14.6)	NIL			
Median (IQR1,IQR3)	30.2 (19.2,48.3)	20 (14.6,30.3)				
Cutting/scoring balloon, N (%)	11	3.8	463	2.1	0.414	
IVUS, N (%)	35	12	1196	5.3	0.09	

The baseline angiographic characteristics are shown in Table 2. Lesion length and morphology is defined by American Heart Association/American College of Cardiology classification. The lesions in RA group were more complex with higher Type C lesion (68.8% versus 37.9, p value 0.005) and longer lesion (20.6%vursus 14%) compared to non RA group. Utilization of intravascular ultrasound to clarify the lesion morphology and result outcome was low (17.3%).

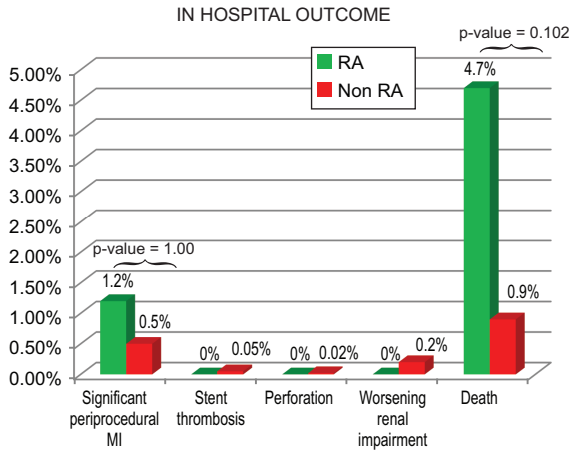


Fig.-2: *Periprocedural in hospital outcome.*

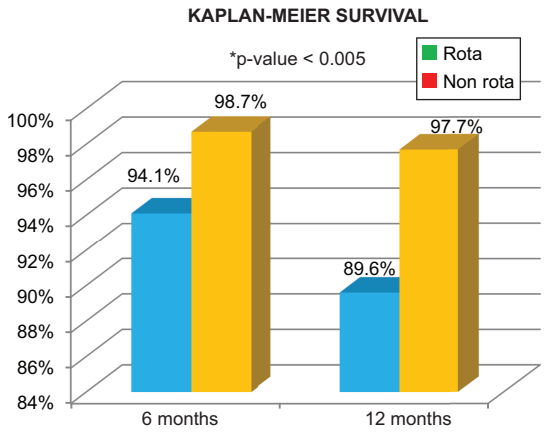


Fig.-3: *Kaplan-Meier survival*

Despite higher patient risk profile, the success rate of revascularization remains high in RA group (99.3%) as in non RA group (97%) (p value 0.89%). More importantly there were no significant difference in inhospital mortality, myocardial infarction and stent thrombosis in both group(p value 0.1).

Angiographic success was not achieved in 2 patients(0.7%) of RA group and 681patients(3%) in non RA group. Death occurred 4.7% patients in RA group in comparison to 0.9% in non RA group (0.102). In 1 year Kaplan –Meier survival graph, there were better survival noted in non RA group(97.7%) compare to RA (89.6%)(pvalue <0.005)(Figure3).

Discussion:

The commercially available Rotablator (Boston Scientific,Natick, Massachusetts), invented by Auth and described by Ritchie and colleagues (22) utilizes an over-the-wire, coaxially driven, diamond-tipped, high-speed speeds (140,000 to 180,000 rpm) rotating elliptical burr to pulverize the atherosclerotic plaque. It produces lumen enlargement by physical removal of plaque and reduction in plaque rigidity, facilitating dilation. The burr preferentially ablates hard, inelastic material, such as calcified plaque, that is less able to stretch away from the advancing burr than is healthy arterial wall (differential cutting). High rotational speeds facilitate longitudinal burr movement across calcific lesions by orthogonal displacement of friction. A guidewire helps to keep the burr's abrasive tip coaxial with the vessel lumen, although wire bias in highly tortuousor angulated segments may predispose to dissection or perforation(2). Unlike balloon angioplasty, which tends to produce intimal splits and medial dissections in calcified lesions, RA yields a relatively smooth luminal surface with cylindrical geometry and minimal tissue injury(2) .The cardinal indication for RA is the calcific lesion, which, in the absence of plaque modification, confers an increased likelihood of procedural failure, stent underdeployment, restenosis, and major complications (23).

This study was sought to describe the short and long term outcome of RA. RA was used primarily in 292 complex lesions (1.3%) with moderate to severe calcification where the operators felt balloon angioplasty and stenting alone would not be sufficient. At one time, RA was involved in up to 10% of percutaneous coronary interventions (PCI)(16)but in the recent series, RA use has fallen to 3% to 5% in select high-volume centers and <1% in others (17).

Lesion characterstics analysis revealed that RA group had higher Type C lesion (68.8% versus 37.9, p value 0.005) and longer lesion (20.6% versus 14%) compared to non RA group. Among these lesions 9.2% were CTO in RA group.

The major findings of this study is despite higher patient risk profile, rotational atherectomy, followed by stenting, is associated with favorable short-term outcomes. Angiographic and procedural success rate remains high in RA group (99.3%) as in non RA group (97%) (p value 0.89%) and complications in terms of inhospital mortality, myocardial infarction and stent thrombosis was similar in both group(p value 0.1). Retrospective series of RA describe high rates of short-term procedural success (range 93.4% to 98.6%), superior to rates reported separately in the absence of preceding plaque modification (6,7,15). The literature describes the use of RA in heavily calcified lesions improve stent expansion(3-6,13) and enable DES deployment in nondilatable, calcified lesions(26,27). Other studies showed RA facilitates procedural success in PCI of complex(American College of Cardiology/American Heart Association types B2 and C) lesions (28,29), including chronic total occlusions (30,31), ostial lesions (32-34), and bifurcation lesions, which may be associated with both bulky plaque and vessel geometry unfavorable for stent deployment.

Several nonrandomized trials have reported that rotational atherectomy shows no obvious difference in the acute success rate or restenosis rate in noncomplex coronary lesions compared with other techniques(35,36). Two previous studies by Kishi and Teirstein reported a disappointing restenosis rate of 57.5and 59.0% after rotational atherectomy in patients with diffuse coronary artery disease, which suggested that debulking of excess tissue with rotational atherectomy was not effective therapy for diffuse coronary artery disease(37,38). In other studies, heavily calcified lesions, RA and DES deployment results in target lesion revascularization rates ranging from 2–10.6% at 6 months to 3 years, which is significantly better than RA and BMS(8-9,24-26). Furthermore, several techniques using rotational atherectomy, such as use of a single burr with burr-to-artery ratio of 0.5 to 0.6-rotational speed of 140,000 to 150,000 rpm, gradual burr advancement using a pecking motion, short ablation runs of 15 to 20 s, and avoidance of decelerations >5,000 rpm. Combined with meticulous technique, optimal antiplatelet therapy, vasodilators, flush solution, and provisional use of atropine, temporary pacing, vasopressors, and mechanical support may prevent slow-flow/no-reflow, which in contemporary series is reported in 0.0%to 2.6% of cases(2).

Beyond immediate procedural success, however, data have not shown a consistent long-term benefit of lesion modification by RA for restenosis and major adverse cardiovascular events (MACE)(2). In this study in 1 year Kaplan –Meier survival graph, better survival was noted in non RA group(97.7%) compare to RA (89.6%)(p value <0.005). Long-term benefit was again absent in the recent ROTAXUS (Rotational Atherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) study, the first randomized trial to directly test the impact of RA on long-term outcomes of DES placement (39). In a series of 240 patients with moderately or severely calcified obstructive lesions treated with or without RA before paclitaxel-eluting stent implantation, there was greater strategy success and short-term lumen gain with RA. However, routine angiographic follow-up at 9 months showed no difference in MACE and greater late lumen loss (40) with an RA strategy.

Conclusion:

The cardinal indication for RA is the calcific lesion, which, in the absence of plaque modification, confers an increased likelihood of procedural failure, stent underdeployment, restenosis, and major complications.

The present study indicates that calcified coronary artery lesions can be successfully treated by high speed rotational atherectomy and the success rate of rotational atherectomy was not reduced by calcification despite the more frequent complex nature of the calcified lesions. Though higher mortality and lower rate of survival were noted in rotational atherectomy group in this study, it should be attributed to the fact that they come from high risk group of patients who have multiple comorbidities.

References:

1. Mota P, Belderb A, Leitão-Marquesa A. Rotational atherectomy: Technical update.Rev Port Cardiol. 2015;34(4):271—278
2. Matthew I. Tomey, Annapoorna S. Kini, Samin K. Sharma. Current Status of Rotational Atherectomy. J Am Coll Cardiol Intv 2014;7:345–53.
3. Whitbourn RJ, Sethi R, Pomerantsev EV, Fitzgerald PJ. High-speed rotational atherectomy and coronary stenting: QCA and QCU analysis. Catheter Cardiovasc Interv 2003;60:167–171.
4. Henneke KH, Regar E, Konig A, et al. Impact of target lesion calcification on coronary stent expansion after rotational atherectomy. Am Heart J 1999;137:93–99.
5. Hoffmann R, Mintz GS, Popma JJ, et al. Treatment of calcified coronary lesions with Palmaz-Schatz stents. An intravascular ultrasound study. Eur Heart J 1998;19:1224–1231.
6. Hoffmann R, Mintz GS, Kent KM, et al. Comparative early and nine-month results of rotational atherectomy, stents, and the combination of both for calcified lesions in large coronary arteries. Am J Cardiol 1998;81:552–557.
7. Moussa I, Di Mario C, Moses J, et al. Coronary stenting after rotational atherectomy in calcified and complex lesions. Angiographic and clinical follow-up results. Circulation 1997;96:128–136.
8. Rathore S, Matsuo H, Terashima M, et al. Rotational atherectomy for fibro-calcific coronary artery disease in drug eluting stent era: Procedural outcomes and angiographic follow-up results. Catheter Cardiovasc Interv 2010;75:919–927.
9. Khattab AA, Otto A, Hochadel M, et al. Drug-eluting stents versus bare metal stents following rotational atherectomy for heavily calcified coronary lesions: Late angiographic and clinical follow-up results. J Interv Cardiol 2007;20:100–106
10. Mauri L, Reisman M, Buchbinder M, et al. Comparison of rotational atherectomy with conventional balloon angioplasty in the prevention of restenosis of small coronary arteries: Results of the Dilatation vs Ablation Revascularization Trial Targeting Restenosis (DART). Am Heart J 2003;145:847–854.
11. Vom Dahl J, Dietz U, Haager PK, et al. Rotational atherectomy does not reduce recurrent in-stent restenosis: Results of the angioplasty versus rotational atherectomy for treatment of diffuse in-stent restenosis trial (ARTIST). Circulation 2002;105:583–588.
12. Warth DC, Leon MB, O'Neill W, et al. Rotational atherectomy multicenter registry: Acute results, complications and 6-month angiographic follow-up in 709 patients. J Am Coll Cardiol 1994;24: 641–648.
13. Tran T, Brown M, Lasala J. An evidence-based approach to the use of rotational and directional coronary atherectomy in the era of drug-eluting stents: When does it make sense? Catheter Cardiovasc Interv 2008;72:650–662.
14. Santos R, Pereira H, et al. Facts on rotational atherectomy fo coronary artery disease: multicentric registry MacIsaac AI, Bass TA, Buchbinder M, et al. High speed rotational atherectomy: Outcome in calcified and noncalcified coronary artery lesions. J Am Coll Cardiol 1995;26:731–736.
15. Kiesz RS, Rozek MM, Ebersole DG, et al. Novel approach to rotational atherectomy results in low restenosis rates in long, calcified lesions: Long-term results of the San Antonio Rotablator Study (SARS). Catheter Cardiovasc Interv 1999;48:48–53.
16. Lasala JM, Reisman M. Rotablator plus stent therapy (rotastent). Curr Opin Cardiol 1998;13: 240–7.
17. Mota P, Santos R, Pereira H, et al. Facts on rotational atherectomy for coronary artery disease: multicentric registry (abstr). Paper presented at:EuroPCR; May 21, 2013; Paris, France.
18. Mangiacapra F, Heyndrickx GR, Puymirat E, et al. Comparison of drugeluting versus bare-metal stents after rotational atherectomy for the treatment of calcified coronary lesions. Int J Cardiol 2012;154:373–6.

19. Tamekiyo H, Hayashi Y, Toyofuku M, et al. Clinical outcomes of sirolimus-eluting stenting after rotational atherectomy. Circ J 2009;73:2042–9.

20. Ryan TJ, Faxon DP, Gunnar RP, and the ACC/AHA Task Force Guidelines for percutaneous transluminal coronary angioplasty. J Am Coll Cardiol 1988;12:529–545.

21. Kini AS. Coronary angiography, lesion classification and severity assessment. Cardiol Clin 2006;24:153–162.

22. Hansen DD, Auth DC, Vracko R, Ritchie JL. Rotational atherectomy in atherosclerotic rabbit iliac arteries. Am Heart J 1988;115:160–5.

23. Bangalore S, Vlachos HA, Selzer F, et al. Percutaneous coronary intervention of moderate to severe calcified coronary lesions: insights from the National Heart, Lung, and Blood Institute Dynamic Registry. Catheter Cardiovasc Interv 2011;77:22–8.

24. Vaquerizo B, Serra A, Miranda F, et al. Aggressive plaque modification with rotational atherectomy and/or cutting balloon before drug-eluting stent implantation for the treatment of calcified coronary lesions. J Interv Cardiol 2010;23:240–248.

25. Mezilis N, Dardas P, Ninios V, Tsikaderis D. Rotablation in the drug eluting era: Immediate and long-term results from a single center experience. J Interv Cardiol 2010;23:249–253.

26. Clavijo LC, Steinberg DH, Torguson R, et al. Sirolimus-eluting stents and calcified coronary lesions: Clinical outcomes of patients treated with and without rotational atherectomy. Catheter Cardiovasc Interv 2006;68:873–878.

27. Schluter M, Cosgrave J, Tubler T, et al. Rotational atherectomy to enable sirolimus-eluting stent implantation in calcified, nondilatable de novo coronary artery lesions. Vascular Disease Management 2007;4:63–69.

28. Levin TN, Holloway S, Feldman T. Acute and late clinical outcome after rotational atherectomy for complex coronary disease. Cathet Cardiovasc Diagn 1998;45:122–30.

29. Reifart N, Vandormael M, Krajcar M, et al. Randomized comparison of angioplasty of complex coronary lesions at a single center. Excimer Laser, Rotational Atherectomy, and Balloon Angioplasty Comparison (ERBAC) study. Circulation 1997;96:91–8.

30. Gruberg L, Mehran R, Dangas G, et al. Effect of plaque debulking and stenting on short- and long-term outcomes after revascularization of chronic total occlusions. J Am Coll Cardiol 2000;35:151–6.

31. Pagnotta P, Briguori C, Mango R, et al. Rotational atherectomy in resistant chronic total occlusions. Catheter Cardiovasc Interv 2010;76: 366–71.

32. Tan RP, Kini A, Shalouh E, Marmur JD, Sharma SK. Optimal treatment of nonaorto ostial coronary lesions in large vessels: acute and long-term results. Catheter Cardiovasc Interv 2001;54:283–8.

33. Koller PT, Freed M, Grines CL, O'Neill WW. Success, complications, and restenosis following rotational and transluminal extraction atherectomy of ostial stenoses. Cathet Cardiovasc Diagn 1994;31: 255–60.

34. Zimarino M, Corcos T, Favereau X, et al. Rotational coronary atherectomy with adjunctive balloon angioplasty for the treatment of ostial lesions. Cathet Cardiovasc Diagn 1994;33:22–7.

35. Fourrier JL, Bertrand ME, Auth DC, et al. Percutaneous coronary rotational angioplasty in humans: Preliminary report. J Am Coll Cardiol 1989;14:1278–1282.

36. Bertrand ME, Lablanche JM, Leroy F, et al. Percutaneous transluminal coronary rotational ablation with Rotablator (European experience). Am J Cardiol 1992;69:470–474.

37. Kishi K, Hiasa Y, Ogata T, et al. Comparison of results of rotational atherectomy for diffuse coronary artery disease in diabetics versus nondiabetics. Am J Cardiol 2001;87:894–896.

38. Teirstein PS, Warth DC, Haq N, et al. High speed rotational atherectomy for patients with diffuse coronary artery disease. J Am Coll Cardiol 1991;18:1694–1701.

39. Abdel-Wahab M, Richardt G, Joachim Buttner H, et al. High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (RotationalAtherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) trial. J Am Coll Cardiol Intv 2013;6:10–9.

40. Mauri L, Orav EJ, Kuntz RE. Late loss in lumen diameter and binary restenosis for drug-eluting stent comparison.Circulation 2005;111:3435–42.

Review Article

Anticipating the Challenging and Unpredictable Long Term Cardiovascular Effects of COVID-19: A Review

Mohammad Arifur Rahman[1], Afzalur Rahman[2], Mohsin Ahmed[3], AKM Monwarul Islam[3], Md. Mesbahul Islam[4], Muhammad Salim Mahmod[5], Tanveer Ahmad[6]

Introduction:

SARS-CoV2 infection can impact all organs structurally and functionally. Persisting symptoms in patients recovering from coronavirus disease 2019 (COVID-19) are common and with close follow-up can be detected in nearly 90% of patients 60 days from the original diagnosis[1]. The most common symptoms are fatigue, dyspnea, joint pain, chest pain, cough, insomnia and headache. Given the well-documented involvement of the circulatory system in COVID-19, including small, moderate and large-sized veins and arteries, coupled with robust immune and resulting local and systemic inflammatory responses, one would anticipate a prolonged recovery period and potentially long-term cardiovascular effects. The following review summarizes the pathogenesis of structural, functional and metabolic abnormalities associated with COVID-19 and postulates long-term cardiovascular effects and management strategies under a broad clinical umbrella referred to as post-COVID-19 syndrome.

Acute stages of COVID-19: setting the stage for prolonged clinical effects

The frequency of cardiac injury, vascular dysfunction and thrombosis in patients with COVID-19, including those persons with either no or minimal symptoms during their initial infection, raises important questions about potential long-term cardiovascular effects: these could include heart failure, life-threatening arrhythmias, sudden cardiac death, impaired myocardial flow reserve from microvascular injury, coronary artery and aorta aneurysm formation, hypertension, labile heart rate and blood pressure responses to activity, accelerated atherosclerosis and both venous and arterial thromboembolic disease[2]. Indeed, events during the acute phase of disease, including those that are clinically unsuspected and undiagnosed[3] will increase the risk for recurring events[4]. How will the medical community follow patients with COVID-19? How will future events be prevented?

The COVID-19 pandemic and its reporting has focused primarily on two areas—the number of cases and the number of deaths. Both statistics are of great importance, yet neither sufficiently captures an equally important metric of morbidity that is responsible for resource utilization, assessment of vulnerable populations, cost, recovery, long-term health effects, and quality of life[5]. A morbidity index of COVID-19 survivors is particularly relevant when

(Bangladesh Heart Journal 2020; 32(2): 147-154)

1. Junior Consultant, Department of Cardiology, Government Employees Hospital, Dhaka, Bangladesh
2. Senior Consultant, United Hospital Ltd, Department of Cardiology, Dhaka, Bangladesh
3. Associate professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh
4. Assistant Professor, Department of Cardiology, Anwar Khan Modern Medical College Hospital, Dhaka, Bangladesh
5. Assistant Professor, Department of cardiology, Dr. Sirajul Islam Medical College Hospital, Dhaka, Bangladesh
6. Specialist, Department of cardiology, United Hospital Ltd, Dhaka, Bangladesh

Address of Correspondence: Dr. Mohammad Arifur Rahman, Junior Consultant, Department of Cardiology, Government Employees Hospital, Dhaka, Bangladesh

DOI: https://doi.org/10.3329/bhj.v35i2.52902

considering co-morbid factors and traits for SARS-CoV-2 infection susceptibility, need for hospitalization, level of care and their collective impact on the severity of illness.

Acute cardiac injury:

Myocardial Infarction stemming from supply–demand mismatch (Type 2) is common in clinical practice and considered to be ischemic in etiology[6]. Patients with COVD-19 can experience hypoxia, hypotension and distributive shock with resulting myocardial injury diagnosed by serial cardiac troponin assays with quantitative values > 99th percentile of the upper reference limit determined in a normal reference population . In addition, COVID-19-associated coagulopathy and hyperinflammation syndrome can cause micro and macro-myocardial injury of non-ischemic etiology[7].

Type 2 myocardial infarction is associated with one-year mortality rates of 10–25% owing to co-morbid conditions and underlying atherosclerotic cardiovascular disease. Similar mortality rates have been reported following non-ischemic myocardial injury. In COVID-19, small vessel inflammation, injury and dysfunction contribute to myocyte damage, as does pericyte injury and impaired myocardial perfusion[7].

Early reports of COVID-19 identified a high proportion of hospitalized patients with reduced left ventricular ejection fraction. Indeed, in one series 35% of patients had an ejection fraction less than 50% and features of stress-induced cardiomyopathy were identified in a number of patients[8]. Patients with COVID-19-associated myocardial injury likely remain at risk for cardiovascular events following hospital discharge. The duration of risk, optimal surveillance and management strategies are under investigation and must be clearly defined.

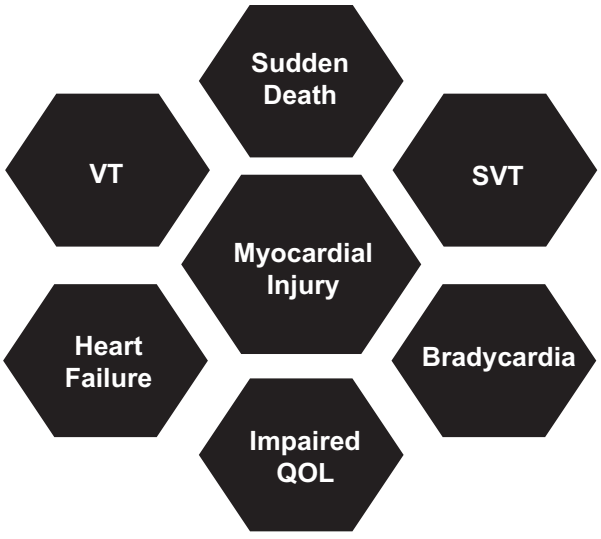


Fig.1: *COVID-19 is associated with ischemic and non-ischemic myocardial injury.*

Viral myocarditis:

Myocarditis occurs in a wide range of acute viral infections, including adenovirus, Human Immunodeficiency Virus (HIV), Epstein-Barr Virus, and Influenza virus to name a few. Observational data, coupled with virologic and molecular diagnostic studies suggest that enteroviruses, including coxsackievirus, parvovirus and adenovirus are among the most common causes of myocarditis.

Animal models of enterovirus-induced myocarditis demonstrate RNA detection in the acute phase and chronic phase of dilated cardiomyopathy. In a murine model of coxsackievirus ²3-myocarditis, features of acute infection including rapid progression of myocardial lesions, infected myocytes and inflammatory cells is followed by a persistent pattern with reduced inflammation and a slow progression of myocardial lesions. Infection is often restricted to atrophic myocytes and fibroblasts[9].

While the virus itself is cytoxic causing myocyte injury, a majority of cases of severe myocarditis and subsequent post-viral cardiomyopathy are governed by a maladaptive or overly robust inflammatory response to viral antigens[10]. Many viruses associated with myocarditis infect the heart secondarily following an initial infection in the lungs or gastrointestinal tract. By contrast, some viruses are highly cardiotropic. For example, parvovirus ²19 can infect the endothelial cells of venules, capillaries and arterioles[11]. Cytokine activation follows, causing apoptosis of endothelial cells, endothelial dysfunction and marked lymphocyte accumulation within the microvasculature. Myocyte injury is the result of perfusion abnormalities rather than direct myocyte viral entry and damage. Myocarditis following a viral infection is viewed under the pathophysiology-based lens of autoinflammatory disease[12].

SARS-CoV-2-associated myocarditis:

Given the duration of viral shedding in SARS-CoV-2 infection and COVID-19, as well as the relatively high density of ACE2 receptors expressed in cardiomyocytes, one might anticipate cases of myocarditis and myopericarditis. Lindner and colleagues performed autopsies on 39 decedents (median age 85 years) with COVID-19. Cardiac tissue contained SARS-CoV-2 in 24 decedents (61.5%). Viral loads above 1000 copies per µq RNA were documented in 16 cases (41.0%). Proinflammatory gene upregulation was present in each decedent with high viral loads[13]. A prospective observational cohort study of 100 adult patients with severe COVID-19 and subsequent recovery compared to age- and sex-matched healthy volunteers and risk

factor-matched patients was conducted by Puntmann and colleagues[14]. The median time from diagnosis and cardiac MRI was 71 (64–92) days. At the time of cMRI high sensitivity (hs) troponin was detectable in 75% of patients, NT pro-BNP (brain naturetic polypeptide) was normal. Compared with the control groups, patients recovered from COVID-19 had lower left ventricular ejection fraction, higher left ventricular volumes, higher left ventricular mass and raised T1 and T2 weighted images. The overall finding suggests that ~ 80% of patients with severe COVID-19 have cardiac involvement and nearly 25% have evidence of ongoing myocardial inflammation three months after diagnosis. Intuitively, these are among the patients who require follow-up and clear management strategies given their inherent risk for poor outcomes.

Natural history and clinical events:

The natural history of viral myocarditis varies considerably, ranging from minimal symptoms to fulminant heart failure, cardiogenic shock, ventricular arrhythmias, post-viral cardiomyopathy and complete resolution without residual structural or functional abnormalities. Patients with preserved left ventricular function at the time of diagnosis tend to have a good long-term prognosis. For those with a moderate-to-severely reduced left ventricular ejection fraction, approximately half will have recovery over the next 6–12 months, 25% will experience chronic systolic dysfunction and 25% will worsen and require advanced mechanical therapies or heart transplantation[15].

The long-term effects of SARS-CoV-2-associated myocarditis are not known, but as summarized above for viral myocarditis could include heart failure, impaired exercise tolerance, atrial tachyarrhythmias, ventricular tachyarrhythmias, bradyarrhythmias and sudden cardiac death. Subclinical myocarditis may portend a particularly high risk for sudden death during moderate-to-high intensity physical activity, raising concern and a cautionary note in the athletic community[16].

Acute vascular injury:

The vascular pathology of COVID-19 is a topic of great interest . As previously described, necropsy and post-mortem biopsies of decedents with COVID-19 have consistently shown endotheliitis and accompanying macro and microvascular thrombosis within arteries, veins, arterioles, capillaries and venules in all major organs. Endothelial cells produce microvesicles in response to inflammatory conditions and inflammatory mediators, including cytokines, thrombin and complement 5a[17]. In turn, microvesicles impair vascular integrity, gap junctions, promote neutrophil binding, release NETs and facilitate tissue-level inflammation.

The wide-spread vasculitis described in patients with COVID-19 likely contributes to thrombosis, hemodynamic instability and autonomic dysregulation. The question being raised is, “how long will the vascular injury persist and at what cost to a full and functional recovery”?

Baroreceptor dysfunction:

The diffuse endotheliitis and vascular injury observed among patients with COVID-19 may have lasting hemodynamic and autonomic regulatory effects. The arterial baroreceptor system is intimately involved on a moment-to-moment basis with maintaining vascular tone and blood pressure homeostasis[18]. For example, arterial baroreceptors (stretch receptors located in the carotid sinuses and aortic arch) provide continuous feedback on blood pressure to the central nervous system, which responds with physiological efferent autonomic activity. Activation of arterial baroreceptors in response to increased blood pressure causes activation of vagal cardio–inhibitory neurons and a decrease of sympathetic neuron discharges to the heart and peripheral resistance bed[19]. The end-result is a decrease in heart rate, cardiac contractility, peripheral vascular resistance and venous return. By contrast, a decrease in sympathetic activity and vagal inhibition, leads to tachycardia and heightened cardiac contractility, vascular resistance and venous return. Any changes to this finely tuned mechanism can cause impaired blood pressure and heart rate responses to a change in posture, sleep and other resting states and physical activity. COVID-19-associated dysautonomia could be one of several manifestations of diffuse vascular injury[20].

Molecular and cellular adaptation, maladaptation and reset states:

Potential role in recovery following COVID-19

The early stages of COVID-19 are driven by a rapidly replicating virus and its direct effects on host cells. The transition stage of disease is less about the virus itself and more aligned with host responses, particularly unregulated immune and inflammatory system activation. SARS-CoV-2 tolerance is an attractive construct because its primary goals are to limit maladaptive response, attenuate tissue/organ damage, preserve physiological function and initiate recovery[21]. By contrast, these same mechanisms if poorly regulated either because of comorbid illness or the virus itself may contribute to long-term pathological effects.

Immune mechanisms:

The variability of symptoms experienced by persons with COVID-19 is one of many areas of investigation. Braun et al. investigated SARS-CoV-2 spike protein reactive CD4+ T cells in patients with COVID-19 and SARS-CoV-2 unexposed healthy donors. Peripheral blood SARS-CoV-2 S-reactive CD4+ T cells were detected in 83% and 35% of samples, respectively. Among healthy donors the S-reactive CD4+ T cells reacted primarily to C-terminal S epitopes that displayed homology to spike glycoproteins of human endemic coronaviruses. S-reactive T cell lines cross-reacted to SARS-CoV-2 C-terminal S protein epitopes. The impact of S-cross-reactive T cells on vaccine response will be an important area of investigation.

SARS-CoV-2 disrupts normal immune responses, leading to both an impaired immune system and, in some cases, an uncontrolled inflammatory response [22] .Under ideal conditions, treatment(s) would be designed to enhance viral immunity and attenuate systemic inflammation. Immune patterns are associated with disease progression and severity in patients with COVID-19. The patterns described to date are as follows: lymphopenia, reduced CD4+ T, CD8+ T, memory helper T cells, natural killer cells and B cells, T cell activation with expression of CD69, CD38, CD44, OX40, IL-2, TNF-±, and IFN-³, T-cell and natural killer T cell exhaustion, decreased basophils, eosinophils and monocytes, increased production of cytokines and increased IgG and total antibodies.

Patients experiencing moderate or severe COVID-19 have pulmonary epithelial cells with a three-fold increased expression of ACE2 receptors compared to healthy controls.

The association between viral infections and long-term metabolic abnormalities is recognized. Wang summarized the recovery pathway among patients with severe acute respiratory syndrome (SARS)—a global epidemic that emerged in 2003 [23]. Lung performance did not return to normal for 6–12 months following. Six min walk distance improved in the first 6 months of recovery, however, it did not reach normal values and physical activity-related quality of life scores were much lower than normal populations even at 1-year. The findings suggest that muscle weakness can persist for a prolonged period after a severe respiratory infection. As with other serious illnesses, neurocognitive impairment (memory, recall, attention and concentration) and physiologic effects (depression, post-traumatic stress) can persist for months to years. While pre-existing conditions contributed, in many instances the acute respiratory illness accompanied by sympathetic activation, altered cerebral microvascular integrity, changes in intracranial pressure, systemic inflammation-associated blood–brain barrier dysfunction and cytokine-mediated hippocampal damage was believed to be primarily responsible.

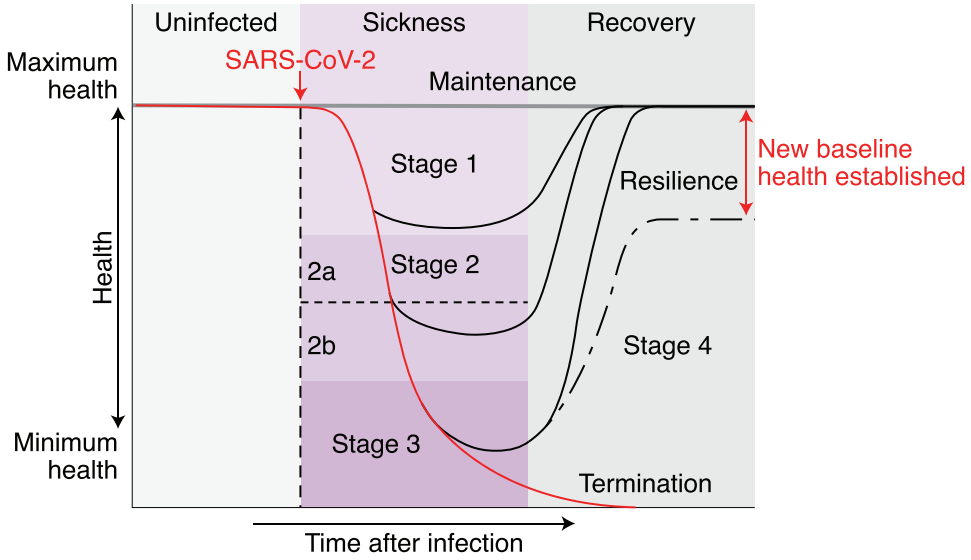


Fig.-2: *The disease phases of patients with COVID-19*

Lipid mechanisms:

The risk for COVID-19 on a high-spectrum of severity is heightened by metabolic and lipid-related comorbid factors. Because lipids play an important role in regulation of immunity, changes in lipidomic profiles could have both near-term and long-term consequences.

Vascular mechanisms:

Ackerman and colleagues performed a detailed necropsy-based analysis of COVID-19 decedents[24] .In all cases there was diffuse alveolar damage with necrosis of alveolar lining cells, Type 2 pneumatocyte hyperplasia and linear intra-alveolar fibrin deposition. A multiplexed analysis identified 79 inflammation-related genes that were differentially expressed compared to influenza H1N1 decedents. Fibrin thrombi of the alveolar capillaries were identified in all cases. In two cases, there were thrombi in precapillary, capillary and post-capillary vessels. Employing a three-dimensional micro-CT of pulmonary specimens, nearly total occlusion of precapillary and postcapillary vessels were observed. The extent of endothelial cell inflammation and thrombosis was associated with structurally deformed capillaries and microvascular corrosion casting. Intussusceptive angiogenesis (nonsprouting angiogenesis) occurred along with endothelial cell disruption of gap junctions and loss of contact with the basal membrane.

The extent of alveolar damage, architectural changes and vascular disruption observed in severe cases of COVID-19 are likely to cause prolonged or life-long functional abnormalities with attendant physiological limitations.

Clinical follow-up strategies:

The frequency of cardiac injury, vascular dysfunction and thrombosis in patients with COVID-19, including persons with either no or minimal symptoms during their initial infection, raises important questions about potential long-term cardiovascular effects. A proactive approach to care following hospital discharge and among patients with persisting or new symptoms with a goal of prevention, education and communication is needed.

The purpose of establishing a COVID-19 Cardiovascular Clinic is to

(1) proactively evaluate patients who have contracted SARS-CoV-2 infection,

(2) identify cardiovascular abnormalities that could portend future serious or life-threatening events, and

(3) establish a foundation for optimal management and follow-up.

Patients with laboratory-confirmed SARS-CoV-2 infection are the focus of the clinic. Those requiring hospitalization, an intensive care unit stay and in whom there was documented cardiac injury (elevated troponin), heart failure, arrhythmias or vascular inflammation (skin or other organ biopsy) will be prioritized for evaluation. An appointment in the COVID-19 Cardiovascular Clinic could be made at the time of hospital or rehabilitation facility discharge. Persons who test positive for Covid-19 who are initially asymptomatic, but then develop shortness of breath, impaired exercise tolerance, declining stamina, persisting fatigue, presyncope or syncope should also be evaluated. Delayed-onset clinical events among SARS-CoV-2 positive persons without initial symptoms, based on prior experience with viruses, will require documentation in medical records, careful history taking and reporting.

Testing and diagnostic platforms:

Patients will have a complete physical examination performed by an experienced clinician. A carefully selected battery of laboratory should be considered (Table1). A carefully selected menu of diagnostic studies to determine the status of cardiac and vascular health could also be performed as clinically indicated (Table2). Patients would receive a COVID-19 Cardiovascular report that summarizes the findings of each recommended test, instructions for a follow-up visit or referral to a specialty clinic or treatment as indicated according to the best available evidence. An existing electronic health record or secured dedicated database should be used for documentation.

Table-I

Covid-19 cardiovascular clinic blood and urine tests

C-reactive protein (CRP)
d-dimer
Von Willebrand Factor (VWF): antigen and activity
Interleukin (IL)-6
Complete blood count with differential
Basic metabolic profile
Urinalysis (protein, active sediment)
Anticardiolipin antibody screen
Ferritin

Table-II

Covid-19 cardiovascular clinic diagnostic menu

ECG
Echocardiogram (with strain calculation)
PET-CT (option if elevated troponin during hospitalization)
Cardiac MRI (preferred for evaluation of suspected myocarditis)
24 h Holter Monitor (If elevated troponin or arrhythmias during hospitalization or a left ventricular ejection fraction <40%)
Pulse wave velocity test
Brachial reactivity test
Heart rate variability test
Venous duplex scan
Pulmonary CT angiography

Expertise and team-based approaches:

Establishing a COVID-19 Clinic, by the very nature of SARS-CoV-2 infection and its widespread target organ involvement, will require a collaborative and multi-disciplinary team of experts. One would anticipate a need for representation from the following specialty and subspecialty groups: cardiology (electrophysiology and heart failure), vascular medicine, pulmonary medicine, nephrology, neurology and infectious disease. Access to expertise in hematology, dermatology, psychiatry, immunology, rheumatology and social services will be a requirement as well.

COVID-19 clinics represent a means to render a continuum of care for patients, but they can also serve as an underpinning for research, including long-term cohort studies and research network development. The natural history of COVID-19 and the many likely forms of post-COVID-19 syndrome can only be understood by establishing initiatives for follow-up, appropriately configured databases, careful documentation with quality controls, audits, experienced staffing, over-sight and sufficient funding.

Understanding the cardiovascular response to SARS-CoV-2 re-infection and Influenza infection will be a particularly important area of research given the common theme in cardiovascular diseases, disorders and conditions of a “second hit phenomenon” that can accelerate pathological abnormalities and lead to clinical events. The bar must be set high to assure that research undertakings meet the vigorous standard needed to inform and advance the field[25].

Concluding thoughts and future directions:

SARS-COV-2 infection is characterized by its protean nature and rapidly evolving understanding of its acute,

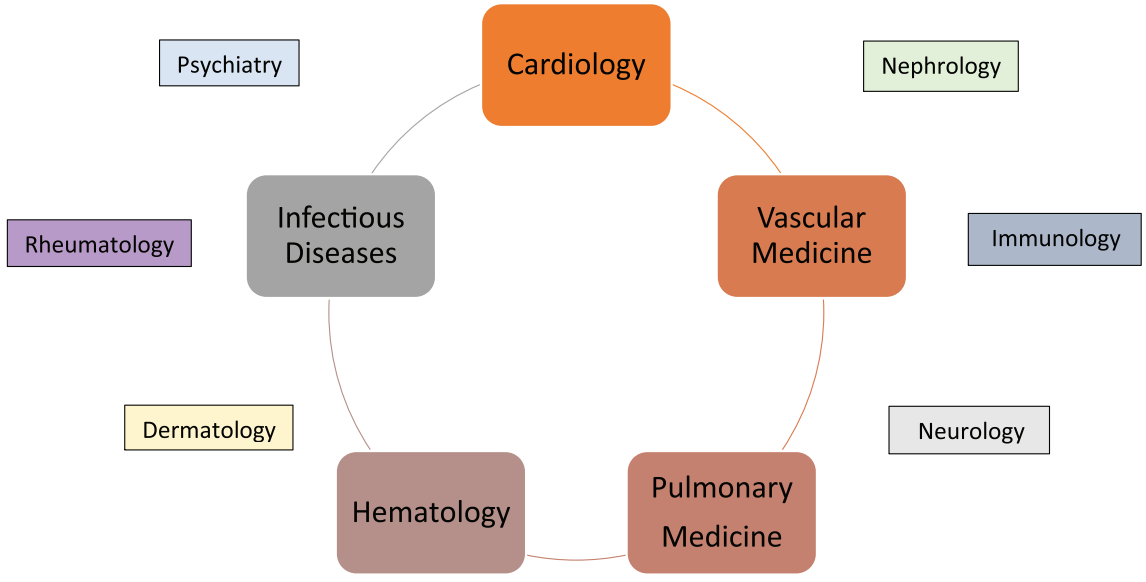


Fig.-3: *COVID-19 clinics for the diagnosis and management of patients with post-COVID-19 syndrome.*

subacute and, in all likelihood, chronic cardiovascular effects. Securing an initial diagnosis and documenting early signs, symptoms, diagnostic studies and complications, followed by an ambulatory clinic or office visit for “recovered” patients will be a vital step toward understanding COVID-19 and its comprehensive management. Research platforms must be established to translate new knowledge of post-COVID-19 syndrome to optimal patient care.

References

1. Carfì A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. JAMA. 2020;324:603–605.
2. Becker RC. Toward understanding the 2019 Coronavirus and its impact on the heart. J Thromb Thrombolysis. 2020 doi: 10.1007/s11239-020-02107-6.
3. Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, Heinrich F, Mushumba H, Kniep I, Schröder AS, Burdelski C, de Heer G, Nierhaus A, Frings D, Pfefferle S, Becker H, Bredereke-Wiedling H, de Weerth A, Paschen HR, Sheikhzadeh-Eggers S, Stang A, Schmiedel S, Bokemeyer C, Addo MM, Aepfelbacher M, Püschel K, Kluge S. Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study. Ann Intern Med. 2020;173:268–277.
4. Bompard F, Monnier H, Saab I, Tordjman M, Abdoul H, Fournier L, Sanchez O, Lorut C, Chassagnon G, Revel M-P. Pulmonary embolism in patients with COVID-19 pneumonia. Eur Respir J. 2020;56:2001365.
5. 7. Paulino M, Dumas-Diniz R, Brissos S, Brites R, Alho L, Simões MR, Silva CF. COVID-19 in Portugal: exploring the immediate psychological impact on the general population. Psychol Health Med. 2020
6. 10. DeFilippis AP, Chapman AR, Mills NL, de Lemos JA, Arbab-Zadeh A, Newby LK, Morrow DA. Assessment and treatment of patients with Type 2 myocardial infarction and acute nonischemic myocardial injury. Circulation. 2019;140: 1661–1678.
7. 11. Becker RC. COVID-19 update: Covid-19-associated coagulopathy. J Thromb Thrombolysis. 2020;50:54–67.
8. 12. Jain SS, Liu Q, Raikhelkar J, Fried J, Elias P, Poterucha TJ, DeFilippis EM, Rosenblum H, Wang EY, Redfors B, Clerkin K, Griffin JM, Wan EY, Abdalla M, Bello NA, Hahn RT, Shimbo D, Weiner SD, Kirtane AJ, Kodali SK, Burkhoff D, Rabbani LE, Schwartz A, Leon MB, Homma S, Di Tullio MR, Sayer G, Uriel N, Anstey DE. Indications for and findings on transthoracic echocardiography in COVID-19. J Am Soc Echocardiogr. 2020 doi: 10.1016/j.echo.2020.06.009.
9. 13. Mall G, Klingel K, Albrecht M, Seemann M, Rieger P, Kandolf R. Natural history of coxsackievirus B3-induced myocarditis in ACA/Sn mice: viral persistence demonstrated by quantitative in situ hybridization histochemistry. Eur Heart J. 1991;12:121–123.
10. 14. Pollack A, Kontorovich AR, Fuster V, Dec GW. Viral myocarditis–diagnosis, treatment options, and current controversies. Nat Rev Cardiol. 2015;12: 670–680.
11. 15. Bültmann BD, Sotlar K, Klingel K. Parvovirus B19. N Engl J Med. 2004;350:2006–2007.
12. 16. Lasrado N, Yalaka B, Reddy J. Triggers of inflammatory heart disease. Front Cell Dev Biol. 2020;8:192.
13. 18. Lindner D, Fitzek A, Bräuninger H, Aleshcheva G, Edler C, Meissner K, Scherschel K, Kirchhof P, Escher F, Schultheiss H-P, Blankenberg S, Püschel K, Westermann D. Association of cardiac infection with SARS-CoV-2 in confirmed COVID-19 autopsy cases. JAMA Cardiol. 2020 doi: 10.1001/jamacardio.2020.355.
14. 19. Puntmann VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, Shchendrygina A, Escher F, Vasa-Nicotera M, Zeiher AM, Vehreschild M, Nagel E. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19) JAMA Cardiol. 2020 doi: 10.1001/jamacardio.2020.3557.
15. 20. Herskowitz A, Campbell S, Deckers J, Kasper EK, Boehmer J, Hadian D, Neumann DA, Baughman KL. Demographic features and prevalence of idiopathic myocarditis in patients undergoing endomyocardial biopsy. Am J Cardiol. 1993;71:982–986.
16. 21. Maron BJ, Udelson JE, Bonow RO, Nishimura RA, Ackerman MJ, Estes NA, 3rd, Cooper LT, Jr, Link MS, Maron MS. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 3—

hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and other cardiomyopathies, and myocarditis—a scientific statement from the American heart association and American college of cardiology. Circulation. 2015;132:e273–e280.

17. 34. Chatterjee V, Yang X, Ma Y, Cha B, Meegan JE, Wu M, Yuan SY. Endothelial microvesicles carrying Src-rich cargo impair adherens junction integrity and cytoskeleton homeostasis. Cardiovasc Res. 2019 doi: 10.1093/cvr/cvz238.

18. 35. Robles-Cabrera A, Michel-Chávez A, Callejas-Rojas RC, Malamud-Kessler C, Delgado G, Estañol-Vidal B. The cardiovagal, cardiosympathetic and vasosympathetic arterial baroreflexes and the neural control of short-term blood pressure. Revista de Neurologia. 2014;59:508–516.

19. 36. Kirchheim HR. Systemic arterial baroreceptor reflexes. Physiol Rev. 1976;56:100–177.

20. 37. Pennisi M, Lanza G, Falzone L, Fisicaro F, Ferri R, Bella R. SARS-CoV-2 and the nervous system: from clinical features to molecular mechanisms. Int J Mol Sci. 2020 doi: 10.3390/ijms21155475.

21. 38. Ayres JS. Surviving COVID-19: a disease tolerance perspective. Sci Adv. 2020 doi: 10.1126/sciadv.abc1518.

22. 40. Yang L, Liu S, Liu J, Zhang Z, Wan X, Huang B, Chen Y, Zhang Y. COVID-19: immunopathogenesis and immunotherapeutics. Sig Transduct Target Ther. 2020;5:128.

23. 48. Wang CH, Liu CY, Wan YL, Chou CL, Huang KH, Lin HC, Lin SM, Lin TY, Chung KF, Kuo HP. Persistence of lung inflammation and lung cytokines with high-resolution CT abnormalities during recovery from SARS. Respir Res. 2005;6:42. doi: 10.1186/1465-9921-6-42.

24. 52. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, Vanstapel A, Werlein C, Stark H, Tzankov A, Li WW, Li VW, Mentzer SJ, Jonigk D. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. N Engl J Med. 2020 doi: 10.1056/NEJMoa2015432.

25. 53. Pundi K, Perino AC, Harrington RA, Krumholz HM, Turakhia MP. Characteristics and strength of evidence of COVID-19 studies registered on ClinicalTrials.gov. JAMA Internl Med. 2020 doi: 10.1001/jamainternmed.2020.2904.

Case Report

Percutaneous Closure of Acquired Hole- First Case Report from Bangladesh

Tawfiq Shahriar Haq[1], Naharuma Aive Hyder Chowdhury[2], Abdul Mazid khan[3], Jesmin Hossain[2], Fazila-Tun-Nesa Malik[4]

Abstract:

Rupture sinus of Valsalva (RSOV) is an uncommon condition with a wide spectrum of presentation, ranging from an asymptomatic murmur to cardiogenic shock or even sudden cardiac death. Our case presented at 62 yrs with progressive onset of dyspnea, palpitation with deterioration of exercise capacity. Diagnosis of ruptured sinus of Valsalva was made by echocardiography, it was aneurysmal and opened into right ventricular outflow tract. Coronary artery disease was excluded by coronary angiogram. Probable cause of rupture was atherosclerosis.We closed percutaneously with ADO I device. The procedure was completed uneventfully. Patient discharged with duel antiplatelet and is on follow up.

Key word: *Ruptured sinus of Valsalva (RSOV), Amplatzer duct occluder I (ADO I), Percutaneous closure, atherosclerosis.*

(Bangladesh Heart Journal 2020; 32(2): 155-158)

Introduction:

Ruptured sinus of Valsalva is a rare cardiac anomaly which is mostly due to congenital, can be also acquired. Presentation vary from asymptomatic to sudden cardiac shock even death. It can be diagnosed simple noninvasive echocardiography. Surgery is the choice of treatment, but isolated uncomplicated case can be closed by percutaneous closure though it is very much challenging. Percutaneous closure can avoid many hazards of surgery so now a days it is becoming more acceptable and demanding treatment option.

Case report:

62-year-old man was admitted to our hospital with the complain of progressive onset of dyspnea, palpitation, and deterioration in exercise capacity. He had no history of fever, trauma or any previous surgery. On examination, he was functionally New York Heart Association class III, pulse-70/min, blood pressure-160/60 mmhg, with continuous murmur IV/VI in left parasternal area. Chest X-ray showed cardiomegaly with increased pulmonary blood flow. Transthoracic & trans oesophageal echocardiography was performed and showed non coronary sinus ruptured into proximal right ventricular outflow tract (maximum & minimum diameter of RSOV, and the length of the aneurysm were taken). The ventricular septum showed no defect and no aortic regurgitation was present.

Cardiac catheterization was performed and did not reveal any coronary artery disease and showed noncoronary sinus ruptured into right ventricular outflow tract; the mean pulmonary artery pressure was 40/15 mmHg and the Qp/Qs was 1.8:1. The RSOV was crossed with a 6F Judkin Right catheter (Cordis Corporation) and a 0.035" × 260 cm straight tipped Terumo wire (Terumo Corp, Japan) from the aortic side. The wire was manipulated into pulmonary artery (PA) and snared through the right femoral vein with a 10 mm Goose Neck Snare (Microvena, MN, USA), to form an arteriovenous loop. The delivery sheath

1. Associate Professor, Department of Cardiology, National Heart Foundation & Research Institute, Dhaka, Bangladesh
2. Assistant Professor, Pediatric Cardiology, National Heart Foundation & Research Institute, Dhaka, Bangladesh
3. Assistant Professor, Department of Cardiology , National Heart Foundation & Research Institute, Dhaka, Bangladesh
4. Professor & Chief consultant Cardiology, National Heart Foundation & Research Institute, Dhaka, Bangladesh

Address of Correspondence: Dr. Naharuma Aive Hyder Chowdhury, National Heart Foundation Hospital & Research & Institute, Dhaka, Bangladesh. Email: naharuma.hyder@gmail.com

DOI: https://doi.org/10.3329/bhj.v35i2.52903

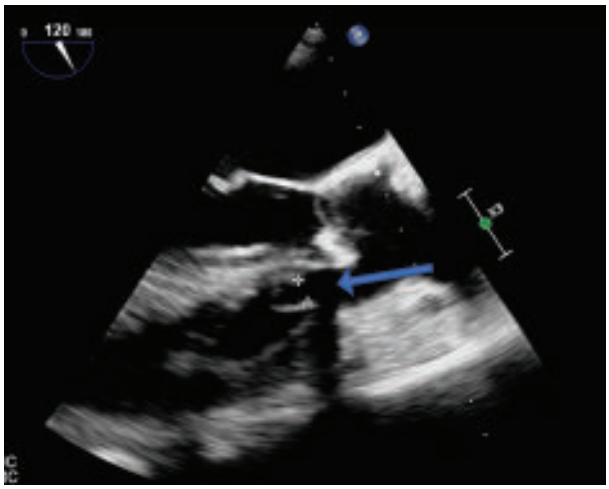


Fig.-1: *TEE showed ruptured non coronary sinus into right ventricular outflow tract.*

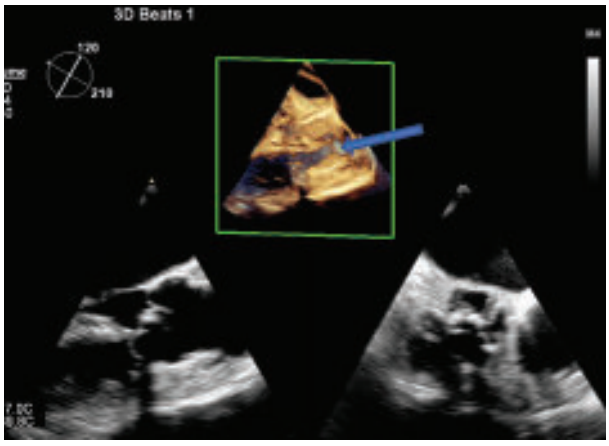


Fig.-2: *TEE 3D showed ruptured non coronary sinus from different plane into right ventricular outflow tract.*

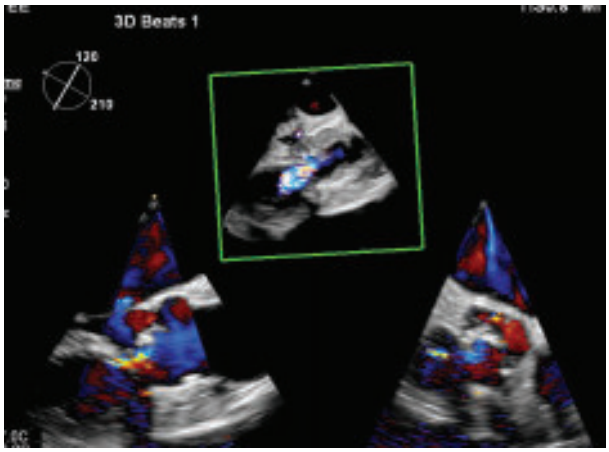


Fig.-3: *TEE 3D color mode showed ruptured non coronary sinus from different plane into right ventricular outflow tract with left to right shunt.*

was passed from the venous end and pushed over the wire across the RSOV. The device was loaded into the sheath. The aortic retention disc was opened into the ascending aorta and the entire system was pulled back till it anchored at the aortic end of the RSOV. At this point, the other end of the device was delivered by stabilizing the loading cable and pulling back the sheath. The entire maneuver was performed under fluoroscopic and transesophageal echo guidance. A check angiogram was done to confirm the position of the device. Once it was found to be optimum & quantify no AR & then the device was released. He was given Aspirin (5 mg/kg/day) and clopidogrel for six months following the procedure.

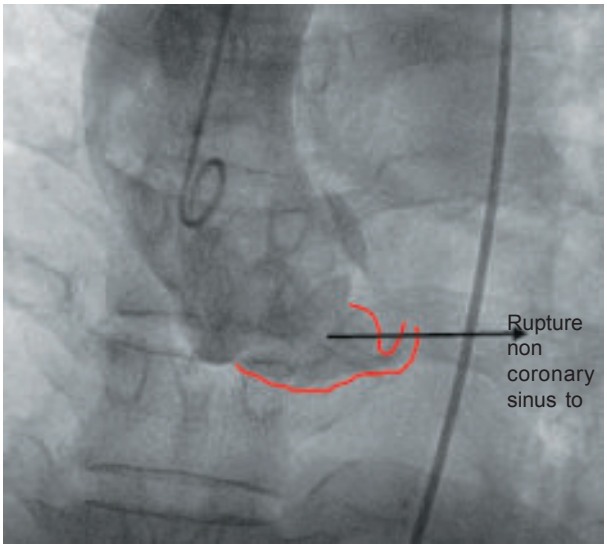


Fig.-4: *Root aortogram showing aneurysmal ruptured non coronary sinus to Right ventricular outflow tract.*

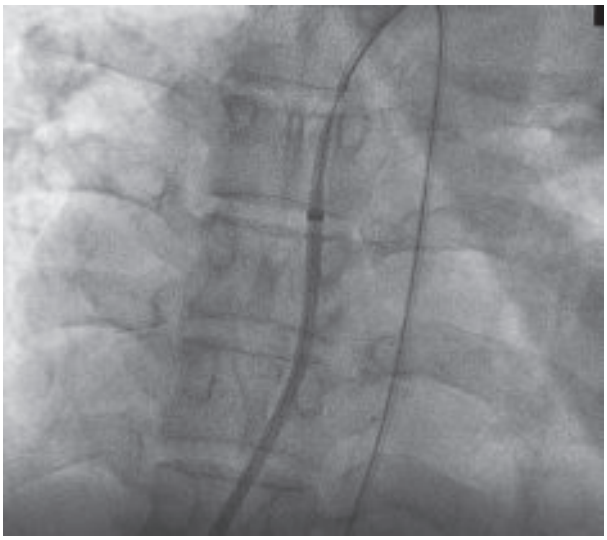


Fig.-5: *Introducing delivery sheath through antegrade approach.*

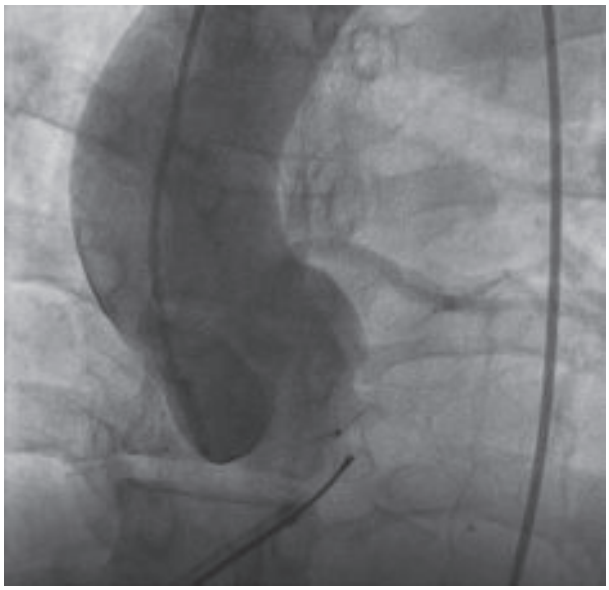


Fig.-6: *Deployment of ADO I device and confirming its secured and stabilized position.*

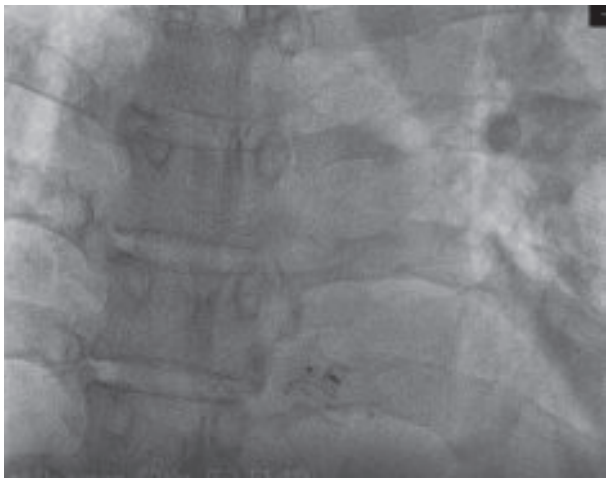


Fig.-7: *Deployed device with stabilized position.*

Discussion:

A sinus of Valsalva aneurysm is a rare cardiac anomaly where the root of the aorta may become aneurysmal & forms thin-walled saccular or tubular outpouchings. [1] They develop as a consequence of incomplete fusion of the distal bulbar septum and truncal ridges, leading to a weakness between the aortic media and the annulus fibrosus of the aortic valve.There is subsequent aneurysmal enlargement at this weak point caused by the high pressure head at the aortic root.[2,3]This dilatation progresses to rupture into the cardiac chambers(most frequently to the right ventricle or right atrium or mediastinum).[3,4] Valsalva aneurysms may involve all 3 sinuses, more frequently the right (75%– 90%) and noncoronary (10%–25%), and rarely the left coronary sinus are involved.[5] The left sinus is not derived embryologically from bulbar septum and therefore is rarely affected by congenital lesions. This anomaly can be unrecognized for many years.[6,7]RSOV are mostly congenital and comprise 0.15%–0.24% of congenital cardiac anomalies.[3]The incidence of rupture is higher in adolescence & adulthood in Eastern compared to Western populations.[8] In addition to a congenital etiology, these aneurysms may occur secondary to trauma, infective endocarditis, or tertiary syphilis, periaortic inflammation, atherosclerosis, aortic dissection, iatrogenic injuries to the sinuses during VSD closure or during debridement of a calcified aortic or mitral valve may also result in aneurysm formation. Ruptured Sinus of Valsalva (RSOV) are often associated with other congenital defects, most commonly VSD and aortic regurgitation [5]. The presence of an aneurysm may lead to a compression of an adjacent chamber, a coronary artery or the conduction system, leading to myocardial ischaemia and/or conduction disturbances. Symptoms occur in 80% of patients, most commonly between 30 and 45 years of age.[5]There is wide spectrum of presentation, ranging from an asymptomatic murmur to cardiogenic shock or even sudden cardiac death.[3] Symptoms are shortness of breath, chest pain, and fatigue, exercise intolerance, symptomatic heart failure. Symptoms depend upon severity of the shunt and presence of associated lesions.[5] There are different classification system.Guo et al. proposed a new system of simple surgical classification for right-sided defects according to rupture site.[9] This classification system identifies four types of rupture: type I, a rupture or protrusion into the right atrium; type II, a rupture or protrusion into the right atrium or right ventricle, near or at the tricuspid annulus; type III, a rupture or protrusion into the right ventricular outflow tract, under the pulmonary valve; and type IV, other types of ruptures or protusions.[9] Another system of angiographic classification uses the shape of the left-to-right shunt jet in order to facilitate the selection of occluders for percutaneous closure.[10] The four types of shunt jets identified are: type I, window-like; type II, aneurysmal; type III, tubular; and type IV, other rare conditions.10 Our patient is under type III (according to anatomy) & type II (according to angiography). Echocardiography is the gold standard for the diagnosis of RSOV and the identification of other co-existing congenital anomalies. [3] Catheterization is carried out in patients who require an evaluation of their coronary artery anatomy or if an interventional procedure is planned. [5] We have done cardiac catheterization to exclude coronary issue. Treatment of RSOV is surgical or percutaneous transcatheter intervention. Traditionally, surgical closure has been the mainstay of treatment for RSOV, with an

operative mortality rate of <5% and excellent long-term outcomes.[8,11] Nevertheless, these patients remain at risk of prolonged hospital stays and postoperative complications such as chest pain and septicemia, making percutaneous device closure an attractive alternative.[8]Lately isolated RSOV have been successfully closed percutaneously using transcatheter devices.[4]

Percutaneous closure RSOV was first attempted by Cullen et al in 1994 using a Rashkind umbrella. Since then a few reports have been published with the use of different available closure devices.[12-15]The size of the device used for RSOV closure must be accurately assessed, since a large device may interfere with coronary blood flow or aortic valve cusp movement. However, a device of suboptimal size might dislodge and embolize, or result in a significant residual shunt. Success rates up to 90% have been reported in catheter-based closures. Complications, although rare, include cardiac perforation, fistula formation, thrombosis, and device embolization into the systemic or pulmonary circulation. complications result in acute symptoms and hemodynamic compromise, requiring urgent surgical retrieval. Post-deployment follow-up includes the assessment of coronary blood flow, aortic valve function, and the presence of thromboembolism. After the deployment of a device, a short course of anticoagulants or antiplatelet drugs is recommended to prevent thromboembolism until the endothelialization of the device occurs .[16]

Conclusion:

Transcatheter closure of RSOV is an effective and safe treatment modality for isolated RSOV. Reduced pain for the patient, absence of surgical scar, shorter hospitalization and convalescence time are also important advantages. In patients where on-pump surgery is high risk, due to poor general condition and comorbidities, transcatheter device closure can be lifesaving. Extended follow-up is required to assess the long-term outcome of these patients.

Reference:

1. Takach TJ, Reul GJ, Duncan JM, et al. Sinus of Valsalva aneurysm or fistula: management and outcome. Ann Thorac Surg 1999;68:1573-7.
2. Chang CW, Chiu SN, Wu ET, Tsai SK, Wu MH, Wang JK. Transcatheter closure of a ruptured sinus of Valsalva aneurysm. Circ J. 2006;70:1043–7. [PubMed] [Google Scholar]
3. Shah RP, Ding ZP, Ng AS, Quek SS. A Ten-Year review of ruptured sinus of Valsalva: Clinico-pathological and echo-Doppler features. Singapore Med J. 2001;42:473–6. [PubMed] [Google Scholar]
4. Trehan VK, Mukhopadhyay S, UmaMahesh CR, Yusuf J, Arora R. Successful transcatheter closure of ruptured sinus of Valsalva Aneurysm. Indian Heart J. 2002;54:720–2. [PubMed] [Google Scholar]
5. Moustafa S, Mookadam F, Cooper L, et al. Sinus of Valsalva aneurysms: 47 years of a single center experience and systematic overview of published reports. Am J Cardiol 2007;99:1159-64.
6. Walters MI, Ettles D, Guvendik L, Kaye GC. Interventricular septal expansion of a sinus of Valsalva aneurysm: a rare cause of complete heart block. Heart. 1998; 80:202-3.
7. Sher RF, Kimbiris D, Segal BL, Iskandrian AS, Bemis CE. Aneurysm of the sinus of Valsalva: its natural history. Postgrad Med. 1979; 65:191-3.
8. Chu SH, Hung CR, How SS, Chang H, Wang SS,Tsai CH, Liau CS, Tseng CD, Tseng YZ, Lee YT. Ruptured aneurysms of the sinus of Valsalva in oriental patients. J Thorac Cardiovasc Surg 1990; 99:288-98
9. Guo HW, Xiong H, Xu JP, Wang XQ, Hu SS. A new and simple classification for sinus of Valsalva aneurysms and the corresponding surgical procedure. Eur J Cardiothorac Surg 2013; 43:1188–93. doi: 10.1093/ejcts/ezs673.
10. Liu S, Xu X, Chen F, Zhao Z, Zhang Y, Wang C, et al. Angiographic features of ruptured sinus of Valsalva aneurysm: New classification. J Cardiol 2014; 64:139–44. doi: 10.1016/j. jjcc.2013.12.004.
11. van Son JA, Danielson GK, Schaff HV, Orszulak TA, Edwards WD, Seward JB. Long-term outcome of surgical repair of ruptured sinus of Valsalva aneurysm. Circulation 1994; 90:II20–9.
12. Cullen S, Vogel M, Deanfield JE, Rdinqton AN. Images in cardiovascular medicine. Rupture of aneurysm of the right sinus of Valsalva into the right ventricular outflow tract: treatment with Amplatzer atrial septal occluder. Circulation. 2002;105: E1-E2.
13. Rao PS, Bromberg BI, Jureidini SB, Fiore AC. Transcatheter occlusion of ruptured sinus of valsalva aneurysm: innovative use of available technology. Catheter Cardiovasc Interv. 2003; 58:130-4.
14. Fedson S, Jolly N, Lang RM, Hijazi ZM. Percutaneous closure of a ruptured sinus of Valsalva aneurysm using the Amplatzer Duct Occluder. Catheter Cardiovasc Interv.2003;58:406-11.
15. Arora R, Trehan V, Rangasetty UM, Mukhopadhyay S, Thakur AK, Kalra GS. Transcatheter closure of ruptured sinus of Valsalva aneurysm. J Interven Cardiol. 2004; 17:53-8.
16. Cullen S, Somerville J, Redington A. Transcatheter closure of a ruptured aneurysm of the sinus of Valsalva. Br Heart J 1994; 71:479-80.

Our Teacher: Prof Abu Zafor

(01.12.1938-03.05.2020)

Prof. Dr. Abdullah Al Shafi Majumder
General Secretary, Bangladesh Cardiac Society

(Bangladesh Heart Journal 2020; 32(2): 159-160)

Prof Abu Zafor was one of the architects of the National Institute of Cardiovascular Diseases and the Institute was the foundation of cardiovascular science in our country. In that sense he will be remembered forever by the cardiologists and the cardiac surgeons of the country.

He hailed from Pabna and passed MBBS from Dhaka Medical College in 1963. He went to UK and in 1971, he obtained MRCP. He returned back in 1976 and joined Rajshahi Medical College , later IPGM&R. In 1980, he joined the ICVD. He became the Director of the Institute in 1989 and worked till 1994. He was transferred as the Professor of Cardiology in IPGM&R from where he retired from the government services in 1995.

He was a great teacher, a teacher by heart, with unique characteristics. He used to teach not a topic but the idea behind the topic. He tried to spread the philosophy of teaching to his students. He used to light the torch to follow the path of learning.

As a clinical teacher he was superb. He was an example for us as a role model in the bed side teaching. He very often made extensive round of seeing the admitted patients. He expected that the doctor in charge of the bed should have thorough knowledge regarding the condition of the patient. His clinical assistant /registrar was assigned to coordinate duty doctors without any excuse

He made in-depth reading of electrocardiogram. He made us understand that critical observation of electrocardiogram might provide decisive clue for the diagnosis of a disease. He was often found in the echocardiogram room to provide hands-on training to

At NICVD, 29th November, 2014

Bangladesh heart j Vol. 35, No. 2
July 2020

his students and the junior doctors. There is no exaggeration when we hail him as the " Pioneer in Echocardiography" of Bangladesh.

In the early days of the Institute, he was a regular operator in the cath lab. He had keen interest in implanting the permanent pacemaker. He personally brought the first pacemaker in Bangladesh while returning to the country. 5th November 1977 marks a historic day for the treatment of cardiovascular diseases in Bangladesh, as Prof. Dr. Zafar performed the installation of this Pacemaker in IPGM&R for the first time in the history of Bangladesh.

He was the person from whom the students could learn the scientific information regarding the operation of a pacemaker. It was a great opportunity for the students as there was not easy access to the latest scientific development in the eighties. (His acceptance as an operator of permanent pacemaker was evident by the fact that he implanted permanent pacemaker on Late National Professor Mohammed Ibrahim).

There are many examples of his humane qualities. I may cite one case. Once he became annoyed with a doctor working in his unit. Later he came to know that he had a child who needed special care and from then he became soft to him and provided a part time job in his chamber! In another situation he used to refer his patients to a junior doctor with instruction that in any problematic case he would review the case in hospital echo machine ,if necessary!

He was a man of integrity and honesty to the highest quality to me, like his other students he was an "Idol" whom we cherished to follow in our professional life.