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

BMDC RECOGNIZED

BANGLADESH HEART JOURNAL

VOL. 33 NO. 1 JANUARY 2018

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Official Journal of
Bangladesh Cardiac Society

BANGLADESH HEART JOURNAL

VOL. 33, NO. 1, JANUARY 2018

Published by :
Dr. S.M. Mustafa Zaman
Publicity Secretary
Bangladesh Cardiac Society
Room # 362, 2nd Floor
(Middle Block)
National Institute of
Cardiovascular Diseases
Sher-e-Bangla Nagar
Dhaka-1207, Bangladesh
Telephones:
Office: +8801799925522
E-mail: bangladeshheartj@yahoo.com

Printed by :
Asian Colour Printing
130, DIT Extension Road
Fakirerpool, Dhaka-1000
Phone : 49357726, 58313186

We gratefully acknowledge the contribution of the Reviewers of this issue of Bangladesh Heart Journal

VOL. 33, NO. 1, JANUARY 2018

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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.

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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.

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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.

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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.

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1. Category of manuscript (original research, review article, case report, cardiovascular image, letter to the Editor)
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3. Transfer of copyright to the Bangladesh Heart Journal upon the acceptance of the manuscript for publication
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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.
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- 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.

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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.

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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.

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

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- 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.
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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.
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- 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.

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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:

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Original Article

Comparison of Short-term Outcomes of Percutaneous Coronary Intervention between Young Male and Female Patients with Acute Coronary Syndrome

Fathima Aaysha Cader[1], Afzalur Rahman[2], Mohammad Arifur Rahman[3], Shahana Zaman[3], Md Minhaj Arefin[1], AbeedaTasnim Reza[4], Mohammad Abdul Matin[4], Md. Shariful Islam[4], Fahdia Afroz[4], Abul Hasnat Md. Jafor[5]

Abstract:

Background:Young women undergoing percutaneous coronary intervention (PCI) for acute coronary syndrome (ACS) experience greater short-term adverse events than young men. There is a scarcity of data on the short-term adverse outcomes between young Bangladeshi males and females with ACS undergoing PCI.Objectives: This study was conducted to compare the short-term outcomes of PCI between young males and females presenting with ACS. Methods: This prospective observational study was done in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD) fromApril 2016 to March 2017. 190 young patients with ACS and undergoing PCI were enrolled. They were equally divided into two groups, group I (young females <55 years) and group II (young males <45 years). Results: The mean age of young females and males was 43.8±6.9 years and 40.1±4.3 years respectively. Young women had significantly higher risk factors of hypertension (62.1% vs 33.7%, p<0.0010) and diabetes (57.9% vs 31.6%, p<0.001) in comparison to young men. Overall, young women experienced significantly greater incidence of short-term adverse events in comparison to young men (14.7% vs. 6.3%, p=0.04) and had significantly higher rates of severe bleeding (6.3% vs 1.1%, p=0.04), vascular access site complications (8.4% vs 2.1%, p=0.04) and recurrent ischaemia at 30 days (7.4% vs. 2.1%, p=0.04). Major adverse cardiac events (MACE) were higher among young females, in comparison to young males (4.1% vs 2.1%, p=0.4). Young females experienced significantly higher rates of short-term net adverse clinical events (NACE) than young males (10.5% vs 3.2%, p=0.04). Female gender (odds ratio [OR] 11.7), diabetes (OR 2.5), hypertension (OR 1.78), decreased ejection fraction (OR 1.41) and smaller stent diameter (OR 1.15) were identified as independent predictors of adverse short-term outcomes among young ACS patients undergoing PCI. Conclusion: Young women experienced significantly more adverse short-term outcomes after PCI. They had significantly greater NACE, largely driven by increased rates of major bleeding. Female gender was an independent predictor of adverse short-term outcomes among young ACS patients undergoing PCI.

Key words:Acute Coronary Syndrome, Percutaneous Coronary Intervention, Young Adult, Treatment Outcome.

(Bangladesh Heart Journal 2018; 33(1): 1-9)

Introduction:

Acute coronary syndromes (ACS) are a major cause of mortality in developing countries, and are responsible for a large number of hospitalizations annually.[1] Historically, women with ACS have had worse outcomes in comparison

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37015

to men, in data derived predominantly from the pre-intervention era.[2] Nevertheless, even following PCI, it has been observed that women had more adverse cardiovascular outcomes, a fact that has largely been attributed to their older age at presentation and greater co-morbidities.[3-4]

However, ACS is increasingly prevalent at a younger age, particularly among those of South Asian ethnicity.[5] The prevalence of ACS among young women has also increased.[6]There is disparity in the literature on the definition of "young" with respect to premature CAD and ACS, with the age cut-off varying from ≤40 to ≤55 years in various studies.[7-9] Cardiovascular disease develops 7 to 10 years later in women than in men,[10]leading to a difference in the definition of the "young" ACS patient for each gender,arising from the fundamental differences in the physiology of women and a protective effect of endogenous oestrogens against CAD. As such, "young" patients in relation to ACS have been defined in the literature as females <55 years of age, and males <45 years of age, a similar cut-off that has been adopted in this study.[8,9,11]

Although percutaneous revascularization is generally considered to be associated with lower risk and better recovery in young patients, multiple studies have observed that younger women were more likely than men to experience adverse cardiovascular outcomes, including in-hospital and 30-day mortality, major adverse cardiac events (MACE) and bleeding, despite similarly high angiographic and procedural success.[12-15] Alternatively, a few studies have observed higher MACE among young males undergoing PCI.[16]

Younger women were at more than twice the risk of peri-procedural complications such as coronary dissection and abrupt vessel closure,[15] possibly attributable to their smaller vessel size and increased tortuosity of coronaries.[17] Younger women were also more likely to experience bleeding complications.[12,14,15]The increased adverse outcomes among younger women with ACS may be further attributed to the clustering of cardiovascular risk factors and co-morbidities, most notably diabetes, and also hypertension, cerebrovascular disease, renal impairment and congestive heart failure in comparison to men.[12,14] It has been previously studied in an older Bangladeshi population, that females undergoing PCI have more adverse in-hospital outcomes in comparison to males, particularly coronary vascular injury and bleeding complications.[18] However, there are no contemporary data on gender-related differences in short-term outcomes of young ACS patients undergoing PCI in Bangladesh. This study has been designed to investigate any disparities in the short-term outcomes (i.e. composite of in-hospital and 30-day outcomes) between young male and female ACS patients following PCI and to identify the predictors of adverse cardiovascular outcomes in young ACS patients undergoing PCI.

Methods:

This prospective observational study was conducted over a period of 1 year from April 2016 to March 2017 at the Department of Cardiology, National Institute ofCardiovascular Diseases (NICVD), Dhaka. The study complied with the Declaration of Helsinki. Prior ethical approval was obtained from the ethical review committee of NICVD. Informed written consent was taken from each patient.Young patients were defined as males <45 years and females <55 years in accordance with the literature A total of 190 young patients presenting with ACS, and undergoing PCI during index hospitalisation at NICVD were selected by purposive sampling technique, based on predefined enrollment criteria. Patients with prior MI, mechanical complications of MI, cardiogenic shock, valvular and congenital heart disease, cardiomyopathy, prior revascularization (PCI or coronary artery bypass graft), intravenous contrast allergy, serum creatinine >2mg/dl and those with bleeding disorders were excluded. Study subjects were divided into two groups on the basis of gender. Group I comprised of young females and group II comprised of young males.

Patients' demographic characteristics, risk factors, ACS typeand left ventricular (LV) ejection fraction (EF) were recorded. Coronary angiography was performed by conventional method (right femoral access) by routine operators. All angiograms were evaluated by two experienced cardiologists. Angiographic variables including Gensini Score, ACC/ AHA lesion type of culprit lesion, culprit vessel and number of diseased vessels (single, double, triple) were noted. In case of angiographically significant stenosis, ad hoc PCI to culprit artery was done. All patients were pre-treated with standard dual antiplatelet therapy (DAPT) comprising of aspirin and clopidogrel. PCI variables including stent type, stent diameter and length, peri-procedural events, angiographic, procedural and clinical success were noted. Patients were then followed up for outcome variables. Follow- up comprised of two parts: In-hospital (i.e. for the entire duration of hospital stay until time of discharge) and once again at 30-days. The following in-hospital outcomes were observed and recorded: Vascular access site and peri-procedural complications, bleeding, significant arrhythmias, cardiogenic shock, acute heart failure, MI related to PCI, stent thrombosis repeat revascularization, stroke and death. All patients were further followed up at the completion of 30 days following PCI and above-mentioned outcome variables were recorded, in addition to repeat-hospitalization and recurrent ischaemia. Overall major adverse cardiac events (MACE) and net

adverse clinical events (NACE) were recorded. Outcome data elements were defined according to 2013 ACCF/AHA Key Data Elements and Definitions for Measuring the Clinical Management and Outcomes of Patients with Acute Coronary Syndromes and Coronary Artery Disease: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Data Standards. Presence of short-term outcome was considered as composite of in-hospital and 30-day outcome.[19]A composite or overall adverse outcome was defined as consisting of the occurrence of any one of a set of multiple defined outcome variables.

Data were processed and analyzed using software using SPSS Version 16.0 (Statistical Package for the Social Sciences by SPSS Inc., Chicago, IL, USA, 2007). The test statistics used to analyze the data were descriptive statistics, Chi-squared Test (c^2), unpaired t-Test and Fisher's Exact Test.Multiple logistic regression analysis was performed to identify predictors of short-term adverse outcomes. A p value of < 0.05 was considered statistically significant.

Results:

A total of 190 patients were studied, including 95 young females and 95 young males. The overall mean age was 41.3±5.6 years (range 18-54 years). The mean age of young females was 43.8±6.9 years and young males was 40.1±4.3 years (Table I). A total of 52.6% STEMI, 26.3% NSTEMI and 21.1% UA patients were included with equal distribution between the two genders. Among STEMI patients, 70% were of anterior and 30% were of inferior MI.

Table II shows the distribution of risk factors between the groups. Hypertension (62.1% vs 33.7%, p<0.001) and diabetes (57.9% vs. 31.6%, p,0.001) were significantly more prevalent among young females, while smoking was significantly greater among young males (70.5% vs 0%, p<0.001). Among the young females, 70 (74%) were pre-menopausal, and among pre-menopausal females, 63% had history of taking oral contraceptive pill (OCP). The mean percent of left ventricular (LV) ejection fraction (EF) of study patients was 46.8±10.0. Young females had significantly higher EF in comparison to young males (48.4±9.3 vs 45.1±10.4, p=0.02).

Table III shows the comparison of angiographic characteristics between the two groups. Left main coronary artery (LMCA) (3.2% vs. 1.1%, p=0.61) andLeft anterior descending (LAD) (51.6% vs. 45.3%,p=0.38) were more frequently involved among young females. Young males demonstrated angiographically more severe CAD, with significantly higher numbers of ACC/AHA lesion type B2 (40% vs 25.3%, p=0.03) and C (20% vs 9.47%, p=0.03). Young males also had greater frequency of double and triple vessel disease and higher mean Gensini scores, although not statistically significant (Table III).

Table-I

Distribution of study patients by age

Age in years	Young females (n, %)		Young males (n, %)		p value
<25	3	3.2	2	2.1	0.65
25 – 34	5	5.3	14	14.8	0.02
35 – 44	39	41.1	79	83.1	<0.001
45 – 54	48	50.5	0	0.0	<0.001
Mean ± SD(Range)	43.8±6.9(18-54)		40.1±4.3(22-44)		<0.001

Table-II

Comparison of risk factors for CAD between young females and males

Risk Factors	Young females (n, %)		Young males (n, %)		p value
Smoking	0	0.0	67	70.5	<0.001
Smokeless tobacco	8	8.4	3	3.2	0.21
Hypertension	59	62.1	32	33.7	<0.001
Diabetes mellitus	55	57.9	30	31.6	<0.001
Dyslipidaemia	59	62.1	50	52.6	0.18
Family H/O CAD	41	43.2	33	34.7	0.23

Table-III

Comparison of angiographic characteristics between young females and males

Angiographic Characteristic	Young females (n, %)		Young males (n, %)		p value
Culprit artery					
Left main stem	3	3.2	1	1.1	0.61
Left anterior descending	49	51.6	43	45.3	0.38
Left circumflex	17	17.9	21	22.1	0.46
Right coronary	24	25.3	30	31.6	0.33
Ramus Intermedius	2	2.1	0	0.0	0.47
Number of diseased vessels					
Single	66	69.5	56	58.9	0.13
Double	18	18.9	21	22.1	0.58
Triple	11	11.6	18	18.9	0.15
ACC/ AHA lesion type					
A	38	40.0	14	14.7	<0.001
B1	24	25.3	24	25.3	1.00
B2	24	25.3	38	40.0	0.03
C	9	9.47	19	20.0	0.03
Gensini Score					
Mean ± SD	39.3±27.6		44.0±32.4		0.27

Table IV details the procedural characteristics between the two groups. Mean stent diameter was significantly smaller in young females (2.7±0.3 vs. 2.9±0.4 mm, p=0.02), but no significant difference in mean stent length was seen between the two groups. Young females were significantly less likely to receive a drug eluting stent (DES) (81.1% vs 96.8%, p=0.001). there was no significant difference in terms of angiographic and procedural success between the two groups.

Table V demonstrates the rates of in-hospital adverse outcomes observed between the two groups. Vascular access site complications (8.4% vs 2.1%, p=0.04) and bleeding (13.7% vs. 4.2%, p=0.02) were significantly higher among young females. All other in-hospital adverse outcomes were also observed with greater frequency among young females, albeit not statistically significant.

Table VI depicts the outcomes observed at 30 days follow up of the study subjects. Overall, young females were more likely to experience adverse outcomes in comparison to young males, particularly repeat hospitalization (6.3% vs. 1.1%, p=0.04) and recurrent ischaemia (7.4% vs. 2.1%, p=0.04).

Table VII shows the comparison of composite short-term outcomes between the two groups, which were significantly higher among young females (14.7% vs 6.3%, p=0.04).At 30 days, young females showed higher rates of death (3.2% vs. 1.1%, p=0.62) and major adverse cardiac events (MACE) (4.1% vs. 2.1%, p=0.4), albeit not significant. However, it was seen that 30-day net adverse clinical events (NACE) were significantly higher among young females (10.5% vs. 3.2%, p=0.04), largely driven by their higher rates of GUSTO severe bleeding (6.3% vs 1.1%, p=0.04).

Table VIII demonstrates the binary logistic regression analysis of odds ratio (OR) for characteristics of the subjects likely to develop adverse short-term outcomes. Multivariate analysis revealed that out of the 9 expected variables, female gender, hypertension, diabetes mellitus, decreased EF and smaller stent diameter were found to be the independently significant predictors of adverse short-term outcomes with odds ratios (OR) being 11.7, 1.78, 2.5, 1.41 and 1.15respectively, on multi-variate analysis. Age >40 years did not emerge as an independent predictor of adverse short-term outcome.

Table-IV

Comparison of PCI Procedural characteristics between young females and males

PCI Variables	Young females(n, %)		Young males(n, %)		Total(n, %)		p value
Stent diameter (mm)							
2.25	12	12.6	9	9.5	21	11.1	0.48
2.5	32	33.7	16	16.8	48	25.3	0.007
2.75	15	15.8	34	35.8	49	25.8	0.002
3.0	30	31.6	19	20.0	49	25.8	0.06
3.5	6	6.3	14	14.7	20	10.5	0.04
4.0	0	0.0	3	3.2	3	1.6	0.08
Mean diameter	2.7±0.3	2.9±0.4	2.8±0.4	0.02			
Stent length (mm)							
<20 mm	31	32.6	22	23.2	63	27.9	0.14
>20 mm	64	67.4	73	76.8	137	72.1	
Mean±SD	25.0±9.6	26.6±9.2	25.8±9.4	0.26			
Stent type							
BMS	18	18.9	3	3.2	21	11.1	0. .001
DES	77	81.1	92	96.8	169	88.9	
PCI procedural success							
Angiographic	91	95.8	94	98.9	185	97.4	0.36
Procedural	90	94.7	94	98.9	184	96.8	0.21
Clinical	88	92.7	93	97.9	181	95.2	0.17

Table-V

Comparison of in-hospital outcomes between young females and males

Outcomes variables	Young females (n, %)		Young males (n, %)		p value
Peri-procedural complications	8	8.4	3	3.2	0.21
Cardiogenic shock	6	6.3	4	4.2	0.74
Heart failure	9	9.5	6	6.3	0.42
Vascular access site complications	8	8.4	2	2.1	0.04
Bleeding	13	13.7	4	4.2	0.02
Significant arrhythmia	5	5.3	3	3.2	0.47
Stroke	0	0.0	0	0.0	—
MI	1	1.1	0	0.0	1.00
Stent thrombosis	1	1.1	0	0.0	1.00
Death	1	1.1	0	0.0	1.00

Table-VI

Comparison of 30-day outcomes between young females and males

Outcomes variables	Young females (n, %)		Young males (n, %)		p value
Repeat hospitalization	6	6.3	1	1.1	0.04
Recurrent ischaemia	7	7.4	2	2.1	0.04
Heart failure	5	5.3	3	3.2	0.47
MI	0	0	0	0.0	-
Stent thrombosis	0	0	0	0.0	-
Bleeding	2	2.1	0	0.0	0.47
Significant arrhythmia	1	1.1	3	3.2	0.62
Stroke	0	0.0	1	1.1	1.00
Repeat revascularization	0	0.0	0	0.0	-
Death	2	2.1	1	1.1	1.00

Table-VII

Comparison of composite/ overall adverse outcomes between young females and males

Outcomes	Young females(n, %)		Young males(n, %)		Total(n, %)		p value
Composite/ overall	14	14.7	6	6.3	20	10.5	0.04
Overall MACE*	4	4.1	2	2.1	6	3.2	0.4
Overall NACE*	10	10.5	3	3.2	13	6.8	0.04

*MACE: Major adverse cardiac event; *NACE: Net adverse clinical event.

Table-VIII

Multivariate binary logistic regression analysis for determinants of adverse short-term outcome.

Variables of interest	OR (95% CI)	P value
Smoking	1.30 (0.599 – 2.210)	0.11
Hypertension	1.78 (1.101 – 3.694)	0.03
Dyslipidemia	1.29 (0.105 – 3.109)	0.30
Diabetes mellitus	2.50 (1.211 – 5.321)	0.004
Decreased EF <55%	1.41 (1.002 – 3.420)	0.02
Gensini Score	1.07 (0.201-2.212)	0.55
Smaller stent diameter <2.5mm	1.15 (1.111-3.289)	0.02
Age >40 years	1.03 (0.412 – 1.782)	0.70
Female gender	11.7 (1.72 – 25.414)	0.02

Dependent variable: short-term adverse outcome
Independent variables: smoking, hypertension, dyslipidemia, diabetes mellitus, decreased EF<55%, Gensini score, smaller stent diameter <2.5mm, age >40 years, female gender

Discussion:

This prospective observational study presents the comparison of short-term outcomes of young ACS patients undergoing PCI. The mean age of young females was significantly higher than young males (43.8±6.9 vs 40.1±4.3 years, p=0.001), which were slightly higher than the patient population of the PROMETHEUS study (48.6±5.6 years vs. 48.1±6.0 years),[12]but is comparable to an Indian study by Patted, et al. (2017).[16] The younger mean age in this study possibly reflects the earlier onset of premature atherosclerosis among South Asian populations in comparison to Western populations.[6]

Equal numbers of all presentations across the spectrum of ACS were taken from both groups in order to ensure matching. The majority of this young ACS population undergoing PCI presented with ST-elevation myocardial infarction (STEMI), accounting for 52.6% of all subjects. Anterior MI was more frequent than inferior MI. These findings concur with those of an Indian study, in which an overwhelming majority of patients underwent PCI due to STEMI.[16] In contrast, however, Chandrasekhar, et al. (2016) observed in the PROMETHEUS study, that unstable angina (UA) comprised almost half of the study population (approximately 46%) and STEMI comprised only approximately one quarter.[12]

This study observed that young females had higher frequencies of baseline risk factors, particularly hypertension and diabetes. Several other studies have made similar observations.[12,14] Diabetes is a particularly strong risk factor for coronary artery disease (CAD) in women and is associated with a heightened cardiovascular mortality particularly in women <55 years (Lansky, et al., 2004). Some studies suggest that diabetes may also negate the protective effects of estrogen on vascular function, and increase the risks of post PCI complications.[20,21] Smoking, however, was observed exclusively among young males (70.5%). While no females reported cigarette smoking, 8.4% of them gave a history of taking smokeless tobacco. These findings concur with Indian populations[16] and some Western studies in which fewer females were known to be smokers.[2,13] They differ from more recent studies where smoking was significantly more frequently observed among young females.[12,14,22]

Young females had significantly better LV systolic function than young males, and angiographically less severe CAD reflected by less frequency of multivessel disease (30.5% vs 41% for young females vs males respectively) and lesser Gensini scores. These findings concur with previous studies.[12,14]Prior studies have reported that intracoronary stents have been used less frequently among young women with ACS, although the use of DES has been more frequent

among females or comparable among both genders.[12,22] On the contrary, in our study, significantly fewer young females received a DES (81.1% vs 96.8%, p=0.001), possibly due to financial constraints. Despite this, women have been shown to derive greater benefit from DES due to reduced intimal hyperplasia,[23] and as such, a greater use of DES should be advocated.

There was no significant difference between angiographic and procedural success between the two groups, which concurs with most prior studies wherein adverse outcomes were reported, despite comparable procedural success.[13,14] At 30 days, young females showed lesser clinical success owing to increased recurrent ischaemia, however, this was not statistically significant.

Young women had greater incidence of all the individual outcome variables studied, except stroke. They also had significantly higher rates of short-term composite adverse outcomes, predominantly due to significantly higher rates of recurrent ischaemia, bleeding and vascular access site complications. Significantly increased vascular access site complications was also observed in Lansky, et. al. (2004)[13] where 9.4% vs 2.3% was reported for young women vs men respectively. Argulian, et. al. (2006)[15] also observed similar outcomes (7.6% vs 3.5% for young women vs men respectively).

Bleeding complications in patients with ACS are a significant predictor of adverse outcomes, morbidity and mortality.[22] In particular, patients with STEMI constitute a high-risk subset of acute patients requiring urgent revascularisation on a background of aggressive pharmacological treatment including intravenous (IV) anticoagulation, IV glycoprotein IIb/IIIa inhibitors, thrombolysis and DAPT. As such, ACS patients undergoing PCI are more prone to vascular access complications which represent a source of major bleeding.

Multiple previous studies have also observed increased bleeding and vascular complications among young women, particularly those undergoing PCI for STEMI.[14,15,25,] Such increased bleeding risk has been attributed to decreased coagulation reserve, potential overdose of anticoagulant or antiplatelet agents, and differences in platelet biology of women.[15,26] Several studies have also found that younger women were more likely than men to experience peri-procedural complications such as coronary dissection and abrupt vessel closure, possibly attributable to their smaller vessel size leading to difficulty in vessel manipulation and increased susceptibility to mechanical vessel injury.[15,17,26] Young females showed a non-significant increase in such peri-procedural complications in our study. Furthermore, young women had significantly smaller coronary arteries as reflected by the smaller diameter stents implanted in them (2.7±0.3mm vs. 2.9±0.4mm for males). Chandrasekhar, et al. (2016) also reported smaller stent diameters (2.94±0.5 vs. 3.1±0.5mm for females and males respectively).[12] Smaller stent diameter was also a significant predictor of poor outcome on multi-variate logistic regression analysis in this study.

Estrogen, traditionally known to exert a protective effect on vascular endothelial function in pre-menopausal women, has also been suggested as a possible reason for the increased risk of vascular injury complications in younger women, given that most women <55 years old are premenopausal.[15] Estrogen may increase the level of various coagulation factors and inflammatory markers and affects vascular endothelial function and its reaction to circulating vasoactive factors. Alternatively, the protective influence of estrogen may be over-ridden by the presence of risk factors, particularly diabetes, resulting in worse outcomes for young women with ACS compared with young men.[15] (Argulian, et al., 2006). Further studies on the presence of specific estrogen receptors and their relationship with adverse outcomes among women are warranted.

At 30 days follow up, young females reported significantly more repeat hospitalisation (6.3% vs. 1.1%, p=0.04) most likely due to significantly higher recurrent ischaemia (7.4% vs. 2.1%). Some authors have postulated that the morbidity of angiographically non-obstructive (i.e. non-atherosclerotic) CAD is greater in women, leading to recurrent angina and adverse outcomes.[23,27]

Young females had greater incidence of combined in hospital and 30-day major adverse cardiac events (MACE) in our study (4.1% vs 2.1% for young women and men respectively), which was not statistically significant (p=0.4). Lansky, et al. (2004) also observed no significant difference in major in-hospital complications constituting MACE (3.1% vs 0.6% respectively).[13] Neither did Argulian, et al. (2006) who found rates of 4.1% vs 4.0% for males and females respectively.[15] Abramson, et al. (2003) reported an adjusted relative risk of 1.78 for increased in-hospital mortality post PCI for females over males.[17] Srinivas, et al. (2007) reported a statistically significant increase of post-PCI in-hospital mortality following acute MI in young females (0.42% vs. 0.05%; p=0.0007), with female sex found to be an independent predictor of MACE.[14] Chandrasekhar, et al. (2016) reported a 90-day MACE of 9.6% for young females in comparison to 7.6% for young males.[12] In contrast to the above studies, a recent Indian study by Patted, et al. (2017) reported an insignificant increase in MACE among young males undergoing PCI in a predominantly ACS sample population.[16]

Consequent to a significantly greater bleeding risk and insignificant increase in MACE, both groups were evaluated for net adverse clinical events (NACE), a term first defined in the HORIZONS-AMI study, and found that women had significantly higher incidence of short-term NACE (10.5% vs 3.2%, p=0.04), largely owing to their increased rates of major bleeding.

On multivariate logistic regression analysis, this study showed that hypertension, diabetes, reduced ejection fraction, smaller stent diameter and female gender were independent predictors of adverse short-term outcomes in ACS patients after PCI. Both Srinivas, et al. (2007) and Lansky, et al. (2004) in their studies found that female gender was an independent predictor of mortality, vascular complications and MACE.[13,14] The presence of greater co-morbidities among females is a contributing factor to their adverse outcomes, as observed by Chandrasekhar, et al. (2016).[12] There are many differences in mechanisms of ACS and plaque characteristics between young males and females that may be attributed to such differences in post-PCI outcome (Chandrasekhar and Mehran, 2016).[23] These biological differences in atherosclerosis between men and women have not been entirely clarified, and further studies using intravascular ultrasound (IVUS) and optical coherence tomography (OCT) may be helpful in defining predictors of gender-based adverse outcome among young patients.

In addition to female gender, risk factors such as hypertension and diabetes mellitus also emerged as independent predictors of adverse outcome among young ACS patients undergoing PCI. Young females with ACS are known to present with a greater clustering of these risk factors in comparison to young males, and the presence of such co-morbidities, rather than female gender per se may have been responsible for their increased incidence of adverse cardiovascular outcome. Alternatively, the fact that young women have more hypertension and diabetes could also mean the presentation of ACS itself is more often than not, complicated by these co-morbidities in young women, and could be considered as a holistic clinical entity leading to adverse outcomes, rather than separate disease processes. Having said that, in order to overcome this limitation, further studies with matching of the number of hypertensive and diabetic patients among the two genders are warranted, to independently test purely for the effect of gender on adverse outcome after PCI.

Limitations:

This study was not without limitations. The study population was relatively smallsingle center study.Sampling method was non-random, so there was risk of selection bias.It was not a single operator study, therefore there may be variation in outcome according to operator expertise.

Conclusion:

This study demonstrated that young women presenting with ACS had significantly more short term adverse outcomes after PCI than young men. Despite angiographically less severe CAD, young women had significantly increased rates of recurrent ischaemia and repeat hospitalisation. They also had higher rates of MACE including death, although not statistically significant. Young women had significantly higher rates of bleeding and vascular complications, in comparison to young men, resulting in significantly greater incidence of NACE, a composite of MACE and major bleeding. Female gender, diabetes, hypertension, decreased ejection fraction and smaller stent diameter were identified as independent predictors of adverse short-term outcomes.

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Original Article

Clinical Characteristics and Angiographic Profile of Acute Coronary Syndrome Patients in a Tertiary Hospital of Bangladesh

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Abstract

Aims: Coronary artery disease is a devastating disease precisely because an otherwise healthy person in the prime of life may die or become disabled without warning. The objectives were to study the clinical profile, risk factors prevalence, angiographic distribution and severity of coronary artery stenosis in acute coronary syndrome (ACS) patients admitted in Cardiology Department of Dhaka Medical College Hospital, Dhaka. Materials and Methods: A total of 800 patients of ACS were analyzed for various risk factors, angiographic patterns and severity of coronary artery disease at DMCH, Dhaka, Bangladesh. Results: Mean age of presentation was 51.27±8.80 years. Majority were male 628 (78.5%) and rest were females (21.5%). Most patients had ST elevated myocardial infarction (STEMI) 509 (63.6%) followed by non-STEMI (NSTEMI) 207 (25.9%) and Unstable Angina (UA) 84 (10.5%). Risk factors: smoking was present in 388 (48.5%), hypertension in 289 (36.13%), diabetes in 235 (29.38%), dyslipidaemia in 169 (21.13%) and obesity in 356 (44.5%) patients. Single-vessel disease was present in 30.32% patients, Double-vessel disease was present in 23.23% patients and Triple vessel disease was present in 27.15% patients. Conclusion: STEMI was the most common presentation. ACS occurred earlier in comparison to Western population. Smoking was most prevalent risk factor. Diabetic patients had more multivessel disease.

Key words: Acute Coronary Syndrome, Angiogram, Bangladesh.

(Bangladesh Heart Journal 2018; 33(1): 10-15)

Introduction:

Coronary artery disease is a global health problem reaching an epidemic in both developed and developing countries and is the leading cause of mortality and morbidity worldwide[1,2]. In 1990 coronary artery disease accounted for 28% of world's 50.4 million deaths and 9.7% of the 1.4 billion lost disability adjusted life years. By 2020 the world's population will grow to 7.8 billion and 32% of all deaths will be caused by coronary artery[3]. The South Asian countries have among the highest incidence of coronary artery disease globally[4]. Estimates from the global burden of disease study suggests that by the year 2020, this part of the world will have more individuals with atherosclerotic coronary artery disease than in any other region[4, 5]. Data related to different aspects of CAD in Bangladesh are inadequate but it is highly prevalent in Bangladesh[6]. While the death rates related to CAD have been declining for the past three decades in the west, these rates are rising in

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37018

Bangladesh. In the last three decades, the prevalence of CAD has increased from 1.1% to about 7.5% in urban population of Delhi, India and from 2.1% to 3.7% in the rural population[7]. In Asian Indians, CAD tends to occur at a younger age with more extensive angiographic involvement[8] contributed by genetic, metabolic, conventional and nonconventional risk factors[9,10]. The objectives of this retrospective study were to study the clinical profile, prevalence of risk factors and distribution of coronary artery stenosis in acute coronary syndrome (ACS) patients admitted in Cardiology Department of Dhaka Medical College Hospital, Dhaka.

Materials and Methods:

Eight hundred patients presented to Cardiology Department of Dhaka Medical College Hospital with first episode of ACS were analyzed. The clinical presentations of patient were categorized as unstable angina (UA), non-ST elevated myocardial infarction (NSTEMI) and STEMI according to American College of Cardiology/American Heart Association (ACC/AHA) definitions and treated as per ACC/AHA recommendations[11,12]. Patients with concomitant valvular heart disease or cardiomyopathy were excluded from this study.

The following data were included for analysis: Age, gender, CAD risk factor profile, current cigarette/ bidi smoking history; dyslipidemia defined as the presence of any of the following: patients on lipid lowering drugs or total cholesterol >240 mg/dl, triglycerides (TG) >150 mg/dl, low-density lipoprotein >130 mg/dl, and high-density lipoproteins (HDL) <50 mg/dl for female and <40 mg/dl for male; diabetes mellitus with symptoms of diabetes and plasma glucose concentration e”200 mg/dl (11.1 mmol/L) or fasting blood sugar e”126 mg/dl (7.0 mmol/L) or 2-hours post-prandial glucose e”200 mg/dl (11.1 mmol/L); hypertension (systolic blood pressure e”140 and/or diastolic e”90 mmHg and/or on anti hypertensive treatment); family history of CAD (first degree relatives before the age of 55 years in men and 65 years in women); obesity defined using the body mass index (BMI) with a value >25.

Clinical manifestations, left ventricular ejection fraction, hematologic indices, coronary angiographic findings and treatment strategy were reported. Selective coronary angiogram was done using standard technique. Expert opinion on coronary angiography was taken by two cardiologists. Significant CAD was defined as a diameter stenosis >70% in each major epicardial artery. Normal vessels were defined as the complete absence of any disease in the left main coronary artery (LMCA), left anterior descending (LAD), right coronary artery (RCA), and left circumflex (LCX) as well as in their main branches (diagonal, obtuse marginal, ramus intermedius, posterior descending artery, and posterolateral branch). Patients were classified as having single-vessel disease (SVD), double-vessel disease (DVD) or triple vessel disease (TVD) accordingly.

Statistical analysis

The results were reported as mean ± standard deviation for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student’s *t*-test for the continuous variables and the Chi-square test for the dichotomous variables. $P < 0.05$ were considered as statistically significant. All the statistical analyses were carried out via Statistical Package for Social Sciences version 20 (SPSS, IL, Chicago Inc., USA).

Results:

Among 800 ACS patients majority were male 628 (78.5%) and 172 (21.5%) were female. The mean age of presentation was 51.27±8.80 years. Most common presentation in ACS was STEMI with 509 (63.6%) patients followed by NSTEMI 207 (25.9%) and UA 84 (10.5%). Baseline characteristics are mentioned in Table 1.

Table-I

Baseline characteristics of the study population (N = 800)

Variables	Minimum	Maximum	Mean
Age	16	88	51.27
Waist Circumference	45	172	90.36
Hip Circumference	40	185	106.82
FBS (mmol/l)	2.1	21	7.12
HbA1C	4.8	14	6.74
Total Cholesterol (mg/dl) (%)	78	400	177.69
LDL (mg/dl)	56	270	112.99
HDL (mg/dl)	18	71	37.40
TG (mg/dl)	83	1125	190.49
S creatinine (mg/dl)	0.38	2.30	1.60
ESR (mm in 1st hour)	7	85	26.55
Echocardiography (%)	22	78	53.29

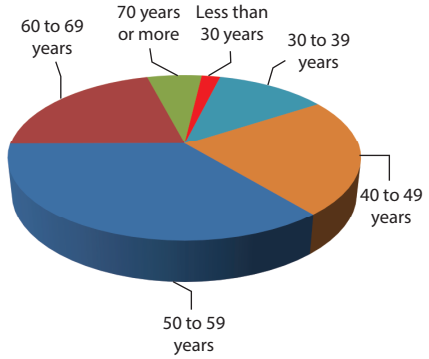

Fig.-1: *Age distribution of the study population (N= 800)*

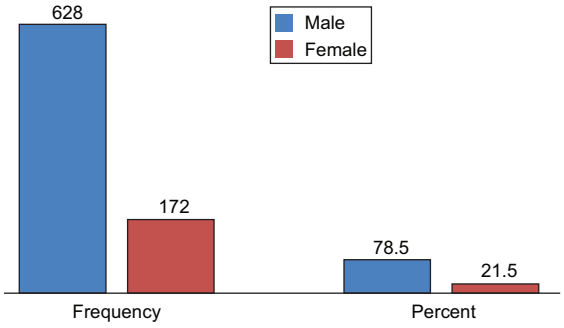

Fig.-2: *Distribution of study population according to sex (N=800)*

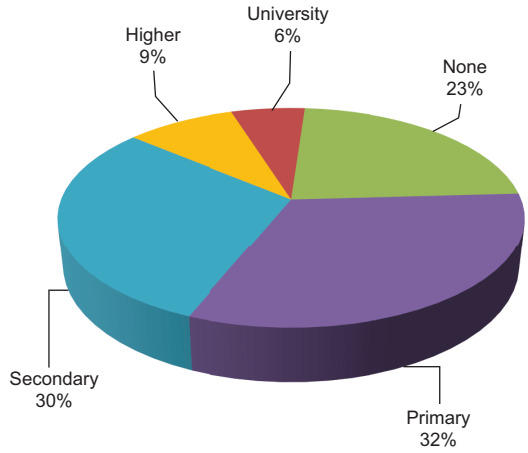

Fig.-3: *Distribution of study population according to educational status*

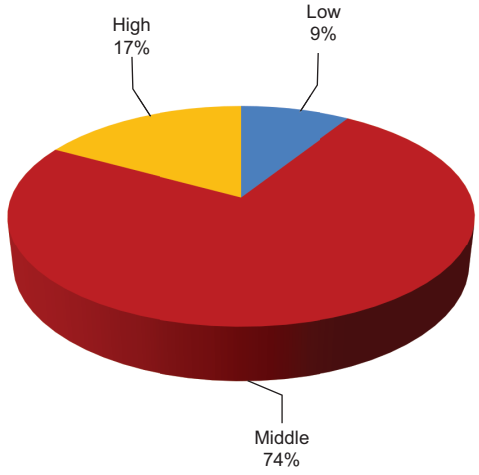

Fig.-4: *Distribution of study population according to level of income (N=800)*

Risk factors analysis

A total of 235/800 (29.38%) patients were diabetic and 289/800 (36.13%) patients were hypertensive. Smoking and tobacco users were 388/800 (48.50%) patients. Active smoking in our study was noticed only in male patients. Women were rather betel nut/tobacco leaf chewers. Dyslipidemia was present in 169/800 (21.13%) patients. Obesity in 356/800 (44.5%) patients and family history of CAD was significant in 25/800 (3.13%) patients. (Table 2)

Table-II

Distribution of study population according to clinical risk factors

Clinical Risk Factor	Frequency	Percent
Ischemic Heart Disease	255	31.85
Family History of CAD	25	3.13
Obesity	356	44.5
Diabetes	235	29.38
Hypertension	289	36.13
Previous PTCA	21	2.62
Smoking & tobacco use	388	48.5
Previous CABG	12	1.54
OCP	36	4.46
Dyslipidemia	169	21.13
Menopause	32	4.00
Alcohol	5	0.62

Angiographic profile

SVD was seen in 30.32% patients, DVD in 23.23% patients, TVD in 27.15% patients, normal coronary vessels in 17.19% and nonsignificant lesion were seen in 2.11% patients out of 800 patients.

Table-III

Distribution of study population according to extent of disease

Extent of Disease	Frequency	Percent
Single Vessel	243	30.32
Double Vessel	186	23.23
Triple Vessel	217	27.15
Normal Coronaries	137	17.19
Insignificant CAD	17	2.11

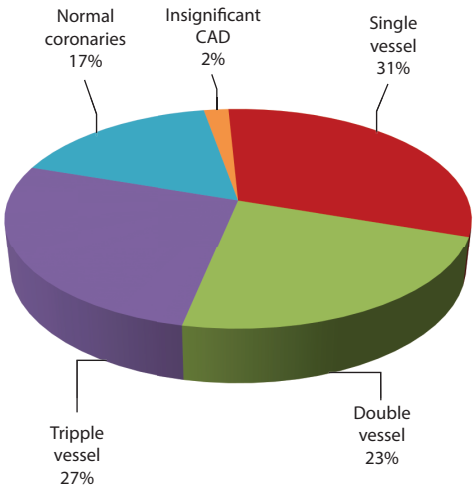

Fig.-5: *Distribution of study population according to extent of disease*

Discussion:

Epidemiological studies have revealed that the prevalence of CAD is increasing along with the rising prevalence of conventional risk factors for CAD in Bangladesh[31]. Present health transition from predominance of infections to the preponderance of cardiovascular disorders, such as hypertension, diabetes and CAD is now responsible for 53% of all deaths[10,13]. At present developing countries contribute a greater share to the global burden of cardiovascular disease than developed countries[14]. The disease is very common in westernized population affecting the majority of adults over the age of 60 years. It is also rising in developing countries. This retrospective study was carried out at the Department of Cardiology, DMCH, Dhaka during the period of January 2016 and December 2017. Coronary artery disease tends to be more aggressive and manifests at a younger age[15]. The mean age of the study population was 51.27±8.80 years as compared to 52±10.8 years in a study reported by Maqbool Jafary et al[16] and 58±11 years by Sahed et al[17] in Pakistan and 62±5 years in COURAGE trial[18] conducted in USA. It is also similar to the study done by Islam AEMM et al[19] where the mean age in male was 51±9.8 and female 47.2±9.67. This signifies that Bangladeshi patients are relatively younger as compared to the western people. The skewed gender distribution (males 78.5% versus females 21.5%) of the study population can be attributed to the gender bias and atypical presentation, which is also a feature in INTERHEART study and its South Asian cohort (overall male, 76% and South Asian cohort, 85%)[20]. The study showed that the prevalence of diabetics was 29.38%, which is higher than the reported prevalence in INTERHEART study but near to other Indian studies (CREATE, Jose and Gupta)[10,21]. Diabetes mellitus alone was a risk factor in 7.13% patient and combined with hypertension and diabetes mellitus were been in 22.25% patients. Diabetes mellitus is well known to have an adverse influence on the prognosis of patients with acute myocardial infarction[22]. Majority of the patients suffered from TVD (40.66%) which was also higher in Akanda et al[23] (42.11%) conducted in Bangladesh. Hypertension is another conventional risk factor implicated in CAD. In this study 36.13% patients were hypertensive. The prevalence of hypertension in South Asian cohort of INTERHEART study[16] (31.1%) is comparatively lower than this study but is similar to Akanda et al[23] (35%). The higher prevalence of diabetes and hypertension in this region could be explained by the comparatively higher development and increasing epidemic of CAD[24]. Tobacco smoking is a known modifiable risk factor for CAD. In our study, 388 (48.5%) patients were smoker or tobacco leaf/betel nut chewers. All reported data show that smoking is the commonest risk factor encountered in patients with acute myocardial infarction[25,26]. The male preponderance and smoking being the major risk factors has been well documented in many studies in this subcontinent[27,28,29,30]. However in contrast to this study, smoking is not a major risk factor in the COURAGE trial (29% vs 60%). The prevalence of obese patients was only 44.5% which is less than the prevalence seen in South Asian cohort of INTERHEART study (44.2%). Single-vessel involvement was 30.32% in all groups of ACS including UA, NSTEMI and STEMI, followed by triple-vessel (27.15%) and double vessel disease (23.23%). Akanda et al[23] also showed more single vessel involvement. Angiographically, the absolutely normal vessels were present in 14.25% cases have been attributed to complete recanalization whether spontaneously or post-thrombolysis. The study limitations include the noninclusion of factors like detailed dietary habits, exercise frequency and substance abuse.

Conclusion:

CAD is highly prevalent in Bangladesh, as well as is a major health challenge for us. Despite decrease in cardiovascular disease mortality in developed countries, substantial increases have been experienced in developing countries like ours. Along with the classical risk factors, genetic make-up and environmental factors unique to our population may contribute. The rapid changes in lifestyle, unhealthy habits (smoking, sedentary life style etc.), dietary factors, economic development and higher prevalence of diabetes and hypertension are considered to be responsible for the increase of mortality. Overall, SVD was most prevalent in ACS patients. Diabetic patients had more multi-vessel disease than non-diabetics. Hence large-scale, preferably,

nation-wide survey and clinical research should be conducted to determine the different aspects of CAD in Bangladesh as well as to identify the magnitude of problem and timely primary and secondary prevention strategies should be vigorously pursued.

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Original Article

Preoperative Aspirin Use and Outcomes in Off-pump Coronary Artery Bypass Grafting Surgery

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Abstract:

Introduction: Aspirin, the most widely used platelet function inhibitor extremely effective at blocking the production of thromboxane in platelets, rendering the platelets incapable of functioning normally, and thus preventing thrombosis. The practice of empirically discontinuing aspirin preoperatively should be abandoned because evidence strongly supports continued use of aspirin in patients for secondary prevention of CAD, CVD, or PVD when undergoing surgery.

Methods and Materials: This Observational study was conducted at Department of Cardiac Surgery, NICVD, Dhaka, who underwent off pump CABG (OPCAB), divided in two groups, Group A: 24 patients who stopped and Group B: 24 patients who are continuing aspirin throughout the perioperative period. Post operative blood loss, requirement of blood transfusion, post-operative MI, ICU stay, Total hospital stay (days) and early post-operative complication (Stroke, New arrhythmia in ECG, 30 days mortality) were recorded and included in the study.

Results: The key finding of the present study is that preoperatively continued aspirin use was not associated with increased risk of post-operative blood loss, blood transfusion requirements and need for re exploration after OPCAB.

Conclusions: Preoperative aspirin therapy should be continued till off-pump CABG without interruption.

Key words: Aspirin, Coronary Artery Bypass, Off-pump.

(Bangladesh Heart Journal 2018; 33(1): 16-21)

Introduction:

The platelet is integral to the initiation of thrombosis. Platelets are anucleate cells produced daily from bone marrow megakaryocytes and have a lifespan of 8 to 10 days.[1] Drugs that affect platelet function are a fundamental part of primary and secondary management of atherosclerotic thrombotic disease.

Aspirin, the most widely used platelet function inhibitor mediates its effects through the arachidonic acid (AA) - thromboxane A_2 (TxA_2) pathway. The conversion of AA to prostaglandin occurs throughout the body and is catalyzed by the enzyme cyclooxygenase (COX). There are 2 isoforms of COX, termed COX-1 and COX-2. Aspirin irreversibly inactivates COX through acetylation of the amino acid serine, with a 170-fold affinity for COX-1 over COX-2. By inactivating COX-1, aspirin renders the platelet incapable of synthesizing prostaglandin H_2. Consequently, aspirin is extremely effective at blocking the production of thromboxane in platelets, rendering the platelets incapable of functioning normally, and thus preventing thrombosis and the damaging cardiovascular events that may result.[2]

Aspirin may further diminish the risk of cardiovascular disease through its ability to decrease inflammation by blocking C-reactive protein, although this benefit probably only occur at higher doses than those used clinically.[3]

Surgical intervention induces a catecholamine surge which in turn augments inflammation and platelet reactivity, the

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37019

link between peri-operative stressors and inadvertent thrombosis becomes more clear.[4] Moreover, it has been demonstrated that this catecholamine-induced platelet reactivity is only partly counteracted by aspirin therapy.[5]

A growing body of evidence supports a platelet rebound phenomenon in the setting of acute aspirin withdrawal. This rebound period is characterized by increased thromboxane production, decreased fibrinolysis, and a resultant clinical prothrombotic state.[6]

On the basis of the available evidence, the practice of empirically discontinuing aspirin preoperatively should be abandoned. The evidence strongly supports continued use of aspirin in patients on it for secondary prevention of CAD, CVD, or PVD when undergoing surgery. Routine discontinuation of aspirin 7 to 10 days preoperatively is not only unjustified but likely significantly compounds patient's thromboembolic risk because of the described aspirin withdrawal syndrome that occurs contemporaneously during this time interval. For an at-risk patient, the hypercoagulable state engendered by the surgical procedure compounded by the aspirin withdrawal syndrome creates an ideal scenario for a major cardiac or vascular thromboembolic complication.[7]

In 2010, the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery recommended that preoperative aspirin should not be stopped[8] and in 2011, the American College of Cardiology Foundation and the American Heart Association guideline for coronary artery bypass grafting (CABG) recommended that aspirin (100 to 325 mg daily) should be administered to CABG patients preoperatively.[9] Some well-conducted studies have shown that aspirin use before coronary artery bypass procedures is safe without an associated increase in hemorrhage-related risks and could reduce in-hospital mortality.[10]

The relationship of aspirin to graft patency after conventional CABG has been studied extensively at both the clinical and the pathophysiologic levels, and it is generally accepted as established fact that aspirin therapy increases graft patency.[11]

Tuman and his colleagues compared perioperative use of aspirin versus placebo in patients undergoing coronary artery bypass graft (CABG). They found no significant differences in postoperative hematocrit, mediastinal bleeding, transfusion requirements and need for re exploration.[12] Srinivasan and his colleagues retrospectively examined and found similar result.[13]

However, few published data have evaluated the effect of preoperative continuation of aspirin therapy on perioperative graft patency after off-pump coronary artery bypass (OPCAB). OPCAB has offered a promising alternative strategy that had the potential to decrease perioperative morbidity, mortality, and cost by eliminating cardiopulmonary bypass, but there is growing concern that OPCAB is associated with reduced graft patency. Platelet inhibition with aspirin has been shown to reduce the rates of acute and sub-acute bypass graft occlusion.

To evaluate the potential effects of preoperative continuation of aspirin therapy in patients undergoing OPCAB, we performed this study.

Materials and Methods:

This observational study was conducted at Department of Cardiac Surgery, NICVD, Dhaka from July 2015 to July 2016. Total 48 patients who will undergo OPCAB were selected for the study divided in two groups, Group A: 24 patients who stopped Aspirin 5 days before operation and Group B: 24 patients who are continuing aspirin throughout the perioperative period. Patients were excluded from the study if there is history of MI within 6 weeks, hepatic dysfunction, renal dysfunction, Redo CABG, combined CABG and conversion CABG. Patient taking anticoagulant, patient with history of stenting and patient requiring end-arterectomy were also excluded from the study. Detailed history of each patient under study and important and relevant findings on thorough physical examinations and investigations were recorded. A standard anesthetic and heparin protocol used throughout the study. All patients was routinely given aspirin 75 mg daily postoperatively, with the first dose of aspirin (75 mg) being administrated on the operative day 6 hrs after operation. Following the surgical procedure, all the patients were brought to the Cardiovascular ICU where they were monitored until extubation and stabilization of respiratory and hemodynamic status. Then the patients were transferred to the HDU from there to the ward for routine care. The patients were discharged from the ward and advised for subsequent follow up after 1 month and 3 month.

Post operative mediastinal bleeding, requirement of blood transfusion, need for re exploration, post-operative MI, ICU stay, Total hospital stay (days) and early post-operative complication (Stroke, New arrhythmia in ECG, 30 days mortality) were recorded and included in the study. Statistical analysis of the results was done by SPSS. The results were presented in Tables, Figures and Diagrams etc.

Results:

The present study is intended to assess short term outcome of perioperative continuation of aspirin in patients undergoing OPCAB. A total of 48 (forty eight) patients were recruited for the purpose of the study. The recruited patients were

assigned into two groups according to their preoperative aspirin use. Group A patients (without aspirin, n=24) consists of patients stopped aspirin 5 days before operation. Group B patients (with aspirin, n=24) consists of the patients who have continued aspirin. Postoperative mediastinal bleeding, required amount of blood transfusion, peri and post-operative other parameters were measured in both the groups. The findings of the study obtained from data analyses are presented below.

Table-I

Pre-operative variable

	Group I (n=24)	Group II (n=24)	p-value
Age (years)	52.96±10.02	52.67±8.28	.913
Male	20(83.4%)	22(91.74%)	.383
Female	4(16.66%)	2(9.34%)	
Hypertension	13(54.16%)	14 (58.33%)	.77
Diabetes mellitus	10(41.17%)	10(41.17%)	1.00
Dyslipidemia	19 (79.16%)	17(70.83%)	.44
Haematocrit (%)	38.83±3.49	37.08±8.68	.364
Bleeding time (min)	4.45±1.10	4.43±1.10	.803
Clotting time (min)	5.6±0.88	5.57±.87	.916

Table I shows that the age of the patients undergoing OPCAB ranges from 35 years to 65 years. But most of the patients were in the range of 46 to 60 years (Group A 58.38%, Group B 62.52%). Moreover there was no statistical significant difference between the groups in terms of age (p>0.05). There was no significant difference between the groups in terms of sex. But shows that there is a male dominance among the patients group A (83.3% against 16.66%) and group B (91.74% against 9.34%). Patients in both the groups were statistically identical according to the base line clinical characteristics. Prevalence of diabetes mellitus were almost similar in both group (Group A 41.17% vs Group B 41.17%), Regarding hypertension, dyslipidemia Group A and Group B were almost similar (54.16 % to 58.33%, p=1.00 ; 79.16% to 70.83%, p=.44).

There was no statistically significant difference among the patients Haematocrit, Bleeding

Time and Clotting time in minutes (38.83±3.49 vs 37.08±8.68; p = .364, 4.45±1.10 vs 4.43±1.10, p = .803; 5.6±0.88 vs 5.57±.87, p = .916 respectively).

In pre-operative echocardiographic study left ventricular ejection fraction were studied in all patients. LVEF was divided into two groups. One was more than 50% and other was less than 50%. In group A more than 18 (75%) of the patient had LVEF <50 and 6 (25%) had LVEF>50. In Group-B 17 (70.8%) patient had LVEF < 50 and 7 (29.2%) patient had LVEF > 50. But there was no significant difference in LVEF among the groups.

Pre-operative angiogram shows that there was also no significant difference between the two groups, most of the patients have triple vessel disease, 16 (66.66%) in Group – A and 15 (62.5%) in Group - B.

There was no significant difference between the two groups with regard to operative time, most of the operations perform 4.5 hrs to 6.5 hrs, Group A and Group B respectively 5.60±0.91 & 5.40±0.71. Difference between the two groups with regard to number of graft also not significant but most of the patients given three grafts (Group A 75.06% vs Group B 84.33% respectively). There is no significant difference between 2 groups with regards to activated clotting time, most of the reversal done at 100 – 120 seconds, 91.6 % and 87.5% in Group A and Group – B respectively.

Table-II

Post-operative bleeding and blood transfusion

	Group I	Group II	P – value
Up to removal of DT (ml)	643.33±36.67	648.33±37.61	.643
Blood Transfusion	1.16±0.38	1.12±.33	.69
Reoperation for bleeding	Nil	Nil	N/A

Average amount of bleeding measured at the end of 24 hours and then up to removal of drain tubes. There was no significant difference between the two groups with regard to bleeding. At 24 hours 371.67±72.15 ml blood loss measured in Group A and 370.83±71.98 ml in Group –B. During removal of drain tube total 643.33±36.67 ml and 648.33±37.61 ml in Group-A and Group-B respectively. Shows there was no significant difference between the two groups with regard to blood transfusion. Most of patients needed 1 unit blood transfusion in both group (Group A 83.4% vs Group B 87.57%). No patient required reoperation for bleeding. (Table II).

Table-III

Post-operative ECG changes

	Group I	Group II	P – value
Normal	22(91.74%)	23(95.91%)	.221
Q Wave	2 (8.34%)	1 (4.17%)	
ST changes	2 (8.34%)	1 (4.17%)	
New arrhythmia	6 (25.022%)	5 (20.85%)	.731

Post-operative ECG changes shows there was no significant difference between the two groups. Most of patients have normal ECG Group A 91.74% vs Group B 95.91% respectively. ST elevation appears in 2 (8.33%) patients in Group A and 1 (4.16%) patients in Group B. Q wave appears in 2 (8.33%)

patients in Group A and 1 (4.16%) patients in Group B. There was no significant difference between the two groups with regard to new arrhythmia (Group A 25.02% & Group B 20.85%). Post-operative trop I level difference was also non-significant between 2 groups. (Table III)

There was no significant difference between the two groups with regard to ICU stay. But most of the patients stayed 4 days, Group A 83.4% vs Group B 79.23% respectively.

Hospital stay was also not significant between the two groups. But most of patients released less than 10 days (Group A 70.89% vs Group B 75.06%).

Table IV
Follow-up variable

	Group A (n=24)	Group B (n=24)	p-value
30 day mortality	1(4.16%)	0	.074
Ejection Fraction			
1 month	46.66±3.97	46.04±4.65	.633
3 month	55.9±3.7	54.79±4.77	.392
Postoperative complication			
Thromboembolism	Nil	Nil	N/A
DVT	Nil	Nil	N/A
CVA	Nil	Nil	N/A

There was no significant difference between the two groups with regard to 30 days mortality. 1 patients died within 30 days in Group-A. No mortality in Group B aspirin users. There was no significant difference between the two groups with regard to ejection fraction 1 month after discharge. There was no incidence of thromboembolism, DVT or CVA in either group seen upto 3 months of followup. (Table IV)

Discussion:

The effect of preoperative aspirin administration remains unclear in off-pump CABG. With an increasing volume of Off-pump CABG performed in Asian countries which accounts for at least 60% of all the CABG. In consideration of the significant differences in term of postoperative coagulation system between off-pump CABG and on-pump CABG, it is essential to evaluate the preoperatively continued aspirin use until surgery in OPCAB patients.

The age of the patients undergoing OPCAB ranges from 35 years to 65 years. But most of the patients were in the range of 46 to 60 years (Group A 58.38%, Group B 62.52%). Mean ±SD age of the study subjects was 52.96±10.02 and 52.67±8.28 years in Group-A and Group-B respectively which was not statistically significant (p>0.05). Hossain and his colleagues reported the mean age of patients undergoing OPCAB surgery to be 53.80±8.57 years which are similar to this study.

Male sex predominates among the study subjects (91.67% male against 9.33% female). Both the groups were comparable in respect of sex. Hossain S (2013) also reported a male preponderance in patients undergoing OPCAB surgery.

Baseline clinical characteristics in the study in both groups subjects are similar. Most of the patients were hypertensive, diabetic, dyslipidemic (54.16 % vs 58.33%, 41.17% vs 41.17% and 79.16% vs 70.83% respectively).

Xiao and his colleagues reported 35.3% and 36.8% prevalence of DM respectively in Group A and Group B, prevalence of preoperative hypertension were 65.5% and 68.4% in Group A and Group B respectively patients undergoing OPCAB surgery. Our study subjects were comparable in terms of preoperative patient characteristics and cardiopulmonary functional status. So postoperative clinical outcomes were not influenced by these factors.

Preoperative coagulation profiles of Group A and Group B patients were statistically identical. There was no statistically significant difference in haematocrit (38.8±2.34 vs 37.27±2.42%, p= 0.3964), bleeding time (4.24±0.48 vs 4.24±0.5 min, p= 0.965) and clotting time (5.89±0.42 vs 5.88±0.41 min, p= 0.958).

In pre-operative echocardiographic study left ventricular ejection fraction were studied in all patients. LVEF was divided into two groups. One was more than 50% and other was less than 50%. In group A more than 18 (75%) of the patient had LVEF <50 and 6 (25%) had LVEF>50. In Group-B 17 (70.8%) patient had LVEF < 50 and 7 (29.2%) patient had LVEF > 50. But there was no significant difference in LVEF among the groups.

Pre-operative angiogram shows that there was also no significant difference between the two groups, most of the patients have triple vessel disease, 16 (66.66%) in Group – A and 15 (62.5%) in Group - B.

Regarding per operative variables Group A and Group B total operation time is 5.89±0.25 vs 5.01±0.37 hours respectively and have no significant difference between the groups (p>0.05). As heparin used at the beginning of the operation were neutralized at the end of operation by protamine so they are identical in both groups. Total operation time is standard for our country.

Difference between the two groups with regard to number of graft also not significant but most of the patients given three grafts (Group A 75.06% vs Group B 84.33% respectively). Xiao and his colleagues shows the mean number of distal anastomoses were 3.3±0.8 in the patients group who discontinued aspirin for more than 5 days before

surgery versus 3.2±0.8 in the continued aspirin therapy group (p = 0.37). These are similar to our study.[14]

There is no significant difference between 2 groups with regards to activated clotting time, most of the reversal done at 100 – 120 seconds, 91.6 % and 87.5% in Group A and Group – B respectively.

Our study shows post-operative blood losses up to removal of drain tubes was 643.33±36.67 ml vs 648.33± 37.6 ml ; p=.643. In our study there was no significant difference between the two groups with regard to blood loss. Most of patients needed 1 unit blood transfusion in both group (Group A 83.4% vs Group B 87.57%) and also no patient required reoperation for bleeding.

Xiao and his colleagues shows there were no significant differences between preoperative non aspirin and aspirin therapy group with regard to postoperative blood loss (790 ml versus 800 ml, p = 0.60). Although not statistically significant, the rate for reoperation for bleeding was higher in aspirin users group (1.3% versus 2.4%, p = 0.11). There were no significant differences among the two groups in blood transfusion rate (24.4% versus 25.1%, p = 0.76) and transfusion requirements of red blood cells, platelets and fresh frozen plasma.[14]

Post-operative ECG changes shows there was no significant difference between the two groups. Most of patients have normal ECG Group A 91.74% vs Group B 95.91% respectively. ST elevation appears in 2 (8.33%) patients in Group A and 1 (4.16%) patients in Group B. Q wave appears in 2 (8.33%) patients in Group A and 1 (4.16%) patients in Group B. Although not statistically significant but little bit higher rate of ST elevation and Q wave found in Group –A (non aspirin group) .There was no significant difference between the two groups with regard to new arrhythmia (Group A 25.02% & Group B 20.85%). Post-operative trop I level difference was also non-significant between 2 groups.

There was no significant difference between the two groups with regard to ICU stay. But most of the patients stayed 4 days, Group A 83.4% vs Group B 79.23% respectively.

Hospital stay was also not significant between the two groups. But most of patients released less than 10 days (Group A 70.89% vs Group B 75.06%).

There was no significant difference between the two groups with regard to 30 days mortality. About 1 patients died within 30 days in Group-A. No mortality in Group B aspirin users. There was no incidence of thromboembolism, DVT or CVA in none of the patients in either group. Xiao and his colleagues shows there were no significant differences between preoperative nonaspirin and aspirin therapy group with regard to in-hospital mortality (0.1% versus 0.1%, p = 1.00), stroke (0.1% versus 0.3%, p = 1.00) and other thromboembolic manifestation .[14]

Bybee and his colleagues shows thirty-six of the total 1636 patients (2.2%) died in-hospital after coronary bypass surgery. Of the 1316 patients receiving preoperative aspirin therapy, 22 died in-hospital after surgery whereas 14 of the 320 patients not receiving preoperative aspirin therapy died in-hospital after surgery. This resulted in an observed 61% relative reduction in all-cause in-hospital mortality in patients receiving preoperative aspirin therapy (1.7% versus 4.4%) with a univariate OR of 0.37 (95% CI, 0.19 to 0.74; *P*_0.004) for mortality). Patients receiving preoperative aspirin were less likely to die of cardiovascular causes (0.5%) compared with those not receiving preoperative aspirin (2.2%). There was no increased risk of reoperation for bleeding in those receiving preoperative aspirin therapy (3.5% versus 3.4%; OR, 1.02; 95% CI, 0.52 to 1.99; *P*_0.96). There was a trend toward an increased need for postoperative blood product transfusion in the aspirin group, which did not reach statistical significance (OR, 1.25; 95% CI, 0.98 to 1.60; *P*_0.07). There was no significant difference in the rates of postoperative adverse cerebrovascular events in those receiving preoperative aspirin compared with those not receiving preoperative aspirin by univariate analysis (2.7% versus 3.8%; OR, 0.72; 95% CI,0.37 to 1.40; *P*_0.34).[10]

Multiple studies support the safety of low-dose aspirin continuation in the context of cardiac surgery. Tuman and his colleagues compared perioperative use of aspirin versus placebo in patients undergoing reoperation coronary artery bypass graft (CABG). Of 317 total patients, 215 patients had taken aspirin within 7 days of their procedure versus none in their 102 matched controls. They found no significant differences in postoperative hematocrit, mediastinal drainage, the need for reoperation, or transfusion requirements. [12]

Srinivasan and his colleagues retrospectively examined 170 aspirin users presenting for first time off-pump coronary artery bypass compared to 170 matched controls, using propensity matching. They found no differences in mean postoperative blood loss (845 mL vs 775 mL, *P* = 0.157), the rate of reoperation for bleeding (3.5% vs 3.5%, *P* > 0.99), blood product requirements, or in-hospital mortality.[13]

Sun and his colleagues published a review of the mixed evidence surrounding the risks and benefits of aspirin continuation up to the time of CABG surgery. They reported on 6 prospective studies that showed increased bleeding tendency with perioperative aspirin use, compared to 9 studies of varying methodologies (retrospective and

prospective) indicating that perioperative aspirin did not increase transfusion needs. Although the authors do not make a definitive conclusion, they summarize their article by stating that overall, the bleeding risk posed to a patient by continuing on low-dose aspirin (<325 mg) for CABG surgery is likely to be less serious than the risk of a thromboembolic event.

Conclusion:

Preoperatively continued aspirin use was not associated with increased risk of post-operative blood loss, blood transfusion requirements, reoperation for bleeding and composite outcome of in hospital death and stroke in OPCAB. Thus, on the basis of the present study, we recommend that preoperative aspirin therapy should be continued till OPCAB surgery without interruption.

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Original Article

In-hospital Outcome of Use of Low Molecular Weight Heparin in Patients Undergoing Percutaneous Coronary Intervention

Tariq Ahmed Chowdhury[1], Mustafizul Aziz[2], Iftekhar Alam[3], Abuduz Zaher[4], Sayed Azizul Haque[5], Abdul Wadud Chowdhury[6]

Abstract:

This prospective observational study was carried out in the Department of Cardiology of national institute of cardiovascular diseases (NICVD), Dhaka to assess the safety of low molecular weight heparin (LMWH) in patients undergoing percutaneous coronary intervention (PCI).

Safety of low molecular weight heparin in comparison to unfractionated heparin (UFH) was observed in this study. In total data from 100 patients undergoing elective PCI was evaluated. Among them 50 patients in group I received I mg/kg intra-arterial LMWH and rest in group II received UFH.

Demographic profile of individuals in both groups was almost similar. There was no significant difference in major coronary risk factors between the two groups. Patients were monitored during their stay in hospital for any complications like bleeding, haematoma, myocardial infraction and death. No death was observed in any group. Minor bleeding in group I and II (6% vs 105), Major bleeding (2% vs4%) and haematoma (6% vs 10%). Myocardial infraction no incidence in group I and 4% in group II. So complications was more prevalent in group II who were treated with UFH, but those were not statistically significant.

The intra-arterial administration of LMWH in patients undergoing PCI is safe. The risk of acute and sub-acute coronary events and bleeding complications are similar in both groups and in hospital outcome there is less complication with LMWH used during PCI.

Key words: Percutaneous Coronary Intervention, Heparin, Low-Molecular-Weight.

(Bangladesh Heart Journal 2018; 33(1): 22-27)

Introduction:

Unfractionated heparin is the standard choice of anticoagulant used during percutaneous coronary intervention (PCI). There are several recommendation regarding the use of intravenous unfractionated heparin with dose adjusted activated clotting time during PCI.[1, 2] Considering limitations of unfractionated heparin, which include it is sometimes difficult to manage effects of heparin on coagulation, the need for repeated monitoring of coagulation, the narrow therapeutic window, the potential induction of platelet activation, and the risk of thrombocytopenia better anticoagulation regimens are needed for PCI.[3]

As compared with unfractionated heparin, low-molecular-weight heparins (LMWHs) are considered to induce a more stable and predictable anticoagulant dose response thus removing the necessity for coagulation monitoring. LMWH have a longer half-life and a greater ratio of anti–factor Xa activity to anti–factor IIa activity, which reduces the generation

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37020

and activation of thrombin.[3] The important pharmacologic characteristics that distinguish LMWH from UFH include: greater bioavailability; minimal plasma protein and vessel wall binding; more predictable anticoagulant response; ease of subcutaneous and intravenous administration; and inhibition of acute phase release of von-Willebrand factor in acute coronary syndrome.[4]

LMWH have earned their place and established their superiority over UFH in the management of post-surgical deep vein thrombosis[5] and acute coronary syndrome (ACS) including unstable angina (UA) and non ST elevated myocardial infarction (NSTEMI).[6] The efficacy and safety of subcutaneous Enoxaparin a LMWH used in NSTEMI showed enoxaparin plus aspirin was superior to UFH plus aspirin in patients with ACS. The need for urgent revascularization was significantly lower in enoxaparin group. LMWH represent a major advancement in the management of patients with ACS or as part of the strategy in candidates undergoing coronary interventions.[7]

Several trials have shown that the LMWH enoxaparin offer the practical and potential pharmacologic advantages over UFH in multiple applications and logically should also provide a similar benefit during percutaneous coronary intervention (PCI).[8] However, during coronary and non-coronary interventions, UFH is conventionally used more frequently than LMWH. Data from randomized, controlled clinical trials support the administration of LMWH and/or platelet GP IIb/IIIa inhibitor in patients who represent with non ST elevation ACS.[9, 10]

Small or noncomparative trials have evaluated a single intravenous bolus of enoxaparin in different doses form, such as:1 mg, 0.75 mg or 0.5 mg[11, 12] per kilogram of body weight, in patients undergoing PCI with or without the administration of glycoprotein IIb/IIIa inhibitors. However, these uncontrolled studies have not allowed definite conclusions to be drawn about the efficacy of enoxaparin as compared with that of standard anticoagulation regimens involving unfractionated heparin. In a meta-analysis of data from randomized studies comparing intravenous low-molecular-weight heparins and intravenous unfractionated heparin in patients undergoing PCI, there was a nonsignificant trend toward a reduction in major bleeding with LMWHs and no difference between groups in the occurrence of ischemic events. In an additional analysis, a dose of less than 1 mg of enoxaparin per kilogram resulted in fewer ischemic and bleeding events than a dose of 1 mg per kilogram.[13]

The use of LMWH eliminates the need for continuous intravenous infusion, anticoagulation monitoring and dose adjustment associated with UFH.[8] Despite evidence-based support for administering LMWH and/or GP IIb/IIIa receptor blocker to patients undergoing PCI and those presenting with ACS, algorithms for integrating these agents into clinical practice have not been determined. The NICE trials have evaluated this issue in details and the results of these trials are likely to have a major impact on the choice of adjunctive therapy during PCI.[8]

The ease of intravenous use, good & predictable anticoagulation response and absence of monitoring need make LMWH enoxaparin a very affective choice for heparinization

during PCI. So this study is undertaken to assess the suitability and safety of intravenous LMWH to that of unfractionated heparin in patients undergoing elective PCI and to determine in hospital outcome regarding complications of UFH.

Method:

This prospective observational study was done in the department of cardiology of the national institute of Cardiovascular diseases (NICVD) during May 2004 to December 2004. Approval for the study was obtained from the institutional review board. All patients gave written informed consent. Patients undergoing percutaneous coronary intervention at NICVD were included in the study and depending on the type of heparin used patients were divided in two groups. In group I 50 patients were included who received intra-arterial LMWH e.g. Enoxaparine 1mg/kg during PCI. In group II 50 patients were included who received conventional UFH. Patients with Creatinine >2 mg/dl, Platelet count <100000 / mm^3 and with Liver disease (INR> 1.3) were excluded from the study.

All patients initially evaluated by history, physical examination, 12 Lead ECG, CK-MB, and echocardiography. Pre catheterization investigations including CBC, Clotting time, bleeding time, HBsAg, VDRL, anti HCV, anti HIV was done as required. Diagnostic angiogram and PCI was done as standard method. Patients were randomly assigned to receive an intravenous bolus of unfractionated heparin, adjusted for activated clotting time according to current guidelines or intravenous enoxaparin at a dose of 1mg per kilogram.[1] All patients received aspirin (300mg) and thienopyridines two hours prior to the procedure. Patients who were assigned to enoxaparin group received a single intravenous bolus of enoxaparin, without anticoagulation monitoring, after sheath insertion and immediately before PCI. When procedures were prolonged by more than 2 hours, an additional bolus of enoxaparin (half the original dose) was used.[14] Patients who were randomly assigned to receive unfractionated heparin were given an initial intravenous bolus of 10,000 IU after crossing the lesion with

guide wire to achieve a target activated clotting time of 300 to 350 seconds. Unfractionated heparin was re-administered during the procedure when measurements of activated clotting time dropped below the recommended range. Activated clotting time was measured with a standardized Hemochron device (ITC). Sheath removal was done in UFH group at an activated clotting time between 150 and 180 seconds, 4 to 6 hours after the end of PCI. In group I who received 1 mg of enoxaparin per kilogram no monitoring of anticoagulation was required before sheath removal and sheath was removed within 2 to 4 hours after the procedure.[15]

Post PCI continuous monitoring done during the whole hospitalization period. Follow-up for ischemic complication, bleeding events, abrupt closure, vascular events and death was monitored. The occurrence of major or minor bleeding during the first 48 hours after the index PCI, according to pre-specified definitions. Major bleeding: Fatal bleeding. Retroperitoneal, intracranial, or intraocular bleeding. Bleeding that causes hemodynamic compromise requiring specific treatment. Bleeding that requires intervention or decompression of a closed space to stop or control the event. Clinically overt bleeding, requiring any transfusion of ≥1 unit of packed red cells or whole blood, causing a decrease in hemoglobin of ≥3 g/dl or a decrease in hematocrit of ≥10%.

Minor bleeding: Gross hematuria not associated with trauma. Epistaxis that is prolonged, repeated, or requires plugging or intervention. Gastrointestinal hemorrhage Hemoptysis. Subconjunctival hemorrhage. Clinically overt bleeding, causing a decrease in hemoglobin of 2 to 3 g/dl. Hematoma >5 cm or leading to prolonged or new hospitalization. Death from any cause, nonfatal myocardial infarction (defined by a new Q wave in two or more leads or a total creatine kinase level or creatine kinase MB fraction that was ≥3 times the upper limit of the normal range during hospitalization for the index PCI or that was ≥2 times the upper limit of the normal range after discharge), or urgent target-vessel revascularization after the index PCI.[16]

All clinical, angiographic, procedural and follow-up data were prospectively recorded on pre-designed data collection sheet. 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 11.5). Probability less than 0.05 were considered significant.

Result:

In this study mean age of the patients in Group I was 57.04±9.27 years and Group II was 52.18 ± 9.40 years (P value > 0.05). The commonest age group of study patients for group I was 55-64 years age group and for the group II 44-54 years.

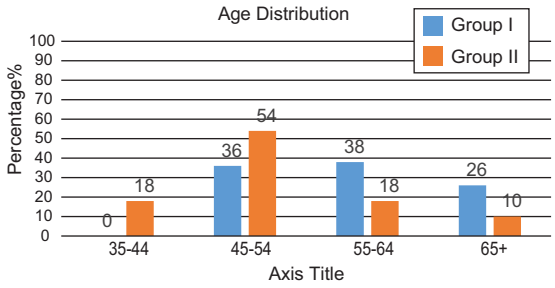

Fig.-1: *Age distribution of study population in percentage among the groups*

Smoking was the most common risk factor among the groups. Incidence of other risk factors were similar in between the groups.

Table-I

Distribution of risk factors in between the groups

Risk factors	Group I		Group II		P value
	n =50	%	n =50	%	
Hypertension	14	28	20	40	0.15^{NS}
Diabetes	10	20	05	10	0.13^{NS}
Smoking	44	88	37	74	0.06^{NS}
Family History of CAD	10	20	10	20	0.60^{NS}
Dyslipidemia	02	04	07	14	0.08^{NS}

Diagnosis of patients among group I was asymptomatic 6 (16%), chronic stable angina 12(24%), unstable angina 8(16%), NSTEMI 10(20%) and STEMI 12(24%).

Table-II

Distribution of groups on the basis of clinical diagnosis

Clinical Diagnosis	Group I		Group II		P value
	n =50	%	n =50	%	
Asymptomatic	08	16	07	14	0.20^{NS}
Chronic Stable Angina	12	24	23	46	0.08^{NS}
Unstable Angina	08	16	04	08	0.07^{NS}
NSTEMI	10	20	08	16	0.19^{NS}
STEMI	12	24	08	16	0.15^{NS}

Whereas in group II asymptomatic 7(14%), chronic stable angina 12(24%), unstable angina 4(8%), NSTEMI 10(20%) and STEMI 17(34%). There is no statistical difference between the groups (P value> 0.05).

In both the groups single vessel was treated in 75 patients and double vessel treated in 21 patients and triple vessel disease was treated in 4 patients.

Table-III

Distribution of the groups on the basis of involvement of number of coronary arteries

Coronary Artery	Group I		Group II	
	n =50	%	n =50	%
LM	00	—	02	04
LAD	25	50	23	46
LCX	04	08	06	12
RCA	14	28	11	22
RCA+LCX	01	02	01	02
LAD+RCA	05	10	05	10
LAD+LCX	01	02	02	04

Among single vessel treated in group I, most common vessel was LAD 25(50%) followed by RCA 14(28%) LCX 4(8%), and in group II, most common vessel was LAD 23(46%) followed by RCA 11 (22%), LCX 6 (12%) and LM 2(4%). Among the double vessel treated in group I, most common vessels were LAD & RCA 5(10%), LAD & LCX 1 (2%), RCA & LCX I (2%) and in group II, most common vessels were LAD & RCA 5(10%), LAD & LCX 2 (4%) and RCA & LCX 1(2%) (P value> 0.05).

In group I single stent was used in 38 (76%) patients double stents were used in 11(22%) and no stent was used in 1(2%) patients.

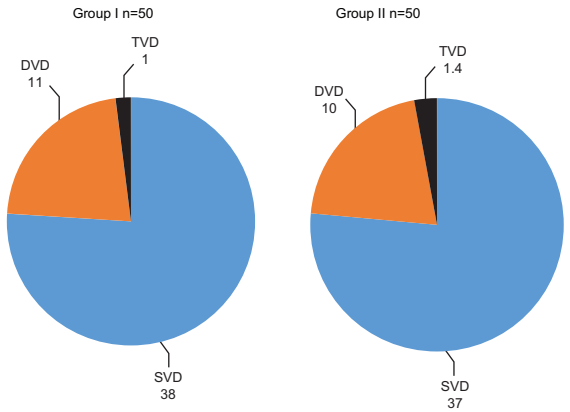

Fig.-2: *Distribution of the groups on the basis of number of coronary arteries treated with stents during PCI.*

However in group II single stent was used in 36(72%) patients, double stents were used in 12(24%) and triple stents were used in 2 (4%) patients. There is no statistical difference between the groups (P value> 0.05).

The incidence of post PCI complications was more prevalent in group II then group I. there was no incidence of death during the study period among the groups.

Table-IV

Distribution of the groups on the basis of post PCI complications

Clinical Diagnosis	Group I		Group II		P value
	n =50	%	n =50	%	
Minor Bleeding	03	06	05	10	0.35^{NS}
Major Bleeding	01	02	02	04	0.50^{NS}
Haematoma	03	06	05	10	0.35^{NS}
Myocardial infraction	00	00	02	04	0.35^{NS}
Death	00	00	00	00	—

None of the patients in group I suffered post PCI myocardial infarction but in group II 08 (16%) patients suffered from post PCI infarction. The prevalence of minor and major bleeding, haematoma was higher in group II compared to group I. There is no statistical dissimilarity between the groups (P value> 0.05).

Discussion:

This was a prospective observational study conducted in the department of cardiology, national Institute of Cardiovascular Disease, Dhaka. There was no published data in Bangladesh comparing effects of two types of heparin in PCI. Hence the result of this study was not possible to be compared with any other Bangladeshi studies but the results have shown similarity with studies done abroad.

Similar pattern of age distribution were reported by Jakub Drozd et.al. There was similar type of risk factor distribution like hypertension, smoking, dyslipidaemia, diabetes mellitus and Family history of CAD in both groups. Similar observation was found by Jakub Drozd et.al.[17]

Heparin has always been used during PCI and in spite of the progress which took place in interventional cardiology it still remains a standard treatment during and after this procedure. The goal of heparin treatment is to decrease the risk of acute restenosis of a vessel undergoing PCI and to prevent thrombo-embolic complications associated with introduction of instruments into the cardio-vascular system. The risk of acute restenosis may be as high as 11%. Acute reocclusion may be complicated by such severe events as death, MI or urgent need for redo PCI. The main limitations of heparin therapy are not fully predictable effects of this agent on the coagulation system due to variable binding to serum protein, platelets and endothelial cells. Therefore, the continuous monitoring of blood coagulation parameters is mandatory. At present, no generally accepted scheme of heparin administration prior to PCI exists. Usually a bolus of

10,000 iu of heparin is given, followed by serial ACT measurements every several minutes. This regimen has two limitations. First, the standard dose *of* heparin is not effective in some patients whereas in some others it is too high. Second, the costs of serial ACT measurements are not negligible. Ogilby et.al.[18] revealed that 11 % of patients had ACT <300 seconds following 10,000 iu of heparin. Doughenty et.al. have demonstrated a very wide range of ACT <250 seconds was measured in 58% of patients, ACT 250-275 seconds in 17%, ACT 275-300 seconds in 12% and >300 seconds in 13% of patients.[19]

The ESSENCE studies have documented the advantages of enoxaparin over standard heparin in patients with acute coronary events resulting in lower risk of death, MI or the need for revascularization.[20] Similar encouraging results were obtained by the TIMI IIB investigations. The promising results of the above mentioned studies encourage the use of LMWH during PCI.[21] Data in literature concerning this topic are very scant. The safety of enoxaparin administration (1 mg/kg) before PCI was examined in the open-label study.[22] The rate of acute coronary complications was 4.9% whereas the rate of bleeding complications- 0.6%. The randomized study REDUCE[23] compared 10,000 iu bolus of standard heparin with reviparin (LMWH) administered at a dose of 7,000 iu anti Xa. A significant reduction in the coronary event rates during the first three days following PCI was documented in the reviparin group (8.2% vs. 3.9%, respectively).[24] Randomized patients to enoxaparin (1 mg/kg) or UFH 10.000 iu, given before PCI. The rate of coronary events, haemorrhage and local bleeding complications was similar in both analyzed groups, however, 30% of patients receiving UFH required additional doses of heparin to achieve the target ACT(>300 s). A study conducted in Poland revealed that in patients with acute coronary events enoxaparin given at a dose of 1mg/kg prior to PCI was equally safe as standard heparin titrated according to ACT.[25]

Safety of enoxaparin in comparison to UFH observed in this study was evaluated in 100 patients. Among them, 50 received enoxaparin and similar number received UFH. Demographic profile of individuals in both groups was almost similar. There was no significant difference of major coronary risk factors between the two treatment groups. Patients were monitored up to hospitalized period for observation of any complications. No death was observed in any group. Major and minor complications was comparatively similar in both groups but relatively there was better outcome in LMWH group.

Study Limitations

Although the results of this study support the hypothesis there are some facts to be considered which might affect the results:

1. The study was a non-randomized and observational study.

2. Number of study population was limited.

3. Duration of follow up period was short.

Conclusion:

The intra-arterial administration of 1 mg/kg of enoxaparin in patients undergoing PCI is

safe. The risk of acute and sub-acute coronary events and bleeding complications are

similar in patients treated with UFH. The study was a non-randomized study with small number of patients. So further comparative study which will be randomized, with larger group will give a clear picture of clinical outcome between patients having enoxaparin and UFH in PCI.

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Original Article

Mortality in Coronary Care Unit of a Tertiary Level Hospital of Bangladesh

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Abstract:

Background and objectives: Cardiovascular disease is the most common cause of death worldwide and Coronary Care Unit (CCU) plays a central role in reducing this mortality. Currently the data on mortality in CCU is very limited in our country. Our purpose of this study to provide data on mortality so that we can focus and improve the factors determining deaths in CCU.

Methodology: The data of all death cases admitted in the CCU of a tertiary level hospital between 1 January 2016 and 31 December 2017 were included for assessing the data on demography, diagnosis, and co-morbidities at the time of death.

Results: Among 802 cases admitted in CCU in two years, 40 patients died (5%). Male was 55% and female was 45%. Most of the death occurred in their 6th decade of life, due to Non-ST-Elevation Myocardial Infarction (NSTEMI) and sepsis, within 24-hour of CCU admission.Common associated co-morbidities were DM (75%), hypertension (42.5%), CKD (27.5%), and hypokalemia (12.5%).

Conclusions: The death rate is much lower in our CCU in comparison to global rate. The common cause of death is still NSTEMI. The common co-morbidities we found are DM, hypertension and CKD. Most of the deathsoccurred within 24-hour of admission.

Key words: Coronary Care Unit, Mortality, NSTEMI

(Bangladesh Heart Journal 2018; 33(1): 28-31)

Introduction:

Cardiovascular death is still the highest cause of death worldwide.[1] Taking this critical situation under consideration, the idea of coronary care unit (CCU)was first introduced in early 1960s by the British Thoracic Society primarily in attempt to reduce the mortality of acute myocardial infarction (MI). Soon it was observed that patients with acute MI treated in CCU had better prognosis than those treated in general wards, mainly due to preventing fatal ventricular arrhythmias by early detection with continuous monitoring.In the late 1960s, it was shown that aggressive medical therapy in the CCU seemed to reduce in-hospital mortality from 26% to 7%.[2]In recent decades, care in CCU has been improved a lot along with the high cost. For common people this is certainly a burden. Still the numbers and facilities of CCU in every country according to their demand is limited.[3]

No doubt, in limited resources countries like Bangladesh, the appropriate management of acute cardiac event is not available in most of the cities. However, in major cities of Bangladesh, there are many tertiary care hospitals capable of dealing with these emergencies. But due to lack of any admission criteria in CCU, department of cardiology has to deal with many non-cardiac emergencies also.[4] BIRDEM General Hospital is a tertiary level hospital and, according to daily patient attendance, it is the largest diabetic hospital in the world.[5] It has a 7-bed CCU with non-invasive facilities for acute cardiac emergencies. As diabetic patients have multiple co-morbidities and has higher risk for cardiac events than those who are non-diabetic,[6-8] our CCU plays a central role in giving almost every kind of emergency management along with cardiac

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37021

diseases. Here we conducted a retrospective observational study on mortality covering the year 2016-17. As there is no sufficient data on mortality in CCU in our country, our objective was to find out the major cause of death and associated co-morbidities, so that we can intensify our goal-directed management.

Materials and methods:

This retrospective observational study was carried out for the year 2016-17 in the CCU of BIRDEM General Hospital which is a tertiary level hospital in the center of capital of Bangladesh.Every death file and registration book of CCU was scrutinizedand data were collected in a predesigned data collection sheet. Information included was the subject's age, gender, date of admission (or date of transfer from other unit), date and time of death, primary cause of death, associated co-morbidities, and whether the primary cause of death cardiac or non-cardiac. All the relevant collected data were compiled on a master chart first. Then organized by using scientific calculated and standard statistical formulas, percentage was calculated to find out the proportion of the findings. Data entry and analysis were done using SPSS for windows version 22.0. Output of data and graphical representation was done using Microsoft Office chart and Microsoft-Word. The results were presented in tables, figures,diagrams etc.

Results:

In the year 2016-17, total 802 patients were admitted in the CCU. Among them, 40 patients (5.0%) died during their stay in the CCU.

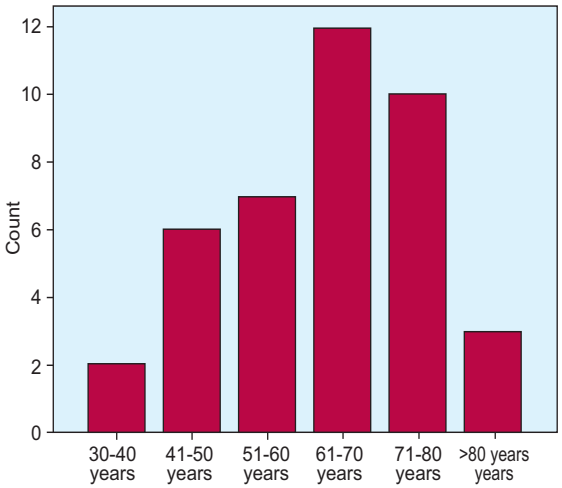

Fig.-1: *Range of age*

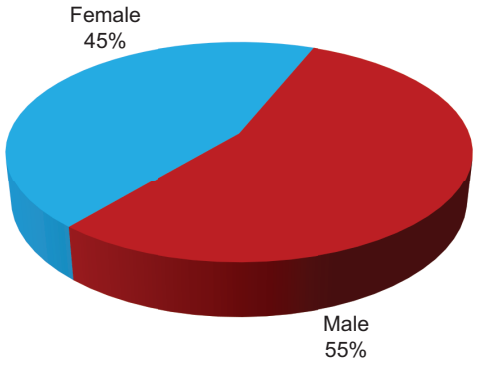

Fig.-2: *Gender distribution*.

It is shown that majority of the subjects were within 6th decade of life and of male sex (Figure 1 and 2).Their main causes of death were acute anterior MI and sepsis. Among 40 deceased subjects, 55% (n = 22) were male, and 45% (n = 18) were female. Most of the patients (32.5%, n = 13) died after 24-hours of stay (Figure 3). The time of death mostly between 12 pm to 6 pm. (Figure 4). The common cause of death was Non-ST Elevation Myocardial Infarction (NSTEMI) (30%, n = 12). Sepsis remains in next position (17.5%, n = 7). Other causes of death were CKD (15%, n = 6), unstable angina (10%, n = 4), acute MI anterior (7.5%, n = 3), acute MI inferior (5%, n = 2), acute stroke (5%, n = 2), dilated cardiomyopathy (DCM) (2.5%, n = 1), ischemic cardiomyopathy (ICM) (2.5%, n = 1), pneumonia (2.5%, n = 1), and acute coronary syndrome (ACS) (2.5%, n = 1) (Figure 5).

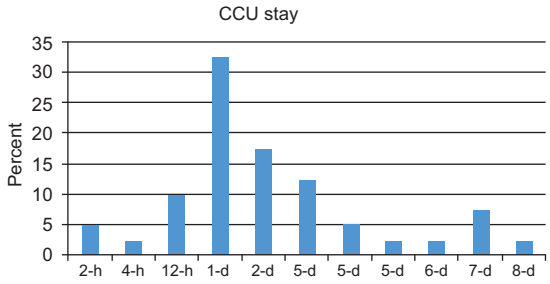

Fig.-3: *Duration of CCU stay*

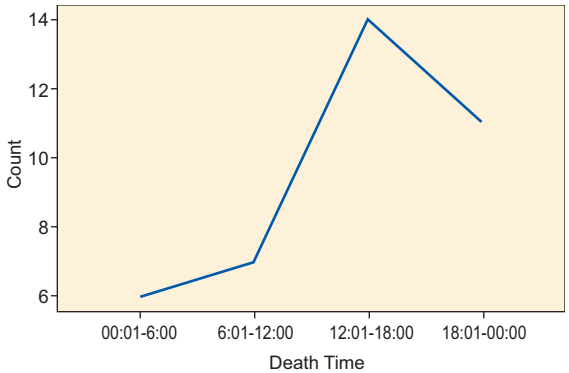

Fig.-4: *Time of death*

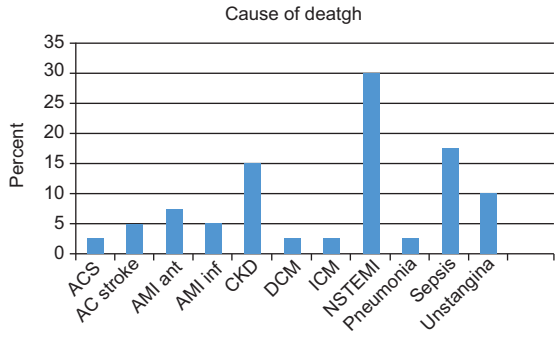

Fig.-5: *Causes of death*

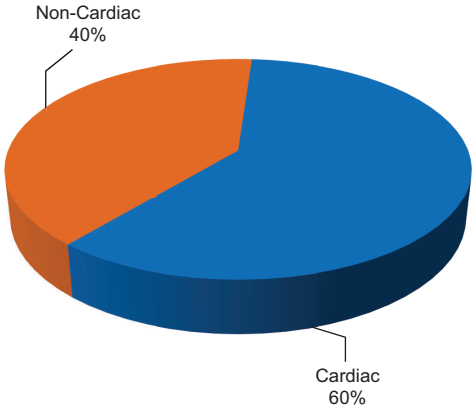

Fig.-6: *Percentage of cardiac and non-cardiac cases*

A good number of cases died from non-cardiac diseases (40%, n = 16) (Figure 6). Cardiac cause was 60% (n = 24).Directly admitted cases in CCU from Emergency Room (ER) were 40% (n = 16), remaining 60% (n = 24) were transferred in from other unit.

Major co-morbidities were DM (75%, n = 30), hypertension (42.5%, n = 17), chronic kidney disease (CKD) (27.5 %, n = 11), and hypokalemia (12.5%, n = 5). However, there was much overlap among cases.

Discussion:

Important findings in our study are: Death rate in CCU is 5.0% and cause of death in CCU is still myocardial infarction as NSTEMI, and due to lack of admission criteria, a good number of non-cardiac deathswere observed.Death rate is higher in 6th decade of life. Death due to NSTEMI was observed more in male than female (17.5%, n = 7 vs 12.5%, n = 5).

Mortality is a very diverse matter globally due to a variety of reasons: Cause of death, associated morbidity, characteristics of patients (eg, age, sex, and family history), treatment received, etc. Despite much limited resource in our country, death rate in our CCU is much lower (5.0%) in comparison to the developed world. The rate ranges from 5.6% to 20.6% in many developed countries.[9-11]They have also many non-cardiac cases (eg, sepsis),[9] but those cases were closely associated with cardiac reason (sepsis following cardiac surgery).

In our CCU, pattern of MI was mostly NSTEMI. This is largely because of associated DM. Because NSTEMI is commonly observed in diabetic patients worldwide.[12-14] In our observation, male patients had more NSTEMI than females. The gender differences in death due to MI was also found in many larger studies in other part of the world.[15-17] Some causes of death were labeled as ACS, because those cases died before getting the confirmatory investigations like cardiac markers (eg, Troponin-I) and before doing echocardiography. They were classified as ACS on the basis of clinical presentation (ie, new angina, increasing angina, and rest angina) and findings of electrocardiogram (ECG).[18]

The study findings that alarmed us are as follows: Most of the death occurred at or around first 24-hour of admission, between 12 to 6 pm, and of age group between 61 and 70 years. This is likely due to referral bias from other centers because we faced most admission in the morning and commonly fatal cases or cases with high morbidity were commonly referred to us. Certainly we need to intensify our management team during this period of time. Moreover, as the associated major co-morbidities are DM, CKD and hypertension, we have to strengthen the root of management of these patients with aggressive control of the diseases along with early identification of their complications.

There are many gross limitations in our study. First, we could not emphasize the background history of the patients that could be more helpful for us to identify the consequences of death, eg, glycemic control, compliance to regular follow up, and personal history (esp, tobacco use). Second, this is a single center based retrospective study. And third, because our hospital is a tertiary level hospital and specialized mainly on diabetes care, there is an obvious chance of referral bias.

The strength of our study are: First, to our knowledge, it is the largest published study in our country till date. Second, previously we had no authentic data about the common cause of death to give emphasis on the treatment. Third, with this study we can encourage and assure our young doctors about their competency and potency in treating critical cardiac patients because of much lower mortality in our CCU than that of many developed world. Fourth, this study proves that we need definite criteria for admission in CCU. Because the appropriate facilities of many CCU are scarce in our country. So it is clear that if non-cardiac cases

will be admitted in CCU, critical cardiac cases who actually need management in CCU will be deprived from CCU care.

However, as we have no provision of invasive procedure like coronary angiogram and intervention, we believe we can improve our care in CCU more if we have these facilities.

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Original Article

Relationship between HDL-Cholesterol and Angiographic Severity of Coronary Artery Disease

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Abstract:

Background: Dyslipidaemias is one of the major risk factor for Coronary artery diseases (CAD).There is an inverse correlation between high density lipoprotein cholesterol (HDL-C) and the risk of coronary artery disease. Understanding the angiographic characteristics of coronary artery diseases (CAD) in low and normal HDL-C patients and its association with severity of CAD is very important for future intervention. Although high-density lipoprotein cholesterol (HDL-C) is well established predictor of future cardiovascular event, little information is available regarding its correlation with the prevalence and severity of angiographically evaluated coronary artery diseases (CAD).

Materials and Methods: This cross-sectional comparative study was conducted in the Department of Cardiology, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from January 2012 to December 2013. We included 100 patients with coronary artery diseases and divided into two groups. 50 patients with low HDL-C (<40 mg/dl) were taken in study group (Group-A) and 50 patients with normal HDL-C (>40 mg/dl) were taken in control group (Group-B) according to inclusion and exclusion criteria. Coronary angiography was performed via the trans-femoral approach using standard techniques. Severity of CAD was determined by vessels score and Friesinger score.

Results: The age [51.1 (SD 8.7) years vs 51.4 (SD 8.2) years; p>0.05] and sex [45 (90.0%) male and 5 (10.0%) female vs 41 (82.0%) male and 9 (18.0%) female; p=0.249] were similar in group-A and group-B. The conventional risk did not show any significant difference between low and normal HDL level group such as age, sex, smoking, diabetes mellitus, hypertension, BMI, hypercholesterolaemia, high serum LDL, hypertriglyceridaemia and family history of CAD (p>0.05 each).

No significant vessel disease [3 (6.0%) vs 14 (28.0%); p=0.008] and single vessel disease [11 (22.0%) vs 25 (50.0%); p=0.020] were significantly fewer in group A than that of group-B; while double vessel disease [14 (28.0%) vs 5 (10.0%); p=0.039] and triple vessels disease [22 (44.0%) vs 6 (12.0%); p=0.002] were significantly higher in group-A than that of group-B. Friesinger score 0 [3 (6.0%) vs 11 (22.0%); p=0.033] and Friesinger score 1 to 4 [6 (12.0%) vs 24 (48.0%); p=0.01] were significantly fewer in group A than that of group-B; while Friesinger score 5 to 9 [20(40.0%) vs 9 (18.0%); p=0.041] and Friesinger score 10 to 15 [21 (42.0%) vs 6 (12.0%); p<0.004] were significantly higher in group-A than that of group-B. Among all respondents conventional risk factors were not statically significant between the groups. A significant negative correlation was found between serum HDL-C (mg/dl) and number of diseased vessel (r=0.370; p<0.001) and also Friesinger score (r=0.388; p<0.001).

Conclusion: It may be concluded that low HDL-C level is associated with angiographically more severe coronary artery diseases reflected by vessels score and Friesinger score as compared to normal or high HDL-C level.

Key words: Coronary artery diseases, HDL, Lipoprotein angiographiy

(Bangladesh Heart Journal 2018; 33(1): 32-38)

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37023

Introduction:

Cardiovascular disease is one of the leading causes of morbidity and mortality in the world.[1] It is responsible for about 30% of deaths worldwide.[2,3] By 2020, it is predicted that coronary artery disease will claim 25 million lives annually and that coronary artery disease (CAD) will surpass infectious disease as the world´s number one cause of death and disability.[4]

The South Asian countries of India, Pakistan, Bangladesh, Sri-Lanka, and Nepal contribute the highest proportion of the burden of cardiovascular diseases (CVDs) compared to any other region globally.[5,6] Estimates from the Global burden of Disease Study suggests that by the year 2020 this part of the world will have more individuals with atherosclerotic cardiovascular disease than any other region.[7]

Deaths related to CVD also occurs 5 to10 years' earlier in South Asian countries than they do in Western countries. This has raised the possibility that South Asians exhibit a special susceptibility for coronary artery disease that is not explained by traditional risk factors.[8]

Factors such as age, family history, abnormal blood lipid profile, hypertension, diabetes mellitus and smoking have been shown to be effective on coronary artery disease incidence.[9] Although such factors are also thought to determine the severity and extent of coronary atherosclerosis.[10]

Dyslipidemias, including high low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) concentrations and low high-density lipoprotein cholesterol (HDL-C) concentration, are risk factors for CHD.[11] One of the major predisposing factors to atherosclerosis is an abnormal lipoprotein metabolism and it may be present in over 70% of patients with premature CAD.[12]

Low-density lipoprotein (LDL) seems to be the major target of oxidative modification, making it particularly atherogenic.[13] Identification of factors protecting against oxidative modification of LDL are therefore of major interest. High-density lipoprotein (HDL) has been shown to have antioxidative potential; however, the mechanism(s) of its action is not known. One mechanism might be the enzymatic removal of lipid peroxides accumulating on the LDL particle by enzymes present on HDL.[14] Thus high concentration of LDL cholesterol and low levels of HDL cholesterol are able to promote atheroma formation and are recognized as particularly important risk factors for atherosclerosis and CAD.[12]

Persons with low HDL cholesterol levels are at increased risk of coronary heart disease, restenosis after angioplasty, and death from cardiovascular causes, especially if such parsons are male or have diabetes.[15] In addition, angiographic studies have shown a correlation between low HDL cholesterol levels and increased number of diseased coronary arteries. Low HDL C values were associated with an increased both triple vessel disease and left main coronary artery. One study found a fourfold increase in the rate of restenosis after angioplasty in patients with low HDL cholesterol levels.[16]

Severity of CAD is inversely correlated with levels of HDL-C in both men and women. In multivariate analysis HDL-C is inversely related to the mean percentage increase in coronary artery stenosis than other lipid.[17]

In angiographic studies the relation between HDL-C levels and CAD has varied widely ranging from significant inverse correlation with HDL-C and were the only significant predictor of the number of lesions.[18]

Materials and method:

This cross-sectional comparative study was conducted in department of cardiology, MAG Osmani Medical College and hospital, Sylhet, Bangladesh during the period from 1st January 2012 to 31st December 2013 to explore the association of low HDL-cholesterol with angiographic severity of coronary artery diseases of patient include chronic stable angina (CSA) and acute coronary syndrome (ACS). Considering the inclusion criteria like patient with coronary artery diseases irrespective of age and sex and exclusion criteria like prior coronary revascularization either CABG or angioplasty,congenital heart diseases,valvular heart diseases,cardiomyopathy,renal insuffiency,LDL-C more than 130 mg/dl,patient refuses to undergo CAG or enroll in the study. 100 patient getting guideline directed anti lipid therapy after initial diagnosis of coronary artery diseases and treated conservatively who subsequently underwent coronary angiogram were included in this study by purposive sampling.Fasting lipid profile was measured following a 12 hour fast and serum total cholesterol (TC),triglyceride (TG) and high density lipoprotein(HDL-C) were determined by standard method using CX 7 SYNCHRON clinical system. LDL cholesterol(LDL-C) was calculated using the Friedewald equation. 50 patient were in Group-A with low HDL-C and 50 patient were in Group-B with normal HDL-C level within index hospital admission, the enrolled patient underwent coronary angiography (CAG) and was analysed by visual estimation and severity was assessed by vessels score and Friesinger score.

Vessel score is the number of vessels with a significant stenosis (for left main coronary artery 50% or greater and for others 70% or greater reduction in luminal diameter.[19] Score ranges from 0 to 3, depending on the number of vessel involve. Left main coronary artery was scored as single vessel disease.[20]

Score 0 = no vessel involvement.

Score 1 = single vessel involvement.

Score 2 = double vessel involvement.

Score 3 = triple vessel involvement.

The Friesinger score,[21] ranges from 0 to 15. Each of the three main coronary arteries is scored separately from 0 to 5.

Score 0: No arteriographic abnormality

Score 1: Trivial irregularities (lesion from 1-29%)

Score 2: Localized 30-68% luminal narrowing

Score 3: Multiple 30-68% luminal narrowing of same vessel;

Score 4: 69-100% luminal narrowing without 100% occlusion of proximal segments

Score 5: Total obstruction of a proximal segment of a vessel.

Statistical Analysis:

Data were processed and analyzed with the help of computer program SPSS (Statistical package for social sciences) 16 version. Quantitative data were analyzed by mean and standard deviation; and comparison was done between two groups by Z-test. Qualitative data was analyzed by rate, ratio, and percentage; and comparison was done between two groups by Chi-Square test. A probability (p) value of <0.05 was considered statistically significant.

Result:

Mean age was found 50.1+8.7 and 51.4+8.2 years in group–A and group-B respectively (p>0.05)In both group maximum patient age belongs to 41-50 years. Male were predominant in both groups, 45(90%) in group-A and 41(82%) in group-B. Risk factor including smoking, HTN, DM and obesity was 26(52%) vs. 29(58%), 29(58%) vs. 26(52%), 19(38%) vs. 23(46%) and 22(44%) vs. 19(38%) in group-A and group-B respectively and regression analysis shows there was no statistically significant difference among the other variables. Fasting blood sugar , serum creatinine and serum HDL-C was found 141.82±37.9 vs. 140.42±38.37 mg/dl, 1.18±0.13 vs. 1.21±0.16 mg/dl and 33.86±3.39 vs. 46.96+4.96 mg/dl in group-A and group-B respectively. HDL-C difference was found statistically significant between two group (table I).

Regarding coronary artery involvement vessel score O and vessel score 1 was 3(14%) vs. 14(28%) and 11(22%) vs. 25(50%) in group-A and group-B respectively which was statistically significant (p<0.05).On the other hand vessel score 2 and vessel score 3 was 14(28%) vs. 5(10%) and 22(44%) vs. 6(12%) in group-A and group-B (table III) which is statically significant. Left main coronary artery involvement 6(12%) vs. 4(8%) in group-A and group-B respectively was not statistically significant (table III).

Friesinger score 0 [3 (6.0%) vs 11 (22.0%) p=0.033] and Friesinger score 1 to 4 [6 (12.0%) vs 24 (48.0%) p=0.01] were significantly fewer in group A than that of group-B; while Friesinger score 5 to 9 [20(40.0%) vs 9 (18.0%) p=0.041] and Friesinger score 10 to 15 [21 (42.0%) vs 6 (12.0%) p<0.004] were significantly higher in group-A than that of group-B(table-III).

Table-I

Characteristics of study population (n= 100)

Variables	Group A(n=50)		Group B(n=50)		p value
Age (years)	50.1± 8.7		51.4± 8.2		p>0.05
FBS (mg/dl)	141.82 ± 37.99		140.42 ± 38.37		p = 0.855
Creatinine (mg/dl)	1.18 ± 0.13		1.21 ± 0.16		p = 0.217
Serum Cholesterol	186.94 ± 31.03		196.14 ± 25.13		p = 0.107
Serum HDL	33.86 ± 3.39		45.96 ± 4.96		p < 0.001
Serum LDL	113.64 ± 23.16		107.86 ± 25.12		p = 0.235
Serum TG	177.28 ± 60.20		164.78 ± 24.85		p = 0.118
	n	%	n	%	
Male	45	90	41	82	p = 0.249
Female	5	10	9	18	
Smoking	26	52	29	58	p = 0.546
DM	19	38	23	46	p = 0.418
HTN	29	58	26	52	p = 0.546
F/H of IHD	12	24	7	14	p = 0.202
Obesity	24	44	19	38	p = 0.542

Table-II

Distribution by type of coronary artery disease (n=100)

	Group A (n=50)		Group B (n=50)		p value
	n	%	n	%	
Type of CAD					
Chronic stable angina	6	12	6	12	
Unstable angina	20	40	15	30	p = 0.467
NSTEMI	7	14	13	26	
STEMI	17	34	16	32	

Table-III

Comparison of coronary angiographic severity between two groups (n=100)

Coronary angiographic severity	Group A (n=50)		Group B (n=50)		P value
Vessel score	n	%	n	%	
No involvement	3	6	14	28	p = 0.008
Single vessel	11	22	25	50	p = 0.020
Double vessel	14	28	5	10	p = 0. 039
Triple vessel	22	44	6	12	p = 0.002
LMCA	6	12	4	8	p = 0.505
FriesingerScore					
0 (Normal)	3	6	11	22	p = 0.033
1-4 (Mild)	6	12	24	48	p = 0.01
5-10 (Moderate)	20	40	9	18	p = 0.041
11-15 (Severe)	21	42	6	12	p = 0.004

Discussion:

Age of the patients ranged from 30 to 70 years with the mean age of 50.8 (SD 8.5) years. The mean age of the patients of Group-A and Group-B were almost similar [50.1 (SD 8.7) years vs 51.4 (SD 8.2) years; p>0.05). This result was consistent with the study of Zaher et al.[22] that the mean age of their patients with coronary artery disease was 49.85 ± 9.89 years. This result was also correlated with the study of Arnesen et al.[23] that the mean age of the patients with coronary artery disease was 51.3 ± 7.3 years.

This result also demonstrated that 41 (41.0%) patients were in the age group of 41 to 50 years, 34 (34.0%) patients were in the age group of 51 to 60 years, 13 (13.0%) patients were in the age group up to 40 years and 12 (12.0%) patients were in the age group of above 60 years. Similar result was reported in the study of Shirin et al.[24] that 15.0% of patients were in the age group of 31 to 40 years, 32.5% of patients were in the age group of 41 to 50 years, 37.5% of patients were in the age group of 51 to 60 years, 11.3% of patients were in the age group of 61 to 70 years and 3.8% of patients were in the age group of above 70 years.

Among the total 100 patients, 86 (86.0%) patients were male and 14 (14.0%) patients were female with a ratio of 6.14: 1. There was no significant difference of sex between the groups (p=0.249). This result was supported by the study of Alam et al.[25] that 92.8% of their series of patients were male and 7.2% patients were female. Shirin et al.[24] reported that 80.0% of their series were male and 20.0% of patients were female.

In the current study 55.0% of patients were smoker and 45.0% of patients were non-smoker. There was no significant difference of smoking status between low HDL-C group and normal HDL-C group (p=0.546). This result was correlated with the study of Asakura et al.[26] that 56.0% of their patients were smoker. This result was also correlated with the study of Kabir et al.[27] that 60.0% of their patients of CAD were smoker.

Among the total 100 patients in the present study, 42.0% of patients were diabetics and 58.0% of patients were non-diabetics. There was no significant difference of diabetes mellitus between the groups (p=0.418). This result was correlated with the study of Bertoluci et al.[28] that 48.6% of their CAD patients were diabetics.

Among the total 100 patients in this study, 55.0% of patients were hypertensive and 45.0% of patients were

normotensive. This result was similar to the study of Habib et al.[29] found that the prevalence of hypertension was 54.9% was of their CAD patients. This result was also supported by Okamatsu et al.[30] that 54.0% of their patients were hypertensive. In this regards Asakura et al.[26] found 60.0% of their patient were hypertensive.

Among the total 100 patients in the current study, 19.0% of patients had family history of CAD and 81.0% of patients had no family history of CAD. There was no significant difference of family history of CAD between group-A and group-B (p=0.202). Khadem-Ansari et al.[20] reported that the history of familial CHD was 27.3% of their CAD patients. Senaratne et al.[32] found 28.2% of their South Asian patients had family history.

Among the total 100 patients in the present study, type of CAD was unstable angina in 35 (35.0%), ST-elevation MI in 33 (33.0%), non-ST-elevation myocardial infarction (MI) in 20 (20.0%) and chronic stable angina in 12 (12.0%) patients. No significant difference was found between Group-A and Group-B in terms of type of CAD (p=0.467). This result was supported by the study of Kabir et al.[27] that stable angina in 18% unstable angina in 36% and MI in 46% of their series of CAD patients.

In this series no significant vessel involvement was in 17.0%, single vessel disease in 36.0%, double vessel disease in 19.0% and triple vessel disease in 28.0% of cases. Kazemi et al.[33] reported that single vessel disease in 22.3%, double vessel disease in 21.8% and triple vessel disease in 23.4% and no vessel disease in 32.5% of their patients underwent coronary angiogram.

No vessel disease and single vessel disease were significantly fewer in group A than that of group-B; while double vessel disease and triple vessels disease were significantly higher in group-A than that of group-B. Safeer and Cornell,[16] found that low HDL cholesterol levels was associated with increased number of diseased coronary arteries and increased incidence of triple vessel disease. Drexel et al.[34] found that 21.8% single vessel disease, 26.5% double vessel disease and 51.7%- triple vessel disease in low HDL-C level in patients with CAD.

Friesinger score 0 [3 (6.0%) vs 11 (22.0%); p=0.033] and Friesinger score 1 to 4 [6 (12.0%) vs 24 (48.0%); p=0.01] were significantly fewer in group A than that of group-B; while Friesinger score 5 to 9 [20(40.0%) vs 9 (18.0%); p=0.041] and Friesinger score 10 to 15 [21 (42.0%) vs 6 (12.0%); p<0.004] were significantly higher in group-A than that of group-B. In this regards French et al.[35] found that more significant coronary artery lesions associated with low HDL-C patients (77.0%), Ballantyne et al.[36] found that percentage of diameter stenosis was more in low HDL-C patients. Rahman et al.[37] found low HDL-C associated with large lesions.

In the present study there was a significant negative correlation between serum HDL (mg/dl) and number of disease vessel (p<0.001). This result was consistent with the study of Tarchalski et al.[12] that there was inverse association between HDL-C level and the number of diseased coronary vessel.

The conventional risk factors were statistically similar in low and normal HDL level group smoker, diabetes mellitus, hypertension, hypercholesterolaemia, high serum LDL, hypertriglyceridaemia and family history of CAD in both multivariate analysis. This results were some different from the study of Zaher et al.[22] These may be due to selection criteria and difference in the study group selection. Zaher et al.[22] selected patients with CAD as case and without CAD as control. But in the present study both groups were patients with CAD and difference in HDL-C level between group i.e CAD with low HDL-C in study group and CAD with normal HDL-C in control group.

Conclusion:

From the findings of the present study it may be concluded that low HDL-C level is associated with angiographically more severe coronary artery diseases in comperison to normal or high HDL-C patientas reflected by vessels score and friesinger score.

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Original Article

Association of Body Mass Index with In-Hospital Left Ventricular Failure after Percutaneous Coronary Interventions

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Abstract:

***Background*: Obesity is an independent cardiovascular risk factor. The most common anthropometric measurement used to quantify obesity is body mass index (BMI). Percutaneous coronary intervention (PCI) is associated with various types of complications. The relationship between BMI and in-hospital complications particularly left ventricular failure (LVF) after PCI has not been thoroughly investigated, especially in Bangladesh.**

***Methods:* This cross sectional observational study was conducted at National Institute of Cardiovascular Diseases, on total 100 patients who underwent PCI with two equally divided groups on the basis of BMI of Asian ethnicity: Group I (BMI < 23 kg/m2) and Group II (BMI e" 23.0 kg/m2). In-hospital LVF after PCI were observed and recorded.**

***Results*: The mean BMI of study population was 23.9 ± 1.9 kg/m^2. The sum of occurrence of adverse in-hospital outcomes was 14.0%. Complications were significantly (p < 0.01) higher in Group I than Group II. Among all adverse in-hospital outcomes, only acute left ventricular failure was found to be statistically significant between groups (p < 0.01). The difference of mean duration of hospital stay after PCI was higher in Group-I which was statistically significant (p < 0.01). Diabetes mellitus and dyslipidemia were found to be the independent predictors for developing adverse in-hospital outcome (OR= 1.68 and 1.46; 95% CI = 1.25 – 2.24 and 1.16 – 1.83; p = 0.018 and 0.040, respectively). BMI was inversely associated with in-hospital outcomes after PCI (OR = 0.95; 95% CI = 0.91 – 0.98; p = 0.007).**

Conclusion: BMI is inversely associated with in-hospital LVF after PCI. The underweight and normal weight people are at greater risk to experience in-hospital LVF than overweight and obese people following PCI.

Key words: Obesity, Body Mass Index, Left Ventricular Dysfunction, Percutaneous Coronary Intervention.

(Bangladesh Heart Journal 2018; 33(1): 39-46)

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37024

Introduction:

Ischemic heart disease (IHD) is a major and increasing health care issue in Bangladesh.[1] Only a limited number of small-scale epidemiological studies are available. IHD prevalence was between 2.7% and 3.4% in two studies with a rural sample and 19.6% with an urban sample of working professionals.[2] Despite marked disparity in values, there seems to be a rising prevalence of coronary artery disease (CAD) in Bangladesh.[3] Globally, 30% of all deaths can be attributed to cardiovascular disease, of which more than half are caused by CHD.[4]

With the combination of sophisticated equipment, experienced operators, and modern drug therapy, coronary angioplasty has evolved into an effective nonsurgical modality for treating patients with CAD.[1,5]The number of PCIs is expected to grow modestly (1% to 5%) over the next decade as a result of the aging population and an increased frequency of diabetes and obesity.[6]

Institute for Health Metrics and Evaluation at University of Washington reported 17% of adults of Bangladesh as overweight or obese.[7]Overweight and obesity are established risk factors for major debilitating chronic diseases including hypertension, type II diabetes mellitus, dyslipidemia, stroke, and CAD.[8–11] There are limited data, however, on the relationship of body mass index (BMI) as a prognostic risk factor for outcomes following revascularization procedures such as PCI.[12] A number of studies have shown that lean patients (<20 kg/m^2) and those with normal BMI (20–24.9 kg/m^2) are at a higher risk for adverse in-hospital outcomes and post-PCI complications than overweight (25–29.9 kg/m^2) and obese (≥30 kg/m^2) patients.[12–14]. This unexpected phenomenon was explained by "obesity paradox".[12]

Methods

In the Department of Cardiology, National Institute of Cardiovascular Diseases and Hospital, Dhaka, this cross sectional observational study was conducted during the period from November 2015 to October 2016. By purposive sampling technique total 100 patients who underwent PCI in NICVD during this period were selected. Study subjects were divided on the basis of their BMI in accordance with Asian ethnicity into two equal groups each containing 50 patients: Group I (BMI < 23 kg/m^2) and Group II (BMI ≥23.0 kg/m-^{2}). Patients with chronic kidney diseases, chronic liver disease, chronic obstructive pulmonary disease, valvular heart disease, congenital heart disease, cardiomyopathy, previous history of revascularization (PCI or CABG) were excluded from the study. Patients undergoing primary PCI, transradial interventions were not included, also. No ethical violation was made in conducting the study.

After having matched the inclusion and exclusion criteria the patients were selected for this study. Weight and height were measured and recorded in all participants by a standard medical scale and stadiometer, respectively. Self-reported weight or height was not accepted. BMI was calculated, categorized and recorded accordingly. PCI was done by transfemoral approach. Following PCI patients were monitored at Coronary Care Unit for at least 24 hours. Post-PCI development of in-hospital left ventricular failure along with common adverse outcomes were observed and recorded, i.e., bleeding, stroke, vascular access site complications, post-PCI ischemic chest pain, myocardial infarction with PCI, significant arrhythmia, acute stent thrombosis, repeat revascularization, contrast induced nephropathy, cardiogenic shock, cardiovascular death.

To adjust for the potential confounders in predicting the association between BMI and in-hospital outcomes, logistic regression analysis was performed. Univariate logistic regression analysis was performed to specify the odds ratio (OR) for overall adverse in-hospital outcomes. Multivariate logistic regression analysis was then performed by using SPSS 23.0 to investigate independent predictors for adverse in-hospital outcomes. Variables yielding p values ≤0.05 in univariate analysis were selected for multivariate model. Statistical significance was assumed if $p \leq 0.05$ throughout the study.

Results:

Out of 100 studied patients 84% were male and 16% were female. Male to female ratio was 4.5:1. No significant association (p>0.05) was found between the groups in terms of sex distribution. The mean age of the patients was 51.1 ± 9.57 years and the mean age difference between two groups was not statistically significant (p>0.05). In both of the groups the highest percentages of patients were in the age range of 41-50 years (Table-I).

Table II shows that among the different risk factors dyslipidemia, hypertension and diabetes mellitus were significantly more in group II (<0.05). The other risk factors i.e., smoking and family history of CAD were not significantly different between the groups (p >0.05).

The difference of means of height was insignificant (p>0.05) across the groups. But that of weight was found to be significant (p=0.001). BMI was significantly (p=0.001) higher in group II than group I. The breakdown of total patient would be 81 in Group I and 19 in Group II with statistically significant difference

($p = 0.001$) of mean BMI across the group had their conventional non-Asian BMI cut-off value be used (Table III).

The difference of means of height between the two sex groups was significant (p=0.001). The difference of means of weight across these groups was also significant (p<0.01). BMI was higher in female patients than in male but the difference between them was not statistically significant in any group (p>0.05) (Table IV).

Table V compares the distribution of clinical presentations between the groups. The percentage of STEMI was the highest in both groups. No statistically significant difference was noted between the two groups ($p > 0.05$).

Table - I

Comparison of the study groups by their demographic characteristics (N = 100).

Age in years	BMI				Total (N =100)		*p*-value
	Group I (n = 50)		Group II (n = 50)				
	Number	%	Number	%	Number	%	
d" 40	4	8.0	5	10.0	9	9.0	[a]0.11[NS]
41-50	23	46.0	25	50.0	48	48.0	
51-60	17	34.0	14	28.0	31	31.0	
> 60	6	12.0	6	12.0	12	12.0	
Mean ± SD	51.2 ± 11.4		50.9 ± 9.1		51.1 ± 9.57		[b]0.91[NS]
Sex							
Male	43	86.0	41	82.0	84	84.0	[a]0.92[NS]
Female	7	14.0	9	18.0	16	16.0	

Group I = Patients with BMI <23 kg/m^2
Group II = Patients with BMI ≥ 23 kg/m^2
NS= Not Significant (p>0.05)
[a]p-value reached from chi-square test and Fisher exact test
[b]p-value reached from unpaired t-test

Table-II

Comparison of the study groups according to their risk factors (N = 100)

Risk factors	BMI				Total (N =100)		*p*-value
	Group I (n = 50)		Group II (n = 50)				
	Number	%	Number	%	Number	%	
Smoking	20	40.0	24	48.0	44	44.0	0.587[NS]
DM	9	18.0	21	42.0	30	30.0	0.038[S]
Hypertension	11	22.0	23	46.0	34	34.0	0.048[S]
Dyslipidemia	7	14.0	20	40.0	27	27.0	0.022[S]
Family history of CAD	14	28.0	14	28.0	28	28.0	0.931[NS]

Group I = Patients with BMI < 23 kg/m^2
Group II = Patients with BMI ≥23 kg/m^2
DM = Diabetes mellitus
CAD = Coronary Artery Disease
S = Significant ($p < 0.05$)
NS = Not Significant ($p > 0.05$)
p-value reached from chi-square test

Table-III

Comparison of the study groups by their height, weight and BMI (N=100).

Parameters	BMI		Total(N =100)	*p*- value
	Group I (n = 50) Mean ± SD	Group II (n = 50) Mean ± SD	Mean ± SD	
Height(in meter)	1.61 ± 0.07	1.63 ± 0.06	1.62 ± 0.06	0.26^{NS}
Weight(in kilogram)	55.5 ± 5.5	65.7 ± 5.9	63.4 ± 7.2	0.001^{S}
BMI cutoff value 23 kg/m^2	21.3 ± 1.4	24.7 ± 1.4	23.9 ± 1.9	0.001^{S}
	*Group I (n=81)	*Group II (n= 19)		
BMI cutoff value 25 kg/m^2	23.3 ± 1.5	26.7 ± 1.3	23.9 ± 1.9	0.001^{S}

Group I = Patients with BMI <23 kg/m^2
Group II = Patients with BMI ≥23 kg/m^2
* = Had non-Asian BMI category been used in this study
S= Significant (*p*<0.05)
NS= Not Significant (*p*>0.05)
p-value reached from unpaired t-test

Table-IV

Comparison of height, weight and BMI within each study groups by sex of the patients (N = 100).

Study group	Male (n= 84)		Female (n= 16)		Mean±SD(N =100)	*p*-value
	Number	Mean ± SD	Number	Mean ± SD		
Height in meter	84	1.64 ± 0.04	16	1.51 ± 0.06	1.62 ± 0.06	0.001^{S}
Weight in kilogram	84	64.5 ± 6.3	16	56.4 ± 8.6	63.4 ± 7.2	0.006^{S}
Group I(n = 50)	43	21.2 ± 1.4	7	21.9 ± 0.8		0.436^{NS}
Group II(n = 50)	41	24.6 ± 1.3	9	25.3 ± 1.9		0.169^{NS}
	84	23.9 ± 1.9	16	24.5 ± 2.3	23.9 ± 1.9	0.294^{NS}

Group I = Patients with BMI <23 kg/m^2, Group II = Patients with BMI ≥23 kg/m^2.
S= Significant (*p*<0.05)
NS= Not Significant (*p*>0.05)
p-value reached from unpaired t-test

Table - V

Comparison of the study population by clinical presentations (N = 100)

Diagnosis	BMI				Total (N =100)		*p*-value
	Group I (n = 50)		Group II (n = 50)				
	Number	%	Number	%	Number	%	
CSA	6	12.0	5	10.0	11	11.0	0.27^{NS}
UA	6	12.0	7	14.0	13	13.0	
NSTEMI	9	18.0	11	22.0	20	20.0	
STEMI	29	58.0	27	54.0	56	56.0	

Group I = Patients with BMI < 23 kg/m^2
Group II = Patients with BMI ≥ 23 kg/m^2
CSA = Chronic Stable Angina
UA = Unstable Angina
NSTEMI = Non-ST-segment Elevation Myocardial Infarction
STEMI = ST-segment Elevation Myocardial Infarction
NS = Not Significant (*p* > 0.05)
p-value reached from chi-square test

Table VI shows that the baseline LV function measured by echocardiography between the two study groups was not statistically significant (p > 0.05). The difference of mean LVEF was also insignificant statistically (p > 0.05) between the groups. Post-PCI echocardiography to assess LV function was not done routinely.

Table VII compares the involvement of vessels between the groups. There was no statistical significance of difference between the two groups ($p > 0.05$).

Table VIII compares the types of stent used between the groups. DES outnumbers BMS in each groups. No significant difference was found between the groups ($p > 0.05$).

The adverse in-hospital outcomes were significantly ($p<0.01$) higher in Group I than Group II. Among all adverse in-hospital outcomes, only acute LVF was found to be statistically significant between the two study groups ($p< 0.01$) (Table IX).

Smoking and family history of CAD were not included in multivariate model as univariate analysis yielded them as statistically insignificant in the current study (OR = 1.29 and 1.10; 95% CI = 0.82– 1.78 and 0.46 – 1.75; p=0.273 and 0.087, respectively). Hypertension and left ventricular ejection fraction (LVEF) that were significant (OR = 1.51 and 1.53;95% CI = 1.05 – 2.10 and 1.32 – 1.78; p=0.026 and 0.049, respectively) in univariate analysis were found to be insignificant (OR = 1.36 and 1.15; 95% CI = 0.92 – 1.95 and 0.98 – 1.35; p=0.114 and 0.087, respectively) in multivariate regression analysis. Diabetes mellitus and dyslipidemia were found to be the independent predictors for developing adverse in-hospital outcome after PCIs (OR= 1.68 and 1.46; 95% CI = 1.25 – 2.24 and 1.16 – 1.83; p=0.018 and 0.040, respectively). BMI was inversely associated with adverse in-hospital outcome after adjustment by multivariate logistic regression analysis (OR = 0.95; 95%CI = 0.91–0.98; p=0.007) (Table X).

Table - VI

Comparison of the study groups according to their LVEF (N = 100)

LVEF	BMI				Total		*p*-value
	Group I (n = 50)		Group II (n = 50)		(N =100)		
	Number	%	Number	%	Number	%	
<50	23	46.0	29	58.0	52	52.0	[a]0.79[NS]
>50	27	54.0	31	62.0	58	58.0	
Mean ± SD	53.4 ± 8.2		52.1 ± 8.1		53.3 ± 8.1		[b]0.69[NS]

Group I = Patients with BMI < 23 kg/m^2
Group II = Patients with BMI ≥23 kg/m^2
LVEF = Left Ventricular Ejection Fraction
NS = Not Significant ($p > 0.05$)
[a]*p*-value reached from chi-square test
[b]*p*-value reached from unpaired t-test

Table-VII

Comparison of the study groups by involvement of vessels (N = 100)

Vessels involved	BMI				Total		*p*-value
	Group I (n = 50)		Group II (n = 50)		(N =100)		
	Number	%	Number	%	Number	%	
LAD	16	32.0	12	24.0	28	28.0	0.07[NS]
RCA	19	38.0	21	42.0	40	40.0	
LCX	7	14.0	10	20.0	17	17.0	
LAD & RCA	5	10.0	6	12.0	11	11.0	
RCA & LCX	1	2.0	0	0.0	1	1.0	
LAD & LCX	2	4.0	1	2.0	3	3.0	

Group I = Patients with BMI < 23 kg/m^2
Group II = Patients with BMI ≥ 23 kg/m^2
LAD = Left Anterior Descending Artery
RCA = Right Coronary Artery
LCX = Left Circumflex Artery
NS = Not Significant ($p > 0.05$)
p-value reached from chi-square test and Fisher exact test

Table-VIII

Comparison of the study groups according to the types of stent used (N = 100)

Types of stent used	BMI				Total (N =100)		*p*-value
	Group I (n = 50)		Group II (n = 50)				
	Number	%	Number	%	Number	%	
DES	27	54.0	29	58.0	56	56.0	0.07^{NS}
BMS	16	32.0	15	30.0	31	31.0	
DES & BMS	7	14.0	6	12.0	13	13.0	

Group I = Patients with BMI < 23 kg/m^2
Group II = Patients with BMI ≥23 kg/m^2
DES = Drug Eluting Stent
BMS = Bare Metal Stent
NS = Not Significant ($p > 0.05$)
p-value reached from chi-square test

Table - IX

Comparison of the study groups by in-hospital outcomes after PCI (N=100).

Types of stent used	BMI				Total (N =100)		*p*-value
	Group I (n = 50)		Group II (n = 50)				
	Number	%	Number	%	Number	%	
Adverse outcomes	11	22.0	3	6.0	14	14.0	0.006^{S}
Chest pain	2	4.0	1	2.0	3	3.0	0.630^{NS}
Arrhythmia	2	4.0	0	0.0	2	2.0	0.058^{NS}
Access site complications	1	2.0	1	2.0	2	2.0	0.630^{NS}
Acute LVF	4	8.0	0	0.0	4	4.0	0.007^{S}
Shock	2	4.0	0	0.0	2	2.0	0.058^{NS}
Death	0	0.0	1	2.0	1	1.0	0.594^{NS}

Group I = Patients with BMI < 23 kg/m^2
Group II = Patients with BMI ≥23 kg/m^2
S = Significant ($p < 0.05$)
NS = Not Significant ($p > 0.05$)
p-value reached from chi-square test and Fisher exact test

Table - X

Univariate and multivariate logistic regression analyses of variables associated with adverse in-hospital outcomes.

Variables of interest	Univariate analysis		*p*- value	Multivariate analysis		*p*- value
	OR	95% CI of OR		OR	95% CI of OR	
Smoking	1.29	0.82 - 1.78	0.273			
Hypertension	1.51	1.05–2.10	0.026	1.36	0.92 – 1.95	0.114
Diabetes	1.97	1.61 – 2.41	0.011	1.68	1.25 – 2.24	0.018
Dyslipidemia	1.54	1.11 – 1.72	0.034	1.46	1.16 – 1.83	0.040
Family history	1.10	0.46 – 1.75	0.087			
LVEF	1.53	1.32 – 1.78	0.049	1.15	0.98 – 1.35	0.087
BMI	0.89	0.87 – 0.92	0.004	0.95	0.91 – 0.98	0.007

Discussions:

Obesity measured on the basis of BMI is an independent cardiovascular risk factor. A number of studies have shown that the lean patients and those with normal BMI are at a higher risk for adverse in-hospital outcomes and post-PCI complications than overweight and obese patients. This is contrary to the common clinical perception that overweight and obese patients would be at a higher risk of adverse outcomes following PCI. To date, there is not a complete understanding of this complex effect.

The age distribution of the studied patients was very close to the other relevant studies.[15,16] The sex distribution of this study population is not comparable to the overall population of Bangladesh because there were fewer females in this study. In Bangladesh, almost all of the studies reported an overwhelming majority of male patients.[17–19] Females were found to be more obese than male in the current study as well as in the other studies.[20-21] In comparison with Europeans, the mean stature of Bangladeshi counterparts is 1.3 cm to 11.8 cm shorter.[22] BMI tends to be higher among shorter adults, especially women.[23]

In-hospital adverse outcomes after PCI was significantly higher in Group I. Compared with normal-weight individuals, overweight and obese patients had lower in-hospital adverse outcomes after PCI.[24] Among all the adverse in-hospital outcomes, only LVF was found to be significantly more in Group-I. A study on 1,203 individuals with class IV heart failure found that higher BMI was associated with better survival, and multivariate analysis showed an inverse association between BMI and mortality.[25] BMI was inversely associated with post-PCI adverse in-hospital outcome after adjustment by multivariate logistic regression analysis in this study. Gruberg et al.[12] noticed that very lean patients (BMI <18.5) and those with normal BMI are at the highest risk for in-hospital complications and cardiac death. Patients at the extremes of BMI (<18.5 and >40kg/m^2) were also at increased risk of adverse outcomes after PCI.[26] Park et al. found that low BMI was associated with increased risks of adverse in-hospital outcomes and death.[27] They also found no excess risks of these events to be associated with a high BMI. A Japanese real-world multicenter registry analysis reported that lean patients, rather than obese patients were at greater risk for in-hospital complications during and after PCI.[27] Although obesity via its negative impact on systolic and diastolic function predisposes to overt heart failure, clinical evidence suggests that overweight/obese patients with heart failure paradoxically seem to have a better clinical prognosis than do their lean counterparts with clinical heart failure. In essence, obesity is a risk factor for developing heart failure, but after the onset of heart failure, obesity is a positive predictor for survival. The existence of this obesity paradox has led physicians to question whether obesity should be treated when associated with heart failure.[25]

Conclusion:

BMI was inversely associated with in-hospital left ventricular failure after PCI in this study. The underweight and normal weight people were at greater risk to experience in-hospital adverse outcomes than overweight and obese people following PCI. Though obesity is a recognized risk factor for cardiovascular diseases, once cardiovascular disease is developed, this obesity seems to play protective roles and provide some benefits. This 'Obesity Paradox' leads us to reshuffle and reorganize our plans whether we should take aggressive attempts or schemes to lose weight of an obese patient once he or she develops coronary artery disease. Verily it calls for more research and observations.

Limitations of the study

There are some facts to be considered which might have affected the result of the current study.

- The study population was heterogeneous, including patients with different severities of CAD, ranging from chronic stable angina to myocardial infarction.
- The complexity of the lesions, procedural complications, use of anticoagulants and antiplatelets were not recorded which might have affected the incidence of complications in each of the BMI groups.

Conflict of interest- None.

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Original Article

Correlation between Echocardiographic Epicardial Fat Thickness and Angiographic Severity of Coronary Artery Disease

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Abstract:

Background: Epicardial adipose tissue (EAT) is a visceral adipose tissue surrounding the heart and the coronary arteries. Because of its endocrine and paracrine activity, secreting pro-inflammatory and anti-inflammatory cytokines and chemokines, it has been suggested to influence coronary atherosclerosis development. Objectives: To identify the relationship between echocardiographic epicardial fat thickness and the extent of coronary artery disease (CAD). Methods: Considering the inclusion and exclusion criteria, a total 87 patients with established or suspected coronary artery disease admitted for coronary angiogram were included in this study. After taking written consent, initial evaluation of the patients was done by history, clinical examination and relevant investigation. Variables, risk factors for CAD and investigation reports were recorded in data sheet. Echocardiography and coronary angiography were done. EAT thickness measurements by echocardiography were compared with coronary angiographic findings. Results: Echocardiographic EAT thickness was significantly higher in patients with CAD in comparison to those with normal coronary arteries 7.14±1.81 mm vs 4.08±1.06mm (p <0.001). Furthermore, EAT thickness increase with the severity of CAD. EAT is 4.08±1.06 mm in patients with normal/non-significant CAD (n=20), 5.75±0.96 mm in single vessel CAD (n=24), 6.54±1.09 mm in double vessel CAD (n=16) and 8.75±1.45 mm in patients with triple vessel CAD (n=27). Conclusions:EAT thickness was significantly higher in patients with angiographically detected CAD in comparison to those with normal coronary arteries. Furthermore, EAT thickness increased with the severity of CAD; i.e. it was thicker in multivessel coronary artery disease than in single vessel or non-significant coronary artery disease.

Key words: Coronary Artery Disease, Echocardiography, Adipose Tissue, Angiography.

(Bangladesh Heart Journal 2018; 33(1): 47-53)

Introduction

Different types of adipose tissue, particularly subcutaneous and visceral adipose depots, are now recognized as having distinct quantitative characteristics.[1,2]Visceral adiposity is a fat deposition around internal organs. It is metabolically active.[3] It is strongly correlated with diabetogenic features (e.g., impaired insulin sensitivity, increased insulin levels),

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37025

atherogenic features (e.g., increased triglycerides, decreased high density lipoproteins), prothrombotic factors (e.g., increased fibrinogen, Factor VII, plasminogen activator inhibitor-1) and proinflammatory cytokines (e.g., interleukin-6 [IL-6] and tumor necrosis factor-a [TNF- a]).[4]Epicardial adipose tissue (EAT) is considered as visceral fat deposited around the heart, particularly around epicardial coronary vessels. Epicardial fat may directly affect the coronary arteries and myocardium through paracrine actions of locally secreted adipocytokines and other bioactive molecules, contributing to the development of coronary artery disease (CAD).[5]

It is increasingly evident that visceral adipose tissue (VAT) is an important CAD risk factor.[6,7]Recently, it was reported that EATmeasured by transthoracic echocardiography was well correlated with abdominal VAT assessed by MRI and computed tomography and that echocardiographic EAT thicknesscould be used as a reliable imaging indicator of VAT.[8,9]Epicardial fat defined as an echo-free space between the outer wall of the myocardium and the visceral layer of pericardium.[10]The highest diameter of this fat is on right ventricular free wall. Transthoracic echocardiography provides a reliable measurement of epicardial fat thickness (EFT).[3]The subcostal four chamber and parasternal long and short axis echocardiogram views show this finding in best way.[11,12]A normal upper-limit value for EFT has not been established yet.[13]

Although epicardial fat is readily visualized on high speed CT and MRI, widespread use of these methods for its assessment is not practical. In this context, Echocardiographic assessment of EAT could be a simple and practical tool for cardiovascular risk stratification in clinical practice and research.The general objective of this study was to identify the relationship between echocardiographic epicardial fat thickness and the extent of coronary artery disease. There were some specific objectives also, i.e., to measure epicardial fat thickness by transthoracic echocardiography; to measure the severity of coronary artery disease by CAG; to establish echocardiographicepicardial fat thicknessmeasurement as a simple, non-invasive, time efficient and reliable imaging indicator for cardiovascular risk

Methods:

This was a cross-sectional analytical study conducted in the Department of Cardiology, Dhaka Medical College&Hospital over a period of one year (July, 2015 to June 2016) on 87 purposively sampled patients with myocardial infarction, unstable angina and stable angina who underwent echocardiography and CAG and who fulfilled the inclusion and exclusion criteria. To minimize the confounding effects, the following patients were excluded from the study, i.e., pericardial effusion, abnormal images on transthoracic echocardiography or poor echo window, history of coronary artery bypass graft surgery (CABG), history of percutaneous coronary intervention (PTCA), cardiomyopathy, severe comorbidities- like malignancy, chronic kidney disease, patients unwilling to given consent, moderate to severe degree of valvular heart disease, etc.

Prior to the commencement of this study, the research protocol was approved by the Research Review Committee of Department of Cardiology and the Ethical Committee of DMCH, Dhaka. Detailed history, clinical examination and relevant investigation reports of all patients were recorded in pre-designed data collection sheet at the beginning of the study. Cardiac catheterizations and coronary angiography was performed using the Judkin's technique. All standard views were taken. In selected cases additional views were taken. CAG was analyzed by visual estimation. 70% or more luminal stenosis was considered significant except in left main coronary artery lesion where 50% or more luminal stenosis was considered significant. The reporters of CAG had no prior knowledge of the echocardiographic findings.The report was defined as single vessel disease, double vessel disease and triple vessel disease as follows- i) Single-vessel disease: Presence of ≥70% diameter lumen narrowing in either the left anterior descending, left circumflex or right coronary artery or a major branch. ii) Double-vessel disease: Presence of ≥70% diameter lumen narrowing in two of the three major epicardial vessel systems. iii) Three-vessel disease: Presence of ≥70% diameter lumen narrowing in all three major epicardial vessel systems. Each patient underwent transthoracic echocardiography (TTE) by Vivid 7 (GE, USA) in the left lateral decubitus position the next day after CAG. EAT thickness was measured on the free wall of right ventricle from the parasternal long-axis views. EAT was identified as the anterior echo-lucent space between the outer wall of the myocardium and the visceral layer of pericardium on the two-dimensional echocardiography and its thickness was measured in still images on the free wall of the right ventricle along the midline of the ultrasound beam with best effort to be perpendicular to the aortic annulus in parasternal long axis view, at end-diastole for 3 cardiac cycles. The average value from 3 cardiac cycles for each echocardiographic view was used for the statistical analysis. The offline measurement of EAT thickness was performed by two cardiologists, expert in echocardiography who would be unaware of the clinical and angiographic findings.All the data were compiled duly in the data collection sheet for statistical analysis and interpretation.

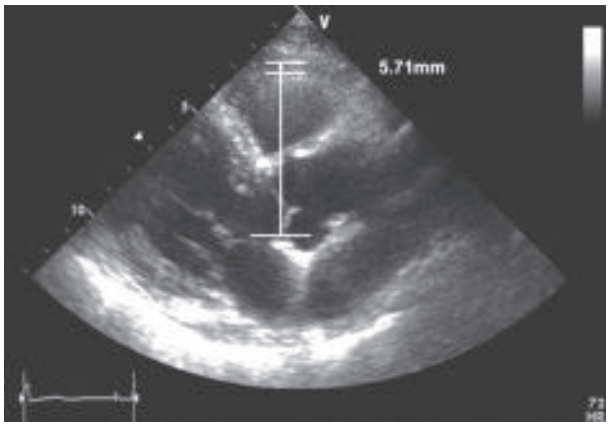

Fig-1: Example of measurement of epicardial fat thickness (EAT). Epicardial fat was identified as an echo-free space in the pericardial layers on the 2-dimensional echocardiography and its thickness was measured perpendicularly on the free wall of the right ventricle at end-diastole.

Statistical analysis was conducted using SPSS 22software on Windows 7. Continuous parameters were expressed as mean± SD and categorical parameters as frequency and percentage. Comparison between groups (continuous parameters) was done by unpaired t test. Categorical parameters were compared by chi-squared test. Comparisons among groups (continuous parameters) was done by ANOVA test.Correlation analyses were done by Pearson correlation coefficient test. The significance of the results as determined in 95.0% confidence interval and a value of p <0.05 was consider to be statistically significant.

Results:

A total 87 patients were selected for the study of which 67 had CAD and 20 had normal coronary angiogram. Baseline characteristics, risk factors for CAD and echocardiographic EAT thickness were compared and presented in different tables and figures below.

Table-I shows that patients with CAD were older. Mean age was 53.25±10.27 years in patients with CAD and 46.80±8.25 years in patients without CAD (p=0.012). Male (77.6%) was predominant in patients with coronary artery disease, but in patients without coronary artery disease, female (65.0%) was found as predominant gender. The mean EAT thickness of the patients was 6.44±2.11 mm (range 2.20-11.0 mm). It was significantly thicker in patients with CAD (7.14±1.81mm) than those without CAD (4.08±1.06mm) (p=<0.001).

Diabetes mellitus anddyslipidemia were more common in patients with significant coronary artery disease (p<0.05). There was no significant inter group difference on smoking, hypertension and BMI (p>0.05). Waist circumference were statistically significant in patients with CAD (p =0.009).

Table II shows the distribution of EAT between male and female patients, mean EAT was 6.81±1.94 in male and

Table-I

Baseline characteristics of patients (n=87)

Characteristics	CAD (-) (n=20)		CAD (+) (n=67)		P value
Age (years)	46.80±8.25		53.25±10.27		$^{a}0.012^{s}$
Body mass index (kg/m^2)	23.68±1.95		24.74±3.23		$^{a}0.170^{ns}$
Waist circumference (cm)	85.25±7.41		90.75±8.29		$^{a}0.009^{s}$
Epicardial adipose tissue (mm)	4.08±1.06		7.14±1.81		$^{a}<0.001^{s}$
Sex	n	%	N	%	
Male	9	45.0	52	77.6	$^{b}0.005^{s}$
Female	11	65.0	15	22.4	
Smoking	6	30.0	35	52.2	$^{b}0.080^{ns}$
Hypertension	7	35.0	37	55.2	$^{b}0.112^{ns}$
Diabetes mellitus	4	20.0	31	46.3	$^{b}0.036^{s}$
Dyslipidaemia	10	50.0	57	85.1	$^{b}0.001^{s}$

CAD (-)= normal coronary artery. CAD (+) = coronary artery disease, s = significant, ns=not significant, ^{a} = p value reached from unpaired 't' test. ^{b}= p value reached from chi-square test

Table-II

Comparison of EAT between male and female patients (n=87)

Gender	Male (n=61) Mean±SD	Female (n=26) Mean±SD	P value
EAT	6.81±1.94	5.58±2.27	0.012^{s}

EAT = epicardial adipose tissue,p value reached from unpaired t-test, s= significant

5.58±2.27 in female patients. There is statistical significant difference between male and female patients (p=0.012).

Table III shows a significant positive correlation between epicardial adipose tissue (EAT) thickness and Age (r=0.373, p<0.001), BMI (r=0.275, p=0.01), waist circumference (r=0.471, p<0.001), TC (r=0.272, p=0.011), TG (r=0.305, p=0.004) and LDL (r=0.271, p=0.011) and negative correlation with HDL (r=-0.298, p=0.005).

The data of echocardiographic EAT thickness were arranged in quartiles and the incidence of CAD was assessed which are showed in Table-IV. The range of thickness was 2.20-5.00mm (n=20) in 1st quartile, 5.01-6.00mm (n=23) in 2nd quartile, 6.01-8.00mm (n=23) in 3rdquartile and 8.01-11.0mm (n=21) in 4th quartile. Table IV shows the percentage of significant coronary artery disease according to the quartiles of echocardiographicEAT thickness. CAD were found in 12(60.0%) patients in 1st quartile, 16(69.6%) patients in 2nd quartile, 19(82.6%) patients in 3rdquartile and 20(95.2%) patients in 4th quartile. The increasing percentage of CAD in the quartiles was significant (p <0.05).

Table-V shows that EAT thickness is 4.08±1.06 mm in patients with normal/non-significant CAD (n=20), 5.75±0.96 mm in single vessel CAD (n=24), 6.54±1.09 mm in double vessel CAD (n=16) and 8.75±1.45 mm in patients with triple vessel CAD (n=27). The increasing thickness of EAT in more severe form of coronary artery disease was significant (p<0.001).

Table – III

Correlation between epicardial adipose tissue (EAT) thickness and clinical and laboratory parameters

	r	p-value
Age	0.373	<0.001[s]
BMI	0.275	0.010[s]
Waist circumference	0.471	<0.001[s]
TC	0.272	0.011[s]
Triglyceride	0.305	0.004[s]
HDL-C	-0.298	0.005[s]
LDL-C	0.271	0.011[s]

r =Pearson's correlation co-efficient, s= significant (p< 0.05).

Table –IV

Incidence of coronary artery disease according to the quartiles of epicardial adipose tissue (EAT) thickness (n=87)

Quartiles	CAD (+) (n=67)		CAD (-) (n=20)		P-value
	n	%	n	%	[a]0.039[s]
1st quartile (2.20-5.00) (n=20)	12	60.0	8	40.0	
2nd quartile (5.01-6.00) (n=23)	16	69.6	7	30.4	
3rd quartile (6.01-8.00) (n=23)	19	82.6	4	17.4	
4th quartile (8.01-11.0) (n=21)	20	95.2	1	4.8	

s=significant (p<0.05), a=p-value reached from chi-square test, 1st quartile=Below Q_1, 2nd quartile=Q_1 to below Q_2, 3rd quartile=Q_2 to below Q_3, 4th quartile = Q_3 and above, CAD (-) =normal coronary artery, CAD (+) =coronary artery disease

Table-V

Epicardial adipose tissue (EAT) thickness and severity of coronary artery disease (CAD)

Investigation	Normal/non-significant CAD (n=20) Mean±SD	Single vessel CAD (n=24) Mean±SD	Double vessel CAD (n=16) Mean±SD	Triple vessel CAD (n=27) Mean±SD	p-value
EAT thickness (mm)	4.08±1.06	5.75±0.96	6.54±1.09	8.75±1.45	[a]<0.001[s]

EAT= epicardial adipose tissue, CAD=coronary artery disease, a= p value reached from 'one way ANOVA' (F=64.04), s= significant (p<0.05)

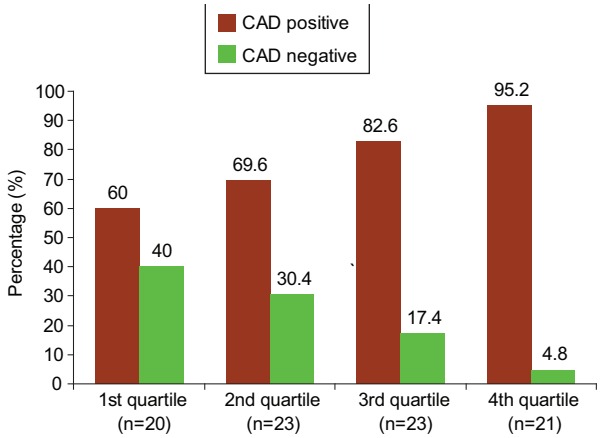

Fig-2: *Bar diagram showing the Incidence of coronary artery disease (CAD) according to the quartiles of echocardiographic epicardial adipose tissue thickness (EAT). (Q= Quartile)*

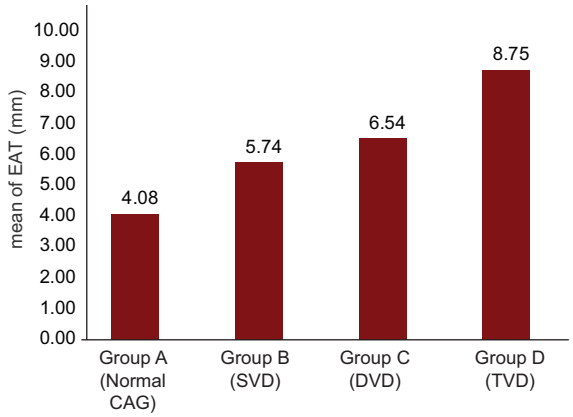

Fig-3: *Epicardial adipose tissue (EAT) thickness and severity of angiographic coronary artery disease (CAD).*

Discussion:

This cross sectional, analytical study was conducted on 87 patients with established or suspected coronary artery disease who were admitted to Department of Cardiology of Dhaka Medical College &Hospital, Dhaka and underwent coronary angiogram. After exclusion, a total 87 patients were included. Echocardiographic measurement of epicardial adipose tissue (EAT) thickness was done accordingly after admission. Based on coronary angiogram, 67 patients had coronary artery disease (CAD) and 20 patients had normal coronary angiogram.

In this study, mean EAT thickness was found 6.44±2.11 mm. EAT thickness may be different according to the race. In a study in USA, conducted by Iacobellis et al.[13] median values of EAT thickness was 9.5 mm in men and 7.5 mm in women. Mean EAT thickness was found 6.1 mm in a study conducted by Sadeaet al.[14] on European population. Mean EAT thickness was found 6.3 mm in a study conducted by jeong et al [15]. In this study the EFT in CAD group was significantly higher than in normal group (7.14±1.81 mm vs 4.08±1.06 mm, p<0.001). These findingsare consistent with study of Shimiraniet al[3] who found significantly higher the EFT in CAD group than in normal group (5.4±1.9 mm vs 4.4±1.8mm, p=0.0001).We found EATto be thicker in men than in women (6.81±1.94 mm vs 5.58±2.27 mm; p =0.012), which was consistent with the study of Sadea et al.[14]whereEAT was also found significantly thicker in men than in women (6.5± 1.6mm vs 5.5± 1.8mm; P<0.001). But, Ahn et al[16]. did not find any difference of EAT thickness between men and women.

EAT thickness showed definite relationship with some clinical and biochemical parameters. In this study, shows a significant positive correlation between EAT thickness and age (r=0.373, p<0.001), BMI (r=0.275, p=0.01), waist circumference (r=0.471, p<0.001), TC (r=0.272, p=0.011), TG (r=0.305, p=0.004) and LDL (r=0.271, p=0.011) and inversely correlated with HDL-C (r=-0.298, p=0.005). Ahnet al[16]. revealed similar findings in their study.Shemiraniet al.[3]found that EFT had a positive correlation with LDL, BMI (p=0.001), serum triglyceride (p=0.04) and WC (p=0.04), which correlate with this study.Jeonget al[15]. stated a significant correlation was revealed between EAT and age (r=0.332, p<0.001), body mass index (r=0.142, p=0.044) and waist circumference (r=0.229, p=0.001).

In this study, significant CAD was found in 60% patients in 1st quartile, 69.6% patients in 2nd quartile, 82.6% patients in 3rd quartile and 95.2% patients in 4th quartile of EAT thickness. The increasing percentage of CAD in higher quartiles was significant (p<0.039). This finding was consistent with those of some previous studies, which also showed that EAT was significantly thicker in subjects with CAD than those without CAD.[14,15]

EAT thickness showed significant variation among patients with normal/non-significant CAD, single vessel CAD, double and triple vessel CAD. The thickness was 4.08±1.06 mm in patients with normal/non-significant CAD (n=20), 5.75±0.96 mm in single vessel CAD (n=24), 6.54±1.09 mm in double vessel CAD (n=16) and 8.75±1.45 mm in patients with triple vessel CAD (n=27) in this study. This increasing thickness of EAT in more severe form of coronary artery disease was statistically significant (p <0.001). This finding of correlation between EAT thickness and the severity of CAD was compatible with that of previous two studies.[14,15]

Data of this study strongly support that there is association between EAT thickness and the presence and severity of angiographically detected CAD. Two potential mechanisms for this association have been proposed: First, EAT is a component of visceral adiposity and is related to cardiovascular risk factors[13] ; secondly, EAT has paracrine and endocrine functions. It can secrete numerous bioactive molecules (adipokines) such as adiponectin, resistin and inflammatory cytokines, like- interleukin (IL) - 1b, IL-6, tumor necrosis factor- alpha etc[17]. Sacks et al. pointed out the paracrine and vasocrine signaling effects of epicardial adipokines for the development of atherogenesis. It is evident that EAT thickness is part of active adipose tissue that mediates coronary circulation via secretion of inflammatory mediators and adipokines.[18]

Conclusion:

Epicardial adipose tissue (EAT) thickness, which can easily be and non-invasively evaluated by transthoracic echocardiography, is significantly higher in patients with angiographically detected coronary artery disease in comparison to those with normal coronary arteries. Furthermore, EAT thickness increases with the severity of coronary artery disease; i.e it is thicker in multivessel coronary artery disease than in single vessel or non-significant coronary artery disease.

Study limitations

There may be selection bias because this study included only those patients pre-selected to undergo coronary angiography.As epicardial adipose tissue has a three-dimensional (3D) distribution, two dimensional (2D) echocardiography may not assess the total amount of epicardial adiposity completely. Epicardial adipose tissue thickness can be measured as a mean of values from parasternal long axis and short axis views.In this study, the value measured from the parasternal long axis view was used. A large, prospective, cohort study might be necessary to elucidate the clinical significance of epicardial adipose tissue (EAT) thickness in the general population.

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Original Article

Angiographic Analysis of Trans-Radial Percutaneous Coronary Intervention Cases by the Backup Support of Guide Extension Catheter

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Abstract:

Background: **The guide extension catheter – *Guidezilla* (Boston Scientific, United States of America) is a useful adjunctive tool in percutaneous revascularization of complex coronary lesions, and provides an extension to the guide catheter with better coaxial alignment, support and stability.*Objective:* The objective of this study was to describe the usefulness and easy deliverability of stent by *Guidezilla*in the trans-radial treatment of complex coronary lesions as our initial experience.*Methods:*This prospective observational study was conducted at the Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute (ICHRI), Dhaka from July 2016 to September 2017. The transradial approach was used in all cases. Clinical, angiographic and procedural data of percutaneous coronary interventions performed using *Guidezilla*, including indications for use of *Guidezilla* were collected and analyzed. *Results:*A total of 19 procedures (in 18 patients) were evaluated. 57.89% of cases were related to left circumflex coronary artery or obtuse marginal branch. The commonest challenge for use of *Guidezilla*was proximal angulation (63.15%) and calcification (47.4%). Commonest type of lesion was ACC/ AHA Type C lesion (63.2%). Successful stent deployment was achieved in 16 of the 19 procedures (84.2%). Among the unsuccessful cases, there was stent damage in one case and distal dissection after deployment of a stent in other. Stent deployment was not possible in two cases, due to diffuse lesion and heavy calcification.*Conclusions:*Guide extension catheter is a good trans-radial back-up support for calcified, complex and tortuous coronary anatomy, which otherwise may have been considered unsuitable for PCI. The use of such support can reduce the necessity for the more expensive alternative of deploying multiple small stents in order to traverse the lesions.**

Key words: Percutaneous Coronary Intervention, Angiography, Catheter.

(Bangladesh Heart Journal 2018; 33(1): 54-60)

Introduction:

The guide extension catheter- Guidezilla is a useful tool in the armamentarium of the interventional cardiologist. As a modified "mother and child" system, it provides an extension to the guide catheter with better coaxial alignment and stability.Its usefulness in everyday cardiac catheterization laboratory practice is indisputable, particularly, where the radial artery is used as a default vascular access route for all types of percutaneous coronary intervention (PCI). A good back-up represents one of the most important conditions to ensure guidewire, balloon advancement and successful deployment

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37026

of stent, which contributes to PCI success.[1]There is difficulty in the use of angioplasty balloons and stents in the presence of calcification, marked tortuosity andchronic total occlusions, leading to a considerable failure of stent deployment (approximately 3%).[1,2]Balloon anchor technique makes delivery of *Guidezilla* through complex, Transradialanatomy easy. This sort of device not only reduces the incidence of surgical revascularization, but also reduces the expense of the patients, in terms of a reduced cost due to a reduced number of stents deployed. Prior to the availability of this device in our catheterization laboratory, it was customary to deploy two or more small length stents in order to traverse the tortuosity and proximal angulation of the vessels. This represents an economic burden for a developing country like Bangladesh, a country only beginning to approachthe lower limit of middle income Gross Domestic Product (GDP), because in addition to the cost of the stent, the majority of the population does not have health insurance coverage.

The use of Buddywire technique,stiffer guide wire, anchoring balloon technique, and deeper intubation of the guide catheter are some of the other measures used to improved back up support in complex lesions.[3-5] Thus, the use of *Guidezilla* is suitable when facing unexpected delivery challenges during PCI, obviating the need for guide catheter exchange.[6]Furthermore, use of *Guidezilla* can also reduce the amount of dye injected, thus it has distinct benefit for patients with chronic kidney disease (CKD)[7] and the elderly, whose renal reserve is poor. There are also other commercially available monorail guide extender catheters, such as *GuideLiner®* catheter (Vascular Solutions Inc.), *Kiwami (*Terumo, Tokyo, Japan), and *Cokatte* (Asahi Intecc).

The GuideExtension Catheter-*Guidezilla* 6F (5-in-6) (Boston Scientific, USA) that was used in this study has a minimal internal diameter of1.45 mm. This catheter consists of a monorailsystem, which extends to the distal end of the guide catheter ('mother-child' fashion), with a length of 25 cm, a thickness of1Frless than the guide catheter and a design that minimizes trauma onthe artery wall. The monorail continues proximally with a thin hypotube.The 1x1 braidof *Guidezilla* helps to straighten the vessel without lengthening it.The technique begins with engaging the guiding catheter(mother) and positioning the guide.Once the guide catheter and guide wire are placed, the Guide Extension catheter can be advanced over the guide wire through the hemostatic valve as an extension to the guide catheter. Subsequently, the procedure can be continued as usual, without need for disconnection and reattachment.

Material & Methods:

This prospective observational study was conducted at the Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute (ICHRI), Dhaka, Bangladesh during the period extending from July 2016 to September 2017. Demographic characteristics, risk factors, left ventricular ejection fraction (EF), angiographic and procedural data of PCI done in patients with the use of Guide Extension Catheter - *Guidezilla* were collected. The Transradial approach was used in all cases.

All consecutive cases oftrans-radial PCI where *Guidezilla* was used for support,were prospectively included in the study. A total of 19 procedures were performed in the 18 patients. The study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Informed written consent was taken from patients or next of kin. Prior ethical approval was obtained from the ethical review committee of ICHRI.

Image Acquisition and interpretation:Coronary angiography was donebytrans-radial route, either right or left. Right radial approach was used as default vascular access route. Left radial route was reserved for graft vessel angiography where LIMA grafts were made in post coronary artery bypass graft (CABG) cases. Routine pre-medication was administered with special attention to those with prior history of allergy. Iodinated contrast media was used. In cases of CKD, iso-osmolar non-ionic media Iodixanol (*Visipaque)* was used. Image interpretation and was performed by two independent readers and disagreement between readers regarding treatment strategy was resolved by Heart Team discussion. Coronary arteries were segmented according to a modified version of the American College of Cardiology(ACC)/ American Heart Association (AHA) 15-segment model (which includes the ramus intermedius, if present, as segment 16).[8] Each coronary segment was visually analyzed with regard to the presence of stenosis and its severity was classified as follows: no lesion, eccentric plaque (<30% diameter), mild lesion (30–49% stenosis), moderate lesion (50–69% diameter stenosis), severe stenosis (70–98% of diameter), subtotal stenosis (99%), or total occlusion (100%). Obstructive coronary artery disease (CAD) was defined as a stenosis ≥70% in at least one coronary segment, except left main stem where stenosis ≥50% was considered significant.[9]Significant lesions were classified according to Modified ACC/AHA Task Force Criteria for Lesion Morphology as Type A, B1, B2 and C lesions.[10]

The indication for *Guidezilla* use, efficacy and peri-procedural complications were noted. Success of the procedure was defined as the achievement of optimal angiographic outcome with no significant residual stenosis and a distal Thrombolysis in Myocardial Infarction (TIMI) 3 flow after stenting.[9] All peri-procedural complications were noted.

Patients were followed up during hospital stay and any adverse outcomes were noted.Data were processed and analyzed using software using SPSS 16.0 (Statistical Package for the Social Sciences by SPSS Inc., Chicago, IL, USA, 2007).

Results:

A total of 19 consecutive procedures (in 18 patients) were evaluated, (15 males and 3 females). Mean age was 62.3 ± 11.2 years and (range 43-81) years. 15 (83.33%) males and 3 (16.67%) females were included. Table I shows the baseline patient characteristics. A great majority of the subjects were dyslipidaemic (77.8%), followed by hypertensive (72.2%) and diabetic (66.7%). Smoking and CKD each comprised of 27.8% each. The most frequent indication for PCI among the study subjects was stable ischaemic heart disease (SIHD) which constituted 38.9%, followed by unstable angina (UA) comprising 33.3%. Non-ST elevation myocardial infarction (NSTEMI) and ST elevation myocardial infarction (STEMI) comprised of 16.7% and 11.1% respectively.The majority (55.6%) of patients undergoing PCI had normal LV systolic function, defined as LVEF of e"55%; (38.9% patient) had mild LV dysfunction (LVEF 45-54%) and 5.6%moderate LV dysfunction (LVEF 30- 44%) LV systolic dysfunction respectively.Majority (38.9%) of patients underwent PCI with the indication of stable ischaemic heart disease (SIHD) followed by unstable angina (33.3). Two (11.1%) of the patients presented with STEMI.

Table I

Patient baseline characteristics

Total Patients (n=18)	
Age in years (Mean ± SD)	62.3 ± 11.2 (range 43-81)
Gender	
Male	15 (83.33%)
Female	3 (16.67%)
Risk factors	
Diabetes	12 (66.7)
Hypertension	13 (72.2)
Dyslipidaemia	14 (77.8)
Smoker	5 (27.8)
Chronic kidney disease	5 (27.8)
Left ventricular ejection fraction (EF) %	
Normal (LV EF e"55%)	10 (55.6)
Mild LV dysfunction (LV EF 45 -54%)	7 (38.9)
Moderate LV dysfunction (LV EF 30 - 44%)	1 (5.6)
Indications for Percutaneous Coronary Intervention	
ST elevation myocardial infarction	2 (11.1)
Non- ST elevation myocardial infarction	3 (16.7)
Unstable angina	6 (33.3)
Stable ischaemic heart disease	7 (38.9)

Table II depicts the overall summary of lesion characteristics, procedural details, and complications. In all cases, it was possible to properly use the *Guidezilla*, obtaining a deep and selective intubation of the target artery. The target vessel was the left circumflex (LCx) coronary artery or obtuse marginal (OM) branch in the majority of cases (57.89%), followed by left anterior descending artery (26.3%) and right coronary artery (15.8%). The commonest challenge encountered requiring increased back-up support of Guide Extension Catheter was proximal angulation (63.2%) and severe calcification (47.4%). In two cases (10.5%) the indication for use was chronic total occlusion (CTO). Commonest type of lesion was ACC/ AHA lesion Type C (63.2%), followed by type B2 lesion (26.3%). Successful stent deployment was achieved in 16 of the 19 procedures (84.2%).

Table-II

Lesion characteristics, procedural details, and complications

Target vessel, n (%)	
LAD	5(26.3)
LCX	11(57.9)
RCA	3(15.8)
Proximity/ location of lesion, n (%)	
Proximal	5(26.3)
Mid	9(47.4)
Distal	5(26.3)
ACC/ AHA Lesions type, n (%)	
A	0 (0.0)
B1	2(10.5)
B2	5(26.3)
C	12(63.2)
Challenge requiring *Guidezilla,*n (%)	
Severe calcification	9(47.4)
Proximal tortuosity	4(21.1)
Chronic total occlusion	2(10.5)
Proximal angulation	12(63.2)
Stent type, n (%)	
BMS	2(11.1)
DES	16(88.9)
Procedural success, n (%)	16(84.2)
Procedural failure, n (%)	3(15.8)
Complications, n (%)	
Major complication	1(5.3)
Stent damage/ fracture	1(5.3)
Distal dissection	1(5.3)

Table III demonstrates the key angiographic, procedural data and procedural success pertaining to each case in which *Guidezilla* was used. In case number 6, PCI was opted for despite a relatively high Syntax score of case 27, as the patient refused to undergo coronary artery bypass graft (CABG) surgery.

Table-III

Summary of angiographic, procedural data and procedural success pertaining to each case

Case no.	Culprit artery	ACC/AHA lesion type	Syntax Score	Challenge	Guide	Wire	Balloon support	Stent type and size, mm	Result
1	M to D-RCA	C	17	Tortuosity and calcification	AR2	Sion Blue	no	Cre8 4x38, AvantGarde3.5 ×12, CC Flex3.0x08	Distal dissection
2	P-LAD	C		Proximal angulation and calcification	JL 3.5	Sion Blue	no	Xience Prime2.75x28	Success
3	M-LCx to OM2	B2	8	Proximal angulation	JL 3.0	Sion Blue	no	Promus Element Plus 2.75x28, 3.0x38	Success
4	PLB	C	20.5	Tortuosity	JR 3.5	Sion Blue	no	Endeavor Resolute2.25x24, 3.0x12	Success
5	M-LCx to Principal OM	C	11	Proximal angulation	XB 3.5	Sion Blue	no	Promus Element Plus 2.5x20	Success
6	P-LAD	B2	27	Proximal angulation and calcification	JL 3.5	Sion Blue	no	Promus Premier2.5x16	Success
7	M-LCx to Principal OM	C	12	Tortuosity	JL 3.5	Sion Blue	no	Promus Element Plus2.5x32	Success
8	M-LCx	B1	3	proximal angulation	JL 3.0	Sion Blue	yes	Promus Premier2.25x32	Success
9	Principal OM	C		CTO, proximal angulation, Calcification	XB 3.0	PT2	no	AvantGarde-Stent damage	Failure
10	D-LCx	C		proximal angulation and calcification	BL 3.0	PT2	yes	Xience V 2.5x23,2.75x18	Success
11	P-LAD	C	18	Calcification	XB 3.5	Sion Blue	no	Promus Premier2.5x38	Success
12	P-LCx	C		CTO,Calcification and proximal angulation	JL 3.5	PT2	yes	Stent not deployed	Failure
13	M-RCA	C	25.5	Tortuous and calcification	JR 3.5	Sion Blue	no	Promus Premier2.75x24	Success
14	P-LAD	B2		Calcification	JL 3.0	Sion Blue	no	Promus Premier2.25x32	Success
15	OM2	B1	13	Proximal angulation	JL 3.0	Sion Blue	no	Promus Element Plus2.5x20	Success
16	D-LCx	B2	5	Proximal angulation	BL 3.5	Sion Blue	no	Xience Alpine 2.75x23	Success
17	M-LCx to Principal OM	C		Proximal angulation	XB 3.5	Sion Blue	no	Ultimaster3.0x38	Success
18a	D-LAD	B2		high LM take-off, proximal angulation	JL 3.0	PT2	no	Promus Premier-2.25x20	Success
18b	L-PDA	C		high LM take-off, calcification, distal-most lesion	JL 3.0	Sion Blue	yes	Stent not deployed	Failure

3 cases were recorded as unsuccessful (Case numbers 9, 12 and 18b), all of which were related to LCX or OM branch as the target vessel. Among them, there was stent damage in case number 9, which was observed prior to deployment of stent and as such is considered to be a complication mediated by Guidezilla. As such, two small cobalt chromium stents sized 2.25x16mm and 2.5x16mm were deployed instead of the longer DES stent which was damaged (Figures 1 and 2) in order to traverse the proximal angulation.

Distal dissection *after* deployment of stent was noted in case number 1, and as such, was a complication that was not mediated by *Guidezilla*.Drug eluting stents (DES) were predominantly used among the patients in this series, with the exception being in case 9, described above.

Stent deployment was not possible in two cases (numbers 12 and 18b). In case number 12, failure of stent deployment in proximal LCXwas due to heavy calcification, proximal angulation and the lesion being a CTO in an 81-year-old elderly male.

In case number 18b, stenting of the left- posterior descending artery (L-PDA) was unsuccessful due to heavy calcification, high left-main take off and distal-most location of the target lesion. The majority of stents deployed were drug-eluting stents (88.9%), except two cases (11.1%) in which cobalt chromium stents were deployed. Only a single major complication related to *Guidezilla* was reported, that of stent damage in case number 9.

Minor complications such as radial spasm was observed in 3 cases, and pressure dampening in 4 cases both of which are known to be acceptable complications in the trans-radial use of Guide Extension Catheter.Radial spasm was successfully overcome by the use of injectable fentanyl and verapamil. Pressure dampening was managed by careful pullback of the guide extension catheter, and thus was devoid

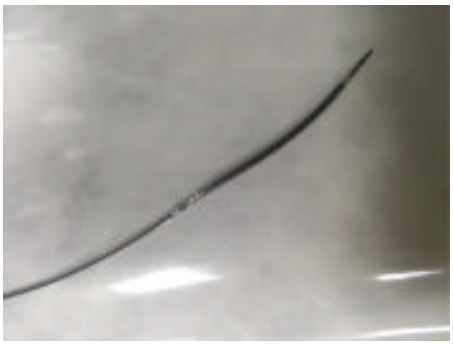

Fig.-1: *Image shows the deformed distal end of stent balloon showing stent strut fracture*

Fig.-2: *Zoomed in view of distal end of stent balloon showing stent strut fracture (arrow).*

of patient-related ischaemic symptoms. In-hospital follow up of all patients was uneventful, with no further complications detected.

Discussion:

The strength of support offered by the radial approach is significantly lower thanthat for femoral access, which confers an extra difficultyin the percutaneous treatment of complex coronary lesions.[11] The results of this study show that the Guide Extension Catheter was useful tool for approaching challenging coronary lesionsusing radial access. Most of the lesions in our study were of ACC/AHA types B2 and C, reflecting the complexity of the lesions requiring extra back-up support.

In our present study, the lesion morphologyis very much similar to Dursun et al. (2016)[12] who presented a 64 patients study using the *GuideLiner*® catheter, with the majority of patients having ACC/AHA types B2/C lesions.In the present study success of stent deployment is 16 out of 19 cases (84.2%), which also very much resembles the study by to Dursun et al. (2016)[12], although it was through trans-femoral route. In addition, we found that this device showed an excellent safety profile since no coronary dissection was induced. This is also true for our study, there was no major complication other than a stent damage in undeployment condition.

García-Blas et al. (2015)[13] reported the usefulness and Safety of a Guide Catheter Extension System of PCI done by trans-radial route. In a study that showed striking similarities to our study in terms of patient profile, number and success rates, they reported successful stent deployment in 16 cases out of 18(81%) in comparison to 84.1% reported in our study.Unsuccessful cases were a chronic total occlusion and a diffusely diseased LAD. They also reported a single coronary dissection as the only significant peri-procedural complication.

Our results also complied with that of Insights from the *Twenty GuideLiner registry reported by de Man FH et al. (2012)* [14]who reported similar lesion morphologies and but differences in terms of challenges requiring the use of guide extension catheter.Where 23% of lesions were calcified and 17% were CTO. In comparison, our series reported 47.4% of heavy calcification and 10.5% CTO.[14] They reported a device success rate of 93% (65/70) with only two minor complications of air embolism and stent dislodgement.Our study also reported a single significant complication of stent damage (stent fracture at the distal end of the stent) prior to its deployment, which is a complication mediated by *Guidezilla*.

The most common indication for *Guidezilla* use for back-up support in a complex coronary lesion where there is difficulty or inability to place a stent or balloon. This problem occurs mainly in complex calcified lesions or tortuous arteries, as reflectedin the type of lesions treated in our series. Using *Guidezilla* support resulted in optimal angiographic results in 84.21% ofcases in our series, cases in which successful stent deployment would not have been otherwise been possible. These results are also consistent with thosefrom other studies, so we believe that this level of efficacy makes this device a very useful tool and a first-line alternativein this kind of selected cases.[14-17]Thus, deep coronary intubation with a guide catheter is oneof the strategies that can increase support, but is limited byits aggressiveness on the vessel wall.[5] Moreover, whileintubating the guide, aortic wall contact is lost and the stabilityof the catheter decreases. The specific design of theproximal hypotube of *Guidezilla* minimizes arterial wall trauma and allows theguiding catheter to remain steady in the aorta while theextensor device advances in the artery.

The complication of stent damage described is the deformation or even dislodgement of the stent before its deployment. This may occur at the transition between the hypotube and the monorail, especially if this area is locatedon a curve of the guide catheter.[14,18,19]This is one of the challenges encountered while using *Guidezilla* and operators need to be wary of this complication, as occurred in case number 9 in our series.

The present study, albeit small, provides some “real-life” insight into efficacy, limitations, and the potential risk of this device. However, it is not without limitations. Thispreliminary study included a relatively small number of patients from a single center, and as such may not be able to provide a scientific level of insight in terms of efficacy andcomplications, that may have been derived from a larger, randomized study. Furthermore, we cannot exclude that in certain cases, alternative techniques to improve back-up and support (e.g., deep intubations or buddy wires) could also have led to procedural success.

Conclusion:

The percutaneous treatment of complex coronary lesions is still a challenging problem, especially when using the Transradial approach. This study has demonstrated the safe and effective use of Guidezilla for the percutaneous treatment of complex lesions in the presence of unfavorable tortuous coronary anatomies and in complex, heavily calcified lesions, which may have otherwise been considered unsuitable for PCI. Its use increased the support for advancing angioplasty balloons and stents using the radial approach, thereby improving the success rate of the procedures. Furthermore, with this back-up support it is possible to deploy a single longer stent in lesions which were previously stented with two small stents owing to complex anatomy. Thus, it has good economic value as well. Procedural success rate was high and there were no major complications. In case of the failure of “traditional tips and tricks” to improve the back-up in challenging cases, it can be employed as a “bail-out strategy”. However, with the growing experience with such a device, it can also be used as a first strategy to face anatomical difficulties.

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Original Article

Role of Heparin in Arterial Line Flushing Solution on Platelet Count and Indwelling Arterial Catheter Patency after Cardiac Valvular Surgery

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Abstract:

Background: Heparin can cause thrombocytopenia but what is it's effect on platelet when used in solution for flushing indwelling arterial catheter is not clear. This study was designed to find out any effect of heparin on platelet count and to see the efficacy of normal solution as flushing solution.

Method:This was a prospective randomized comparative clinical trial in the Department of Cardiovascular Surgery of National Institute of Cardiovascular Diseases Hospital, Sher - e - Banglanagar, Dhaka,Bangladesh during the period from july 2016 to june 2017. Total sixty patients who underwent single valve replacement surgery were divided into two groups and were evaluated for heparin effect and compared for arterial catheter patency rate.

Results: Platelet count on third postoperative day is 226517+- 60185/ml and 245957+-52826/ml in heparinized flush solution and normal saline flush solution group respectively. The difference of mean is not significant with p value 0.188. Arterial catheter patency rate was 50.0% in heparinized flush solution group and 43.3% in normal saline flush solution group on third postoperative day which signifies no difference between the groups with p value 0.607.

Conclusion: The use of heparin in normal saline in continuous flushing devices for an arterial catheter does not significantly reduce platelet counts in cardiac valve surgery patients in comparison to normal saline. It seems that there is no difference in the use of heparinized and normal saline solutions to maintain indwelling arterial catheter patent.

Key words: Heparin, Platelets, Cardiac Surgical Procedures.

(Bangladesh Heart Journal 2018; 33(1): 61-66)

Introduction:

Heparinized saline solution is used to prevent occlusion in the arterial catheters and central venous pressure monitoring catheters. Even at low dose, heparin administration can be associated with serious complications. Normal saline solution can maintain patency of arterial catheters and central venous pressure monitoring catheters.[1]

Arterial catheters are widely used in intensive care unit for continuous haemodynamic monitoring and frequent assessment of arterial blood gas analysis. Arterial catheters

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37027

including radial, brachial, femoral, dorsalis pedis and axillary artery are used in the intensive care unit for continuous blood pressure monitoring, repeated blood sampling, and when there is inability to measure indirect blood pressure.[2] Invasive arterial blood pressure measurements are more accurate.[3] Flush system is used to maintain patency of arterial catheter. For this purpose, heparinized solution or normal saline should be used. Heparinized solution is used to prevent occlusion in these catheters. Heparin is an anticoagulant drug used to prevent and treat thrombosis.[4] Unfractionated heparin is a standard anticoagulant that affects multiple sites of internal and external coagulatory system and inhibits blood clotting.[5] Heparin administration can be associated with serious complications. It has a number of drug interactions, as well as potentially serious side effects. Heparin, even with low dose, can cause thrombocytopenia and bleeding.[6] The absolute risk of heparin-induced thrombocytopenia (HIT) with unfractionated heparin is 1%-5%. [7] Normal or isotonic saline has sodium and chloride concentrations of 154 mEq/L.[8] Normal saline solution can maintain patency of arterial and central venous pressure monitoring catheters. Heparinized solutions had no effect on prolonging patency and improving function of catheters and even caused changes in activated partial thromboplastin time (APTT) while the normal saline solution increases accuracy of coagulatory tests. Use of normal saline solution prevents patient exposure to the risks associated with heparinized solution and thus increase patient safety.[9]

Normal saline should be used as an alternative to heparin in arterial line and central-venous catheters. Low-dose heparin (1U/ml) should be added to the infusion set to maintain patency of arterial catheters. Extra precautionary measures must be taken when heparin therapy in instituted. Nurses and other healthcare professionals need to be reeducated on the side effects and complications of heparin therapy in order to prevent unnecessary complications and to provide safe and effective .[10]

Thrombocytopenia define as a drop in platelet count by 30% to $<100\times10^9$/l or a drop of >50% from the patient's baseline platelet count.[11] Heparin induce thrombocytopenia is defined as a decrease in platelet count during or shortly following exposure to heparin.[12] HIT is the most important and most frequent drug-induced type of thrombocytopenia. It is associated with significant morbidity and mortality if unrecognized. Despite thrombocytopenia, bleeding is rare, rather HIT is strongly associated with thromboembolic complications involving both the arterial and venous system. The risk of HIT is high with prolonged use of heparin for post-operative thromboprophylaxis. However, case studies have also demonstrate the possibility of developing HIT with minimal heparin exposure via intravascular flushes to maintain the patency of indwelling arterial or venous catheter.[13]

Methods:

This prospective randomized comparative clinical trial was conducted in the Department of Cardiac surgery, National Institute of Cardiovascular Disease (NICVD), Sher-E-Bangla Nagar, Dhaka, Bangladesh from July 2016 to June 2017. This study included sixty patients who underwent single valve replacement surgery, either MVR or AVR and shifted to the intensive care unit with arterial line catheter. The inclusion criteria for the study included 18- 60 years of age, time passed from the insertion of catheter less than 6 hours, usage of arterial line extension catheters with 20 cm, 20 gauze size, patient's blood platelet of 150000 or above, PT (Prothrombin Time) of 11-12.5 seconds, PTT (Partial Thromboplastin time) in the range of 35-45 seconds. The patients having risk of bleeding, known hypersensitivity to heparin, requiring therapeutic heparin and TPN (Total Parenteral Nutrition) during study was excluded from the study. Sampling was performed by random sampling method using random numbers generated by MS Excel software's RANDBETWEEN Function The participants were divided into two groups, one without heparin and other with heparin in normal solution. In the heparinized group, heparin (ROTEXMEDICA, TRITTAU, GERMANY) with the product number of 40124 was used. The solution was prepared by a 1000 IU of heparin added to a half liter of normal saline; hence each milliliter of the prepared solution contained 2 IU of heparin. 3 mL of the heparin solution was used for each flush. In normal saline group patients, 3 mL 0.9% sodium chloride will be used for each flush. Patients were unaware of the used method. Catheters were examined for blood return and flushing every hour using patients medical data sheets. Arterial catheter was remain upto 72 hours. During the examination of catheters, all patients were lying on their backs. If flushing or taking blood sample from the catheter was not possible, it was considered non-functional and removed. Platelet count was measured manually preoperative, post pump and daily for 4 postoperative days then on 7^{th} and 14^{th} postoperative days. The maximum time of study was 14th days and the collected data during the first 4 days were recorded every four hours in the previously prepared checklist. At the end of 1^{st} week and 2^{nd} week platelet count were recoded and whole data were analyzed by SPSS software version 23. In this study for describing the features of research units, descriptive statistics (mean, standard deviation and distribution frequency) was used. For analyzing the data, Kaplan Meier survival analysis, log rank test and Cox regression was performed and for comparing the ratios, the Chi-square test was used. $p < 0.05$ was considered significant.

The statistical package for the social science program (SPSS-22.0 Inc) was used to evaluate all data. The tests statistics were used to analyze the data are student's t test. The qualitative data were presented as frequency with

corresponding percentage. For all analytic test s, the level of significance was set at 0.05 and a p value of <0.05 was considered significant. The summarized data were presented in the form of tables and charts.

Results:

Table-1 shows that patients maximum patients within 31-40 years in both groups. The mean age of Group-A was 36.3 yrs and that of Group –B was 35.7±10.3 years. The mean difference between the two groups was not statistically significant.

Table-I

Distribution of patients by age (n=60)

Age (years)	Group		p value
	Group-A (n=30)	Group-B (n=30)	
	No. (%)	No. (%)	
< 20	0(0.0%)	3(10.0%)	
21-30	7(23.3%)	5(16.7%)	
31-40	13(43.3%)	13(43.3%)	
41-50	10(33.3%)	6(20.0%)	
51-60	0(0.0%)	3(10.0%)	
Total	30(100.0%)	30(100.0%)	
Mean±SD	36.3±6.7	35.7±10.3	0.790^{ns}

Group-A: Heparinized flush solution group
Group-B: Normal saline group
Data were analysed using Student's t-test and were presented as mean ± SD

Table-II shows that females were predominant in both Group. 60.0% patients were female in Group A and 63.3% in Group B. There is no significant difference between the groups in respect to sex (p = 0.790).

Table-II

Comparison of patients by sex between Group-I and Group-II

Genders	Group		p value
	Group-A (n=30) No. (%)	Group-B (n=30) No. (%)	
Male	12(40.0%)	11(36.7%)	0.790
Female	18(60.0%)	19 (63.3%)	
Total	30(100.0%)	30(100.0%)	

Group-A: Heparinized flush solution group
Group-B: Normal saline group
Chi square test was done to analyze the Data. Degree of freedom (df) =1
Figure in the parenthesis denoted corresponding percentage.

Name of operation

Table-III shows type of operation, maximum 73.3% cases had MVR in Group A and 56.7% in Group B. AVR were 26.7% in Group A and 43.3% in Group B. No significant difference between two groups.

Table-III

Distribution of the study by name of operation

Name of operation	Group		p value
	Group-A (n=30) No. (%)	Group-B (n=30) No. (%)	
MVR	22(73.3%)	17(56.7%)	0.175
AVR	8(26.7%)	13 (43.3%)	
Total	30(100.0%)	30(100.0%)	

Group-A: Heparinized flush solution group
Group-B: Normal saline group
Chi square test was done to analyze the Data. Degree of freedom (df) =1
Figure in the parenthesis denoted corresponding percentage.

Platelet count

Table-IV showed comparison of platelet count between two groups. There is no statistically significant difference

Table-IV

Comparison of platelet count in two groups in different POD.

Platelet count	Group-A (n=30)Mean±SD	Group-B (n=30)Mean±SD	P value
Pletelet count pre operative	247583±55675	235813±54708	0.412 ^{ns}
Pletelet count post pump	215883±58210	222580±52422	0.633 ^{ns}
Pletelet count 1st POD	206530±64441	212543±48768	0.685 ^{ns}
Pletelet count 2nd POD	208363±58003	222177±55580	0.350 ^{ns}
Pletelet count 3rd POD	226517±60185	245957±52826	0.188 ^{ns}
Pletelet count 4th POD	241217±57558	258190±55012	0.247 ^{ns}
Pletelet count 7th POD	240517±57379	257713±53655	0.236 ^{ns}
Pletelet count 14th POD	245850±52680	244337±56796	0.915^{ns}

Group-A: Heparinized flush solution group
Group-B: Normal saline group
Data were analysed using Student's t-test and were presented as mean ± SD

between Group A and Group B at preoperative period, post pump, 1st POD, 2nd POD, 3rd POD, 4th POD, 7th POD and 14th POD (p >0.05).

Arterial line

Table-V shows arterial line patency in study patients. 100% patients had arterial line patent in 1st POD in both groups. In 2nd POD 86.8% patients had patency in Group A and 76.7% in Group B. At 3rd POD 50.0% patients had patency in Group A and 43.3% patients in Group B. No significant difference between two groups (p> 0.05).

Table-V

Distribution of the study by arterial line

Arterial line	Group		p value
	Group-A (n=30) No. (%)	Group-B (n=30) No. (%)	
1st POD	30(100.0%)	30(100.0%)	1.000 ns
2nd POD	26(86.7%)	23 (76.7%)	0.316 ns
3rd POD	15(50.0%)	13(43.3%)	0.607ns

Group-A: Heparinized flush solution group
Group-B: Normal saline group
Chi square test was done to analyze the Data. Figure in the parenthesis denoted corresponding percentage.

Hospital stay and ICU stay

Table showed that mean hospital stay and ICU stay were not significant difference between Group A and Group B (p>0.05).

Table-VI

Comparison of hospital stay between two groups

Hospital stay	Group-A (n=30) Mean±SD	Group-B (n=30) Mean±SD	p-value
Hospital stay	11.41±3.12	12.14±3.69	0.411ns
ICU stay	5.63±2.23	4.64±2.47	0.108ns

Group-A: Heparinized flush solution group
Group-B: Normal saline group
Data were analysed using Student's t-test and were presented as mean ± SD

Discussion:

This study found no statistically significant difference between heparinized flush solution group and normal saline group at preoperative period, post pump, 1st POD, 2nd POD, 3rd POD, 4th POD, 7th POD and 14th POD (p >0.05) on platelet counts. Over time for individual patients who had arterial lines for 4 days or longer, Counts showed an early decline and then recovery to normal levels in both the heparinized and normal saline groups. The parallel study done by Hall *et al* comparing arterial catheter line in the two groups showed no difference at the 95% confidence interval using the central limit theorem.[14] Sixty-five patients were recruited over 8 months: 35 in the normal saline group and 30 in the heparinized saline group. The mean platelet count was 256.6×10^9/L for the heparinized saline group, compared with 234.6×10^9/L for the normal saline group. Comparison of means with the central limit theorem showed there was no significant difference at the 95% confidence interval.

In 1991, Clifton conducted a double-blind, randomized study comparing the effects of heparin solutions (4 IU/mL) and normal saline solutions on patency of arterial catheters. They concluded that heparinised solutions were preferable for reducing the rate of catheter occlusions and other malfunctions and that they did not significantly alter platelet count. However, their study included only 30 patients, and patients were excluded from the study if baseline platelet counts were below 50×10^9/L.[15]

Another study of 35 ICU patients compared use of either heparin (4 IU/mL) or 1.4% sodium citrate, both in 0.9% sodium chloride solution, as a continuous flush solution. Again, platelet counts were similar in the two groups.[16]

The results of the current study showed no statistically significant difference regarding the patients' demographic characteristics such as age and gender between heparinized flush solution group and normal saline group. The most common site of arterial catheters similar to those of the previous studies was radial artery. The proportion of arterial catheters placement sites including radial, brachial and femoral arteries were similar to those of the previous studies and there was no statistically significant difference between the two groups.[17]

In present showed arterial line patency, 100% patients had arterial line patent in 1st POD in both groups. In 2nd POD 86.8% patients had patency in Group A and 76.7% in Group B. At 3rd POD 50.0% patients had patency in Group A and 43.3% patients in Group B. No significant difference between two groups (p> 0.05). It is Similar to those of the previous studies.[17] In a current systematic review study Kordzadeh *et al* determined that, heparinized saline solution may be superior for long term use in arterial line.[18] However the current study assessed this issue in short term period and found no significant difference. Cardiac valve surgery and in the current study there was no statistically significant difference between the two groups, but in the other studies were not surveyed. Variable alteration during three days of patients follow up including catheters patency and other parameters did not significantly change that was similar to the obtained results of the studies in which patients were followed up from several days to 12 months.[17,6,19] Based on the finding of the current double blind randomized clinical

trial, use of heparinized saline solutions compared with normal saline solutions did not prolong the patency of arterial and central venous catheters in short term postoperative period. Finding of the study suggested that normal saline solution can be used as the standard solution to prevent catheter occlusion after cardiac surgery. Therefore, all medical centers are suggested to prevent heparin complications such as allergic reaction, local tissue injury, bleeding, thrombus and thrombocytopenia related to use of heparin in patients with arterial and central venous catheter; normal saline solution can be used to prevent catheter patency as a safe alternative solution.

It seems that the use of heparinized saline and normal saline solution in preventing patency of arterial line has no difference. Our finding only applicable to cardiac valve surgery patients that have arterial line catheters for short time period (3 three days) post-operatively. Therefore these data could not be generalizable to chronic medical situations.

A randomized, double-blind, placebo-controlled trial by Del Cotillo et al. concluded that use of heparinized solutions did not increase catheter patency.[17] Hall et al. found a similar conclusion that heparin as a continuous flush at 3U/ml did not improve the function of arterial lines as compared with saline flush.[14] Leighton concludes that it is practical to maintain arterial lines with normal saline as it has the same benefit as heparin without the risks associated with heparin.[20] However, Clifton *et al.* contradicts the conclusion that normal saline is beneficial.[15] Their study states that use of normal saline as a continuous flush for radial artery catheters is associated with increased frequency of catheter occlusions compared with heparin.

Lapum et al. were neutral in their results and concluded that no significant differences were found between intravascular catheters flushed with heparinized solution and those flushed with nonheparinized solutions.[21,4,22] Majority of the studies mentioned above used heparin at varying doses (0.25 U/mL or 1U/mL). Studies done to determine the effective dose of heparin conclude that 0.25 U/mL is sufficient for maintenance of arterial catheters.[23] Majority of the available data suggest that heparin saline given as a continuous flush at low doses improved catheter patency. However, heparin as an intermittent flush is ineffective.

Limitation:

Arterial catheter patency was assessed only for three postoperative days. so, findings regarding prolonged maintenance of indwelling catheters by heparinized or normal saline solutions were not representative. It would be better to have large sample size to predict patency rate of indwelling arterial catheter.

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Original Article

Effect of Pre-operative Amiodarone on Atrial Fibrillation after Off-Pump Coronary Artery Bypass Surgery

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Abstract:

Background: Atrial Fibrillation (AF) is common in early recovery period after cardio-thoracic surgery. There have been several pharmacological and non-pharmacological strategies suggested for prevention against AF after coronary artery bypass grafting. The purpose of this study was to evaluate the effect of oral amiodarone in the prevention of atrial fibrillation in patients who underwent off pump coronary artery bypass graft (OPCAB).

Methods: This interventional study was conducted from February 2017 to January 2018 in the department of cardiac surgery, National Institute of Cardiovascular Disease (NICVD) Dhaka, Bangladesh. By purposive sampling a total of 100 patients having sinus rhythm who will undergo OPCAB were selected for the study. Among them 50 patients (Group-A) got amiodarone (600mg/day started 3 days prior to surgery) and 50 patients (Group-B) did not get amiodarone. Two (2) patients of group-A were excluded from the study due to conversion to on pump from off pump during operation. So, finally group A had 48 patients and group-B had 50 patients. Preoperative electrocardiography (ECG), serum electrolytes (e.g. potassium & magnesium), thyroid function test, liver function test and echocardiogram were done in all patients under study. Per-operative occurrence of AF was assessed on operation theatre monitor. Each patient was evaluated by continuous ECG up to 5th post-operative day (POD). Serum potassium & magnesium were measured in every alternative day up to 5th POD. ECG with long lead tracing was done for all patients on the day of hospital discharge & was recorded. Data were analyzed by SPSS 24.0 (Statistical Package for the Social Sciences) and tested by student T-test and Chi-square test. P < 0.05 was considered significant.

Results: Pre-operative baseline characteristics were similar in both groups. Per-operative and post-operative AF occurred more frequently in group B than group A. Those were 10(20.83%) and 32(64.0%) per-operative, 9(18.75%) and 31(36.0%) immediate post-operative period respectively in group A and group B. The result was statistically significant (P value<.05). Post-operative amiodarone used in all patients who developed AF irrespective of groups. This also decreased AF significantly. There were statistically no significant difference found in postoperative serum electrolytes and use of inotropes, anti-arrhythmic drugs. All patients recovered well.

Conclusion: This study concluded that preoperative oral administration of amiodarone can prevent the occurrence of atrial fibrillation in patients undergone Off Pump Coronary Artery Bypass (OPCAB).

Key wards: Amiodarone, Postoperative atrial fibrillation,

(Bangladesh Heart Journal 2018; 33(1): 67-73)

Introduction:

Atrial tachyarrhythmias are common during early recovery after cardiothoracic surgery, occurring with a frequency ranging from 10% to 30% [1, 2]. Atrial fibrillation (AF) often occurs in patients after both conventional and off-pump

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37028

Coronary Artery Bypass Graft (OPCAB)[3,2]. AF after OPCAB most often develops between the second and fifth postoperative day with a peak incidence in the 2nd to 3rd postoperative days [1]

The incidence is mainly dependent on the type of operation as well as on patient characteristics. As the population is aging and number of cardiac surgical operations is increasing, incidence of AF has gradually increased recently. Moreover, AF brings about several problems, including hemodynamic derangement, thromboembolic complications, longer time of hospital stay, and higher costs.[3]

There have been several pharmacological and non-pharmacological strategies suggested for prevention against AF after coronary artery bypass grafting (CABG). The mechanism of atrial fibrillation involves two processes, focal triggers of enhanced automaticity and multiple wavelets of macro-reentry activation migrating across the atria[4]. Risk factors for developing atrial fibrillation include inflammation, oxidative stress, and atrial morphology Also ²-blockers withdrawal, right coronary artery occlusion, reduced left ventricular function & left ventricular hypertrophy are risk factors as well[5]. However the aging is a constant independent predictor for the incidence of AF after OPCAB [1]. Although AF in the early postoperative period is often sudden and self-limiting but can be continued for weeks and leads to increased morbidity, cardiac loss, embolic complications and the need for pacemaker[6]

Amiodarone acts as anti-arrhythmic drug mainly by blocking potassium (K+) channel and increasing the refractory period. It can be given both in oral & intravenous form. Usual dosage varies from 600-1200 mg/day as loading and 200-600 mg/day as maintenance. It can cause bradycardia, QT prolongation, hypotension, AV conduction disturbances, peripheral vasodilation, hypo or hyperthyroidism, chemical pneumonitis & pulmonary fibrosis, photosensitivity, ocular deposition, peripheral neuropathy etc. Most of these complications are dose dependent & rare in short term low dose use [7]

Preoperative prescription of amiodarone is an interventional method which may reduce the incidence of AF after cardiac surgery[6]. Using low-dose intravenous or oral administration for 3-5 days before and after CABG surgery has reduced the incidence of AF.[3]

Despite the high frequency of AF encountered during clinical practice, the concept of a proactive preventative measures became very appealing. Therefore the present study investigated the role of preoperative oral amiodarone in prevention of AF following OPCAB.

Materials and methods:

It is an interventional study conducted in department of cardiac surgery, National Institute of Cardiovascular Disease (NICVD), Dhaka, Bangladesh during the period of 1st February 2017 to 31st January 2018 with the consent of ethical committee of this institute. By purposive sampling a total of 100 patients having sinus rhythm will undergo OPCAB were selected for the study. Among them 50 patients (Group-A) got amiodarone and 50 patients (Group-B) did not get amiodarone. Two (2) patients of group-A were excluded from the study due to conversion to on pump from off pump during operation. So, finally group A had 48 patients and group-B had 50 patients. Patients with sinus bradycardia (Heart rate below 60 beats/min), on other anti-arrhythmic drugs (Except ²-blockers), Redo, Urgent or Emergency CABG, patients with thyroid or liver dysfunction were excluded from the study. The objective of this study was to evaluate the effect of pre-operative oral amiodarone in the prevention of atrial fibrillation for patients undergoing OPCAB. Also to evaluate incidence of postoperative AF after OPCAB in both groups and to compare the outcome between two groups. The patients under study were hospitalized at least 7 days before surgery. Preoperative ECG, serum electrolytes (e.g. potassium & magnesium), thyroid function test, liver function test and echocardiogram were done in all patients under study. Amiodarone (Trade name: Pacet) was prescribed at a dosage of one tablet (200 mg) three times daily (600mg/day) 3 days prior to surgery. Other medical therapy was unchanged. Per operative occurrence of AF was assessed on operation theatre monitor. After OPCAB surgery, each patient was transferred to intensive care unit and then at 3rd postoperative day was transferred to a step down or high dependency unit (HDU).

In intensive care unit (ICU) & HDU, patients were evaluated by continuous ECG monitoring. Inotropic supports given to each patient up to 5th postoperative day. Serum potassium & magnesium were measured in every alternative day up to 5th postoperative day. An episode of atrial fibrillation was counted if it persisted for more than five minutes. Electrocardiography (ECG) with long lead tracing was done for all patients on the day of hospital discharge & was recorded. At the end of study, patients' data was analyzed by SPSS software version 24.0. The numerical data obtained from the study was analyzed and significance of difference was estimated by using statistical methods. Continuous variables were expressed as mean values ± standard deviation and compared using Student's t-test. Categorical variables were expressed as frequencies with percentages and compared using Chi-square test when and where appropriate. $P < 0.05$ was considered significant.

Result:

Total 100 patients were selected for OPCAB. Among them 50 patients (Group A) got amiodarone and 50 patients (Group B) did not get amiodarone. 2 patients of group A were excluded from the study due to conversion to on pump from off pump during operation. So, finally group A had 48 patients and group B had 50 patients. The findings of the study obtained from data analysis are presented below.

Table-I

Comparison of Preoperative data between two groups (N=98)

Preoperative variables	Group A (n=48) No. (%)	Group B (n=50) No. (%)	P value
Age(years)	60.68±7.47	60.06±6.16	-
Sex	40(83.33%)	45(90.0%)	-
Male	8(16.67%)	5(10.0%)	
Female			
Pulse rate			
Normal	45(93.75%)	48(96.0%)	0.646 ns
Tachycardia	3(6.25%)	2(4.0%)	
Pulse rhythm			-
Regular	48(100.0%)	50(100.0%)	
AF	0(0.0%)	0(0.0%)	
ECG			
Normal	48(100.0%)	50(100.0%)	-
AF	0(0.0%)	0(0.0%)	
TFT			
Euthyroid	48(100.0%)	50(100.0%)	-
Hypothyroid	0(0.0%)	0(0.0%)	
Hyperthyroid	0(0.0%)	0(0.0%)	
LFT			
Normal	48(100.0%)	50(100.0%)	-
Abnormal	0(0.0%)	0(0.0%)	
LVEF			
≥ 50%	23(47.92%)	20(40.0%)	0.545ns
< 50%	25(52.08%)	30(60.0%)	
Coronary artery involved			
Single	4(8.33%)	3(6.0%)	
Double vessel	16(31.25%)	17(34.0%)	.565 ns
Triple vessel	28(60.42%)	30(60.0%)	

Table-II

Comparison of per-operative data between two groups (N=98)

Per operative variables	Group A (n=48) No. (%)	Group B (n=50) No. (%)	P value
Occurrence of AF (monitor)			
Yes	10(20.83%)	32(64.0%)	<0.001*
No	38(79.17%)	18(36.0%)	
Grafts given			
One	9(18.75%)	6(12.0%)	
Two	14(29.17%)	17(34.0%)	0.629ns
Three	25(51.08%)	27(54.0%)	

Figures in the parentheses indicate corresponding percentage; ns = not significant, *significant
Chi-squared Test was done to analyze the data.

Table-III

Comparison of immediate Postoperative data between two groups (N=98)

Postoperative variables	Group A (n=48) No. (%)	Group B (n=50) No. (%)	P value
Postoperative ECG			
Normal	39(81.25%)	19(38.0%)	<0.001*
AF	9(18.75%)	31(62.0%)	
Postoperative BP			
Low	7(14.6%)	0(0.0%)	<0.001*
Normal	41(85.4%)	36(72.0%)	
High	0(0.0%)	14(28.0%)	
Postoperative use of anti-arrhythmic drug			
Yes	10(20.8%)	32(64.0%)	0.097^{ns}
No	38(79.2.0%)	18(36.0%)	

Figures in the parentheses indicate corresponding percentage; ns = not significant, *significant
Chi-squared Test was done to analyze the data.

Table-IV

Postoperative ECG monitoring between two groups (N=98)

Postoperative ECG monitoring	Group A (n=48) No. (%)	Group B (n=50) No. (%)	P value
Continuous ECG (ICU) in 1st POD			0.006*
Normal	39(81.2%)	27(54.0%)	
AF	9(18.8%)	23(46.0%)	
Continuous ECG (ICU) in 2nd POD			<0.001*
Normal	38(79.2%)	22(44.0%)	
AF	10(20.8%)	28(56.0%)	
ECG in HDU in 3rd POD			<0.001*
Normal	48(100.0%)	30(60.0%)	
AF	0(0.0%)	20(40.0%)	
ECG in HDU in 4th POD			0.063^{ns}
Normal	48(100.0%)	45(90.0%)	
AF	0(0.0%)	5(10.0%)	
ECG in HDU in 5th POD			0.240^{ns}
Normal	48(100.0%)	50(100.0%)	
AF	0(0.0%)	0(0.0%)	
12 Lead ECG on discharge			0.068^{ns}
Normal	48(100.0%)	50(100.0%)	
AF	0(0.0%)	0(0.0%)	

In table 1 showed preoperative pulse rhythm, ECG, TFT, LFT were normal in all patients (100%). Pulse rate were normal in 93.75% and 96% of group A and group B respectively, tachycardia in 6.25% and 4% of group A and group B respectively. LVEF was ≥ 50% in 47.92% and 40% of group A and group B respectively and was < 50% in 52.08% and 60% of group A and group B respectively. Regarding coronary artery involvement, single vessel involvement was 8.33% and 6% in group A and group B respectively; Double vessel involvement was 31.25% and 34% in group A and group B respectively; Triple vessel involvement was 60.42% and 60% of group A and group B respectively. All the results were statistically not significant. (P>0.05).

In table-2, per-operatively one graft was given for 18.75% and 12% in group A and group B respectively; two grafts were given for 29.17% and 34% in group A and group B respectively; three grafts were given for 52.08% and 54% in group A and group B respectively. P value was >0.05 which is statistically not significant.

Regarding AF occurrence (seen in monitor) per operatively, AF occurred 20.83% in group A and 64% in group B; AF did not occur 79.17% in group A and 36.0% in group B. The result was statistically significant (P value <0.05).

In table 3, postoperative pulse was normal in 81.25% and 38.0% of group A and group B respectively; was AF in 18.75% and 62.0% of group A and group B respectively. The result was statistically significant (P value <0.05).

Postoperative BP was low in 14.6% and 0.0% of group A and group B respectively; was normal in 85.4% and 72.0% of group A and group B respectively and was high in 0.0% and 28.0% of group A and group B respectively. The result was statistically significant (P value <0.05).

Postoperative antiarrhythmic drugs were used in 20.8% and 64.0% of group A and group B respectively and not used in 79.2% and 36.0% of group A and group B respectively. The result was statistically not significant (P value >0.05).

In table 4 postoperative ECG in 1st POD was normal in 81.2% and 54.0% of group A and group B respectively and AF was present in 18.8% and 46.0% of group A and group B respectively. Postoperative ECG in 2nd POD was normal in 79.2% and 44.0% of group A and group B respectively and AF was present in 20.8% and 56.0% of group A and group B respectively. Postoperative ECG in 3rd POD was normal in 100.0% and 60.0% of group A and group B respectively and AF was present in 0.0% and 40.0% of group A and group B respectively. On 3rd and 4th POD, ECG was normal in all patients of group A with no AF. But in group B, AF was present in 40% and 10% patient respectively. The results were statistically significant up to 3rd POD (P value <0.05).

Regarding 12 lead ECG on discharge, ECG was normal in all patients of both groups. The results were not statistically significant (P value ≥0.05).

Discussion:

Ever since the establishment in 1981, National Institute of Cardiovascular Diseases (NICVD), Dhaka is performing a major role in cardiac surgery. This study was carried out in the department of cardiac surgery during the period of February, 2017 to January, 2018. As NICVD plays the central role in the field of cardiac surgery and off pump coronary artery bypass (OPCAB) in Bangladesh, study population was chosen from the institute. On average, around 300 CABG (both on pump and off pump) cases are performed at NICVD in every year[8]. Total 100 patients were selected for this study, divided into two groups. Out of them 50 patients (Group A) was intended to receive oral amiodarone before surgery and 50 patients (Group B) did not receive any amiodarone. But two cases were excluded from group A due to conversion from off pump to on pump CABG. Finally total 98 cases were included under study (48 for Group A and 50 for Group B). The aim of this study was to determine whether preoperative oral amiodarone have any effect in the prevention of atrial fibrillation in patients undergone OPCAB.

The mean age of group A patients were 60.68 ± 7.47 years and group B patients were 60.06± 6.16 years both ranging from 40 to 70 years. Analysis revealed that no statistically significant mean age difference was found between group A and group B patients (p>0.05). Homogenously both group had highest percentage (54.17% for group A and 50.0% for group B) of age group from 61-70 years.

In the study, majority of the patients were male in both groups. In group A and group B, 83.33% and 90.0% were male and the rest 16.67% and 10.0% were female respectively. Homogenous distribution of sex was also present in both groups.

Preoperative pulse rhythm, ECG, TFT, LFT were normal in all patients (100%). In group A and group B, pulse rate were normal in 93.75% and 96% and tachycardia in 6.25% and 4% respectively. Several studies also found preoperative normal heart rate, normal BP and normal liver function test [8,9,11]

In echocardiography, LVEF was e" 50% in 47.92% and 40% of group A and group B respectively and was < 50% in 52.08% and 60% of group A and group B respectively. Results were statistically not significant

Regarding coronary artery involvement, triple vessels involvements were found in majority of the patients. Statistically, single vessel involvement was 8.33% and 6% in group A and group B respectively; Double vessel involvement was 31.25% and 34% in group A and group B respectively; Triple vessel involvement was 60.42% and 60% of group A and group B respectively. All the results were statistically not significant. Several studies also found majority of patient with triple vessels involvement followed by double vessels and single vessel[2]

Three grafts or more were given in majority of the patients. Per operatively, one graft was given for 18.75% and 12% in group A and group B respectively; two grafts were given for 29.17% and 34% in group A and group B respectively; three grafts were given for 52.08% and 54% in group A and group B respectively. P value was >0.05 which is statistically not significant. Onk and colleagues also found majority of patients (60%) requiring three grafts [5,12]

Per operatively, AF occurred more frequently in group B than group A. AF occurred 20.83% in group A and 64% in group B; AF did not occur 79.17% in group A and 36.0% in group B. The result was statistically significant (P value <0.05).

Postoperative pulse was within normal limit in majority of the patients in both groups (81.25% and 38.0% in group A and group B respectively. Postoperative AF was high in group B in comparison to group A (18.75% and 36.0% in group A and group B respectively). The result was statistically significant (P value <0.05).

Group A showed hypotension more in comparison to group B postoperatively (14.58% and 0.0% of group A and group B respectively). Postoperative BP was normal in 85.42% and 72.0% of group A and group B respectively and was high in 0.0% and 28.0% of group A and group B respectively. The result was statistically significant (P value <0.05). Esmail with his colleagues found systolic BP 125±15 mm(Hg) and diastolic BP 76±10 mm(Hg) which were also within normal limit.[1, 13]

Dopamine was used in 93.8% and 100% of group A and group B respectively. In few patients (6.0% and 18.0% of group A and group B respectively) dobutamine was used in exchange of dopamine after 1st postoperative day. But majority of the patient in both groups did not require dobutamine (94.0% and 82.0% of group A and group B respectively). Some patients required adrenaline (14.0% and 28.0% of group A and group B respectively) along with either dopamine or dobutamine. Noradrenaline was also used in 10.0% and 24.0% of group A and group B respectively with dopamine or dobutamine. No inotropic drugs were used in high dose. All the results were statistically not significant (P value >0.05).

Postoperative AF was found in both groups in different proportions. Amiodarone (trade name: Pacet) was given in some patients of group A (18.8%) up to 1st POD. But amiodarone was required up to 3rd POD in Group B (46.0%). Postoperative ECG in 1st POD was normal in 81.2% and 54.0% of group A and group B respectively. Postoperative ECG in 2nd POD was normal in 79.2% and 44.0% of group A and group B respectively and AF was present in 20.8% and 56.0% of group A and group B respectively. Postoperative ECG in 3rd POD was normal in 100.0% and 60.0% of group A and group B respectively and AF was present in 0.0% and 40.0% of group A and group B respectively. On 3rd and 4th POD, ECG was normal in all patients of group A with no AF. But in group B, AF was present in 40% and 10% patient respectively. The results were statistically significant up to 3rd POD (P value <0.05).

Both preoperative serum potassium and magnesium was normal in both group. Postoperatively, normal serum potassium and magnesium were found in majority of the patient. Mild hypokalemia and hypomagnesaemia was found more in group A than group B. This electrolyte imbalance may be due to excessive diuretics use and fluid and salt restriction. Though amiodarone itself can cause hypokalemia and hypomagnesaemia, but it is rare in low dose and short term use[14].

In 1st POD, serum potassium was normal in 92.0% and 96.0% of group A and group B respectively; was low in 8.0% and 4.0% of group A and group B respectively. Electrolyte imbalances were corrected accordingly. In 3rd POD potassium was normal in 90.0% and 94.0% of group A and group B respectively; was low in 10.0% and 6.0% of group A and group B respectively. In 5th POD potassium was normal in 90.0% and 96.0% of group A and group B respectively; was low in 10.0% and 4.0% of group A and group B respectively. All the results were statistically not significant (P value >0.05). Regarding serum magnesium, in 1st POD magnesium was normal in 94.0% and 98.0% of group A and group B respectively; was low in 6.0% and 2.0% of group A and group B respectively. In 3rd POD magnesium was normal in 92.0% and 96.0% of group A and group B respectively; was low in 8.0% and 4.0% of group A and group B respectively. In 5th POD magnesium was normal in 88.0% and 92.0% of group A and group B respectively; was low in 12.0% and 8.0% of group A and group B respectively. All the results were statistically not significant (P value >0.05).

Postoperative pulse and BP were normal in majority of the groups. Few members of group A showed bradycardia and hypotension. But they were self-limiting and reverted to

normal in short duration. Postoperatively, Pulse was low in 10.0% and 0.0% of group A and group B respectively; was normal in 62.0% and 64.0% of group A and group B respectively; was high in 28.0% and 36.0% of group A and group B respectively. Blood pressure was low in 6.0% and 0.0% of group A and group B respectively; was normal in 74.0% and 70.0% of group A and group B respectively; was high in 20.0% and 30.0% of group A and group B respectively. All the results were statistically not significant (P value >0.05). This observations were similar to the study of William H, et al.[15]

There was no incidence of death in the study population

Conclusion:

In conclusion, our study results suggest that amiodarone administered according to this scheme reduces the onset of post-operative AF in a safe and well-tolerated manner. Thus, prophylactic treatment can be considered effective and should be used routinely for patients undergoing CABG in order to prevent AF thereby reduce the duration of hospital stay and costs.

Conflict of interest: We have no conflicts of interests to disclose.

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Case Report

Idiopathic Thrombocytopenic Purpura in Patients with Ischaemic Heart Disease - A Therapeutic Challenge

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Abstract:

Idiopathic thrombocytopenic purpura (ITP) and myocardial infarction (MI) in an individual patient is a rare combination. MI mandates thrombolytic and antiplatelet therapy which increases the risk of bleeding in ITP. So far, no guideline deals with management protocol for ischaemic heart disease (IHD) in ITP patients. Here, we describe 2 cases of IHD who developed ITP while on antiplatelet therapy.

Key Words: Idiopathic Thrombocytopenic Purpura, Coronary Artery Disease, Thrombocytopenia.

(Bangladesh Heart Journal 2018; 33(1): 74-77)

Introduction:

Idiopathic thrombocytopenia purpura (ITP), also called immune thrombocytopenic purpura,is an autoimmune disorder with a low platelet count and mucocutaneous bleeding. Autoantibody-mediated platelet destruction, as well as, impaired platelet production both contribute to the pathophysiology of ITP. Quantitative as well as qualitative deficiency in platelet function leads to a bleeding tendency. On the other hand, ITP tends to increase the risk of cardiovascular diseases (CVD) e.g., IHD, stroke, transient ischemic attack and heart failure.[1]ITP may even lead to a prothrombotic state which may be related to endothelial damage caused by antigenic mimicry between platelets and endothelial cells[2] or, related to administration of intravenous immunoglobulin (IVIG) for the treatment of ITP[3].Occurrence of acute coronary syndrome[4-6], deep vein thrombosis and pulmonary embolism[7,8], and ischaemic stroke[9-11]has been described in association with ITP. Thrombolytic and antiplatelet therapy, the integral part of standard management of these patients, certainly increases the risk of bleeding in the context of already compromised platelet function. So far, no consensus exists regarding the optimal revascularization strategy and antiplatelet treatment policy in patients with ACS or stable coronary artery disease who have simultaneous ITP. Here, we present 2 cases of old MI who developed ITP while on antiplatelet drugs.

Case 1

A 71-year-old hypertensive man was on aspirin along with standard treatment for stable coronary artery disease with the history of postero-infero-lateral MI 1 year back. He was allergic to clopidogrel. During routine follow up, his serial platelet counts were 115,000 and 45,000/mm^3 over 4 weeks. However, he had no obvious bleeding manifestations, and there was no bony tenderness, lymphadenopathy or organomegaly. Also, he did not have fever recently and take any new drug. He was referred to a haematologist. Bone marrow examination was suggestive of ITP. Platelet count further dropped to 10,000/mm^3, however, no obvious bleeding occurred. Aspirin was withheld for fear of bleeding,

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DOI: http://dx.doi.org/10.3329/bhj.v33i1.37029

oral methyl prednisolone followed by azathioprine was given. Platelet count rose to 55,000/mm^{3}but the general condition of the patient deteriorated and he developed significant adverse effects characterized by mouth ulceration, glucose intolerance and hepatitis. Methyl prednisolone and azathioprine were stopped, the patient improved rapidly, and the platelet count remained between 30,000 and 60,000/ mm^3. Aspirin was reintroduced with close clinical and haematological monitoring. The platelet count remained unchanged, no bleeding encountered, and the patient remained stable.

Case 2

A 65-year-old diabetic man with history of inferior MI was on clopidogrel along with other medications. He refused any invasive procedures. During routine follow up, his platelet count was 65,000/mm^3, however, he did not have any bleeding manifestations. His hemoglobin was 12.6 g/dL, erythrocyte sedimentation rate (ESR) 20 mm in first hour, serum creatinine 1.03 mg/dL, and SGPT 35 units/L. Bone marrow examination by a haematologist revealed features suggestive of ITP. Clopidogrel was continued while the patient was on close clinical and haematological monitoring. There was no bleeding manifestations, and he was doing well in 9-month follow up.

Discussion:

Simultaneous occurrence of IHD and ITP is rare because of the physiological role of platelets in coagulation. Nevertheless, acute MI has been reported in even severely thrombocytopenic patients.[12]On the other hand, ITP developing in otherwise stable coronary artery disease (CAD)patients, as is the issue in the 2 cases presented here, has not been reported adequately. Presence of thrombocytopenia of ITP poses serious management problems in ACS, as well as, in stable CAD patients in which a good balance between the prevention of thrombosis and haemorrhagic risk demands.

Patients with acute ST-elevation MI and ITP have successfully been managed with thrombolytic therapy with limited experience.[13]Coronary revascularization either by percutaneous coronary intervention (PCI) or by coronary artery bypass graft (CABG) surgery seems to be safe and feasible, having a good early outcome and a low complication rate.[14]Historically, CABG was preferred to PCI in ITP patients with CAD because majority of the coronary artery lesions can be dealt with in a more predictable way and antiplatelet therapy can be managed with greater flexibility with CABG in comparison to PCI.[15]In fact, despite low platelet count, CABG has successfully been carried out with some increase in bleeding risk compared to CABG in the general population.[16-9] On the other hand, available data suggest that PCI, including primary PCI, can be safe and feasible in carefully selected patients.[16, 20-6]Li-Sha et al. reported a 75-year-old patient with ITP who underwent 3 separate coronary interventions for recurrent ACS and in-stent restenosis, including PCI and cutting-balloon angioplasty and using unfractionated heparin, dual antiplatelet therapy and platelet transfusion.[21]They also analyzed the reported 18 cases of ITP who underwent PCI between 1999 and 2013; pre-procedural platelet count ranged from 3 × 109/L to 322 × 109/L (mean 78.5 ± 81.5 × 109/L). Glycoprotein IIb/IIIa inhibitors were administrated during 4 PCI procedures, clopidogrel before and during PCI in 9, ticlopidine in 1, aspirin in 9, and no antiplatelet drug before and during PCI in 5. One instance (5.6 %) of major bleeding[27] and 6 minor bleeding were observed. Ten patients (55.6 %) were discharged on double antiplatelet therapy, 3 on single antiplatelet drug, while 3 patients did not receive any antiplatelet agent. Performance of PCI in a patient with ITP requires sufficient inhibition of platelet function to prevent stent thrombosis, but not enough to cause bleeding. For this reason, most expert opinions recommended bare-metal stent (BMS) as opposed to drug-eluting stent (DES) to minimize the duration of dual antiplatelet therapy in case bleeding occurs.[14]However, DES has also been implanted successfully.[16]Platelet transfusion and IVIG have been used in some cases of ITP to reduce the risk of bleeding during coronary revascularization.IVIG may paradoxically induce thromboembolic events including myocardial infarction.[28-30]Since severe bleeding is uncommon when the platelet count is above 30,000/mm^3, treatment is usually initiated when the count falls below 30,000/mm^3.[31]

Antiplatelet therapy in the setting of ITP and IHD should be used with great caution. Dual antiplatelet drugs e.g., combination of aspirin and clopidogrel, when indispensable, should be used generally only for short time, with special attention to the indication, platelet count, and bleeding risk. In both the cases presented here, mostly single antiplatelet drug was used, in the first case only aspirin because of suspected clopidogrel intolerance, and in the second case only clopidogrel because of gastrointestinal intolerance. Aspirincan be safely continued after CABG and PCI unless clinical bleeding occurs, or until the platelet count falls to 10,000–20,000/mm^3.[32]This may probably be applicable to those otherwise stable CAD patients with ITP who did not have any revascularization strategy, as are the cases presented here.

Actually, in ITP, in contrast to the more common findings of petechiae and purpura, severe haemorrhage, such as intracranial haemorrhage, overt gastrointestinal bleeding,

and haematuria, is uncommon. This was illustrated in a systematic review of prospective clinical studies, which included 5336 adults with ITP[33];the incidence of intracranial haemorrhagewas 1.4%, while that of other severe bleeding was 9.6%. In a population-based study that included 3771 patients with ITP, the risk of severe bleeding at disease onset was <1%[34]. Predictors of severe bleeding include the degree of thrombocytopenia (from <10,000 to <20,000/mm^3), previous minor bleeding, and chronic ITP (i.e., diagnosis >12 months prior).[33]

Take-home message:

Combination of ITP and IHD including ACS, though rare, does occur. Presence of thrombocytopenia in ITP is not protective to ACS.

Despite increased risk of haemorrhage, major bleeding rarely occurs until platelet count falls below 20,000 to 10,000/mm^3.

No established protocol exists for management of IHD in the setting of ITP, or ITP in case of chronic IHD. Treatment should be individualized.

Safety of thrombolytic therapy is limited by inadequate experience.

Growing evidence favours coronary revascularization including PCI and CABG.

BMS may be preferable to DES. Periprocedural anticoagulants and antiplatelets may be used, certainly with careful monitoring. Platelet transfusion is rarely needed.

For maintenance therapy, single antiplatelet drug, preferably aspirin, canusually be safely given or continued as long as platelet count is approximately more than 30,000/mm^3, or there is evidence of bleeding.

Antiplatelet drugs should be withdrawn when platelet count falls below 10,000/mm^3, or there is active major bleeding, and treatment should probably be started to raise platelet count.

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