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Our Teacher: Prof Abu Zafor
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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.

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

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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). Number of references should be limited to 50.

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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: JPEG 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 up to 5 most recent references. The text need not be divided into sections. The number of authors should not exceed 3.

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1. Category of manuscript (original research, review article, case report, cardiovascular image, letter to the Editor)
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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.

• Author names and affiliations. Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. Present the authors’ affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower case superscript letter immediately after the author’s name and in front of the appropriate address. Provide the e-mail address of each author.

• Corresponding author. Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.

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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.

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

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

g. Figures and graphics
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• Each figure/illustration should be provided with a suitable legend that includes enough information to permit its interpretation without reference to the text.
• All photomicrographs should indicate the magnification of the prints.
• When symbols, arrows, numbers or letters are used to identify parts of the illustrations, each one should be explained clearly in the legend.

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

   More than six authors:
   

2. **Organization as author**
   

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

4. **Volume with supplement**
   

5. **Issue with supplement**
   

6. **Type of article indicated as needed**
   

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

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

3. **Organization(s) as author**
   

4. **Chapter in a book**
   

5. **Conference proceedings**
   

6. **Dissertation or thesis**
   

**Other Published Material**

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Article with document number in place of traditional pagination:


Article with a Digital Object Identifier (DOI):

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3. Homepage/Web site

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3. The submission file is in Microsoft Word file format, and the figures are in JPEG 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.
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7. All authors have read the manuscript and agree to publish it.

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Abstract:

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

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

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

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

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

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

Historically, the first reported balloon angioplasty of the LMCA was performed in 1979 by Gruntzig. Later, in 1989, a series of 129 patients' cases were reported, with 10% in hospital and 64% 3-year mortality. By the mid-1990s, development of stenting techniques, DAPT allowed interventionist to do LM stem PCI again. LM stem PCI by BMS characterized high procedural success rate with 17-20% and 10-20% mortality in 1st year. The availability of drug eluting stents for the treatment of ULMCA stenosis showed significant reduction of restenosis and target lesion revascularization (TLR).

Several observational single and multicenter registries showed that PCI of ULMCA by second or third generation DES had a good efficacy and safety profile.

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

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

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

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

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

<table>
<thead>
<tr>
<th>Table-I</th>
</tr>
</thead>
</table>

Demographic Profile of patient | Male | Female |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>117</td>
<td>29</td>
</tr>
<tr>
<td>Age (yrs.)</td>
<td>59.0±11.0</td>
<td>56.0±14.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8±3.8</td>
<td>29.8±3.6</td>
</tr>
<tr>
<td>SBP(mmHg)</td>
<td>125.0±14.8</td>
<td>124.0±17.7</td>
</tr>
<tr>
<td>DBP(mmHg)</td>
<td>76.2±8.9</td>
<td>75.0±9.9</td>
</tr>
<tr>
<td>No. of CAD Risk Factor</td>
<td>3.0±1.0</td>
<td>2.0±1.0</td>
</tr>
<tr>
<td>LVEF %</td>
<td>52.0±8.9</td>
<td>53.6±8.1</td>
</tr>
</tbody>
</table>

Data were presented as Means±SD

![Fig.-1: Percentage Distribution of CAD Risk Factors](image)
disease (CAD) risk factors for hypertension (HTN) 67.8\% (n=99), Dyslipidemia 56.2\% (n=82), diabetes mellitus (DM) 75 (51.4\%), smoking 31.5\% (n=46), family history (FH) 21.2\% (n=31). Number of CAD risk factors were more in male, as all smokers in this study were male. In this study, 19.2\%(n=28) patient had CABG in the past and not considered as or belong to UPLMCA. Table 2. Shows the average stent diameter according to location for ostial LM and LM shaft 3.7 mm, LM-LAD 3.4 mm, LM-LCX 3.3 mm and LM-RI 2.8 mm., indicating small size coronary vessel in this part of world. LVEF is almost same in both sex; in male 52 vs female 53%. Figure 2. Showed the distribution of lesion in the studied population.

**Table-II**

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

Table 2: Percentage Distribution of Stented Territory of LM

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

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

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

LM-LAD lesion PCI followed by LM shaft lesion are the commonest LM segment lesions stented. Figure 3. Showed the distribution of common drug eluting stents. Common DES were, Everolimus 69.9\% (n=102), Sirolimus 12.3\% (n=18), Zotarolimus 9.6\%(n=14), BMS 4.8\% (n=7), Sirolimus with Epithelial Progenitor Cell 3.4\% (n=5), and Biolimus 2.1\% (n=3)

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

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

**Fig.-4:** Percentage Distribution of Re-look CAG in the Studied Patient
Dual antiplatelet therapy (DAPT), patients receiving Clopidogrel were 57.5% (n=85), Ticagrelor 28.8% (n=42), and Prasugrel 13.7% (n=20).

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

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

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

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

(a) 90% distal LM and 70% proximal LAD lesion, (b & c) 3.5 x 48 Everolimus Eluting Stent positioning, (d) Deployment of stent, while JL Catheter tip hanging at LM ostium, (e) Final cine after post dilation by 4.0 x 10mm NC balloon, showed well apposed stent.
Figure 8. Shows both pre-post PCI IVUS Image of LM stem PCI
Left panel **Fig 8a:** showed Pre PCI IVUS images, showed stenotic lesion, Right Pane **Fig 8b.** post PCI IVUS image; well expanded stent and next one showed with complete apposition of and expansion of stent without edge tear.

![Image](a)

![Image](b)

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

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

![Image](a)

![Image](b)

![Image](c)

![Image](d)

![Image](e)

![Image](f)

**Fig.-9:** a. 50% distal LM and 90%Proximal LAD and 70% Proximal LCX lesion, b. 3.5 x 15 Everolimus Eluting stent in LCX deployed after kissing balloon, c. LM-LAD stenting by a 4.0 x23 Everolimus Eluting Stent, d. Further Kissing of both stent, e. POT of LM stent by 4.5 x 10 mm balloon at 18ATM, f. Final cine after post dilation by 4.0 x 10mm NC balloon showed well apposed stent.
Everolimus Eluting 2.5 x 15 mm stent deployed covering the LCX ostium. Then, LM-LAD stenting done by 4 x 23 mm Everolimus eluting stent. Further optimization by kissing ballooning of both stent and POT of LM by a 4.5 x 10 mm balloon at 18ATM done. IVUS was done in LM-LAD which was showed LM-LAD & LCX were well dilated with clear bifurcation area.

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

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

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

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

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

Repeat revascularization rates during follow up after PCI compared to CABG were greater for lesion in distal LM but similar for LM ostium or shaft in previous studies. Metanalysis of several RCTS (PRE-COMBAT, SYNTAX, NOBLE, EXCEL) reported primary safety endpoint of death, MI, stroke was similar between PCI and CABG. Patients with UPLMCA disease, CABG and PCI results similar safety composite endpoint of death, myocardial infarction, or stroke. Among patients with isolated LM or + 1 vessel CAD PCI is associated with lower all-cause
mortality compared to CABG.\textsuperscript{28} In our present observational study, only 14.4\% (n=21) patients had relooked CAG and none of them underwent PCI, only three underwent CABG due to significant ISR. So, based on this finding, is very primitive to say that PCI is superior to CABG in our patient population. We need to have a set protocol for mandatory check CAG at least 3-6 months after PCI of LM and, need a multicenter LM registry. So, as to compare and better analyze, PCI outcome according to lesion location (shaft vs ostial vs distal LM).

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

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

Unprotected LM stem disease is a heterogenous condition that includes various degrees of anatomic location and severity of LM lesions, and various possible sets of concurrent lesions of other coronary segments.\textsuperscript{38} Age is also an important predictor of LM stem PCI. Mortality was high > 60\% in isolated LM PCI in patients over 75 years of age, as high as 75\% in those with associated other coronary involvement among with LM stem, while being lower in younger patients.\textsuperscript{39} when performing LM PCI, patient comorbidities such as diabetes, renal failure, acute coronary syndrome on presentation, left ventricular dysfunction, concomitant valvular disease, previous cerebro-vascular events are possible key important factor for procedural outcomes.

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

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

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

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

Acknowledgement:
Akhter Hossain, Sr. Cath Technician for IVUS assistance

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Abstract

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

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

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

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

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

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

Faizus Sazzad¹, Ashlynn Ai Li Ler², Geetha Ganesh³, Marcus Kung⁴, Theo Kofidis⁵

Introduction:
In the era of changing prospects of clinical practice in coronary revascularization surgery, beating heart coronary artery bypass surgery (BECAB) is gaining popularity worldwide as well as in Bangladesh. On
average, more than 10,000 patients undergo coronary artery bypass graft (CABG) surgery each year. As coronary artery disease continues to remain one of the most common forms of heart disease and is the single most significant cause of death in the adult Bangladeshi population, the volume of CABG surgeries has only been increasing over the last decade.

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

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

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

Methods:

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

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

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

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

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

<table>
<thead>
<tr>
<th>Certainty assessment</th>
<th>No. of patients</th>
<th>Effect</th>
<th>No. of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Beating</th>
<th>Arrested</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Assessed with: Trop l¹, BMI, AF, DM &amp; EuroScore¹¹,¹³,¹⁴,¹⁵,¹⁶,¹⁷,¹⁸,¹⁹,²⁰</td>
<td>5</td>
<td>NCC NCT</td>
<td>serious a</td>
<td>serious b</td>
<td>not serious</td>
<td>not serious</td>
<td>none</td>
<td></td>
<td></td>
<td>120/120 (100.0%)</td>
<td>180/240 (75.0%)</td>
<td>not estimable</td>
<td>✧✧✧✧ LOW</td>
<td>CRITICAL</td>
<td></td>
</tr>
<tr>
<td>B. Assessed with: Low EF, Radial Artery¹²,²¹</td>
<td>2</td>
<td>RCT</td>
<td>serious b</td>
<td>serious b</td>
<td>not serious</td>
<td>not serious</td>
<td>publication bias strongly suspected b</td>
<td></td>
<td></td>
<td>30/200 (15.0%)</td>
<td>30/60 (50.0%)</td>
<td>not estimable</td>
<td>✧✧✧✧ VERY LOW</td>
<td>CRITICAL</td>
<td></td>
</tr>
<tr>
<td>C. Assessed with: BIMA, Coronary Endarterectomy¹⁷,²²</td>
<td>2</td>
<td>RCS RSS</td>
<td>serious a</td>
<td>serious c</td>
<td>not serious</td>
<td>not serious</td>
<td>strong association</td>
<td></td>
<td></td>
<td>134/2781 (4.8%)</td>
<td>0/0</td>
<td>not estimable</td>
<td>✧✧✧✧ MODERATE</td>
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<tr>
<td>D. Assessed with: NCD HS-CRP²³</td>
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<td>CSS</td>
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<td>serious b</td>
<td>not serious</td>
<td>not serious</td>
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<td></td>
<td></td>
<td>30/30 (100.0%)</td>
<td>100/100 (100.0%)</td>
<td>not estimable</td>
<td>✧✧✧✧ LOW</td>
<td>CRITICAL</td>
<td></td>
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<tr>
<td>E. Assessed with: MPV, Skeletonized IMA, BT, CEA, Aspirin Use, AF, RD, Low EF, DM, Euroscore, Tranexamic Acid use, Syntax Score and LM disease¹⁵,¹⁶,¹⁷,²⁰,²¹,²²,²³,²⁴,²⁵</td>
<td>14</td>
<td>PCS PIS PCS</td>
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<td>serious a</td>
<td>not serious</td>
<td>not serious</td>
<td>strong association</td>
<td></td>
<td></td>
<td>2204/3304 (66.7%)</td>
<td>362/362 (100.0%)</td>
<td>not estimable</td>
<td>✧✧✧✧ MODERATE</td>
<td>CRITICAL</td>
<td></td>
</tr>
</tbody>
</table>

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

### Table-II
Summary of Included Studies

<table>
<thead>
<tr>
<th>Sl</th>
<th>Author</th>
<th>Year</th>
<th>Study Design</th>
<th>Patients</th>
<th>BCAB</th>
<th>CCAB</th>
<th>Place of Study</th>
<th>Interest variable</th>
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<td></td>
<td></td>
<td></td>
<td>BECAB and CCAB</td>
<td></td>
<td></td>
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<td>1</td>
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<td>60</td>
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<td>Troponin I</td>
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<tr>
<td>2</td>
<td>Roy et. al.¹²</td>
<td>2013</td>
<td>Randomized Controlled Trail</td>
<td>60</td>
<td>30</td>
<td>30</td>
<td>National Institute of Cardiovascular Diseases</td>
<td>Low Ejection Fraction</td>
</tr>
<tr>
<td>3</td>
<td>Ahmed et. al.¹³</td>
<td>2018</td>
<td>Cross sectional Study</td>
<td>60</td>
<td>30</td>
<td>30</td>
<td>National Institute of Cardiovascular Diseases</td>
<td>Neurocognitive Dysfunction</td>
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<td>30</td>
<td>30</td>
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<td>5</td>
<td>Alauddin et. al.¹⁵</td>
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<td>Prospective Observational Study</td>
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<td>50</td>
<td>50</td>
<td>Bangabandhu Sheikh Mujib Medical University</td>
<td>Renal Dysfunction</td>
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<td>30</td>
<td>National Institute of Cardiovascular Diseases</td>
<td>Euroscore</td>
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<td>2020</td>
<td>Prospective Observational Study</td>
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<td>Left main disease</td>
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<td>2016</td>
<td>Prospective Observational Study</td>
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<td>2018</td>
<td>Prospective Observational Study</td>
<td>101</td>
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Total (Group/Total) 3190/7197 2518 672

*Unspecified grouping as per study requirement. IMA: Internal Mammary Artery. NICVD: National Institute of Cardiovascular Diseases. BSMMU: Bangabandhu Sheikh Mujib Medical University.
The risk of bias for each individual study was mostly serious to critical. We believe that the retrospective and non-randomised nature of the included studies is responsible for these results. Since most of the studies used in the meta-analysis were observational studies, it has contributed to significant confounding and selection bias. The scientific journals reported that the surgeon’s decision to proceed with BECAB or CCAB was heavily influenced by institutional practice and the expertise of the individual surgeon, which would somewhat explain the bias present in the studies. Moreover, a number of the included studies had missing data for the BECAB and/or CCAB groups, further contributing to the overall bias.

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

Statistical analyses
All forest plots were generated using RevMan 5.36. All meta-analyses were carried out using random-effects models to account for statistical variability across all studies that provided data of the clinical outcomes of coronary revascularization surgery. Pooled analyses of our results were carried out using the OpenMetaAnalyst Software37. We reported all the pooled results with 95% confidence intervals (95% CIs).

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**Fig.-1:** The systematic search revealed a total of 341 papers, of which 225 remained for review after duplicates were removed. After implementation of inclusion and exclusion criteria 29 articles were selected for full-text review. Following the full-text assessment of these articles, 25 studies remained for inclusion into the present study.
Results
A total of 341 potential articles were identified from all databases (Figure 1). 25 studies included 7197 patients (2518 from BECAB, 672 for CCAB and 4007 with no assigned group) were selected following standard inclusion criteria for further analysis.

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

Based on screening of titles and abstracts, irrelevant studies that did not satisfy our inclusion criteria were excluded, leaving 29 articles for full-text review. Following the full-text assessment of these articles, studies that lacked data on coronary revascularization surgery (n=4) were excluded, leaving 25 papers11-35 for inclusion into the present study.

The PRISMA statement flow diagram shown in Figure 1 highlights the aforementioned screening process. We were aware that 4 studies from Ranjan et. al20,24,33,35 and 2 studies each from Alam et. al16,27 all published in different years had been included in our meta-analysis as seen in Table 1. Assessment of the full texts verified that these studies were performed on completely different study populations, and were therefore included separately in our meta-analysis. To aid the identification of these papers, we made use of superscripted referencing throughout the present manuscript to properly distinguish the different publications.

Quality of evidence
From our risk of bias assessment of the included studies, we determined that 2 randomized controlled trials were associated with high risk of performance bias due to the outcome assessors not being blinded to the type of intervention12,32 (Table-2). For the 14 prospective observational studies,15,18-27,30,31,35 there was high risk of bias in confounding factors. The non-randomized clinical trials11,14,16,28,34 were also significantly biased due to absence of randomization. Additionally, the bias in selection of patients was observed in retrospective studies17,33 which is typical of studies that are retrospective nature. The included cross-sectional13,29 studies were also devoid of comparative groups and thus had low significance to our study due to their small sample sizes. We determined that the evidence provided by these studies (and the included studies overall) was still of an acceptable quality (Table 1).

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

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

Primary Outcomes
With the data from 5 studies and a total of 360 patients, we observed significantly lower operative times associated with BECAB as compared to CCAB (MD: -52.30, CI: -67.73 to -36.86, p<0.0001) (Figure 2A). There was no significant difference in the number of grafts used from 3 studies and 240 patients (MD: 0.15, CI: -0.54 to 0.84, p=0.67) (Figure 2B). There was also no significant difference in in-hospital mortality when data from 3 studies and 240 patients were compared (RR: 0.70, CI:0.22 to 2.25, p=0.55) (Figure 2C).

Secondary Outcomes
Comparing data from 3 studies and 180 patients, there was no significant difference in the rates of postoperative atrial fibrillation between the BECAB and CCAB groups (RR: 0.80, CI: 0.21 to 3.08, p=0.75) (Figure 3D). We observed shorter ventilation times associated with the BECAB group (MD: -8.64, CI: -9.47 to -7.82, p<0.0001) in
Fig. 2: Forest plots showing (A) less operation time associated with BECAB, (B) no significant difference in the number of grafts used and (C) no significant in-hospital mortality.

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

Analysis of Pooled Data
Our pooled analysis of 4 studies showed that the average blood loss for BECAB patients was 500.303 [352.099, 648.507] ml ($I^2=99.62\%$, $p<0.001$). This was lower than the average blood loss for CCAB patients from 3 studies, which was 656.513 [453.537, 859.490] ml ($I^2=99.68\%$, $p<0.001$). With data from 7 studies, the average incidence rate of perioperative MI for the BECAB group was 0.020 [0.000, 0.042] ($I^2=63.84\%$, $p=0.011$), which was lower than that of CCAB group at an average rate of 0.081 [0.038, 0.136] ($I^2=34.51\%$, $p=0.191$). The pooled average incidence rate of AKI with or without the need for dialysis was 0.006 [0.002, 0.012] ($I^2=0.00\%$, $p=0.543$) for the BECAB group, which was lower than that of the CCAB group, with an average rate of 0.087 [0.055, 0.124] ($I^2=0.00\%$, $p=0.896$). Pooled analysis of 6 studies showed that the average rate of respiratory complications in the BECAB group was 0.020 [0.000, 0.058] ($I^2=70.65\%$, $p=0.004$), which was also lower than that of our pooled analysis of the CCAB group at a rate of 0.090 [0.043, 0.151] ($I^2=18.41\%$, $p=0.294$). The rate of low output syndrome pooled from 2 studies was 0.123 [0.106, 0.141] ($I^2=0.00\%$, $p=0.369$) for the BECAB group, while the pooled analysis of the CCAB group from 2 studies was 0.179 [0.108, 0.262] ($I^2=0.00\%$, $p=0.877$). Finally, the average follow-up EF pooled from 5 studies for BECAB patients was 52.324 [48.200, 56.448] ($I^2=98.64\%$, $p<0.001$), while pooled analysis of average EF of 3 studies for CCAB patients was 52.443 [42.097, 62.788] ($I^2=99.68\%$, $p<0.001$) (Table 3).
Fig.-3: Forest plots showing (D) no significant difference in postoperative atrial fibrillation, (E) less ventilation time associated with BECAB, (F) shorter ICU stay associated with BECAB and (G) no significant difference in hospital stay.
### Table-III

#### Analysis of Pooled Data

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<td>Badruzamanet et. al&lt;sup&gt;11&lt;/sup&gt;</td>
<td>58.10±6.40</td>
<td>63.10±6.40</td>
<td>60.6±6.40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Roy et. al&lt;sup&gt;12&lt;/sup&gt;</td>
<td>46.26±2.01</td>
<td>42.9±1.7</td>
<td>44.5±1.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kabir et. al&lt;sup&gt;15&lt;/sup&gt;</td>
<td>51.6±2.8</td>
<td>51.4±2.9</td>
<td>51.5±2.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R Karim et. al&lt;sup&gt;21&lt;/sup&gt;</td>
<td>55.34±3.97</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Salekin et. al&lt;sup&gt;23&lt;/sup&gt;</td>
<td>50.46±5.06</td>
<td>NA</td>
<td>50.46±5.06</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Overall pooled</td>
<td>52.342</td>
<td>[48.200, 56.448]</td>
<td>I²=98.64%, p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>[42.097, 62.788]</td>
<td>I²=99.68%, p&lt;0.001</td>
</tr>
</tbody>
</table>
Discussion:

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

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

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

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

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

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

Conclusion:

In an adult Bangladeshi CABG population, BECAB was associated with shorter operation times, ventilation times and ICU stay as compared to CCAB. Additionally, we observed lower pooled average rates of perioperative MI, stroke/TIA, AKI, respiratory complications and low output syndrome in the BECAB cohort. At the very least, these results may suggest that the clinical outcomes of BECAB are non-inferior to that of CCAB. However, whether these clinical outcomes can be judged to be better than CCAB is a matter that requires more evidence from further research and data from randomized controlled trials.
Funding
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Declaration of conflicting interests
The Authors declare that there is no conflict of interest.

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

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

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

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

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

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

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

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The National Kidney Foundation of USA began the Dialysis Outcomes and Quality Initiative (DOQI) in 1995, now referred to as the Kidney Disease Outcomes and Quality Initiative (KDOQI), which published a large evidence-based set of clinical guidelines to help improve healthcare outcomes among patients with end stage renal disease. One major focus of KDOQI is optimal arteriovenous access management, which has led to the creation of the National Vascular Access Improvement Initiative (NAVII) and its Fistula First campaign. KDOQI makes it clear that all patients with stage IV or stage V chronic kidney disease who opt for hemodialysis should undergo autologous fistula creation. In order to preserve viable access sites, they recommend a radio-cephalic arteriovenous fistula (RCAVF) as the first and best option. If not feasible, then a brachiocephalic arteriovenous fistula, followed by a basilic vein transposition should be created in the non-dominant arm. Prosthetic arteriovenous bridge grafts and tunneled dialysis catheters are mentioned as last resorts in patients with no autologous options. These recommendations are based upon available data that suggests that AVF have superior patency, fewer complications, require fewer reinterventions, and ultimately improve patient survival. The quality of vascular access for hemodialysis should be suitable for repeated puncture and allow a fast blood flow rate for high-efficiency dialysis with minimal complications. Therefore, long-term functioning AVF needs a well-trained surgeon to create it and enough time allowed for maturation. The dialysis staff must be well versed in cannulation of the AVF, and there should be a minimal need for corrective interventions. Yet it must be recognized that, under the present circumstances, an ideal approach really does not exist. Current literature suggests the arteriovenous fistula to be the preferred type of vascular access for hemodialysis. Once established, fistulas have longer patency and lower rates of complications compared with arteriovenous grafts and catheters. Fistula complications are associated with morbidity, mortality, and a high economic burden. Objectives of our study were to understand the complications after fistula creation, long term follow up during dialysis and also to figure out the management techniques of these complications. The objectives also include understanding the role and importance of Duplex study for fistula creation and for evaluation of complications. We present our experience on facing complications and management technique of AVF.

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

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

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

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

b. Patient on hemodialysis with temporary dialysis catheter.

c. Failed arteriovenous fistula.

**Exclusion Criteria**

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

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

c. Fistula creation for renal transplantation

**Results:**

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

**Table-I**

<table>
<thead>
<tr>
<th>Type of Arteriovenous Fistula (n=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of fistula</td>
</tr>
<tr>
<td>Radio-cephalic</td>
</tr>
<tr>
<td>Brachio-cephalic</td>
</tr>
<tr>
<td>Brachio-basilic</td>
</tr>
<tr>
<td>Ulnar-basilic</td>
</tr>
<tr>
<td>Brachio-axillary straight graft fistula</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

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

**Table-II**

<table>
<thead>
<tr>
<th>Choice of Upper Limb for Fistula Creation (n=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choice of Upper limb</td>
</tr>
<tr>
<td>Left Upper Limb</td>
</tr>
<tr>
<td>Right Upper Limb</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

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

**Table-III**

<table>
<thead>
<tr>
<th>Causes of Renal Failure (n=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>CKD</td>
</tr>
<tr>
<td>Obstructive Uropathy</td>
</tr>
<tr>
<td>Polycystic Kidney disease</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

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

**Table-IV**

<table>
<thead>
<tr>
<th>Complications of Arteriovenous Fistula (n=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complication</td>
</tr>
<tr>
<td>Haematoma</td>
</tr>
<tr>
<td>Bleeding</td>
</tr>
<tr>
<td>Seroma</td>
</tr>
<tr>
<td>Infection</td>
</tr>
<tr>
<td>Ischaemic Steal Syndrome</td>
</tr>
<tr>
<td>Thrombosis</td>
</tr>
<tr>
<td>Pseudoaneurysm</td>
</tr>
<tr>
<td>Aneurysm</td>
</tr>
<tr>
<td>Anastomotic Rupture</td>
</tr>
<tr>
<td>Anastomotic stenosis</td>
</tr>
<tr>
<td>Arterialized vein stenosis</td>
</tr>
<tr>
<td>Canulation site infection</td>
</tr>
<tr>
<td>Venous Hypertension</td>
</tr>
</tbody>
</table>

In this study, the most common complication was stenosis of arterialized vein (4.13%). Repeated use of cannulation for dialysis followed by inflammation and fibrosis was the leading cause of stenosis. Stenosis was also commonly found at the anastomotic site (2.48%). Probably anastomotic stenosis occurred due to venous intimal hyperplasia. All stenoses was managed successfully by endovascular intervention with balloon angioplasty. The
The second most common complication was infection. Cannulation site infection (3.31%) was followed by infection at the site of fistula creation (2.48%). These were managed successfully by regular careful dressing and proper use of antibiotics after culture sensitivity test.

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

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

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

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

Creation of Arteriovenous fistula is an important surgery for the vascular surgeons. Almost all AV fistulas were done with local anesthesia, but Brachio-basilic transposition fistula and one graft fistula (PTFE) was done under brachial block. Distal radio-cephalic fistula gives more length and more patency rate than others, so surgeons as well as patients first choice was distal radio-cephalic fistula. In a study done in Brazil, 52.5% of the study population was Distal Radio-cephalic fistulae, 16% was Proximal Radio-cephalic, 15% was Brachio-basilic fistulae. Most of the arteriovenous fistula (97.52%) in our series were made for Chronic Kidney Diseases[1]. Other causes of End Stage Renal Disease were obstructed uropathy (1.65%) and polycystic kidney disease (0.83%).

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

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

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

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

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

Two bleeding fistulas were found in immediate postoperative period within one and half hours of Brachio-cephalic fistula creation. Re exploration was done. Bleeding point was identified and proper hemostasis was done. There was no ischemic steal syndrome and anastomotic ruptured AVF in our series, but there was found a case of venous hypertension. Diagnosed
clinically by the signs of upper limb swelling and edema and was confirmed by venography. This venous hypertension of AVF complication was managed by stenting in central venous stenotic site.

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

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

Md. Sadaqul Islam Sikdar¹, Md Mamunur Rashid², Md Khalekuzzaman³, Iftekhar Alam¹, Mst. Nazmun Nahar⁴, Md. Shariful Islam⁵, Lipi Debnath⁶, Abdullah Al Masud⁷

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Informed written consent was taken from each patient before enrollment. Meticulous history was taken and detailed clinical examination was performed. Risk factors profile including smoking, hypertension, dyslipidaemia and family history of premature coronary artery disease (CAD) were noted. All necessary screening tests for coronary angiogram were done. Resting ECG of all patients was done at a paper speed of 25 mm/s and 10mm standardization at admission using Fukuda ECG machine (Model: FX-2111) Denshi Co Ltd. Japan. All angiography views were evaluated by two experienced cardiologists who were blinded to the study. Ventricular ejection fraction (LVEF) was measured by Tichoitz’s method. Blood Sample was taken for fibrinogen before the day of CAG. Fibrinogen measured by automatic system by Stago-Compact Max using STA: Fib-2 reagent using clot based method.

Coronary angiogram was done either by right femoral or right radial route by Trinias C12 unity system, Shimadzu, Japan. All angiography views were evaluated by two experienced cardiologists who were blinded to the study. The severity of the CAD was assessed by Vessel score and Gensini score.
From the categorical viewpoint, significant coronary artery disease was defined as > 70% stenosis in any of the three major coronary artery, stenosis <70% in major epicardial coronary arteries were termed non-obstructive CAD. Extent of CAD was defined as insignificant, single, two or three vessel CAD. Score ranges from 0 to 3 were assigned depending on the number of vessels involved. Left main coronary artery was scored as single vessel disease.

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

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

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

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

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

---

### Table I

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Group I (n=87)</th>
<th>Group II (n=45)</th>
<th>Total (N=132)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td>31 – 40</td>
<td>04</td>
<td>4.6</td>
<td>07</td>
<td>15.6</td>
</tr>
<tr>
<td>41 – 50</td>
<td>47</td>
<td>54.0</td>
<td>19</td>
<td>42.2</td>
</tr>
<tr>
<td>51 – 60</td>
<td>22</td>
<td>25.3</td>
<td>13</td>
<td>28.9</td>
</tr>
<tr>
<td>&gt;60</td>
<td>14</td>
<td>16.1</td>
<td>06</td>
<td>13.3</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>52.7±8.7</td>
<td></td>
<td>50.4±8.7</td>
<td></td>
</tr>
</tbody>
</table>

---

Fig.-1: Sex distribution among the study groups
Table-II

*Distribution of risk factors in between the study groups*

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Group I (n=87)</th>
<th>Group II (n=45)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td>Hypertension</td>
<td>58</td>
<td>66.7</td>
<td>21</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>42</td>
<td>48.3</td>
<td>11</td>
</tr>
<tr>
<td>Smoking</td>
<td>49</td>
<td>56.3</td>
<td>17</td>
</tr>
<tr>
<td>Family H/O of CAD</td>
<td>35</td>
<td>40.2</td>
<td>16</td>
</tr>
</tbody>
</table>

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

Table-III

*Distribution of vessel score in between the patient groups.*

<table>
<thead>
<tr>
<th>Vessel Score</th>
<th>Group I (n=87)</th>
<th>Group II (n=45)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td>Score - 0</td>
<td>10</td>
<td>11.5</td>
<td>16</td>
</tr>
<tr>
<td>Score - 1</td>
<td>34</td>
<td>39.1</td>
<td>11</td>
</tr>
<tr>
<td>Score - 2</td>
<td>29</td>
<td>33.3</td>
<td>12</td>
</tr>
<tr>
<td>Score - 3</td>
<td>14</td>
<td>16.1</td>
<td>06</td>
</tr>
</tbody>
</table>

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

Table-IV

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

<table>
<thead>
<tr>
<th>Vessel involvement</th>
<th>Fibrinogen (Fg) gm/L</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Number(N=132)</td>
<td>Mean</td>
</tr>
<tr>
<td>No Vessel</td>
<td>26</td>
<td>3.39</td>
</tr>
<tr>
<td>SVD</td>
<td>45</td>
<td>4.01</td>
</tr>
<tr>
<td>DVD</td>
<td>41</td>
<td>4.29</td>
</tr>
<tr>
<td>TVD</td>
<td>20</td>
<td>4.36</td>
</tr>
</tbody>
</table>

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

Table-V

*Distribution of Gensini score in between the patient groups.*

<table>
<thead>
<tr>
<th>Gensini Score</th>
<th>Group I (n=87)</th>
<th>Group II (n-45)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td>Mild (1-10)</td>
<td>16</td>
<td>18.4</td>
<td>05</td>
</tr>
<tr>
<td>Moderate (11-50)</td>
<td>44</td>
<td>50.6</td>
<td>16</td>
</tr>
<tr>
<td>Severe (&gt; 50)</td>
<td>17</td>
<td>19.5</td>
<td>08</td>
</tr>
</tbody>
</table>

The table VI displays the severity of CAD among the study patients. The mean vessel score and Gensini score was statistically significantly higher in group I.
There is a positive correlation between Fg and coronary artery disease severity in terms of vessel score (r=0.19). It was observed that the Spearman’s correlation statistically significant (p=0.03) by correlation t test (Figure 2).

![Correlation between Fg and vessel score by Spearman’s correlation](image)

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

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

![Correlation between Fg and Gensini score by Pearson’s correlation t-test](image)

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

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

**Table-VII**

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

**Discussion:**

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

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

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

Thompson et al. found fibrinogen to be a strong predictor of coronary events in patients with angina pectoris. In
those subjects with high total cholesterol, a high fibrinogen level conferred added risk compared with those with low fibrinogen. Patients in the highest fibrinogen quintile had three times the risk of a coronary event than those in the lowest quintile.

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

**Discussion on the results of the present study:**

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

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

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

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

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

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

**Limitations of the study**

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

**Conclusion:**

The present study demonstrates that elevated plasma fibrinogen is associated with more severe CAD in type 2 diabetes mellitus patients with chronic stable angina.
There is a positive correlation between the plasma levels of fibrinogen and severity of CAD. High fibrinogen level as an early diagnostic marker of coronary artery disease may have important clinical implications in improving the management strategy and outcome of these patients.

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


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

Lipi Debnath¹, Abdul Wadud Chowdhury², Iftekhar Alam³, Md. Mamunur Rashid⁴, Md. Sadaqul Islam Sikder³
Bijan Kumar Nath⁵

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

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

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

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

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

Introduction:
Various studies have pointed out that South Asians have a higher prevalence of coronary artery disease (CAD) as compared with other ethnicities, with a higher rate at younger ages¹. Traditionally there are some conventional risk factors like age, male sex, positive family history, hypertension, smoking, hyperlipidaemia, metabolic syndrome, diabetes, lack of exercise, obesity, and some emerging risk factors, like C-reactive protein, Homocysteine, Fibrinogen etc².

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

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

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

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

Bottom of Form

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

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

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

Methods:

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

Informed consent was taken from all patients or from the legal guardians. Initial evaluation of the study population by history and clinical examination was performed and recorded accordingly in the preformed data collection sheet. Demographic variables e.g. Age, sex and personal information were recorded. Risk factors of ischemic heart
disease (IHD) e.g. hypertension, smoking, dyslipidaemia, diabetes mellitus, family history of premature CAD and obesity was noted. Necessary laboratory investigations RBS, fasting lipid profile, S. Creatinine, S. Troponin-I was done and recorded. 12 lead resting ECG was done at a paper speed of 25 mm/s and 10mm/mV standardization at admission. Trans-thoracic echocardiography was done by 2D & M-mode and Doppler echo modalities and left ventricular ejection fraction (LVEF) was measured by Tichoitz’s method.

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

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

**Results:**

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

**Table I**

<table>
<thead>
<tr>
<th>Age (in year)</th>
<th>Group I (n=72)</th>
<th>Group II (n=188)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>31 – 40</td>
<td>32</td>
<td>118</td>
<td>62.8</td>
</tr>
<tr>
<td>41 – 50</td>
<td>12</td>
<td>24</td>
<td>12.8</td>
</tr>
<tr>
<td>51 – 60</td>
<td>18</td>
<td>20</td>
<td>10.6</td>
</tr>
<tr>
<td>61 – 70</td>
<td>10</td>
<td>24</td>
<td>12.8</td>
</tr>
<tr>
<td>&gt;70</td>
<td>0</td>
<td>2</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Mean ± SD 50.33±15.50 45.86±18.76 0.073ns

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

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

**Table II**

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Group II(n=72)</th>
<th>Group II (n=188)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI</td>
<td>52</td>
<td>132</td>
<td>70.2</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>8</td>
<td>24</td>
<td>12.8</td>
</tr>
<tr>
<td>UA</td>
<td>12</td>
<td>32</td>
<td>17.0</td>
</tr>
</tbody>
</table>

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

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

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

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

Smoking and dyslipidemia were statistically significant (p<0.05) between two groups but others were not significant (p>0.05) in chi square test. (Table VII)
The mean serum Homocysteine differences were statistically significant and high in group II in HTN, smoker and dyslipidemia, but obesity and F/H of premature heart disease was not statistically significant. (Table VIII)

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

### Table III

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

<table>
<thead>
<tr>
<th>Clinical Diagnosis</th>
<th>Group I (n=72)</th>
<th>Group II (n=188)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serum homocysteine (µmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td>14.14±6.6</td>
<td>19.63±18.1</td>
<td>0.012^s</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>15.89±8.02</td>
<td>18.19±6.0</td>
<td>0.012^s</td>
</tr>
<tr>
<td>UA</td>
<td>12.75±4.88</td>
<td>15.21±5.19</td>
<td>0.001^s</td>
</tr>
<tr>
<td>Group mean</td>
<td>14.11±6.48</td>
<td>18.41±15.49</td>
<td>0.024^s</td>
</tr>
</tbody>
</table>

### Table IV

**Distribution in between the groups of hs-CRP level according to clinical diagnosis (N=260).**

<table>
<thead>
<tr>
<th>Clinical Diagnosis</th>
<th>Group I (n=72)</th>
<th>Group II (n=188)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hs CRP level (mg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td>30.12±33.11</td>
<td>41.26±43.26</td>
<td>0.049^s</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>14.12±12.32</td>
<td>39.67±29.53</td>
<td>0.001^s</td>
</tr>
<tr>
<td>UA</td>
<td>8.12±7.77</td>
<td>28.51±27.61</td>
<td>0.001^s</td>
</tr>
<tr>
<td>Group mean</td>
<td>23.84±30.30</td>
<td>37.48±37.99</td>
<td>0.034^s</td>
</tr>
</tbody>
</table>

### Table V

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

<table>
<thead>
<tr>
<th>S. Homocysteine (µmol/L)</th>
<th>Group I (n=72)</th>
<th>Group II (n=188)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N %</td>
<td>n %</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>16.25 ± 5.81</td>
<td>19.48 ± 16.68</td>
<td>0.108ns</td>
</tr>
<tr>
<td>Female</td>
<td>7.67 ± 3.45</td>
<td>13.69 ± 6.82</td>
<td>0.001^s</td>
</tr>
</tbody>
</table>

### Table VI

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

<table>
<thead>
<tr>
<th>hs-CRP level (mg/L)</th>
<th>Group I (n=72)</th>
<th>Group II (n=188)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N %</td>
<td>n %</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>31.41 ± 32.77</td>
<td>39.97 ± 38.71</td>
<td>0.097ns</td>
</tr>
<tr>
<td>Female</td>
<td>13.13 ± 14.87</td>
<td>26.24 ± 32.75</td>
<td>0.012^s</td>
</tr>
</tbody>
</table>
Discussion:
This cross-sectional study was carried out with an aim to evaluate the serum homocysteine and hs-CRP level in type 2 diabetic and non-diabetic patients with recently diagnosed ACS.

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

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

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

Regarding the clinical association with serum homocysteine level it was observed that the mean serum homocysteine levels were significantly higher in patients with risk factors such as hypertension, smoking, obesity, dyslipidemia, and family history of premature CAD compared to non-risk factor patients.

<table>
<thead>
<tr>
<th>Table-VII</th>
<th>Distribution of risk factors among the study groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factors</td>
<td>Group I (n=72)</td>
</tr>
<tr>
<td>HTN</td>
<td>N</td>
</tr>
<tr>
<td>Smoking</td>
<td>22</td>
</tr>
<tr>
<td>Obesity</td>
<td>12</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>54</td>
</tr>
<tr>
<td>Family history</td>
<td>6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table-VIII</th>
<th>Distribution of the study subjects according to mean serum homocysteine level and risk factors for ACS (N=260)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factors for ACS</td>
<td>Group I (n=72)</td>
</tr>
<tr>
<td></td>
<td>Serum homocysteine (µmol/L)</td>
</tr>
<tr>
<td>HTN</td>
<td>14.86±7.29</td>
</tr>
<tr>
<td>Smoker</td>
<td>15.81±7.12</td>
</tr>
<tr>
<td>Obesity</td>
<td>14.95±10.25</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>14.07±6.10</td>
</tr>
<tr>
<td>F/H Of Premature CAD</td>
<td>14.26±10.09</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table-IX</th>
<th>Distribution of the study subjects according to mean Serum hs-CRP level and risk factors for ACS (N=260)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factors for ACS</td>
<td>Group I (n=72)</td>
</tr>
<tr>
<td></td>
<td>Hs CRP level (mg/L)</td>
</tr>
<tr>
<td>HTN</td>
<td>10.89±35.33</td>
</tr>
<tr>
<td>Smoking</td>
<td>32.03±32.32</td>
</tr>
<tr>
<td>Obesity</td>
<td>34.82±50.88</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>29.59±33.71</td>
</tr>
<tr>
<td>F/H Of Premature Cad</td>
<td>13.35±6.91</td>
</tr>
</tbody>
</table>
homocysteine level in patients with subsets of ACS were significantly (p<0.05) higher in patients without DM. The observed mean homocysteine was $14.4\pm6.4$ µmol/L and $15.2\pm6.0$ µmol/L in male and female patients without DM in group I and II respectively. Kurowska et al., showed the mean (±SD) serum homocysteine level in patients with MI was $14.7\pm6.7$ µmol/L in patients with type 2 diabetes and $16.9\pm7.4$ µmol/L in patients without diabetes. In UA the investigators showed the mean serum homocysteine level was $13.9\pm5.6$ µmol/L in patients with type 2 diabetes and $13.8\pm4.2$ µmol/L in patients without diabetes, which are similar with the current study.

Similarly, the mean hs-CRP level in patients with subsets of ACS was significantly (p<0.05) higher in group II. The mean hs-CRP level of group I and group II was $26.84\pm30.30$ mg/l and $37.48\pm37.99$ mg/l respectively. In the study by Kurowska et al., mean hs-CRP level in patients with MI was $24.3\pm36.6$ mg/l in patients with type 2 diabetes and $29.7\pm40.8$ mg/l in patients without diabetes. In case of UA the hs-CRP level was $6.6\pm6.5$ mg/l in patients with type 2 diabetes and $25.2\pm49.9$ mg/l in patients without diabetes, which were significantly (p<0.05) higher in patients with out DM, which support the findings of current study. Facila et al., concluded that homocysteine over 10 µmol/l was an independent prognostic factor increasing the long term risk of all cause mortality after acute coronary syndrome.

In this present series it was observed that the mean serum homocysteine level was higher in male and female ACS patients without DM. This finding is supported by Kurowska et al., who showed that the mean serum homocysteine level was $14.4\pm5.5$ µmol/L in male patients with T2DM and $15.4\pm6.4$ µmol/L in male patients without diabetes. Kurowska et al., showed the mean (±SD) serum homocysteine level was $14.4\pm7.1$ µmol/L in female patients with T2DM and $15.2\pm6.0$ µmol/L in female patients without diabetes, which was statistically significant (p<0.05) and support the findings of the current study.

Similarly the mean hs-CRP level was higher in male and female ACS patients without DM in this study. Kurowska et al., showed lesser hs-CRP level in male patient, which was $17.0\pm19.8$ mg/l in patients with type 2 diabetes and $31.0\pm50.1$ mg/l in patients without diabetes, that was significantly (p<0.05) higher in ACS patients without DM. Thus support the current study. Kurowska et al showed, the mean hs-CRP level was $17.0\pm38.3$ mg/l in female patients with type 2 diabetes and $20.5\pm33.6$ mg/l in female patients without diabetes, which was significantly (p<0.05) higher in ACS patients without DM, which is consistent with the current study.

On the other hand, Idzior-Waluż et al. CRP levels was significantly higher in women with diabetes than in men which was $4.7\pm3.2$ mg/l vs $4.1\pm7.2$ mg/l in female and male respectively.

Regarding the risk factors dyslipidaemia and smoking was statistically sngificant risk factor in group I and group II respectively. Puri et al. showed that hypertension, smoking, positive family history and dyslipidaemia were the most common risk factors in patients with ACS. The mean serum Homocysteine differences were significantly (p<0.05) higher in patients without T2DM. But obesity and F/H of premature CAD was almost comparable in both groups. Puri et al. showed the mean homocysteine was $23.93\pm10.94$ nmol/ml and $25.41\pm11.88$ nmol/ml in hypertensive and smoker patients respectively. The mean serum hs-CRP differences was significantly (p<0.05) higher in HTN and F/H of premature CAD patients without DM, but other risk factors was not significant (p>0.05) between the two groups.

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

**Conclusion:**

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

**References:**


2. Maron DJ, Rider PM, Grundy SM, Prevention Strategies for Coronary Heart Disease. In: Fuster


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

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

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

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

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

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

Introduction:
Coronary artery disease (CAD) is the leading cause of mortality and morbidity in industrialized countries and it is emerging as public health problem in developing countries. It is established that 30% of all deaths can be attributed to cardiovascular disease, of which more than half are caused by CAD. Globally, of those dying from cardiovascular diseases, 80% are in developing countries not in the western world. By the year 2020, CAD will hold first place in the world health organization’s list of leading cause of disability. Bangladesh has undergone a remarkable demographic transition over last three decades. Striking changes have
also been observed in the lifestyle and food habit in our population.

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

Complications of CAD are acute and chronic. The most common chronic complication of CAD is chronic ischemic heart failure wherein the heart becomes dilated, myocardium become thinned, scarred and fibrosed; as a result systolic LV dysfunction develops, leading to congestive heart failure. In a word this condition known as ischemic cardiomyopathy. Burch and Colleagues in 1970 first used the term Ischemic Cardiomyopathy to describe the condition in which Coronary Artery Disease results in severe myocardial dysfunction. In the United States, the most common form of dilated Cardiomyopathy is ischemic Cardiomyopathy or the Cardiomyopathy that follows myocardial infarction. Dilation of LV and a decrease of ejection fraction occurs in 15-40% of subjects within 12-24 months after anterior MI and in a smaller percentage of subjects after an inferior MI. Based on limited data, it is tempting to speculate that subjects who undergo the remodeling process and develop an ischemic cardiomyopathy are those with particularly heightened compensatory mechanisms, perhaps as result in polymorphic variation in this system. The remodeling process is an attempt of the compromised ventricle to increase its performance by increasing stroke volume, but ultimately, it correlates with an adverse outcome in the long run.

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

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

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

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

Inclusion criteria:
Chronic heart failure patients with dilated Left ventricle with one of the followings:

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

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

Results and Observations:
A total 100 patients of ischemic cardiomyopathy were included in this study. The data analysis of these patients showed mean age was 61±7.9 years ranges from 40 years to 80 years and 79 (79%) were male.
Table I displays the clinical symptoms of the studied ischemic cardiomyopathy patients. The remarkable symptoms presented were dyspnea (92%), chest pain (73%), Paroxysmal nocturnal dyspnea (52%), orthopnea (46%), palpitation (39%), edema (23%), and cardiogenic shock (21%). The rest of the symptoms such as syncope and cardiac arrest were present in 5% patients.

Table II shows NYHA class II, III and IV were observed 25%, 32% and 43% in study population respectively. Majority of the patients were in NYHA functional class IV. Risk factor evaluation shows 40% patients had diabetes, 40% patients had hypertension, 47% were smokers, 25% had family history of coronary artery diseases and 25% patient had chronic kidney diseases.

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

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

Table IV shows majority of the ECG is in sinus rhythm (80%), atrial fibrillation (15%) and ventricular tachycardia / ventricular fibrillation (5%). The sinus tachycardia (71%) was more frequently seen in patients with ischemic cardiomyopathy followed by LBBB (34%), and RBBB (12%). Anterior and inferior surface in pathological Q were found in 65% and 21% respectively. ST-T changes had in 41% patients. PVCs was found in 17% patients of the study population.
Table-V
Echocardiographic structural and functional parameters of the study patients (n=100).

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

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

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

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

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

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

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

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

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

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

In echocardiography anterior wall hypokinetic (left anterior descending artery territory) was 52%, inferior wall hypokinetic (right coronary artery territory) was 12% and overlapping or global hypokineti was 43%. There were similar findings with previous study. Maximum patients left ventricular ejection fraction (LVEF) were moderately impaired i.e. LVEF (30-44%) and the no. of the patients were 62%. The mean left ventricular ejection fraction (LVEF) was found to be 31.9±5.9%. In previous studies it was 26.6±7.8% , 27.8±5.7% and 26±9.5%. The mean LVIDd and LVIDs were found to be 6.5±0.5 and 5.2±0.5 respectively which were similar to previous study.

On echo-color Doppler study 59% patients had mitral regurgitation (MR) grade-I, 20% MR grade-II, 14% MR grade-III and 7% had no MR. Previous study related to ischemic cardiomyopathy and dilated cardiomyopathy also showed similar pictures. We, the physicians have to take challenge to manage these patients daily. Most of the patients are not able to take proper treatment due to economic constrain. Some of these patients have the criteria for modern treatment of heart failure i.e. device therapy alongside to medical management, so that morbidity and mortality can be reduced.

**Limitations of the study:**

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

**Conclusion:**

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

**References:**


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


Original Article

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

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

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

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

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

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

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

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

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

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

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

Materials and Methods:
This cross-sectional observational study was done in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh during September, 2018 to August, 2019. A total of 200 patients with NSTEMI who were admitted into NICVD and underwent coronary angiography (CAG), were included for this study. Those getting medications that alter potassium homeostasis (e.g., diuretics, glucocorticoids, intravenous insulin), having renal impairment, haematological or liver disease, congenital or valvular heart disease, cardiomyopathy, prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were excluded. For each patient, relevant history was taken and clinical examination was done and recorded in predesigned structured data collection sheet. For measurement of serum potassium, 2.5 ml of blood was drawn before the day of CAG under aseptic technique from peripheral veins. The collected blood was then directly put into an automated hematology analyzer (Beckman Coulter AU480/ Siemens Dimension EXL LM) to get the values of serum electrolytes including potassium. Other investigations e.g., complete blood count, serum creatinine, lipid profile, blood sugar, were done as per standard protocol. The study patients were divided into 2 groups on the basis of serum potassium level: mid to high normal (4 to 5.5 mmol/L) constituted the group I and low normal (3.5-3.9 mmol/L) constituted the group II. Echocardiography was done before sending the patient to cath lab. CAG was done by conventional method. From the baseline diagnostic CAG, angiographic severity assessment was done by the SYNTAX scoring system by 2 independent experienced interventional
cardiologists blinded to the identities and clinical information of the patients. All coronary lesions with a diameter stenosis ≥50% in vessels ≥1.5 mm were scored, using the SYNTAX algorithm, which is available on the website www.syntaxscore.com. Patients with SYNTAX scores ≥23 were considered to have moderate to severe CAD according to this definition. For the present study, the patients were divided into 2 groups, those with low SYNTAX scores (≤22) and those with intermediate to high SYNTAX scores (>23). Comparison of SYNTAX scores between group I (low normal serum potassium) and group II (mid to high normal serum potassium) NSTEMI patients was done.

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

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

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

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

High SYNTAX score was more commonly found in group I than in group II (62.1% vs 14.7%), and the difference between the 2 groups was statistically highly significant (p<0.001). On the other hand, low SYNTAX score was more common in group II than in group I (37.9% vs 85.3%), and the difference was statistically highly significant. Mean SYNTAX score was higher in group I than in group II (24.3±8.2 vs. 15.3±7.8), the difference between the groups was statistically significant (p=0.01). (Table 3). Other statistics of SYNTAX score including the 25th and 75th percentile levels, the median, the maximum and minimum values and the inter-quartile ranges of SYNTAX score were higher in group I patients with high serum potassium level than in group II patients with low normal potassium. (Figure 1)

### Table-I

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Group I (n=132)</th>
<th>Group II (n=68)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td>Smoking</td>
<td>78</td>
<td>59.1</td>
<td>36</td>
</tr>
<tr>
<td>Hypertension</td>
<td>80</td>
<td>60.6</td>
<td>48</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>76</td>
<td>57.6</td>
<td>28</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>62</td>
<td>47.0</td>
<td>20</td>
</tr>
<tr>
<td>Family H/o premature CAD</td>
<td>32</td>
<td>24.2</td>
<td>12</td>
</tr>
</tbody>
</table>

Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)
Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)

p value was reached from chi square test. S= Significant (p<0.05), NS = Not significant (p>0.05). CAD = Coronary artery disease
Table-II

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

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

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

Table-III

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

<table>
<thead>
<tr>
<th>SYNTAX Score</th>
<th>Group I (n=132)</th>
<th>Group II (n= 68)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>%</td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td>High (e&quot;23)</td>
<td>82 62.1</td>
<td>10 14.7</td>
<td></td>
</tr>
<tr>
<td>Low (d&quot;22)</td>
<td>50 37.9</td>
<td>58 85.3</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>24.3±8.2</td>
<td>15.3±7.8</td>
<td>&lt;0.001S</td>
</tr>
</tbody>
</table>

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

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

Group I: NSTEMI patients with mid to high serum potassium level (4-5.5 mmol/L)
Group II: NSTEMI patients with low normal serum potassium level (3.5-3.9 mmol/L)

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

Also, a positive correlation was found between serum potassium level and SYNTAX score with correlation coefficient, r=0.49, p<0.001. As serum potassium level increases, SYNTAX score also increases. (Figure II)
Variables associated with high SYNTAX score were further analyzed by logistic regression analysis to find out the determinants of severity of CAD as assessed by high SYNTAX score. Hypertension, dyslipidemia and mid to high serum potassium level were found to be the significant predictors of high SYNTAX score with ORs being 4.37, 2.12 and 10.44 respectively. (Table 4)

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

In this present study, the SYNTAX score of NSTEMI patients differed between group I and group II. The patients in group II with low normal serum potassium had mean SYNTAX score 15.3±7.8 while, patients in group I with mid to high normal serum potassium had mean SYNTAX score 22.6±7.1. Statistically, this difference was highly significant (p<0.001). Zhao et al demonstrated that serum potassium levels were significantly increased in patients with lower (<39 points; 3.90 ±0.02 mmol/L, n=453) and higher (>39 points; 3.9±0.02, n=194) Gensini scores compared with normal patients (3.82±0.03 mmol/L) (p value<0.05). Furthermore, serum potassium level of the high score group was also significantly higher than that of low score group (p=0.05). In another study, Honda et al found serum potassium level on admission as an independent risk factor for target lesion revascularization. Both of the studies had similar findings like the present study in terms of having increased CAD severity with increased serum potassium levels. In this study significantly positive correlation was found between serum potassium level within normal range and SYNTAX score (r = 0.49, p value < 0.001). Within normal range as serum potassium level increases, SYNTAX score also increases. Most of the patients with low normal serum potassium had low SYNTAX score, while most of the patients with mid to high serum potassium had high SYNTAX score. In the USA, serum potassium level was found marginally associated with risk of CVD (hazard ratio per 1mg/dL increment, 1.03; 95% confidence interval, 1.00-1.05; p=.02) a multicenter study.

In this study significantly positive correlation was found between serum potassium level within normal range and SYNTAX score (r = 0.49, p value < 0.001). Within normal range as serum potassium level increases, SYNTAX score also increases. Most of the patients with low normal serum potassium had low SYNTAX score, while most of the patients with mid to high serum potassium had high SYNTAX score. Statistically, this correlation was highly significant (p<0.001). Similar significant positive correlation was found by Zhao et al between serum potassium and the severity of CAD assessed by Gensini score (p <0.05).

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

<table>
<thead>
<tr>
<th>Variables of interest</th>
<th>Regression coefficient (β)</th>
<th>p value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤50 years</td>
<td>0.437</td>
<td>0.27NS</td>
<td>1.54</td>
<td>0.714 – 3.354</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.575</td>
<td>0.12NS</td>
<td>1.77</td>
<td>0.856 – 3.691</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.420</td>
<td>0.25NS</td>
<td>1.52</td>
<td>0.739 – 3.135</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.477</td>
<td>&lt;0.001S</td>
<td>4.37</td>
<td>2.024 – 9.474</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>10.755</td>
<td>0.03S</td>
<td>2.12</td>
<td>1.062 – 4.260</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>0.634</td>
<td>0.13NS</td>
<td>1.88</td>
<td>0.817 – 4.351</td>
</tr>
<tr>
<td>Mid to high serum potassium level</td>
<td>2.346</td>
<td>&lt;0.001S</td>
<td>10.44</td>
<td>4.547 – 23.993</td>
</tr>
</tbody>
</table>

Dependent variable: high SYNTAX Score; Independent variables: age ≤50 years, smoking, diabetes mellitus, hypertension, dyslipidemia, family history of CAD and mid to high normal serum potassium level (4-5.5 mmol/L)

S = Significant, NS = Not significant
Serum Potassium and Angiographic Severity of Coronary Artery Disease

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potassium i.e., 4.5-5.5 mmol/L (odds ratio: 10.44; 95% CI is 4.547-23.993, p<0.001) and hypertension and dyslipidaemia were the independent determinants of increased angiographic severity of CAD (SYNTAX score e’ 22). In the study by Zhao et al and Honda et al higher serum potassium level within normal range was demonstrated as independent predictor for severe CAD.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Results:
In this study, 85 patients of NSTEMI with HbA1c level < 5.7% were considered as group I and 85 patients of NSTEMI with elevated HbA1c level (e” 5.7%- 6.4%) were considered as group II.
Demographic profile of the study population (N = 170)

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

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

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

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Group I n (%)</th>
<th>Group II n (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>66 (77.6)</td>
<td>68 (80.0)</td>
<td>0.700</td>
</tr>
<tr>
<td>Chewing tobacco</td>
<td>34 (40.0)</td>
<td>37 (43.5)</td>
<td>0.640</td>
</tr>
<tr>
<td>Hypertension</td>
<td>43 (50.6)</td>
<td>57 (67.1)</td>
<td>0.062</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>48 (56.5)</td>
<td>50 (58.8)</td>
<td>0.750</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>22 (25.9)</td>
<td>24 (28.2)</td>
<td></td>
</tr>
</tbody>
</table>

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

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

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

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

Comparison of the study patients according to vessel score (N=170)

<table>
<thead>
<tr>
<th>Vessel score</th>
<th>Group I n (%)</th>
<th>Group II n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score- 0</td>
<td>17 (20.0)</td>
<td>6 (7.1)</td>
<td>0.018</td>
</tr>
<tr>
<td>Score- 1</td>
<td>42 (49.4%)</td>
<td>22 (25.9%)</td>
<td>0.0048</td>
</tr>
<tr>
<td>Score- 2</td>
<td>19 (22.4%)</td>
<td>28 (32.9%)</td>
<td>0.048</td>
</tr>
<tr>
<td>Score- 3</td>
<td>7 (8.2%)</td>
<td>29 (34.1%)</td>
<td>0.0018</td>
</tr>
</tbody>
</table>

Association of Haemoglobin A1c Level with the Severity
Md. Mamunuzzaman et al.
According to vessel score, zero (0)-vessel score and 1- vessel score were significantly higher in group I, whereas 2-vessel score and 3- vessel score were significantly higher in group II.

Table V

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

<table>
<thead>
<tr>
<th>Vessel score</th>
<th>HbA1c in %</th>
<th>P  value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>No vessel involvement (n=23)</td>
<td>5.27</td>
<td>0.59</td>
</tr>
<tr>
<td>Single (n=64)</td>
<td>5.47</td>
<td>0.54</td>
</tr>
<tr>
<td>Double (n=47)</td>
<td>5.81</td>
<td>0.47</td>
</tr>
<tr>
<td>Triple (n=36)</td>
<td>6.05</td>
<td>0.57</td>
</tr>
</tbody>
</table>

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

Table VI

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

<table>
<thead>
<tr>
<th>Gensini Score</th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (CAD d+36)</td>
<td>66 (77.6)</td>
<td>39 (45.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Moderate to severe (CAD &gt;36)</td>
<td>19 (22.4)</td>
<td>45 (54.1)</td>
<td></td>
</tr>
</tbody>
</table>

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

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

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

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

The figure shows that there is a positive correlation between HbA1c and coronary artery disease severity in terms of Gensini score (r=0.41; p=0.01).
Discussion:
The mean age of the studied patients was 51.0±9.0 years ranging from 30 to 80 years. Hung et al.\textsuperscript{13}, showed that the mean age of their study population was 51.5 ±13.2 years which was similar to the present study. Sherif, et al.\textsuperscript{8} found the mean age of his study subjects was 55.2±7.6 years. Male female ratio was 4.5:1. Male female ratio was found 5.9:1 and 4.95:1 in study done by Khan\textsuperscript{12} and Uddin\textsuperscript{13} respectively.

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

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

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

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

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

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

References:


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

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

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

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

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

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

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

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

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

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

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

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

Results are reported as median or percentages of the total. For statistical comparison, cases were devided into
two groups based on whether or not undergone RA. Chi square test and Kaplan –Meier analysis were used. Statistical significance was considered a p-value < 0.05.

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

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

<table>
<thead>
<tr>
<th>Table-I</th>
<th>Baseline Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA Group</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
</tr>
<tr>
<td>No of cases</td>
<td>258</td>
</tr>
<tr>
<td>Gender, N (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>190</td>
</tr>
<tr>
<td>Female</td>
<td>68</td>
</tr>
<tr>
<td>Age, Median (IQR1,IQR3)</td>
<td>65.6 (58.1,71)</td>
</tr>
<tr>
<td>Age range, N (%)</td>
<td></td>
</tr>
<tr>
<td>Below than 40 yr</td>
<td>3</td>
</tr>
<tr>
<td>40 – 50 yr</td>
<td>15</td>
</tr>
<tr>
<td>50 – 60 yr</td>
<td>59</td>
</tr>
<tr>
<td>60 – 70 yr</td>
<td>103</td>
</tr>
<tr>
<td>More than 70 yr</td>
<td>78</td>
</tr>
<tr>
<td>BMI, Median (IQR1,IQR3)</td>
<td>25.5 (23.3,28.8)</td>
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<tr>
<td>BIM range, N (%)</td>
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<tr>
<td>Below than 18.5</td>
<td>8</td>
</tr>
<tr>
<td>18.5 – 24.9</td>
<td>93</td>
</tr>
<tr>
<td>25 -29.9</td>
<td>88</td>
</tr>
<tr>
<td>More than 30</td>
<td>43</td>
</tr>
<tr>
<td>Not available</td>
<td>26</td>
</tr>
</tbody>
</table>

**Fig.-1:** Patient’s comorbidities
The baseline angiographic characteristics are shown in Table 2. Lesion length and morphology is defined by American Heart Association/American College of Cardiology classification. The lesions in RA group were more complex with higher Type C lesion (68.8% versus 37.9%, \( p \) value 0.005) and longer lesion (20.6% versus 14%) compared to non RA group. Utilization of intravascular ultrasound to clarify the lesion morphology and result outcome was low (17.3%).

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

Angiographic success was not achieved in 2 patients (0.7%) of RA group and 68 patients (3%) in non RA group. Death occurred 4.7% patients in RA group in comparison to 0.9% in non RA group (0.102). In 1 year Kaplan –Meier survival graph, there were better survival noted in non RA group (97.7%) compare to RA (89.6%) (\( p \) value < 0.005)(Figure 3).
Discussion:
The commercially available Rotablator (Boston Scientific, Natick, Massachusetts), invented by Auth and described by Ritchie and colleagues (22) utilizes an over-the-wire, coaxially driven, diamond-tipped, high-speed speeds (140,000 to 180,000 rpm) rotating elliptical burr to pulverize the atherosclerotic plaque. It produces lumen enlargement by physical removal of plaque and reduction in plaque rigidity, facilitating dilation. The burr preferentially ablates hard, inelastic material, such as calcified plaque, that is less able to stretch away from the advancing burr than is healthy arterial wall (differential cutting). High rotational speeds facilitate longitudinal burr movement across calcific lesions by orthogonal displacement of friction. A guidewire helps to keep the burr’s abrasive tip coaxial with the vessel lumen, although wire bias in highly tortuous or angulated segments may predispose to dissection or perforation (2). Unlike balloon angioplasty, which tends to produce intimal splits and medial dissections in calcified lesions, RA yields a relatively smooth luminal surface with cylindrical geometry and minimal tissue injury (2). The cardinal indication for RA is the calcific lesion, which, in the absence of plaque modification, confers an increased likelihood of procedural failure, stent underdeployment, restenosis, and major complications (23).

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

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

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

Several nonrandomized trials have reported that rotational atherectomy shows no obvious difference in the acute success rate or restenosis rate in noncomplex coronary lesions compared with other techniques (35,36). Two previous studies by Kishi and Teirstein reported a disappointing restenosis rate of 57.5 and 59.0% after rotational atherectomy in patients with diffuse coronary artery disease, which suggested that debulking of excess tissue with rotational atherectomy was not effective therapy for diffuse coronary artery disease (37,38). In other studies, heavily calcified lesions, RA and DES deployment results in target lesion revascularization rates ranging from 2–10.6% at 6 months to 3 years, which is significantly better than RA and BMS (8-9,24-26).

Furthermore, several techniques using rotational atherectomy, such as use of a single burr with burr-to-artery ratio of 0.5 to 0.6-rotational speed of 140,000 to 150,000 rpm, gradual burr advancement using a pecking motion, short ablation runs of 15 to 20 s, and avoidance of decelerations >5,000 rpm. Combined with meticulous technique, optimal antplatelet therapy, vasodilators, flush solution, and provisional use of atropine, temporary pacing, vasopressors, and mechanical support may prevent slow-flow/no-reflow, which in contemporary series is reported in 0.0% to 2.6% of cases (2).

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

Conclusion:
The cardinal indication for RA is the calcific lesion, which, in the absence of plaque modification, confers an increased likelihood of procedural failure, stent underdeployment, restenosis, and major complications.
The present study indicates that calcified coronary artery lesions can be successfully treated by high speed rotational atherectomy and the success rate of rotational atherectomy was not reduced by calcification despite the more frequent complex nature of the calcified lesions. Though higher mortality and lower rate of survival were noted in rotational atherectomy group in this study, it should be attributed to the fact that they come from high risk group of patients who have multiple comorbidities.

References:


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

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Introduction:
SARS-CoV2 infection can impact all organs structurally and functionally. Persisting symptoms in patients recovering from coronavirus disease 2019 (COVID-19) are common and with close follow-up can be detected in nearly 90% of patients 60 days from the original diagnosis¹. The most common symptoms are fatigue, dyspnea, joint pain, chest pain, cough, insomnia and headache. Given the well-documented involvement of the circulatory system in COVID-19, including small, moderate and large-sized veins and arteries, coupled with robust immune and resulting local and systemic inflammatory responses, one would anticipate a prolonged recovery period and potentially long-term cardiovascular effects. The following review summarizes the pathogenesis of structural, functional and metabolic abnormalities associated with COVID-19 and postulates long-term cardiovascular effects and management strategies under a broad clinical umbrella referred to as post-COVID-19 syndrome.

Acute stages of COVID-19: setting the stage for prolonged clinical effects
The frequency of cardiac injury, vascular dysfunction and thrombosis in patients with COVID-19, including those persons with either no or minimal symptoms during their initial infection, raises important questions about potential long-term cardiovascular effects: these could include heart failure, life-threatening arrhythmias, sudden cardiac death, impaired myocardial flow reserve from microvascular injury, coronary artery and aorta aneurysm formation, hypertension, labile heart rate and blood pressure responses to activity, accelerated atherosclerosis and both venous and arterial thromboembolic disease². Indeed, events during the acute phase of disease, including those that are clinically unsuspected and undiagnosed³ will increase the risk for recurring events⁴. How will the medical community follow patients with COVID-19? How will future events be prevented?

The COVID-19 pandemic and its reporting has focused primarily on two areas—the number of cases and the number of deaths. Both statistics are of great importance, yet neither sufficiently captures an equally important metric of morbidity that is responsible for resource utilization, assessment of vulnerable populations, cost, recovery, long-term health effects, and quality of life⁵. A morbidity index of COVID-19 survivors is particularly relevant when

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

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

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

Early reports of COVID-19 identified a high proportion of hospitalized patients with reduced left ventricular ejection fraction. Indeed, in one series 35% of patients had an ejection fraction less than 50% and features of stress-induced cardiomyopathy were identified in a number of patients\(^6\). Patients with COVID-19-associated myocardial injury likely remain at risk for cardiovascular events following hospital discharge. The duration of risk, optimal surveillance and management strategies are under investigation and must be clearly defined.

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

Animal models of enterovirus-induced myocarditis demonstrate RNA detection in the acute phase and chronic phase of dilated cardiomyopathy. In a murine model of coxsackievirus \(^3\)-myocarditis, features of acute infection including rapid progression of myocardial lesions, infected myocytes and inflammatory cells is followed by a persistent pattern with reduced inflammation and a slow progression of myocardial lesions. Infection is often restricted to atrophic myocytes and fibroblasts\(^9\).

While the virus itself is cytoxic causing myocyte injury, a majority of cases of severe myocarditis and subsequent post-viral cardiomyopathy are governed by a maladaptive or overly robust inflammatory response to viral antigens\(^10\). Many viruses associated with myocarditis infect the heart secondarily following an initial infection in the lungs or gastrointestinal tract. By contrast, some viruses are highly cardiotropic. For example, parvovirus \(^\text{SV}19\) can infect the endothelial cells of venules, capillaries and arterioles\(^11\). Cytokine activation follows, causing apoptosis of endothelial cells, endothelial dysfunction and marked lymphocyte accumulation within the microvasculature. Myocyte injury is the result of perfusion abnormalities rather than direct myocyte viral entry and damage. Myocarditis following a viral infection is viewed under the pathophysiology-based lens of autoinflammatory disease\(^12\).

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

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**Fig.1:** COVID-19 is associated with ischemic and non-ischemic myocardial injury.
factor-matched patients was conducted by Puntmann and colleagues. The median time from diagnosis and cardiac MRI was 71 (64–92) days. At the time of cMRI high sensitivity (hs) troponin was detectable in 75% of patients, NT pro-BNP (brain natriuretic polypeptide) was normal. Compared with the control groups, patients recovered from COVID-19 had lower left ventricular ejection fraction, higher left ventricular volumes, higher left ventricular mass and raised T1 and T2 weighted images. The overall finding suggests that ~ 80% of patients with severe COVID-19 have cardiac involvement and nearly 25% have evidence of ongoing myocardial inflammation three months after diagnosis. Intuitively, these are among the patients who require follow-up and clear management strategies given their inherent risk for poor outcomes.

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

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

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

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

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

**Molecular and cellular adaptation, maladaptation and reset states:**
Potential role in recovery following COVID-19

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

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

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

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

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

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**Fig.-2: The disease phases of patients with COVID-19**
Lipid mechanisms:
The risk for COVID-19 on a high-spectrum of severity is heightened by metabolic and lipid-related comorbid factors. Because lipids play an important role in regulation of immunity, changes in lipidomic profiles could have both near-term and long-term consequences.

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

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

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

The purpose of establishing a COVID-19 Cardiovascular Clinic is to
(1) proactively evaluate patients who have contracted SARS-CoV-2 infection,
(2) identify cardiovascular abnormalities that could portend future serious or life-threatening events, and
(3) establish a foundation for optimal management and follow-up.

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

Testing and diagnostic platforms:
Patients will have a complete physical examination performed by an experienced clinician. A carefully selected battery of laboratory should be considered (Table 1). A carefully selected menu of diagnostic studies to determine the status of cardiac and vascular health could also be performed as clinically indicated (Table 2). Patients would receive a COVID-19 Cardiovascular report that summarizes the findings of each recommended test, instructions for a follow-up visit or referral to a specialty clinic or treatment as indicated according to the best available evidence. An existing electronic health record or secured dedicated database should be used for documentation.

Table I

<table>
<thead>
<tr>
<th>Covid-19 Cardiovascular clinic blood and urine tests</th>
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<tbody>
<tr>
<td>C-reactive protein (CRP)</td>
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<tr>
<td>d-dimer</td>
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<tr>
<td>Von Willebrand Factor (VWF): antigen and activity</td>
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<tr>
<td>Interleukin (IL)-6</td>
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<tr>
<td>Complete blood count with differential</td>
</tr>
<tr>
<td>Basic metabolic profile</td>
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<tr>
<td>Urinalysis (protein, active sediment)</td>
</tr>
<tr>
<td>Anticardiolipin antibody screen</td>
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<td>Ferritin</td>
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Table-II

Covid-19 cardiovascular clinic diagnostic menu

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

**Expertise and team-based approaches:**

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

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

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

**Concluding thoughts and future directions:**

SARS-CoV-2 infection is characterized by its protean nature and rapidly evolving understanding of its acute,
subacute and, in all likelihood, chronic cardiovascular effects. Securing an initial diagnosis and documenting early signs, symptoms, diagnostic studies and complications, followed by an ambulatory clinic or office visit for “recovered” patients will be a vital step toward understanding COVID-19 and its comprehensive management. Research platforms must be established to translate new knowledge of post-COVID-19 syndrome to optimal patient care.

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

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

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

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

Cardiac catheterization was performed and did not reveal any coronary artery disease and showed noncoronary sinus ruptured into right ventricular outflow tract; the mean pulmonary artery pressure was 40/15 mmHg and the Qp/Qs was 1.8:1. The RSOV was crossed with a 6F Judkin Right catheter (Cordis Corporation) and a 0.035" × 260 cm straight tipped Terumo wire (Terumo Corp, Japan) from the aortic side. The wire was manipulated into pulmonary artery (PA) and snared through the right femoral vein with a 10 mm Goose Neck Snare (Microvena, MN, USA), to form an arteriovenous loop. The delivery sheath was inserted through the right femoral vein and guided through the pulmonary artery to the right ventricle. The delivery sheath was then exchanged for a longer sheath and the occluder was introduced into the right ventricular outflow tract. The occluder was deployed and the sheath was removed. The patient was discharged without any complications and is on follow up.
was passed from the venous end and pushed over the wire across the RSOV. The device was loaded into the sheath. The aortic retention disc was opened into the ascending aorta and the entire system was pulled back till it anchored at the aortic end of the RSOV. At this point, the other end of the device was delivered by stabilizing the loading cable and pulling back the sheath. The entire maneuver was performed under fluoroscopic and transesophageal echo guidance. A check angiogram was done to confirm the position of the device. Once it was found to be optimum & quantify no AR & then the device was released. He was given Aspirin (5 mg/kg/day) and clopidogrel for six months following the procedure.

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

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

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

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

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

A sinus of Valsalva aneurysm is a rare cardiac anomaly where the root of the aorta may become aneurysmal and forms thin-walled saccular or tubular outpouchings. They develop as a consequence of incomplete fusion of the distal bulbar septum and truncal ridges, leading to a weakness between the aortic media and the annulus fibrosus of the aortic valve. There is subsequent aneurysmal enlargement at this weak point caused by the high pressure head at the aortic root. This dilatation progresses to rupture into the cardiac chambers, most frequently to the right ventricle or right atrium or mediastinum. Valsalva aneurysms may involve all 3 sinuses, more frequently the right (75%–90%) and noncoronary (10%–25%), and rarely the left coronary sinus are involved. The left sinus is not derived embryologically from bulbar septum and therefore is rarely affected by congenital lesions. This anomaly can be unrecognized for many years. RSOV are mostly congenital and comprise 0.15%–0.24% of congenital cardiac anomalies. The incidence of rupture is higher in adolescence & adulthood in Eastern compared to Western populations. In addition to a congenital etiology, these aneurysms may occur secondary to trauma, infective endocarditis, or tertiary syphilis, periaortic inflammation, atherosclerosis, aortic dissection, iatrogenic injuries to the sinuses during VSD closure or during debridement of a calcified aortic or mitral valve may also result in aneurysm formation. Ruptured Sinus of Valsalva (RSOV) are often associated with other congenital defects, most commonly VSD and aortic regurgitation. The presence of an aneurysm may lead to a compression of an adjacent chamber, a coronary artery or the conduction system, leading to myocardial ischaemia and/or conduction disturbances. Symptoms occur in 80% of patients, most commonly between 30 and 45 years of age. There is wide spectrum of presentation, ranging from an asymptomatic murmur to cardiogenic shock or even sudden cardiac death. Symptoms are shortness of breath, chest pain, and fatigue, exercise intolerance, symptomatic heart failure. Symptoms depend upon severity of the shunt and presence of associated lesions. There are different classification systems. Guo et al. proposed a new system of simple surgical classification for right-sided defects according to rupture site. This classification system identifies four types of rupture: type I, a rupture or protrusion into the right atrium; type II, a rupture or protrusion into the right atrium or right ventricle, near or at the tricuspid annulus; type III, a rupture or protrusion into the right ventricular outflow tract, under the pulmonary valve; and type IV, other types of ruptures or protrusions. Another system of angiographic classification uses the shape of the left-to-right shunt jet in order to facilitate the selection of occluders for percutaneous closure. The four types of shunt jets identified are: type I, window-like; type II, aneurysmal; type III, tubular; and type IV, other rare conditions. Our patient is under type III (according to anatomy) & type II (according to angiography). Echocardiography is the gold standard for the diagnosis of RSOV and the identification of other co-existing congenital anomalies. Catheterization is carried out in patients who require an evaluation of their coronary artery anatomy or if an interventional procedure is planned. We have done cardiac catheterization to exclude coronary issue. Treatment of RSOV is surgical or percutaneous transcatheter intervention. Traditionally, surgical closure has been the mainstay of treatment for RSOV, with an
operative mortality rate of <5% and excellent long-term outcomes. Nevertheless, these patients remain at risk of prolonged hospital stays and postoperative complications such as chest pain and septicemia, making percutaneous device closure an attractive alternative. Lately isolated RSOV have been successfully closed percutaneously using transcatheter devices. Percutaneous closure RSOV was first attempted by Cullen et al in 1994 using a Rashkind umbrella. Since then a few reports have been published with the use of different available closure devices. The size of the device used for RSOV closure must be accurately assessed, since a large device may interfere with coronary blood flow or aortic valve cusp movement. However, a device of suboptimal size might dislodge and embolize, or result in a significant residual shunt. Success rates up to 90% have been reported in catheter-based closures. Complications, although rare, include cardiac perforation, fistula formation, thrombosis, and device embolization into the systemic or pulmonary circulation. Complications result in acute symptoms and hemodynamic compromise, requiring urgent surgical retrieval. Post-deployment follow-up includes the assessment of coronary blood flow, aortic valve function, and the presence of thromboembolism. After the deployment of a device, a short course of anticoagulants or antiplatelet drugs is recommended to prevent thromboembolism until the endothelialization of the device occurs.

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

Reference:
Obituary

Our Teacher: Prof Abu Zafor
(01.12.1938-03.05.2020)

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

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

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

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

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

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

He made in-depth reading of electrocardiogram. He made us understand that critical observation of electrocardiogram might provide decisive clue for the diagnosis of a disease. He was often found in the echocardiogram room to provide hands-on training to
his students and the junior doctors. There is no exaggeration when we hail him as the “Pioneer in Echocardiography” of Bangladesh.

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

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

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

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