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Journal of
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INSTRUCTION TO AUTHORS

A. Introduction

The Journal of Invasive and Clinical Cardiology is a biannual, peer-reviewed journal and aims to publish work of the highest quality from all sub-specialties of Cardiology. The aim of the publication is to promote research and serve as platform for dissemination of scientific information in Cardiology.

B. Categories of Articles

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

Original Research:

Original, in-depth research article that represents new and significant contributions to medical science. Each manuscript should be accompanied by a structured abstract of up to 250 words using the following headings: Objective, Methods, Results, and Conclusions. 3 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.

Review Articles:

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

Case Reports:

Only case reports of exceptional quality will be published in the case report format. The text should not exceed 1500 words and is arranged as introduction, case report and discussion. Include a brief abstract of about 150 words. Number of tables/figures should be limited to 3. Include up to 15 most recent references. The patient's written consent, or that of the legal guardian, to publication must be obtained.

Cardiovascular Images:

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

Letter to the Editor:

Letters commenting upon recent articles in Journal of Invasive and Clinical Cardiology 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.

C. Criteria for Acceptance

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

D. Editorial Process

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

E. Cover Letter

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

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

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

F. Manuscript Preparation

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

The Introduction should address the subject of the paper. The Methods section should describe in adequate detail the laboratory or study methods followed and state the statistical procedures employed in the research. This section should also identify the ethical guidelines followed by the investigators with regard to the population, patient samples or animal specimens used. A statement should be made, where applicable, that their study conforms to widely accepted ethical principles

guiding human research (such as the Declaration of Helsinki) and also that their study has been approved by a local ethics committee. The Results section should be concise and include pertinent findings and necessary tables and figures. The Discussion should contain conclusions based on the major findings of the study, a review of the relevant literature, clinical application of the conclusions and future research implications. Following the Discussion, Acknowledgements of important contributors and funding agencies may be given.

a. *Title page information*

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

b. *Abstract*

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

c. *Keywords*

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

d. *Abbreviations*

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

e. *Acknowledgements*

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

f. *Units*

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

g. *Figures and graphics*

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

h. *Tables*

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

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

i. *References*

The authors are responsible for the accuracy and completeness of the references and their citations in the text.

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

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

Examples of correct forms of references are given below:

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

1. *Standard journal article*

   List the first six authors followed by et al.

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

   More than six authors:

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

2. *Organization as author*

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

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

   Vallancien G, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1,274 European men suffering

from lower urinary tract symptoms. J Urol. 2003;169(6):2257-61.

4. *Volume with supplement*

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

5. *Issue with supplement*

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

6. *Type of article indicated as needed*

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

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

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

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

Books and Other Monographs

1. *Personal author(s)*

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

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

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

3. *Organization(s) as author*

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

4. *Chapter in a book*

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

5. *Conference proceedings*

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

6. *Dissertation or thesis*

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

Other Published Material

Newspaper article

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

Unpublished Material

In press or Forthcoming

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

Electronic Material

1. *Journal article on the Internet*

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

Article published electronically ahead of the print version:

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

Article with document number in place of traditional pagination:

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

Article with a Digital Object Identifier (DOI):

Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat

admission to hospital for adverse drug reactions in older adults: retrospective cohort study. BMJ. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752. PubMed PMID: 19129307; PubMed Central PMCID: PMC 2615549.

2. *Monograph on the Internet*

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

3. *Homepage/Web site*

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

G. Submission Preparation Checklist

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

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

H. Submission

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

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Left Main Coronary Artery Disease Management in 2022: What is Changed ?

Imad Sheiban

J Inv Clin Cardiol 2022; 4(1): 1-4

For many years, left main coronary artery (LMCA) disease has remained as the last frontier resisting percutaneous coronary intervention (PCI). Until recently, the most relevant clinical studies in this regard as well as clinical practice guidelines favored surgical revascularization (CABG) almost as the only treatment for the management of this condition. The changes that have occurred over the last 20 years since the advent of drug-eluting stents in clinical practice and their technological advances have been extraordinary. This, added to the data coming from randomized clinical trials that compared both revascularization modalities, has placed percutaneous coronary interventions at a similar level to surgery in a large number of patients. The anatomical, technical, and strategic aspects are essential for the percutaneous management of left main coronary artery lesions given their tremendous clinical variability. Consequently, the choice between PCI and CABG in patients with LMCA disease should take into account the heterogeneity of the disease: location (ostial, body, or bifurcation), with or without involvement of major coronary arteries; comorbidities (with or without diabetes mellitus) age (young versus elderly) and gender (men versus women).

The Syntax score was introduced to facilitate the choice of the type of revascularization (CABG or PCI) accordingly to anatomical complexity[1] which also premised to interpret clinical trials more appropriately and accordingly to more homogeneous anatomical characteristics of coronary artery disease thus leading to its validation in several studies[2-4] and adoption by Scientific Societies Guidelines as an important parameter for choosing between CABG and PCI in patients with coronary artery disease associated or not with LMCA disease . Then we realized that some clinical parameters have an equally important impact on the clinical outcome and consequently the SYNTAX Score was updated and validated by adding some clinical variables with an important impact on the clinical outcome (left ventricular function, renal failure, age, etc.) - SYNTAX Score II - making it even more precise and more adequate[5].

Several clinical studies and meta-analysis reported favorable mid term clinical outcomes with no difference in death and myocardial infarction between PCI and CABG in the treatment of LMCA disease, but all confirmed a significantly higher rates of need for repeat revascularization among patients treated with PCI. However; the 2 largest and targeted randomized trials with 5 year follow up data (EXCEL[6] and NOBLE [7)] showed conflicting results. The EXCEL trial included 1905 patients demonstrated that at 5 years primary composite endpoints (all causes of mortality, myocardial infarction and stroke) had similar incidence in both PCI and CABG group. In contrast, the NOBLE Trial which included 1201 demonstrated superiority of CABG over PCI for the primary composite end point of all cause death, nonprocedural MI, repeated revascularization, and stroke at 5 years. These results are mainly driven by the differences in MI and repeat revascularization rates in both groups.

Adding to this, 3 recent meta analyses[8-10] also demonstrated conflicting results since the non-uniformity of end points across trials makes it difficult to pool studies together for meta analyses. In the meta analysis of 5 randomized trials (4612 patients) done by Ahmad et al[8], both PCI and CABG showed no differences in mortality and clinical events at 10 year follow up.[8] Zhang et al [9] performed a meta analysis of 4 randomized trials including 4394 patients and showed that there are no significant differences in all cause mortality, stroke, or MI in patients with a low or intermediate SYNTAX score (hazard ratio [HR], 1.20; 95% CI, 0.85–1.70), but there was a higher incidence following PCI in patients with a higher SYNTAX score

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(HR, 1.64; 95% CI, 1.20–2.24). In the largest meta analysis, of 23 clinical trials and retrospective studies (13 260 patients),[10] the PCI arm was noted to have significantly higher cardiovascular mortality (incidence ratio, 1.24; 95% CI, 1.05–1.45) and non-cardiovascular mortality (incidence ratio, 1.19; 95% CI, 1.00–1.41) relative to CABG. However, a major criticism of this meta analysis is the heterogeneity of the patient population, with varying clinical presentation limiting broad conclusions about treatment effect.

Despite the previously cited limitations , the results from the clinical trials and the meta analyses led to an important changes in the 2018 European clinical practice guidelines for myocardial revascularization[11] supporting PCI of the LMCA, with a Class I recommendation and level of evidence A in patients with low SYNTAX score (<22) and Class IIa recommendation with level of evidence A in those with intermediate SYNTAX score (23 to 32) ; while in patients with high SYNTAX Score (> 32) CABG was confirmed as the gold standard (Class I – evidence A) and PCI as Class C level of evidence A). Heart Team discussion was also recommended accordingly for a more appropriate decision making[11]. In contrast also the latest American Heart Association/American College of Cardiology / SCAI guidelines have not been influenced by the same studies leaving recommendations for PCI still favoring CABG over PCI in patients with LMCA disease (Class I – evidence BR) independently of location of the disease in the LMCA whereas. PCI is now Class IIa recommendation (Level of Evidence: B R, for both)[12]. As in European Guidelines; CABG is Class I recommendation for patients with associated multivessel disease whiler PCI is Class III).

In non-distal lesions location, particularly if isolated LMCA disease - treated with PCI reported excellent clinical outcome when treated with PCI and latest generation of drug-eluting stents and equipoise CABG [13-15]

Recently the PRECOMBAT[16] trial which included 600 patients reported extended follow up (10 years) focusing on the outcome of patients with or without diabetes mellitus. The 10 year rates of major adverse cardiac or cerebrovascular events, death, MI, stroke, and its composite outcomes were not significantly different after PCI or CABG in patients with and without diabetes mellitus, but the risk of target vessel revascularization and repeat revascularization was consistently higher after PCI, irrespective of diabetes mellitus. However; it should be noted that because of the small number of patients, the PRECOMBAT trial did not have sufficient power to detect statistically significant differences in clinical end points in each subgroup according to diabetes mellitus status. In the diabetic group, the number of patients treated with insulin was only 10%. Patients who are insulin dependent might have worse outcomes, as shown by Bawamia et al,[17] where the impact of diabetes mellitus on mortality outcomes following left main PCI was significant only in the patients treated with insulin. PRECOMBAT results are also consistent with prior results[18-22] In all these studies, there was no significant difference in 3 or 5 year mortality after treatment of patients with LMCA disease with PCI versus CABG in patients with or without diabetes mellitus. However, in the pooled analysis, CABG showed a superior survival rate when compared with PCI in patients with diabetes mellitus and multivessel disease but without LMCA involvement.

R. Wang et al[23] re-evaluated, in an analysis of the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial, whether and how differences in surgical or percutaneous revascularization may affect long-term mortality in patients with or without diabetes using an 'allcomers' design of PCI with the first-generation paclitaxel-eluting stent vs. CABG surgery, and where all randomized patients were eligible for either revascularization approach. 10-year all-cause mortality was not different in diabetic patients treated either with PCI using the paclitaxel drug-eluting stent or with CABG, and diabetes did not discriminate any between-group differences in mortality. As expected, 10-year mortality was higher in diabetic than in non-diabetic patients after multivariable adjustment, and especially in insulin- vs. non-insulin-treated patients regardless of the revascularization modality. Importantly, in the 75% of nondiabetic SYNTAX patients with three-vessel CAD, death was significantly higher with PCI at both 5 years [12.8% vs. 9.3%; hazard ratio (HR) 2.04, 95% confidence interval (CI) 1.22–3.41, P= 0.007] and 10 years (25.9% vs. 17.3%; adjusted HR 1.57, 95% CI 1.28–2.60, P= 0.001). Of note, in diabetic patients, the authors observed lower mortality with CABG vs. PCI only in the subset with three-vessel CAD and the highest (>_33) SYNTAX score tertile, while mortality with CABG vs. PCI in insulin-treated patients was numerically lower[23].

In summary, heterogeneity of definitions of the primary composite end points and other confounders makes it impossible to draw a definitive conclusion for the optimal therapy for left main disease.

In the last decade PCI has improved significantly, with new generations of drug eluting stents that have thinner struts, durable and biodegradable polymers, and optimization of PCI techniques with intravascular imaging, new plaque modification techniques, and optimal pharmacological treatment; these iterations continued to narrow the gap when comparing outcome of CABG versus PCI for left main disease. Further, diabetes mellitus is a heterogenous disease, that is, insulin versus non insulin dependent, controlled versus uncontrolled, and new pharmacological therapeutics that can improve outcome. Therefore, diabetes mellitus should not be a deciding factor for the best treatment option for left main disease. However; at the present time CABG remains the standard of care for patients with diabetes mellitus, complex coronary artery disease, and multivessel coronary disease[11-12].

In summary; recent publications on outcome from large randomized clinical trials and meta analyses demonstrate equipoise regarding the hard endpoints (death, stroke, and MI) between PCI and CABG in patients with left main disease except for those in whom LMCA stenosis is associated with multivessel disease with or without poor left ventricular function. In this later cohort CABG should continue to be considered the gold standard treatment and PCI only in those with contraindication for surgery. Heart Team discussion is essential to select the most appropriate approach.

In daily clinical practice, the number of patients undergoing PCI for LMCA disease is globally increasing and the number of patients undergoing CABG is decreasing which indicate that there is a general and global consensus based on the existing data. It is time to start to evaluate CABG and PCI as alternative strategies for the treatment of LMCA disease and revascularization option should be selected based on patient characteristics, anatomic consideration, clinical presentation, and patient preference. This should be based on detailed informed that puts the patient in the ideal conditions to choose between immediate better quality of life versus higher rate for repeat revascularization with PCI and elderly patients (>75 years) who might accept to pay as price a higher risk for reintervention in the next 5 to 10 years versus worse postoperative outcomes (higher complications and mortality)

The need for new randomized studies in this regard does not seem to be required since continue to generate more confounders. In the meanwhile it is much more important to continue focusing on improving stent technology, tight diabetes control, optimal medical therapy and secondary prevention and sharing the decision of CABG versus PCI with fully informed patient.

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ORIGINAL ARTICLE

Comparison the Appendicular Emptying Velocity of RT Atrium in Patient with Moderate versus Severe Chronic Rheumatic Mitral Stenosis Measured by Pulsed wave Doppler in Transesophageal Echocardiography

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Abstract:

Background: Systemic thromboembolism is a complication of mitral stenosis. Left atrial appendage is a site for thrombus formation. But right atrial appendage(RAA) has not received much attentation as it is not easily imaged by TTE or TEE. It is assumed that RAA function also decreases in patients with rheumatic mitral stenosis may be a source of pulmonary thromboembolism. So in this study, we compared RAA emptying velocity in moderate versus sever chronic rheumatic mitral stenosis patients. Findings of this study will help to predict RAA dysfunction and guide in management.

Objective: To assess comparability of emptying velocity RAA in patient with moderate chronic rheumatic mitral stenosis in moderate versus severe cases

Methodology: This was a cross sectional study, 30 CRHD with moderate versus sever MS patients who underwent TEE were enrolled. Pulsed wave Doppler with cursor position at the tip position of the RAA was done with cursor position at the tip of the RAA was done to obtain emptying velocities. Then RAAev was compared between moderate versus severe mitral stenosis.

Outcome measure: Total 33 patients were screened, 3 patients were exclude due to outlier and inadequate data. Majority patients had moderate MS (53.3%) RAAev (27.43±5.97) were significantly higher than that of sever MS (22.57±6.38), p value 0.039

Conclusion: Appendicular emptying velocity is lower in RAA with chronic sever MS and it has temporal relation with MS severity. It can be used as a reliable, simple and semi invasive tool to early predict thromboembolic risk.

Key word: mitral stenosis; right atrial appendage emptying velocity; transesophageal echocardiography

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Introduction:

In Bangladesh, the proportion of rheumatic heart disease (RHD) among cardiovascular disease patients was about 26 percent in eighties. [1] It ranks 2nd among the cardiovascular disease in Bangladesh. Rheumatic mitral stenosis is common among patients with RHD.[2]. Over 15 million people around the world suffer from RHD. RHD ranks among the leading causes of non communicable diseases in low –income and middle-income countries and accounts for up to 250,000 premature deaths every year worldwide. [3]

Recently, right atrial appendage (RAA) thrombi & RAA function have been reported in patients with AF.[4,5] Almost all the thrombi in the right atrium due to AF were localized in the RAA.[6] All the patients with RAA thrombus had also spontaneous echo contrast in the RA. Presence of spontaneous echo contrast independently predicts the formation of RAA

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thrombus.[7] Another point that is overlooked easily in routine practice is the pulmonary embolism in patients with AF, when pulmonary embolism is encountered in patients with AF and without deep vein thrombosis. In such patients, RAA thrombus might be the source of pulmonary embolism. So RAA thrombus in the setting of AF may be occurs without LAA thrombus.

In routine practice, ignorance about RAA thrombus scanning might cause catastrophic outcome

Visualization of right atrial appendage (RAA) anatomy is more difficult than LAA. The rate of non visualization of RAA anatomy during TEE has been reported to be around 1.3% to 16%.[6] It has been reported that almost all the thrombi in the right atrium due to AF were localized in the RAA. All the patients with RAA thrombus had also spontaneous echo contrast in the RA. Presence of spontaneous echo contrast independently predicts the risk of formation of RAA thrombus.[7] Another point that is overlooked easily in routine practice is the pulmonary embolism in patients with AF, when pulmonary embolism is encountered in patients with AF and without deep vein thrombosis. In such patients, RAA thrombus might be the source of pulmonary embolism. So RAA thrombus in the setting of AF may be occurs without LAA thrombus.

The findings of this study will play an important role in further management like monitoring of the medical therapy (changes of dynamics like RAA dysfunction is determined by measuring RAA emptying velocity in trans- esophageal echocardiography. The mean RAA emptying velocity is slower in AF groups compare to sinus rhythm groups.

Although the LAA emptying velocity is used to evaluate chronic rheumatic mitral stenosis for assess risk but less attention is given to RAA emptying velocity.

Screening not only LAA but also RAA during TEE examination in patient with chronic rheumatic mitral stenosis is important for early detection of RAA dysfunction and related complication and there by prevent morbidity and mortality in MS patient.

The findings of this study will play an important role in further management like monitoring of medical therapy (changes of dynamics like emptying velocity before and after treatment) intervention or surgical procedure.

So comparison RAA emptying velocity in moderate versus sever chronic rheumatic mitral stenosis may decided development of further evaluation method of RAA to support more evidence based treatment strategies for patients with rheumatic mitral stenosis.

Methodology:

This Cross-sectional study was carried out in the University Cardiac Centre(UCC), Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka, Bangladesh from February, 2019 to September, 2019. Patient with moderate to severe rheumatic mitral stenosis patients were undergoing TEE were included in this study. CRHD patients with moderate versus severe MS having pre-existing congenital heart diseases, implanted cardiac devices or mechanical valve replacement and previous cardiac surgery, Patients on anticoagulant cardiomyopathy, established thromboembolic event, previous with history of infective endocarditis, contraindication for TEE, poor echo window and Patients who do not give consent were excluded in this study. All patients with chronic rheumatic heart disease and moderate versus severe mitral stenosis underwent TEE department of cardiology as evidence by their clinician were screened for this study. A total of 30 patients were included in the study.

Peak RAA forward and backward velocities were measure by placing a pulse wave Doppler sample volume just inside the base of the appendage.

Mean RAA emptying velocities of moderate versus sever CRHD wth MS were calculated and comparison and correlation between two mean were done.

Result:

The expected sample size was 30. All patients with chronic rheumatic heart disease and moderate versus severe mitral stenosis undergoing TEE department of cardiology as advised by their clinician will be screened for this study. Right Atrial Appendage (RAA) emptying velocity are measured and compared. Considers of all inclusion and exclusion criteria total 33 patients were taken. Among them two patients were excluded from analysis due to outlier value and one patient was excluded due to incomplete information. Finally 30 patients were taken for analysis. The result is describe here after.

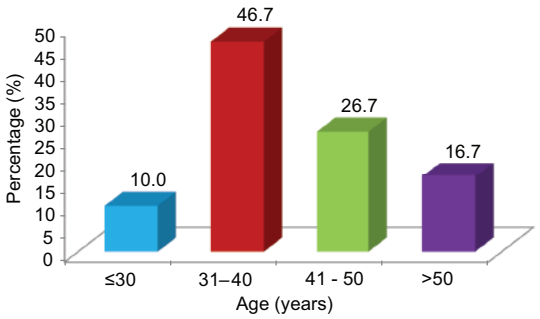


Fig.-1: *Distribution of study population according to age (n = 30)*

Figure in the parentheses indicate percentage
n = number of study population

The mean (SD) age of 30 CRHD with moderate to severe mitral stenosis, was 45.4(±9.9) years, the range was 30-50 years and maximum patients (46.7%) fell in 31-40 age groups.

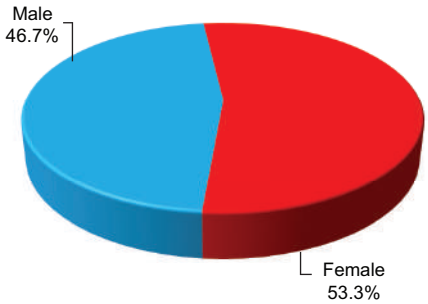


Fig.-2: *Sex distribution of chronic rheumatic mitral stenosis patients*

Figure in the parentheses indicate percentage
n=number of study population

Among the study population 53.3% patients were female. So in our study female were predominant

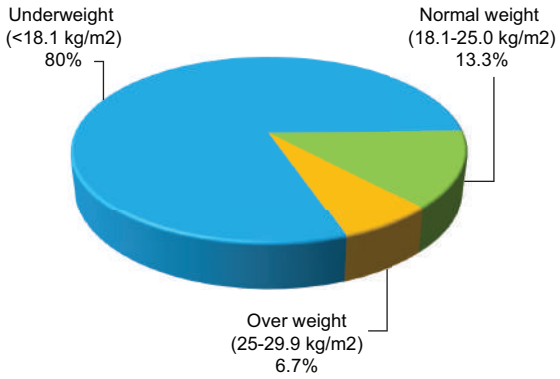


Fig.-3: *BMI of study subjects*

Figure in the parentheses indicate percentage
BMI= Body mass index (kg/m²)

Out of 30 patients, majority of the patient 24cases (80%) were underweight (< 18.1 Kg/m^2), normal body weight (18.1-25.0kg/m^2) were 13.3% and rest of the patients were overweight (25-29 kg/m^2).

Majority of the patients were moderate versus severe according to MVA (cm^2), LA diameter (mm), Mean Trans-mitral gradient, PASP, LVEF. In sever MS pts MVA,Mean trans-mitral gradient, PASP were more compare to moderate MS. LVEF were less in sever MS patient.

Among 30 patient with CRHD with MS, moderate MS were majority of present and 14in number(53.3%).

In chronic rheumatic mitral stenosis in both moderate versus severe cases average RAA emptying velocities

Table-I

TTE findings of the study subjects (N=30)

TTE findings	Moderate MS (n=16)	Severe MS(n=14)	p-value
MVA (cm^2)	1.25±0.12	0.73±0.11	<0.001
LA diameter (mm)	35.0±4.0	42.0±6.0	<0.001
Mean trans mitral gradient	9.63±1.31	15.12±1.52	<0.001
LVEF	61.52±1.93	60.55±2.19	0.207
PASP	49.6±6.3	59.0±6.2	<0.001

Unpaired t test was done

N= number of study subject, n = Number in each group

MVA = Mitral valve area , LVEF = Left ventricular ejection fraction

PASP = Pulmonary artery systolic pressure, LA = Left atrium

TTE = Trans thoracic echocardiography,MS=mitral stenosis

Table-II

Type of chronic rheumatic mitral stenosis of the study subjects (n=30)

Type of chronic rheumatic mitral stenosis	Frequency (n)	Percentage (%)
Severe	14	46.7
Moderate	16	53.3

n= number of study subject

Table-III

Comparison between appendicular emptying velocity of right atrium in patients with chronic rheumatic mitral stenosis (n=30)

	Severe	Moderate	p-value
Chronic rheumatic mitral stenosis	22.57 ± 6.38(14-38)	27.43 ± 5.97(14-35)	0.039

Paired t test was done to measure the level of significance
Data expressed in Mean±SD
s = significant
SD= Standard deviation
RAA= right atrial appendage
MS= mitral stenosis
E°= emptying velocity

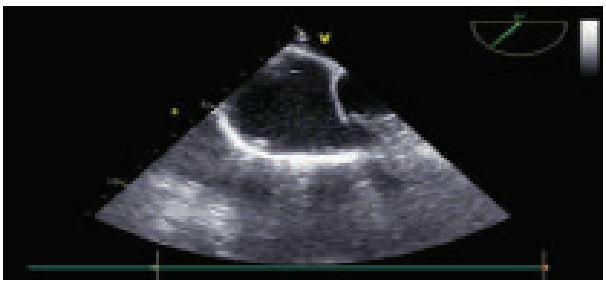


Fig.-4: *Morphology of RAA in TEE in bi-caval view at 90°-140° in midesophagial level*

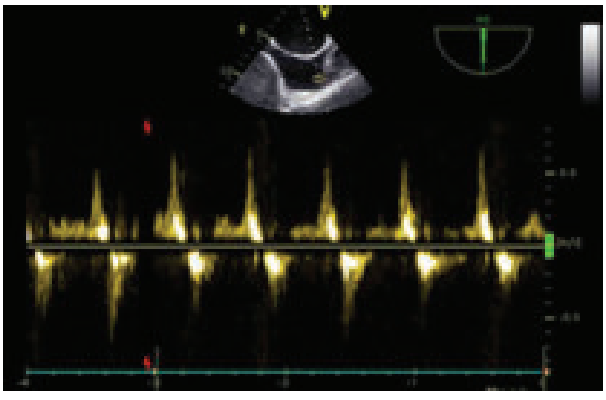


Fig.-5: *Emptying velocity of RAA in PWD(moderate case)*

were significantly higher in moderate chronic rheumatic mitral stenosis than severe chronic rheumatic mitral stenosis

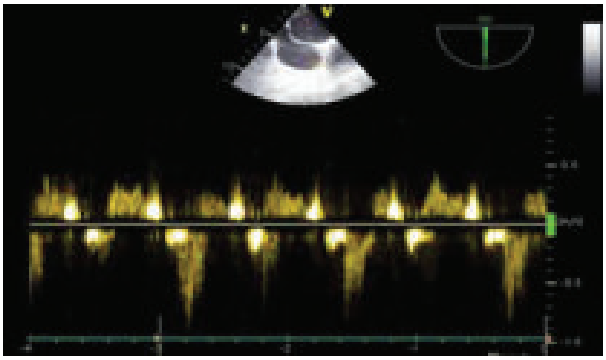


Fig.-6: *Emptying velocity of RAA in PWD(severe case)*

Discussion:

The present research addressed the emptying velocity of Right atrial appendage (RAA) in patient with moderate versus severe chronic rheumatic mitral stenosis by pulse wave echocardiography in TEE and compare the RAA emptying velocity in severe and moderate chronic rheumatic mitral stenosis.

While looking for age distribution of the Chronic Rheumatic Heart Disease (CRHD)patients with moderate versus severe mitral stenosis, it was observed that more than 80% patients fell in 31-40 groups with SD 45.4 (±9.9) year, ranging from 30 to 50 yrs. Considering the baseline characteristics, the mean age of present research subjects is higher as compared with global researches, such as ´World Heart Federation' criteria for echocardiographic diagnosis of rheumatic heart disease-an evidence based guideline concluded that about 38% belonged to juvenile age (<20yrs) group of RHD.[8] It may be fair enough to accept that increased CRHD with MS in this age group may be due to ignorance of symptoms

and delayed to attend the physicians in younger population in our country or may be due to conduction of research among adult population attending in BSMMU echo lab. A research conducted by Sani et al. 2007.[9] among Nigerian population showed that mean age of RHD was 24±12 yrs. which was may be due to sample taken from 5 to 60 years old patients. It is observed through an American research, the mean age at the appearance of symptom is 31 yrs. and progression of mitral stenosis common in the fourth and fifth decades of life. [10] This research quite similar to present one because all were CRHD who attended in BSMMU echo lab for Transesophageal echocardiography(TEE) to detect any complication or further management strategy.

A recent research conducted by Khaled et al. 2019. [11] for observing the frequencies and pattern of chronic rheumatic heart disease in patients undergoing echocardiography in a tertiary level hospital of Bangladesh showing maximum patients fell in 30-39 age group. While dictating Mitral Stenosis with complication, most of the patients are fell in fourth and onward decade.[12,13] So study populations are more vulnerable to development of complication and needed specialized care and regular follow up to prevent dangerous complications like cardio-embolic stroke, pulmonary embolism and others.

A higher female predominance was observed in the present research in patients of CRHD with MS occurred as compared to male and their ratio was 1.18: 1. It was personal view of us that, this female predominance may reflects the higher number of female patients attending hospitals, their socio-economic and cultural issues. On the other hand, many researches shows the female predominance in patients with MS in Bangladesh.[14,15]

In the present research, majority (more than 80%) patients of CRHD with MS had under BMI as most of the patients in previous researches were under weight. The findings of the present research reflects the present health awareness of study population attending to the doctor as well as came to tertiary level hospital like as BSMMU. A recent research conducted by Kruczan et al. 2007[16], in Brazil supports the findings of present research. In their research they found that around 84% of patients with RHD had normal BMI. This finding necessitates the further evaluation of the nutritional status in a patient with CRHD in Bangladesh.

Next most common co-morbid factor was Atrial Fibrillation (AF) which similar to a British research conducted. [17] They state that patients with AF tend to be older than those with sinus rhythm. In the present research, most of the patients were older and CRHD may be related to AF common presentation. AF and advanced age are associated with the development of embolism. [18] A sudden cerebral embolism often kills or cripples patients with mitral stenosis who are otherwise free of symptom and in a fair state of cardiac compensation .The incidence of systemic embolism is low before 35 yrs but it gradually increases from 31.6% to 36% over 36 yrs of age, concluded that approximately 50% of emboli were cerebral, with almost 50% mortality within a year of onset. As the AF is the prominent risk factor found in the present research so it is a matter of concern that needs further attention.

While examine the study populations clinically, all patients were found haemo-dynamically stable with medical management. Transthoracic echocardiogram (TTE) was done to exclude intra cardiac thrombus and SEC and confirmed moderate to severe mitral stenosis. More than 90% patients had mid diastolic murmur in the apical region where few cases had no murmur due to severe mitral stenosis. More than one third of the patients present with arrhythmia. On the other hand rest of patients had sinus rhythm (SR). Most of the chronic MS patients with SR were also chronic low flow state and increase chance to blood stasis leading to thrombus formation as well as embolism.

Another finding of the present research, about 10% of patients was anemic although all patients were clinically stable with medical management and had no hemoptysis or other blood loss history. Wood et al. 1954[17], states that anemia in RHD may be due to hemoptysis of different five types; sudden profuse hemorrhage (pulmonary apoplexy), acute pulmonary congestion, winter bronchitis, presumably due to a combination of bronchial inflammation and pulmonary venous congestion, acute pulmonary edema and pulmonary infraction. Dyspnea was less common in study population which may be due to most of the patient were clinically stable and in medical treatment. Among them, NYHA class I,II,III breathlessness were present in 20%, 10%, 6.2% of patients respectably. Chest pain and Leg oedema were present in 20% and 23.1% of patients respectably.

In the present research, more than 50% had moderate CRHD with MS. Moderate and severe MS were categories by some TTE parameter like MVA, LA diameter, Mean trans mitral gradient, LVEF, PASP. While comparing the emptying velocity of RAA, it was found that patients with chronic rheumatic mitral stenosis, both moderate and severe cases RAA emptying velocities significantly higher moderate chronic rheumatic stenosis compare to severe chronic rheumatic mitral stenosis. It was observed that RAA emptying velocity were significantly lower in sever MS compare to moderate mitral stenosis. The findings of the present research similar to an Egyptian research, where RAA emptying velocity were lower in sever MS (16.1±3.7;16.7±2.9) compare to mild MS (26.5±0.7;17.7±1.6)[18].RAA emptying velocity and atrial myocardial contractile velocities reduce in patient with MS compare to control group which favored the presence of SEC and thrombi.[18] Divitiis et al. 1999[7], shows the presence of SEC in the RAA of patients with AF is a strong predictor of the development of thrombi. The incidence of the RAA thrombus formation is less in patients with MS and AF than in LAA.[19]

Another point that is overlooked easily in routine practice is the pulmonary embolism in patients with CRHD, when pulmonary embolism encountered in patients without deep vein thrombosis and present as shortness of breath where we misdiagnosis as a MS with pulmonary hypertension or chronic heart failure due to RA and RAA (less attention) dysfunction like decrease emptying velocity. So needs comparison RAA emptying velocity in chronic rheumatic mitral stenosis patients for further attention, management and prevent catastrophic complication.

Subramaniam al. 2006 [19], claimed that this may be due to RAA neck width was greater that LAA neck width, yet LAA area was larger-resulting in a greater RAA neck width/area ratio, and lack of RAA remodeling or dilation among patients with AF. Similarly decrease emptying velocity in RAA may be related to stasis of blood in right atrium and development of catastrophic event like pulmonary thromboembolism which need further research.

Conclusion:

In addition to compare the emptying velocity of right atrial appendages in patients with moderate versus severe chronic rheumatic mitral stenosis measured by pulse wave Doppler in TEE, it can be used as a reliable, simple and semi-invasive tool to predict the severity and complication in CRHD with MS. The findings of present research will play an important role in further management like monitoring of the medical therapy, intervention or surgical procedures for patients with CRHD with MS.

Limitations:

Some limitations were encountered in the present research that could not be avoided during research conduction.

- It is a single center study.
- Purposive sampling technique was done so there is a risk of selection bias.
- Below 18 years age population was not included as below this age group were handle by different pediatric cardiology department.

Recomdations:

- Further research involving multiple centers with adequate study population to find out the utility of emptying velocity of RAA to predict the severity and complication in CRHD with MS will represent the actual footage of Bangladeshi patients.
- Future research can be carried out to find whether the emptying velocity of RAA can be used as a prognostic marker or a predictor of clinical outcome in patients with CRHD with MS.
- Research to evaluate the changes of dynamics like emptying velocity before and after treatment.

Conflict of interest:

No conflict of interest

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Myocardial Performance Index as a Tool for Assessment of Right Ventricular Function in Acute Inferior Myocardial Infarction

Md. Rezaul Karim[1], Md. Babul Mia[2], Md. Afzalur Rahman[3], Tariq Ahmed Chowdhury[4], Anisur Rahman Khan[5]

Abstract:

This descriptive type of cross sectional study was conducted to determine the role of myocardial performance index (MPI) for assessment of right ventricular function in acute inferior myocardial infarction (IMI). The study was carried out in Coronary Care Unit, Department of Cardiology, Sir Salimulla Medical College and Mitford Hospital. After exclusion total 72 patients were included in this study of which 24 had acute inferior MI with RV involvement diagnosed by ≥1mm ST segment elevation in V3R-V5R of right sided ECG (group-I) and 48 had acute inferior MI without RV involvement (group-II). All patients underwent echocardiography within 24 hours of admission.

The study revealed that RV MPI was significantly increase (0.57± 0.13) in RVMI patients compared to IMI without RVMI (0.24± 0.12). MPI detected RVMI in 08 patients (0.45± 0.09) who did not have ECG findings of RVMI (Group-II). Repeat MPI estimation after 05 days in 21 RVMI (Group-I) and 08 isolated IMI (Group-II) patients who had RVMPI >0.30, showed dramatic reduction of MPI (0.19± 0.07 and 0.22±0.09) respectively. RV MPI ≥0.30 has high sensitivity (100%) and specificity (89%) for the diagnosis of RVMI in presence of acute IMI

The study recommended that MPI may be a new non invasive echocardiographic gold standard tool in diagnosing RVMI and also assessment of right ventricular function in acute inferior myocardial infarction with high sensitivity and specificity. MPI changes can be serially followed in acute RVMI patients to assess changes in RV function.

Key wards: Myocardial Performance Index, Inferior Myocardial Infarction

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Introduction:

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in Western society and is a worldwide epidemic. In 2001, it was estimated that worldwide, ischemic heart disease (IHD) was responsible for 11.8 percent of all deaths in developing countries and 17.3 percent of all deaths in developed countries.[1] Incidence of IHD is increasing in developing countries including Bangladesh with the improvement of socioeconomic status, urbanization and changes of dietary habits and lifestyle.[2]

Right ventricular myocardial infarction occurs in approximately one third of patients with acute inferior wall myocardial infarction (IWMI), and hemodynamic abnormalities became clinically significant in 10% of these patients.[3] Patients with right ventricular infarctions have much higher rates of significant hypotension, bradycardia requiring pacing support, and in-hospital mortality than isolated IWMI.[4]

Assessment and quantification of right ventricular function often is difficult and challenging.[5] Diagnosis of right ventricular myocardial infarction (RVMI) based on electrocardiographic (ECG) ST segment elevation in lead V_4R in inferior myocardial infarction setting. The Echocardiographic diagnosis of RVMI is straightforward if right ventricular (RV) dilation and

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regional wall motion abnormality are present. These changes are not evident in many RVMI patients. Also, the assessment of RV volume and function is cumbersome due to complex geometry and inaccessible location of the RV.[6]

MPI can be defined as the Doppler-derived sum of isovolumetric contraction and relaxation periods divided by ejection time. MPI reflects combined RV systolic and diastolic function when applied to the right heart. In the setting of acute RVMI, the energy-dependent processes of RV contraction, ejection, and relaxation are likely to be altered. As MPI combines all these important time intervals, it may be a sensitive tool to diagnose "occult" RV ischemia / infarction, which may not manifest clinically and in routine 2D Echo imaging.[7] The MPI value of 0.30 appears to be an ideal cutoff value with a sensitivity of 82% and specificity of 95% for the diagnosis of RVMI in the presence of IMI.[6] The aim of the present study to assess right ventricular function by MPI in patients with acute right ventricular infarction.

Diagnosis of RVMI required a high degree of suspicion based on clinical findings and early recording of ECG (ST elevation in V_4R) through right-sided precordial leads. There are some groups of patients who have RVMI, which may not manifest clinically and in routine 2D Echo imaging and no ECG changes (no ST elevation in V_4R). These groups can be diagnosed by MPI. Right ventricular infarction associated with major complications and considerable morbidity and mortality, and its presence defines a higher risk subgroup of patients with inferior wall MI and has a well-delineated set of priorities for its management.

MPI can reliably diagnose RVMI and it can be used to quantify right ventricular dysfunction and assess acute improvements in RV function. Measurement of MPI is noninvasive, less expensive and easily available.

Methods:

This was a descriptive type of cross sectional study. The study was carried out in Coronary Care Unit, Department of Cardiology, Sir Salimulla Medical College and Mitford Hospital. A total of 72 patients of both sex diagnosed to have acute Inferior wall myocardial infarction (IWMI) were included in this study.

Inclusion criteria:

1. Patients with acute inferior myocardial infarction with or without right ventricular infarction diagnosed by clinical features and conventional 12 lead ECG.

Exclusion criteria:

1. Patients with chest pain for more than 12h.
2. Patients with prior myocardial infarction, chronic obstructive pulmonary disease, high grade AV block, atrial fibrillation, congenital heart disease, valvular heart disease and post CABG.

All suspected AMI patients admitted in CCU were enrolled for the application of inclusion and exclusion criteria. Patients with right ventricular dysfunction other than AMI were excluded clinically. Conventional 12 leads ECG were done for diagnosis of acute inferior MI. Right sided ECG was obtained routinely in all inferior MI patients at the time of initial evaluation. On ECG right ventricular infarction was defined as $\geq$1 mm elevation of ST segment in leads V3R–V5R.[5] Clinical data including clinical history and treatment history was recorded. Clinical features, relevant physical examination and baseline laboratory investigations like random blood sugar, serum creatinine, lipid profile, troponin-I were done.

Patients were divided into two groups based on the presence or absence of RVMI on right sided ECG -

- Group- I: Patients with acute inferior MI with RVMI.
- Group- II: Patients with acute inferior MI without RVMI.

Echocardiography including MPI was done in all patients within 24 hours of admission. All the echocardiograms were reported by experienced physician using VIVID 7. The reporting physician was blinded to the clinical diagnosis. Right ventricular myocardial performance index (MPI) is calculated as follows. The tricuspid inflow is interrogated by pulse wave Doppler (PWD) in the apical four-chamber view and the time interval from end of "A" wave to the onset of the next "E" wave is noted as "a" in milliseconds. Then the right ventricular outflow is interrogated by PWD in the parasternal short axis view. The total pulmonary ejection time is noted as "b." Three consecutive cardiac cycles are averaged to obtain each value for "a" and "b" to correct for heart rate variation and measurement errors. The time interval "a" denotes combination of isovolumetric contraction time (IVCT), ejection time (ET), and isovolumetric relaxation time (IVRT) As the Doppler period "b" is the pulmonary ET, the sum of IVCT and IVRT is derived by subtracting "b" from "a." MPI is calculated as MPI = (a " b)/b and a dimensionless ratio is obtained.

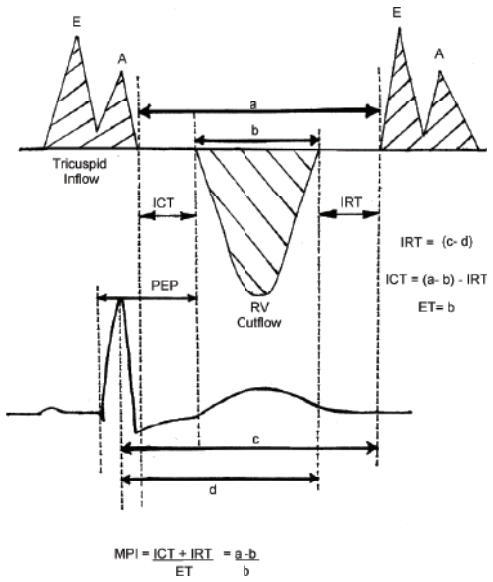


Fig.-1: *Illustration of measurements for myocardial performance index.*

Follow up was done during hospital stay. During the study, complication (cardiac arrest, cardiogenic shock, arrhythmia and heart failure) were recorded. Echocardiography including MPI was done in all RVMI patients after 05 days of admission.

Results:

A total of 72 patients were enrolled in this study. Among the study population 24 were Group-I

(Patients with acute inferior MI with RVMI) and 48 were Group-II (Patients with acute inferior MI without RVMI). Mean age in Group I was 52.25 ± 10.90 (SD) and in Group II was 49.13 ± 10.56 (SD). Among study subjects 60 (83.3%) were male and 12 (16.7%) were females. The male: female ratio was 5:1.

Comparing risk factors among group I and group II study subjects it was found that diabetes mellitus was more common in group I (54.2% in group I and 35.4%) in group II) Family history of IHD was more common in group II (16.7% in group I and 54.2% in group II). Distribution of hypertension and smoking were almost same between the two groups 41.7% and 75% vs. 41.7 and 77.1%) of patients respectively. The clinical triad of hypotension, clear lung fields and

Table-I

Comparison of risk factors in group I and group II study subjects

Risk Factors	Group-I(IMI + RVMI)No (%)	Group-II(IMI)No (%)	p value
Hypertension	10 (41.70%)	20 (41.70%)	Not significant
Diabetes mellitus	13 (54.20%)	17 (35.40%)	Not significant
Smoking	18 (75%)	37 (77.10%)	Not significant
Dyslipidemia	2 (8.30%)	1 (2.10%)	Not significant
Family history of IHD	4 (16.70%)	26 (54.20%)	<.05

p value reached from chi-square test, d.f.

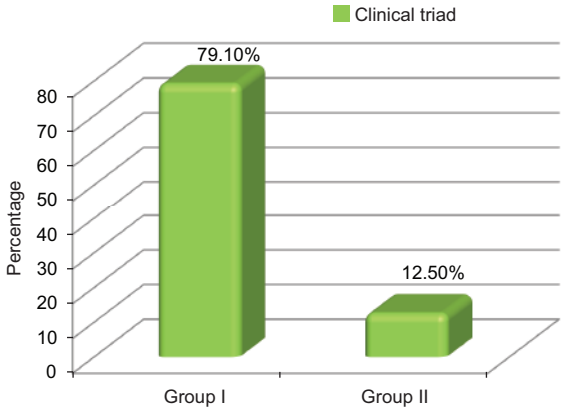


Fig.-2: *Bar diagram showing distribution of* clinical triad (hypotension, clear lung fields and elevated JVP) *in group-I and group-II study subjects*

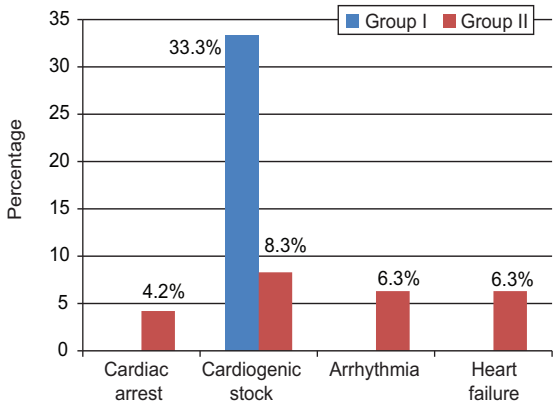


Fig.-3: *Bar diagram showing distribution of complications*

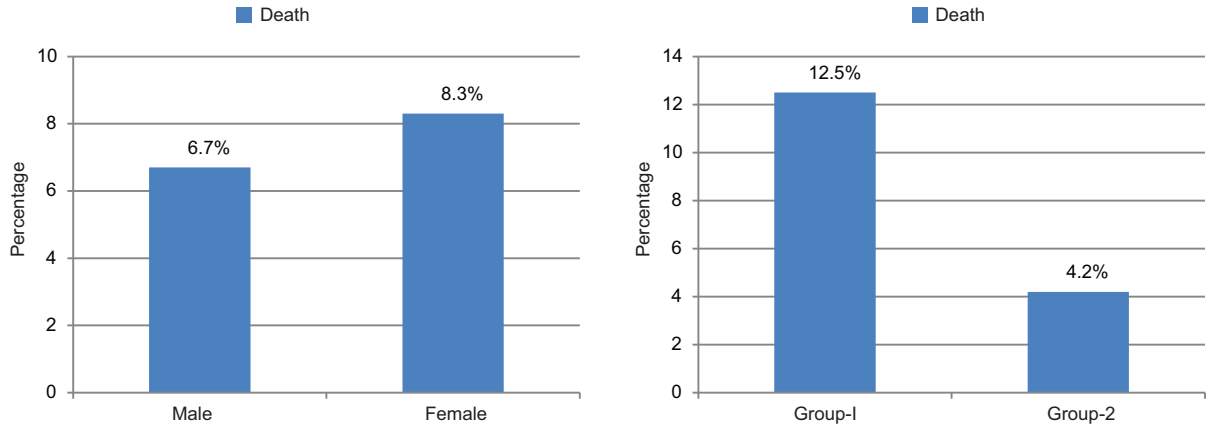


Fig.-4: *Bar diagram showing distribution of mortality in group-I and group-II study subjects.*

elevated JVP found were found 79.1% in group I and 12.5% in group II study subjects.

During hospital stay cardiogenic shock (33.3%) was more common among the RVMI patients. The overall mortality during hospital stay was 6.9%. Mortality was 12.5% in group I and 4.2% in group II. Mortality was more common in females than in males. In males, mortality was 6.7%, and in females it was 8.3%.

All patients underwent echocardiography including MPI within 24 hours of admission. RV MPI in group I patients was significantly increased (0.57±0.13) compared to group II patients (0.24±0.12).

Comparison between MPI and right sided ECG shows 24(100%) patients of group I had MPI more than 0.30. Among group II 40 (83.3%) had MPI <0.30 but 8 (16.7%) patients had MPI >0.30

RVMI follow up echocardiography shows the dramatic reduction of MPI toward normal by 5 days after RVMI. Also, this quick "recovery" of MPI toward normal confirms good tracking of RV function by MPI. RV MPI ≥ 0.30 has high sensitivity (100%) and specificity (88.89%) for the diagnosis of RVMI in the presence of acute inferior MI.

Table-II
Echo parameters

Echo parameters	Group-I (IMI + RVMI) n=24	Group-II (IMI) n=48	X^2 value / p value
RVWMAS	1.35 ± 0.35	1.08 ± 0.19	<.05
ICT+IRT+ET	382.81 ± 32.52	331.56 ± 42.49	Not significant
ET	244.34 ± 23.20	267.75 ± 29.27	Not significant
ICT+IRT	138.43 ± 27.28	63.84 ± 31.06	Not significant
RVMPI	0.57 ± 0.13	0.24 ± 0.12	<.05
LVEF	46 ± 5.12	46.5 ± 5.36	Not significant

p value reached from chi-square test, d.f. = 3
ICT : Isovolumetric contraction time
IRT : Isovolumetric' relaxation time
ET : Ejection time
RVMPI : Right ventricular myocardial performance index
LVEF : Left ventricular ejection fraction

Table-III

Performance of diagnostic test by calculating sensitivity, specificity, accuracy, positive and negative predictive values of RVMPI in diagnosing RVMI

		Right sided ECG		
		Group-I (IMI + RVMI) Positive	Group-II (IMI) Negative	
MPI	RVMPI { >.30 } Positive	True Positive (TP) = 24	False Positive (FP) = 8	Positive predictive value = TP / (TP + FP) = 24 / (24 + 8) = 75%
	RVMPI { <.30 } Negative	False Negative (FN) = 0	True Negative (TN) = 40	Negative predictive value = TN / (FN + TN) = 40 / (0 + 40) = 100%
		Sensitivity = TP / (TP + FN) = 24 / (24 + 0) = 100%	Specificity = TN / (FP + TN) = 40 / (8 + 40) = 83.33%	

Table-IV

Follow-up echo parameters of group-I (IMI+RVMI) patients n=21

Echo parameters	Initial echocardiography	Follow-up echo	Difference	p value
ICT+IRT+ET	383.87 ± 34.28	333.96 ± 23.35	- 49.92 ± 44.45	<.05
ET	244.17 ± 24.46	280.84 ± 18.71	36.67 ± 26.37	<.05
ICT+IRT	139.66 ± 27.78	53.23 ± 19.93	- 86.43 ± 30.17	<.05
RVMPI	0.57 ± 0.13	0.19 ± 0.07	- 0.38 ± 0.12	<.05
LVEF	45.76 ± 5.49	55.62 ± 5.14	9.68 ± 4.13	<.05

p value reached from paired t test, d.f. = 20
ICT : Isovolumetric contraction time
IRT : Isovolumetric‘ relaxation time
ET : Ejection time
RVMPI : Right ventricular myocardial performance index
LVEF : Left ventricular ejection fraction

Table-V

Follow-up echo parameters of group-II (IMI) patients who had RVMPI ≥0.30n=8

Echo parameters	Initial echocardiography	Follow-up echo	Difference	p value
ICT+IRT+ET	379.03 ± 31.96	337.47 ± 25.31	- 41.56 ± 26.37	<.05
ET	261 ± 18.14	276.97 ± 15.04	15.97 ± 13.57	<.05
ICT+IRT	117.53 ± 23.44	60.50 ± 23.22	- 57.04 ± 23.04	<.05
RVMPI	0.45 ± 0.09	0.22 ± 0.09	- 0.23 ± 0.9	<.05
LVEF	45.75 ± 1.83	55.75 ± 6.47	10 ± 6.55	<.05

p value reached from paired t test, d.f. = 7
ICT : Isovolumetric contraction time
IRT : Isovolumetric‘ relaxation time
ET : Ejection time
RVMPI : Right ventricular myocardial performance index
LVEF : Left ventricular ejection fraction

Discussion:

The prevalence of right ventricular infarction in acute inferior myocardial infarction in this study was 33.33% which is consistent with that found in Andersen's study[8] as they were showed the range of frequency of RVMI in patients with inferior MI was 10-50%.

The ECG is a valuable, non-invasive, easily repeatable and inexpensive means of diagnosing right ventricular infarction. ST segment elevation in lead V4R has an overall sensitivity of 88%, specificity of 78% and diagnostic accuracy of 83%. [9]

The clinical triad of hypotension, clear lung fields and elevated JVP in a patient with an inferior MI is virtually pathognomonic of right ventricular infarction.[10] This clinical triad was also found in majority of our patients.

In the current study, the mean age in Group I was 52.25 ± 10.90 years and in Group II was 49.13 ± 10.56 years. Among study subjects 60 (83.3%) were male and 12 (16.7%) were females. The male: female ratio was 5:1.

In Khan's study[9] while comparing group-I (RVMI) and group-II (IMI), it was found that smoking and diabetes mellitus were more common in group-I, while hypertension and family history of IHD were more common in group II. In this current study, diabetes mellitus was more common in group I (54.2% in group I and 35.4% in group II). Distribution of hypertension and smoking were almost same between the two groups 41.7% and 75% vs. 41.7% and 77.1% of patients respectively. Family history of IHD was more common in group II (16.7% in group I and 54.2% in group II).

In Zehender's study[11] in hospital complication in group-I vs. group-II was 64% and 28% respectively, while in this study it was 54.17% and 25% respectively. In Khan's study[9] in hospital mortality in group-I vs. group-II was 23.5% and 18.1% respectively, while in this study, the overall mortality during hospital stay was 6.9%. Mortality was 12.5% in group I and 4.2% in group II. Mortality was more common in female than males. In males, mortality was 6.7%, and in females it was 8.3%.

In Chockalingam's study[6] RVMI does not result in RV dilation and RWMA in a significant number of cases, and mean RV MPI of RVMI patients were 0.53± 0.22, while in this study the MPI in group I patients was significantly increased (0.57±0.13) compared to group II patients (0.24±0.12) and did not find RV dilation in majority of RVMI patients.

The MPI value of 0.30 appears to be an ideal cutoff value with a sensitivity of 82% and specificity of 95% for the diagnosis of RVMI in the presence of IMI.[6]

In this study comparison between MPI and right sided ECG was done and showed 24(100%) patients of group I had MPI more than 0.30. Among group II 40 (83.3%) had MPI <0.30 but 8 (16.7%) patients had MPI >0.30. However in this study sensitivity, specificity, accuracy, PPV and NPV for MPI were 100%, 88.33%, 88.89%, 75% and 100% respectively. So, Myocardial Performance Index (MPI) is a good non invasive tool for assessing right ventricular infarction and significant elevation in RVMI (mean = 0.57) suggests MPI is a reliable test of RV function.

In this current study follow up echocardiography was done in all patients of group-I and group-II (IMI) who had RVMPI ≥ 30 and showed the dramatic reduction of MPI toward normal by 5 days after RVMI. This quick "recovery" of MPI toward normal confirms good tracking of RV function by MPI.

Limitations of the study:

Although the result of this study is statistically significant, there were some limitations of this study.

I. The study performed on relatively small sample size.

II. It was a single center study

III. The invasive hemodynamic assessment was not done

Conclusion:

In the current study Right ventricular infraction was found in approximately one third of inferior MI. Diagnosis of this condition required a high degree of suspicion based on clinical findings and early recording of ECG through right-sided precordial leads. Right ventricular infraction was associated with considerable morbidity and mortality, and its presence defines a high-risk subgroup of patients with inferior myocardial infarction. Significant RV dilation and wall motion abnormality do not occur in over half of RVMI patients limiting the role of routine 2D echocardiography. MPI is a Doppler echo time interval, which can quickly and reliably estimate combined systolic and diastolic RV dysfunction. The narrow range of normal RV MPI increases the diagnostic power of this parameter in the setting of RVMI. The prognostic significance of RV MPI needs to be evaluated in larger series with

long-term follow-up. MPI may be a new non invasive echocardiographic gold standard tool in diagnosing RVMI and also assessment of right ventricular function in acute inferior myocardial infarction with high sensitivity and specificity. MPI changes can be serially followed in acute RVMI patients to assess changes in RV function.

Conflict of interest:

No Conflict of Interest

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Zero Contrast Percutaneous Coronary Intervention - the Light at the End of the Tunnel

Farhana Ahmed [1], Mohammad Arifur Rahman [2], Afzalur Rahman[3]

Abstract:

Recently, new approaches aiming to minimize contrast usage have been proposed, i.e., zero-contrast PCI. However, neither tutorials for these techniques nor reviews of their outcomes exist in the literature, and therefore dissemination of these approaches among the interventional community may be limited. This article presents a step-by-step description on how to perform zero-contrast PCI in different scenario, which should help invasive cardiologists to adopt these techniques in daily practice. A review of clinical studies, case series is also provided. Despite the promising results, such procedures still require some improvements and confirmation of their effectiveness as well as safety in large clinical studies. This article aims to spread these new techniques throughout the interventional community, which is paramount for their further development and wider utilization. Contrast-induced nephropathy is a serious complication after intravascular administration of iodinated contrast media and is associated with numerous adverse outcomes. Its prevalence is particularly high in patients with multiple comorbidities who undergo coronary angiography and percutaneous coronary intervention (PCI). Currently, the only effective method to prevent contrast-induced kidney injury is adequate hydration and a reduction of contrast volume during the intervention.

Keywords: chronic kidney disease, contrast-induced nephropathy, acute kidney injury, zero-contrast angioplasty.

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Introduction

Zero contrast Angioplasty is a technically promising approach for the prevention of contrast induced nephropathy. With the advancement of intracoronary imaging and physiology in the field of coronary angioplasty now it is possible to do coronary angioplasty with no or minimal dye especially by an experienced operator.

Contrast induced nephropathy (CIN) is a common iatrogenic complication associated with adverse outcome including need for Renal replacement therapy (RRT). It is potentially preventable. Despite of some established approaches to prevent CIN include peri-procedural hydration[1] and minimizing contrast volume[2] percutaneous coronary intervention (PCI) in patients with advanced CKD is associated with a high risk of CIN and requirement for RRT, leading to underutilization of PCI in these high-risk patients. Zero contrast percutaneous coronary intervention (PCI) is a new approach in the prevention of contrast Induced nephropathy.[3,4]

With the development of expertise in advance technology like Intravascular Ultrasound (IVUS), Fractional Flow Reserve (FFR)/Instantaneous Wave Free Ratio (IFR) it is possible to do PCI by 'minimal' or 'zero' contrast successfully with successful stent implantation and resolution of ischemia. Zero contrast PCI is creating new era in the field of coronary intervention specially treating those patients with CKD who are suffering from refractory angina and not indicated or fit for Cardiac Bypass surgery. Here we like to describe series of cases which include left anterior descending artery (LAD) bifurcation PCI, LAD ostial PCI by zero contrast or minimal contrast.

Case 1:

Clinical Background**:** 68-year old lady with a history of Type II diabetes mellitus, hypertension, and CKD

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Stage III with an estimated glomerular filtration rate (eGFR) of 30ml/min/1.73 m2 (normal: ≥60mg/min/1.73 m2) presented for diagnostic angiography done for exertional chest pain and patient was on anti-ischemic medication for last 6 months, identified wall motion abnormality in the mid and apical part of anteroseptal wall. Diagnostic angiography (20mL contrast), demonstrated bifurcation lesion involving LAD & Diagonal (Figure 1a and 1b) with Medina 0, 1, 1.

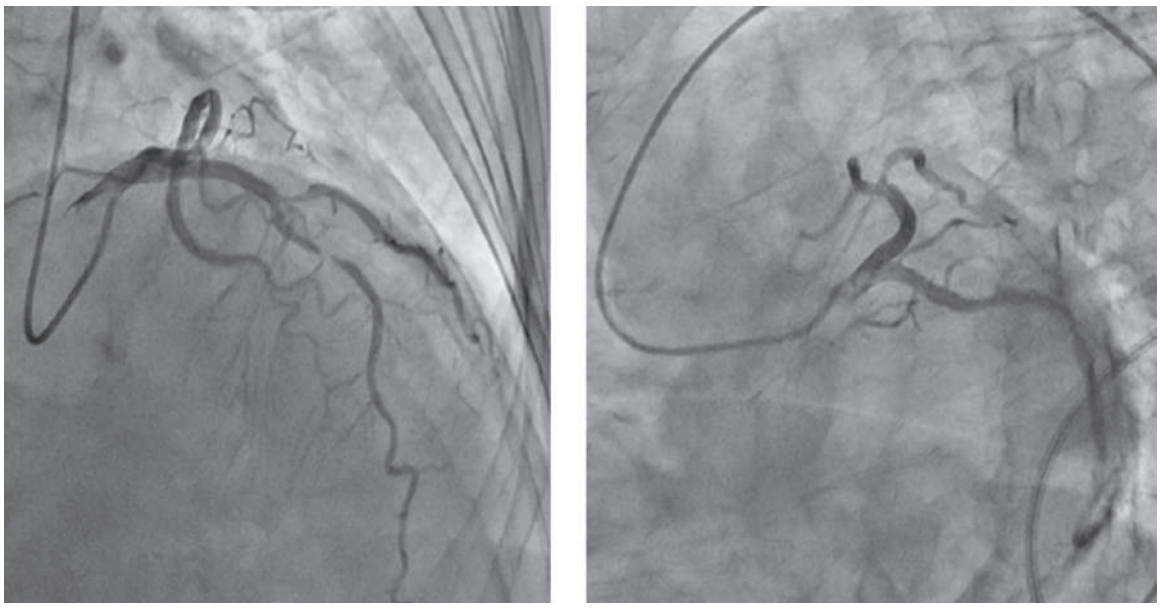
Procedural description:

Seven (7) days after diagnostic CAG patient came back for PCI to LAD. Prior to the procedure, previous angiographic films were uploaded to the monitors as a guide for coronary wiring. We prefer RAO cranial and LAO caudal view of Left coronary artery as reference. Using those images as reference EBU guide catheter was engaged to LM ostium. The bifurcation lesion in Medina 1,1,1 and diagonal was very big sized vessel so our plan was Inverted Culotte technique. Two Floppy wires, one were negotiated through the lesion to distal LAD and another one in Diagonal 2. Diagonal wire was also play role as land mark wire during balloon dilatation as well as stent placement beside IVUS. IVUS done in both LAD to LM and D2 to LAD (Fig: 2a). Proximal and distal Landing zone of LAD determined by IVUS. After pre-dilatation by 2.5×12mm at 12 ATM, DES (1) 2.5×20mm×12 ATM deployed in LAD covering the distal part of lesion beyond diagonal (Fig. 2 b).

After pre-dilatation across diagonal ostium another DES(2) stent 3.5×20mm×12 ATM were placed and deployed from Proximal landing zone of LAD to D2 (Fig:2c), with subsequent post dilatation. After post dilatation patient complained of chest pain with ECG change and drop of pressure, at that time we took a check with 2 ml of Dye and showed plaque shifting to LAD (Fig. 1a). LAD wire was recrossed, dilatation of LAD part of DES (2) done by 3.5×12mm NC balloon. DES (3) 3.5×20mm stent deployed with minimal overlapping of DES (1) and entire LAD portion of DES (2) beyond the proximal end (Fig. 1B). Recrossing of diagonal wire and the procedure were ended by multiple POT and kissing balloon inflation (Fig:2f) & procedure was completed successfully by Inverted Culotte technique. Single check with 3mL of contrast was take record of final result. Total 5 ml dye were used in the procedure. Subsequent S. Cr. and eGFR done on 3rd day and it was remaining same.

Case 2: **Precise LAD ostial PCI by Marker Wire technique**

A 50 years old young man with a history of hypertension, and CKD Stage IV with an estimated glomerular filtration rate (eGFR) of 20ml/min/1.73 m2 (normal: ≥60ml/min/1.73 m2) presented with recent MI anterior with ongoing chest pain and identified wall motion abnormality in anteroseptal wall. Angiography demonstrated significant lesion in LAD (Fig. 3 a & b).



(a) (b)

Fig.-1: *(a & b) Significant stenosis involving LAD & Diagonal*

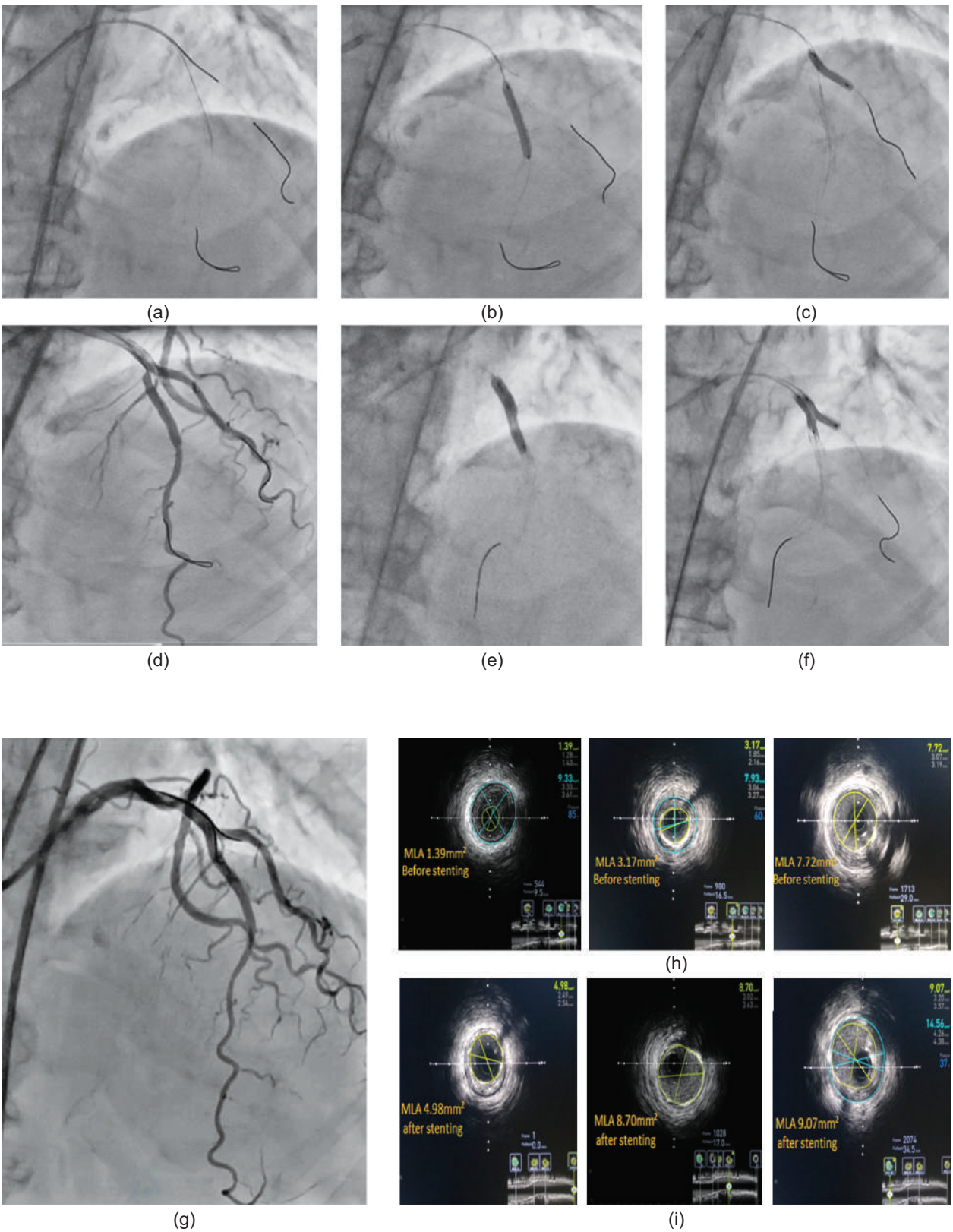


Fig.-2: *(a) Wiring in both LAD & Diagonal & IVUS, (b)(DES I) Stenting to Distal LAD lesion (c)Another stenting (DES 2) from Diagonal to LAD (d)Plaque shifting to LAD (e) Deployed with minimal overlapping (f) Kissing Balloon Inflation (g) Final check (h) IVUS : pre PCI (i) IVUS: Post PCI*

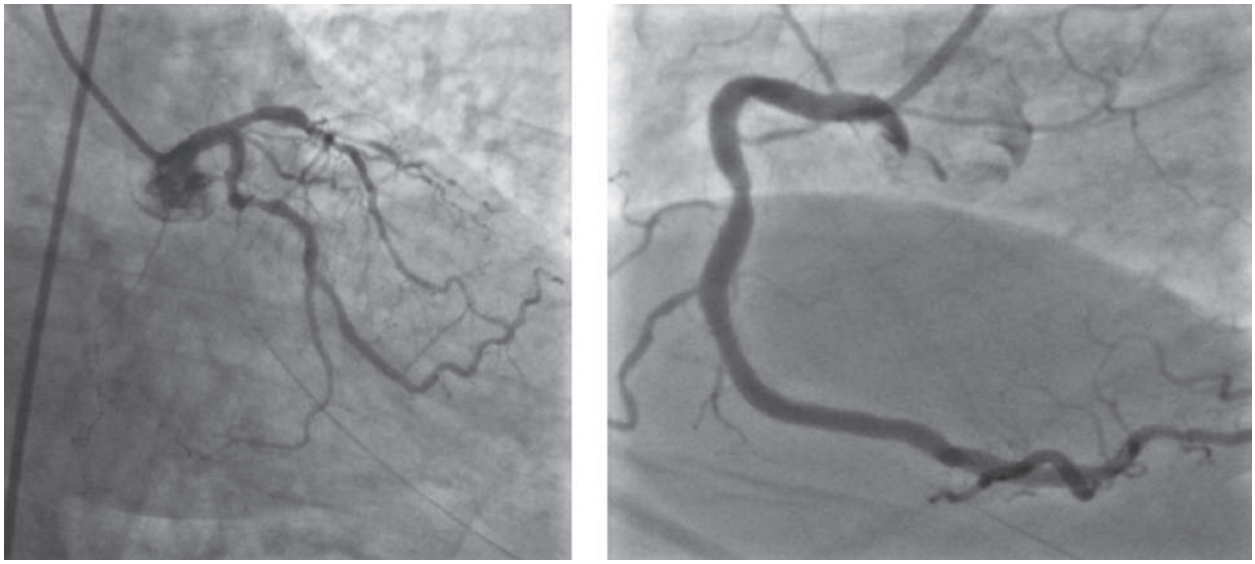
Procedural description:

Lesion was looking simple apparently and we were planned to do PCI to LAD 10 days after diagnostic CAG. Prior to the procedure, previous angiographic films were uploaded to the monitors as a guide for coronary wiring. We prefer RAO cranial and LAO caudal view of Left coronary artery as reference. Using those images as reference EBU guide catheter was engaged to LM ostium. Three Floppy wire, one were negotiated through the lesion to distal LAD and another Two wire, one was in Diagonal 1, another wire was in LCX (Fig. 4a). Diagonal wire and LCX wire were also play role as land mark wire. IVUS was done. IVUS run found significant plaque in LAD ostium too and LM is free of disease. So apparently a simple case turned into a complex one. We decided to place stent precisely in the LAD ostium LM is disease free. During IVUS run we select distal landing zone and approximate length of stent. DES 2.5×38mm were deployed covering the lesion of mid LAD. At this point LCX wire were pulled back and marker portion of the wire were kept in LM to LCX to make a metallic silhouette. The idea was that with blood flow the softer portion of wire will stuck with the roof of carina which acts as marker of ostium. DES 3×20mm (Fig. 4b) were placed to the LAD ostium and deployed. After deployment of stent and post dilatation IVUS was done. IVUS also confirm the placement of stent precisely LAD ostium by this technique. Final check (Fig. 4c) were taken by using 2 ml of dye to keep record and check for any complication. Total 2ml dye was used to finish entire procedure.

Case 3:

Mrs. R, 50 years old lady have history of PCI to LCX 4 years back, now complaining of intractable chest pain for 1 months, gone through CAG in another hospital and found Significant Mid LAD lesion. Patient was not preparing for PTCA at that time. And unfortunately she developed AKI after CAG. So later on, after recovery from AKI (Acute kidney injury) we did PCI to LAD without using any contrast. Here side branch wiring (Fig. 5a) was done to make a silhouette of the coronary system which constitutes a useful road map for the intervention.

At the end of PCI, small amount (3ml) of contrast was injected into a coronary artery in order to exclude complications (especially distal perforation or embolization) and document final angiographic result her hospital stay was uneventful.



(a) (b)

Fig.-3: *(a) Significant Lesion in LAD, (b) Borderline Lesion in RCA*

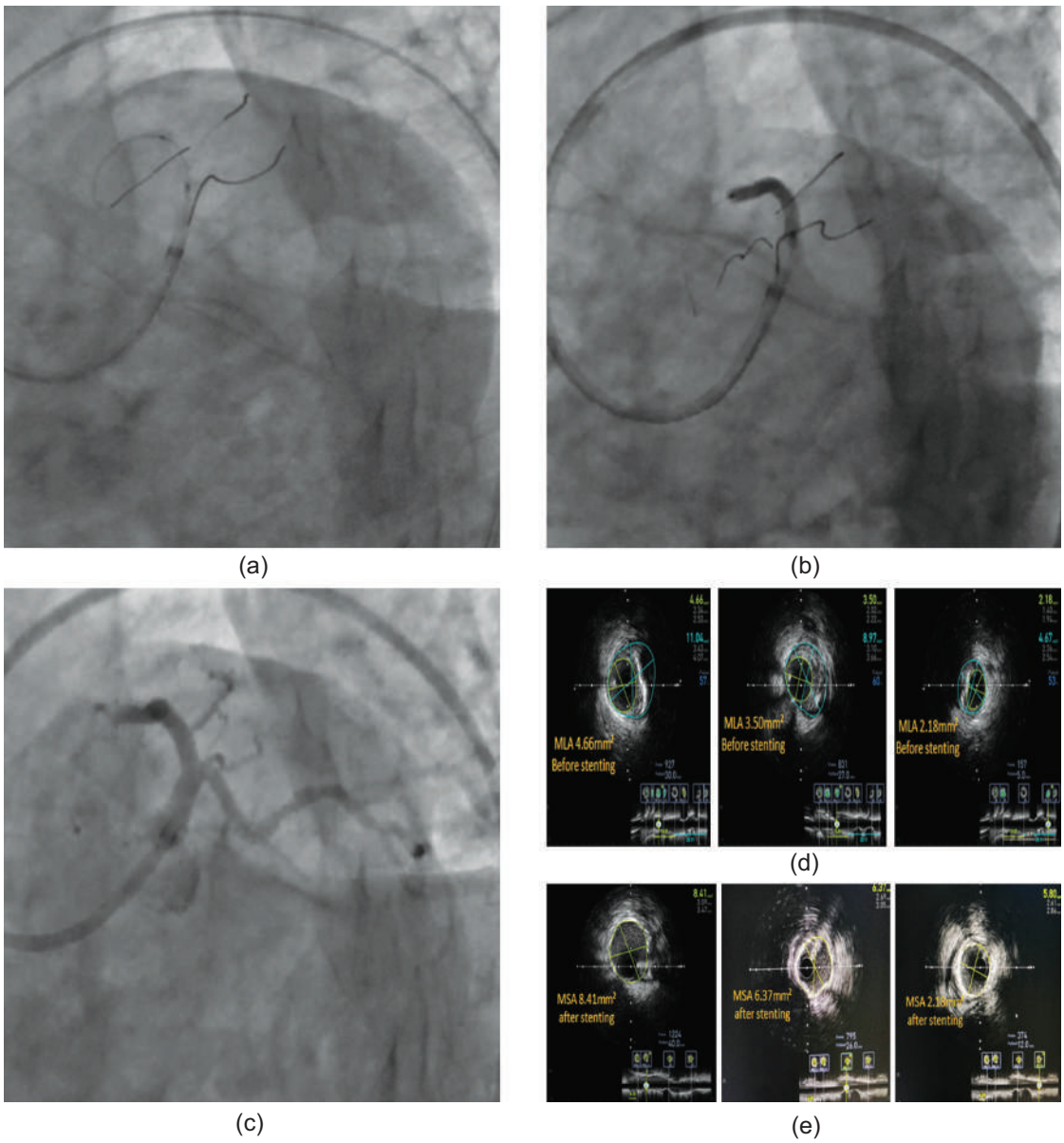


Fig.-4: *(a) Three wire in LAD, Diagonal & LCX to make a metallic silhouette, (b) Softer Portion of LCA wire acts as a Marker of Ostium, (c) Final Result, (d) Pre-IVUS, (e) Post IVUS.*

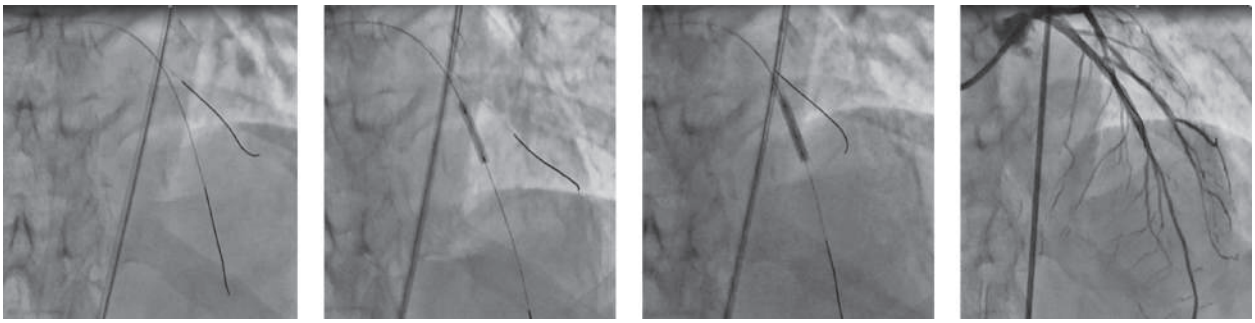


Fig.-5: *(a) Wiring to LAD & Diagonal, (b) Pre-dilatation, (c) Stent deployment, (d) Final Check*

Discussion:

Among high-risk patient subset, patients with advanced CKD are at an even greater risk of adverse events, as CIN is directly correlated with higher rates of adverse clinical events and progression to end stage renal disease.[5] Performing minimal or zero contrast PCI, when indicated, offers the opportunity to improve overall outcomes related to ischemic heart disease without risking worsening renal function or dialysis in this extreme risk group of patients.[6] Zero contrast or minimal contrast PCI is a promising approach to battle against CIN. This approach resulted in safe and successful PCI without CIN or the need for RRT.

Concerns regarding CIN and procedure-related RRT can inhibit the performance of revascularization in patients with advanced CKD, especially those approaching end-stage renal diseases. Pre-existent renal disease is the strongest independent predictor for development of CIN and the requirement for RRT, which develop in 27 and 4% of patients with severe CKD, respectively. Contrast induced nephropathy is independently associated with adverse events including death, MI, and bleeding,[5,7,8] the rates of which dramatically increase if RRT is required, whether temporary or permanent.[8,9]

The strategy of performing zero contrast PCI, staged after ultra contrast diagnostic angiography, facilitates procedural planning as well as staged PCI also allows time for better discussion with patients regarding the treatment options, allowing true informed consent to be obtained. The staged PCI should perform no earlier than 7 days after the angiography because CIN typically occurs within the first week after the contrast exposure.[2]

Both femoral and radial accesses are acceptable for ultra low- or zero-contrast techniques, but patients with advanced renal failure radial arteries should be saved for arteriovenous fistula for hemodialysis. Guide catheter engagement without contrast injection does not pose a problem for an experienced operator. To confirm the proper engagement, one should inject 10–20 ml of saline through the catheter and observe temporal changes in the electrocardiogram [14]. If the catheter is properly inserted, the saline injection induces the T-wave inversion or increases its amplitude along with ST-segment depression or elevation. One may also confirm the appropriate catheter position by introducing a coronary guide wire into the artery, i.e., if the guide wire follows the anatomy of the coronary artery then this is the confirmation of proper engagement.

Careful study of the prior diagnostic angiogram is fundamental to successful wire navigation without using contrast. Significant expertise with IVUS and coronary physiological technology is also quite essential and only highly trained IVUS interpreter operators should attempt these procedures. Use of physiological measurements such as FFR can aid confirmation of the restoration of antegrade flow in the treated vessel at the end of the procedure.

During zero-contrast interventions, the most challenging task is proper stent positioning according to the landing zones determined in IVUS. Besides anatomical land mark several other techniques have been proposed to provide additional assistance for positioning of stent. One of these techniques is “marking wire technique”. Case 2 is the example of marking wire technique. Here One of its biggest challenge was the precise positioning of stents according to landing zones determined by intravascular ultrasound (IVUS). In our case, radio opaque, the softer marker part of PCI wire in LM to LCX make a metallic silhouette. The idea was that with blood flow the softer portion of wire will stuck with the roof of carina which acts as marker of LAD ostium. As LM is free of disease we prefer here precise placement of stent in LAD ostium to prevent undue jailing of LCX as well as metal in LM. The case demonstrate that by marker wire technique precise placement of stent to LAD ostium is possible.

Another technique that helps in orientation within a coronary artery relies on building a metallic silhouette of the vessel with guidewires. Side branches often provide important landmarks for stent implantation. In Case 3 side branch wiring were done to make a land mark for proper positioning of stent.

At the end of the procedure, single injection of small amount (3ml) of contrast into coronary artery can be done in order to exclude complications (especially distal perforation or embolization) and document final angiographic result.

Finally a high level of preparedness and expertise in managing coronary complications is paramount for such procedures. The threshold for using contrast in the event of a suspected complication is low and close monitoring of these patients during the peri-procedural

period is necessary.

Study [3] done on 31 patients with advanced CKD who had clinical indication for PCI based on a prior minimal contrast coronary angiogram were included. Zero contrast PCI was performed at least 1 week after diagnostic angiography using real-time intravascular ultrasound (IVUS) guidance, with pre- and post-PCI measurements of fractional flow reserve and coronary flow reserve to confirm physiological improvement. This approach resulted in successful PCI, no major adverse cardiovascular events and preservation of renal function without the need for RRT within a follow-up time of 79 days in all patients and came to a conclusion that patients with advanced CKD who require revascularization, PCI may safely be performed without contrast using IVUS and physiological guidance with high procedural success and without complications.

Our case series also demonstrate that besides treating simple lesion, complex cases like bifurcation lesion and LAD ostial lesion can also be treated by zero contrast or minimal contrast angioplasty.

In conclusion, zero contrast PCI that can be utilized in experienced centers with expertise with intravascular imaging and physiology to safely revascularize selected high-risk patients with advanced CKD or history of Contrast induced AKI.

Conflict of interest- None

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REVIEW ARTICLE

Correlation between Serum Free Triiodothyronine Level and Prognosis in Patients with Acute ST Elevation Myocardial Infarction

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Abstract:

Acute myocardial infarction is a global health problem with significant incidence of mortality and morbidity. Acute ST-segment elevation myocardial infarction (STEMI) remains one of the leading causes of premature death even after tremendous progression in the management and prevention of coronary artery disease. It is a cardiac emergency and is associated with considerable mortality and MACE including acute heart failure, cardiogenic shock, ventricular tachycardia, ventricular fibrillation or AV block, post MI angina. A predicted outcome for patients with acute STEMI is considered to be a necessary tool for stratifying risk and evaluating the potential impact of different therapeutic interventions. The cardiovascular system is very sensitive to thyroid hormones and a wide spectrum of cardiac changes has long been recognized in overt thyroid dysfunction. In severe illness of non thyroidal origin, including acute STEMI, thyroid hormone system may be rapidly down regulated. Additionally low FT3 is emerging as a risk factor for coronary artery disease. Low FT3 level in acute MI is associated with low LVEF, higher levels of troponin and NT-pro BNP values, more severe form of CAD, longer hospital stay, higher MACE and poor short and long term outcomes. Recently performed studies have showed that serum FT3 level predicts cardiovascular in-hospital adverse outcomes. A low FT3 state after acute myocardial infarction worsens hemodynamics and promotes adverse cardiac events and changes the transcription of many cardiac structural and functional genes, leading to decreased contractility of myocardium, inhibited Ca2+ transport, a worsened diastolic function, calcium overload, myocardial stunning and reperfusion injury.

Methods: We searched Google Scholar and PubMed with keyword STEMI, Triiodothyronine level, In-hospital cardiovascular outcomes and MACE to find out related published articles.

Keywords: STEMI, Triiodothyronine level, In-hospital cardiovascular outcomes, Prognosis, Mortality.

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Introduction:

Coronary artery disease is one of the leading causes of mortality and morbidity throughout the globe.[1] Acute coronary syndrome indicates any group of symptoms caused by obstruction of the coronary arteries.[2] By the year 2020, 32% of all deaths across the world would be caused by coronary artery diseases.[3] In south-east Asian regions, the prevalence of CAD is increasing rapidly due to rising prevalence of the atherosclerosis, which is the main cause of CAD.[4] CAD is highly prevalent in Bangladesh, but data related to various aspects of CAD are inadequate.[5-6] The prevalence rate of CAD in Bangladesh is 1.85% to 3.4% in the rural population and 19.6% in the urban

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population.[7-9] At present, STEMI comprises approximately 25% to 40% of all MI in hospital admissions and in-hospital mortality ranges between 5% to 6% .[10]

Thyroid hormone levels are frequently altered in response to acute myocardial infarction.[11] The most common alteration of thyroid function, known as low triiodothyronine syndrome e(LT3S), is characterized by low levels of FT3, normal levels of thyroid stimulating hormones (TSH) and thyroxine (T4).[12] In the form of free T3 (FT3) as biologically active thyroid hormone , has various effects on the cardiovascular system, including upregulating effective myocardial contractile function, decreasing systemic vascular resistance, as well as improving endothelial function and promoting angiogenesis. So the decrease in FT3 level may lead to decreased cardiovascular protection in patients with AMI.[13-15,23] Thus serum FT3 level assessment can improve risk prediction of in-hospital outcomes in acute STEMI patients. This study will assess correlation between serum free triiodothyronine level and prognosis in patients with acute ST elevation myocardial infarction.

Thyroid Hormones and cardiovascular system

The cardiovascular system is one of the important targets where thyroid hormones act.[16] As the chief biologically active hormone triiodothyronine exerts the main role in accelerating heart rate and cardiac contractility and also decreasing systemic vascular resistance.[17] Triiodothyronine functions by interactions with isoforms type α receptors -α1 or α2, and type β receptors- β1,β2 or β3.[18] Regarding their cardiovascular functions , these receptors are present both on atrial and ventricular cells.[19] By binding to receptors , thyroid hormones increase myosin synthesis and affect sarcoplasmic reticulum activity, movement through the ionic Ca and K channels, response of adrenergic receptors, transmembrane ion gradients and the levels of ATP and of atrial natriuretic peptide.[16] Acting on α receptors, T3 plays a major role in the process of accelerating myocardial contractility and by acting on β receptors, affect diastolic processes and ventricular relaxation.[20] At vascular level it plays a significant role in the maintenance and renewal of endothelial integrity in peripheral arterial resistance and in modulating the arterial response to the renin–angiotensin–aldosterone mechanism activation.[21] T3 also maintains the macrophage response to the deposition of lipids in the vascular walls.[22]

Thyrotropin (Thyroid stimulating hormone,TSH), a glycoprotein released from thyrotroph cells of anterior pituitary gland in response to the hypothalamic tripeptide, TRH (Thyrotropin releasing hormone) stimulates the production of T3 or T4 in the thyroid gland. The anterior pituitary gland is highly sensitive to slight changes in thyroid hormone levels within the reference range. There is a negative feedback control of thyroid hormones by the hypothalamous and pituitary.[23]

Serum FT3 level and cardiovascular outcomes

Changes in the levels of serum thyroid hormones has been seen in several non thyroidal illness, including acute cardiac diseases.[24] Acute myocardial infarction has significant effect on thyroid gland homeostasis and consequences in terms of mortality and morbidity.[19]

The decrease of FT3 levels can be caused by reduced conversion of T4 to T3 and by increased T3 catabolism.[25] Oxidative stress, inflammation and hypoxia Inflammation are found to be involved in the down regulation of T3 levels by affecting the activity of deiodinase and these conditions are often found in acute cardiac diseases.[26-27] Low FT3 level decreases cardiac blood volume, cardiac output, ionotropism , chronotropism and increases afterload, diastolic blood pressure, systemic vascular resistance , vascular wall thickness and stiffness. Changes in the arterial wall elasticity accelerate the progression of atherosclerotic processes.[28] Low FT3 level is also associated with lower EF and cardiac index and higher right atrial, pulmonary artery and pulmonary capillary wedge pressure.[29]

Recently performed several international prospective studies have shown a robust association of sick euthyroid syndrome , subclinical hypothyroidism or overt hypothyroidism with adverse in-hospital outcomes in patients with acute coronary syndrome.[30-31,17] A low FT3 level(<3.5 pmol/L) increases the incidence of immediate and long-term adverse cardiovascular events in STEMI patients.[31] Low T3 syndrome is a very frequent finding and is a predictor of poor immediate in-hospital and long term outcomes in patients with heart failure and STEMI.[32] A study in china has showed that low FT3 levels (<3.1 pmol/L) were significantly associated with worse prognosis in patients with acute STEMI.[17] Another study in China has showed that low FT3 levels were strongly associated with higher levels of markers of

myocardial damage and with low LVEF after STEMI in Chinese patients.[33] Another European study has found that ,among patients <75years of age, with low FT3 exhibited a significantly lower survival rates.[34] A study was performed in Bangladesh showing an association between IHD and thyroid hormone status.[35]

Impact of low Serum FT3 level on in-hospital outcomes

We have found several articles published in several indexed journal about the relation serum FT3 level and in-hospital outcomes in STEMI patients. A Japanese study have showed that the mortality and incidence of MACE were higher in lower FT3 group than in the normal FT3 level group (14.0% vs 2.7% and 66.7% vs 45.5% ,respectively; all P <0.001) . According to a multivariate analysis low FT3 level was the strongest predictor of death and MACE(Hazard ratio of death : 0.142, P<0.001 and HR for MACE : 0.748, p=0.007).[31] A study in China has showed a high incidence of low FT3 level(27.5%) among patients with STEMI. This study has also revealed that low FT3 group had more serious myocardial injury, as assessed by peak cardiac TnI levels and more severe cardiac dysfunction , as assessed by LVEF.[17] A study in Egypt has showed that in low FT3 group myocardial injury as assessed by cardiac Troponin I and Echocardiography (LVEF, LVESD, LVEDD and LAD) was higher in comparison with normal FT3 group.[36] The magnitude of low serum FT3 level is proportional to increase risk of mortality and MACE in AMI patients.[17]

The mechanism which may account for the association between serum FT3 levels and in-hospital adverse outcome with acute STEMI was unknown. However, it is accepted that decreased conversion from T4 to T3 in peripheral tissues due to inflammatory factors, hypoxia and so on result in low FT3 levels. Inflammatory cytokines might also contribute to the incidence of low FT3 levels after acute MI. IL6 reduces type 1 iodothyronine deiodinase (D1) and D2 activity by inducing oxidative stress in peripheral tissues.[37] Increased hypoxia induced factor 1 activates D3 in the heart and other tissues, which might contribute to lowering the FT3 levels.[38] The decrease in FT3 was considered to be adaptive response to acute disease by decreasing catabolism and conserving energy expenditure.[39]

Conclusion:

The incidence of low FT3 is high in patients with acute STEMI and is a strong predictor of short and long term poor prognosis. Prediction of in-hospital outcomes by on admission laboratory measures of FT3 level might help to identify patients at high risk of death or MACE. This can also identify patients who might benefit from further aggressive management steps.

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Conflict of interest

Nothing to declare.

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None

Authorship contribution

MMH planned to write the review, searched literature and drafted the manuscript . MK revised the manuscript. KNI, SMKH, MMR, MMUR, MNH read and approved the final version of manuscript.

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REVIEW ARTICLE

Medical Publications: Where Does Bangladesh Stand

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Abstract:

Background: A country's intellectual and academic status can be determined by the quality and quantity of its published scientific articles. Impact Factor (IF) is a widely accepted tool to discern this status. The aim of this review paper is to get an idea about the status of medical publications in Bangladesh.

Methods: Advanced searches were performed to carry out this study. Various National and International databases were used. Literature searches were performed using ISI, Scopus and PubMed (Medline) computer databases.

Results: Though there are 155 medical and dental journals in Bangladesh, only 4 journals from Bangladesh are indexed in the Scopus database (Scientific Bangladesh, 2019). The output of indexed medical journals from Bangladesh is much less than other South Asian countries like India and Pakistan.

Conclusions: Comparing to our two very neighboring countries India and Pakistan, we still lag behind in terms of medical publications let alone other European countries. Government as well as other concerned authorities should come forward to mitigating this disparity.

Keywords: Bangladesh, Impact Factor, Indexed journal, Medical publication.

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Introduction:

A country's intellectual and academic status can be determined by the quality and quantity of its published scientific articles. Worldwide the quality of medical journals is measured by prestige. It is a vague and a qualitative term that reflects the reputation and popularity of the journal.

Impact Factor (IF) is a widely accepted tool to discern this status. It is a measure of the frequency with which the average article in a journal has been cited in a particular year. It is used to measure the importance or rank of a journal by calculating the times its articles are cited which is an important indicator for evaluating research performance.[1]

The aim of this review paper is to get an idea about the status of medical publications in Bangladesh.

The results from the data analysis are presented in various illustrated charts to show the status of the

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journals listed in the Scopus database at the Bangladesh and South Asian levels.

In spite of the availability of medical journals, the number of indexed journals is very low. An indexed journal is one which has to pass through a review process done by a journal indexer. Though every institution can be an indexer, a trusted and reputable body is more plausible in this regard. There are few journal indexing agencies worldwide: Google Scholar, Scopus, PubMed, EBSCO, IJIFACTOR, EMBASE, DOAJ: Directory of Open Access Journals, ISI Indexing, Medline. These are the most reputed journal indexing agencies where author can check the indexing and apply for it.

Study Methods:

This study is based on Bangladesh Medical Research Publication Database, retrieved from the Bangladesh Medical & Dental Council (BM&DC) website. Advanced searches were performed to carry out this study. Various National and International databases were used. Literature searches were performed using ISI, Scopus and PubMed (Medline) computer databases. Data was then analyzed through MS-Excel. The results from the data analysis are presented in various illustrated charts to show the status of the journals listed in the Scopus database at the Bangladesh and South Asian levels.

Results:

Though there are 155 medical and dental journals in Bangladesh, only 4 journals from Bangladesh are indexed in the Scopus database which means in terms of percentage only 3% journals are indexed.[2]

According to the BM&DC, there are 155 medical and dental journals in Bangladesh. Out of these 155 medical and dental journals, only 12 are dental journals, and the remaining 143 are medical journals.[3]It means that 92% of BM&DC affiliated journals are medical journals.

In most fields, the impact factor of 10 or greater is considered an excellent score while 3 is flagged as good and the average score is less than 1. This is a rule of thumb.[4]

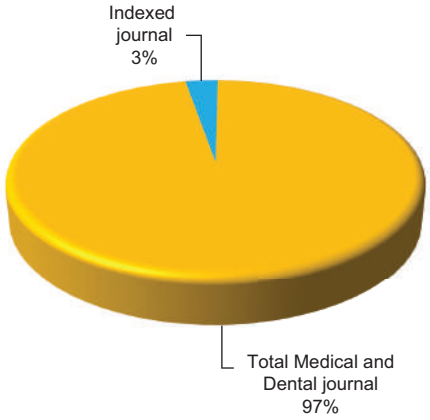


Fig.-1: *The ratio of non-indexed and indexed journals of Bangladesh.*

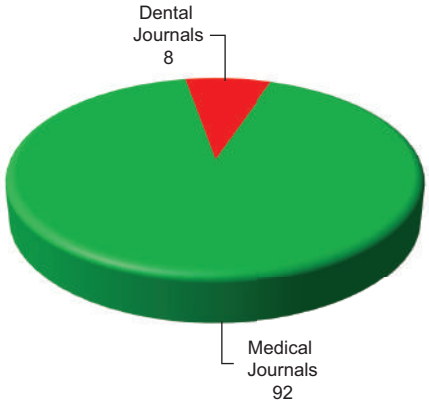


Fig 2: *The ratio of medical and dental journals in Bangladesh.*

Table-I

Medical Journal Bangladesh, Scimago Journal & Country Rank

Title	Type	SJR	H index	Total Docs (2020)	Total Docs (3 years)	Total Refs. (2020)	Total cites (3 years)	Citable docs (3 years)	Cites/Doc. (2 years)	Ref./ Doc. (2020)
Bangladesh Journal of Medical Science	Journal	0.255Q3	10	136	364	3751	223	332	0.68	27.58
Bangladesh Medical Research Council Bulletin	Journal	0.136Q4	19	27	88	576	13	82	0.17	21.33
Journal of Medicine Bangladesh	Journal	0.121Q4	5	30	85	472	18	75	0.24	15.73
Bangladesh Journal of Obstetrics and Gynaecology	Journal		3	40	0	763	0	0	0.00	19.08

In 2018, the authors from Bangladesh published 3135 scientific and technical journal articles. Therefore, in our country 20 articles per million people were published. The corresponding figures for selected countries are: Nepal: 28 articles per million, Vietnam: 45 articles per million, Pakistan: 60 articles per million, Sri Lanka: 64 articles per million, Bhutan: 70 articles per million, India: 100 articles per million, Indonesia: 101 articles per million, Thailand: 182 articles per million, China: 370 articles per million, Malaysia: 750 articles per million, South Korea: 1298 articles per million, Singapore: 1990 articles per million, Australia: 2153 per articles per million. Switzerland has the highest number of articles per million (2508).[5]

It is clearly depicted that the number of indexed medical journals in our country is merely inadequate. In case of India we will get a very different scenario. Among 570 total indexed journals there are 203 medical journals[6]. That means in terms of percentage India has 35.61% medical journals.

In case of Pakistan, despite having less number of medical journals than ours their number of indexed journal is more. Among 97 medical journals they have 6 and 3 indexed journal in PubMed and ISI databases respectively[7].

Table-II

Top ten countries with most research Paper

Country	Document	Citable documents	Citations	Self-Citation	Citations per Document	H index
1.China	788287	744042	971502	512540	1.23	1010
2.United States	766789	624554	933944	412567	1.22	2577
3.United Kingdom	249408	198500	366213	98231	1.47	1618
4.India	217771	191590	165237	69967	0.76	691
5.Germany	216474	174524	266602	77781	1.23	1429
6.Italy	155135	127502	239812	78810	1.55	1135
7.Japan	147341	127408	132663	36591	0.90	1118
8.France	139661	112838	180941	40432	1.30	1286
9.Canada	131684	110247	174238	35780	1.32	1299
10.Russian Federation	129270	119195	75897	32033	0.59	652

(Source: Scimago Journal and Country Rank, retrieved from: https://www.scimagojr.com/countryrank.php)

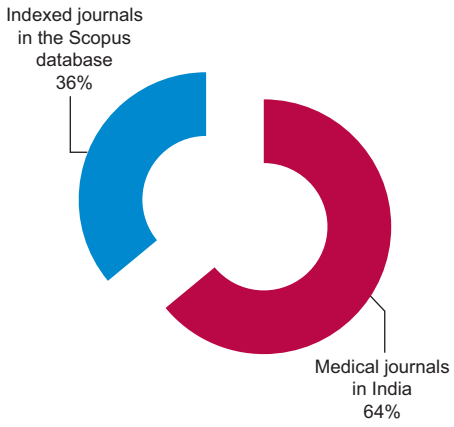


Fig.-3: *The ratio of indexed medical journals in India.*

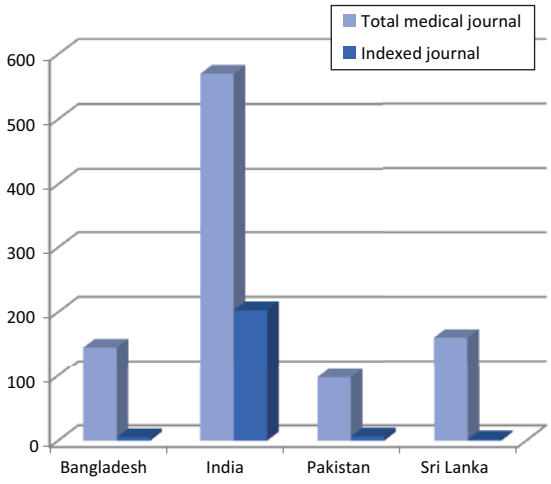


Fig.-4: *Comparative picture of indexed medical journals in South Asian countries.*

Discussion:

In this era of globalization, it's of highly significance to share knowledge and identify novel solutions to locally important problems. Research can serve that purpose conscientiously. The main goal of most medical journals is to improve medical care by publishing sound scientific articles (both research and practice papers) and focusing on topics that are of great importance to its readership. Secondary journalistic goals include improving the impact factor and breaking latest medical news[8].

From earlier discussion it has been noticed that the output of indexed medical journals from Bangladesh is much less than other South Asian countries like India (203) and Pakistan (9). In Pakistan, the total number of medical journals is less than ours, but the number of indexed journals is more. Their total number of medical journals is 97. Of these, journals indexed to the PubMed database are 6 and in the ISI database are 3[7]. On the other hand, Sri Lanka, a South Asian country, has more medical journals than us, but Scopus journals have less than us. Among 160 journals only 2 journals are indexed in the Scopus database[9]. But apart from the impact factor there are many more indicators to be considered.

Being the main scientific core of the societies, it's the duty of the universities to perform a great portion of research work which is supposed to be handled by the faculties and the students. But unfortunately, it has been found that the faculty members are mostly busy with education rather than with research activities. So, mainly in the developing countries research activities are not adequate at the university level[10]. Without involving the students into research activities, it is impossible to incur and maintain a national level development as students play a major role in the development of a country as future researchers[11,12]. Through different studies it was found that most of the medical students, due to some existing barriers, are not willing to carry out research. Those barriers include the lack of information access, language difficulties, administrative regulations, insufficient budgets as well as the lack of knowledge on how to write formal research proposals[13,14,15].

Another important barrier that we found through this extensive review of literatures is the lack of time. Due to lack of time many researchers, as they claimed, couldn't publish enough research works.[16,17] The other main reasons claimed by many respondents included self-reported limited skills in English or in writing, limited submission skill, and difficulty in initiating writing. Limited skill and lack of merely increase the difficulties. It was found that this combination decreased the chance of publishing in a high-impact journals[18]. As there is greater interest in publishing results which will have immediate effects, negative results are often difficult to publish.[19] But as an international initiative has been taken to prevent this publication bias[20], this barrier is losing its power to impede the publishing in high impact-journals. On the other hand, Knowledge gathered from negative results may also be useful in achieving good non-deleterious patient care [21].

Another significant barrier is lack of funding. It has been seen that over decades low-budget assignment on publication is becoming a growing problem[22,23]. According to Pavia et al., publishing in high- and low-impact journals is also dependent of financial resources[18].

In one of the studies author[24] concluded that there are mainly four factors that can be considered as keys to research, i.e. consideration of intrinsic factors like motivation, facilitating the growth of talents, financial factors and use of information systems. Through different studies it has been found that the whole procedure from proposal to publishing is unnecessarily time consuming. So, it has become a necessity to revamp the structure and procedures of universities and their research centers. Moreover, the experiences of the research center managers can be used for the improvement of the bureaucratic procedures in the approval of research proposals.[25]

In a study by Ibrahim Abushouk *et al.*,[26] the inadequate understanding of the statistical concepts and lack of skill in scientific writing were the barriers to research. By Siemens *et al.*,[27] inadequate knowledge and training in research were the barriers to research in students. In a study by Bocar,[28] the lack of skill in analyzing and interpreting the results was one of the obstacles to research in the majority of students.

Ashrafi-Rizi *et al.*[29] mentioned students' inadequate skill and knowledge of research methodology among the main personal barriers to research. This finding was consistent with the body of other research findings.[30-34] However, it was different from the findings of Abedini *et al.*,[35] concerning the research skills in

their target population. It seems that the difference lies in the fact that in the research by Abedini *et al*.,[35] the target population was faculty members, whereas in this research, it was students. Students' knowledge of research technique can be improved by including research methodology courses at various university levels and holding regular practical workshops. Joibari and Sanagoo[36] have mentioned research methodology in the students' curriculum as a top priority.

According to Dadipoor *et al*.[37], university students rated high workload and intensive courses among the key barriers to research. This finding is consistent with that of the studies by Anbari and Jadidi,[37] Ashtyani and Shamsi,[38] Poornaseri *et al*.,[39] Kharraz *et al*.,[40] Russell *et al*.,[41] and Oliveira *et al*.[42] Medical students' tremendous workload in clinics during their education, as well as their rigorous courses, naturally limit their research efforts, even when research facilities are available. A study by Edwards[43] also showed that intensive courses are among the main barriers to research activities. To remove this research barrier, Houlden *et al*.,[44] recommended the introduction of summer research courses in the students' curriculum. The experience of the undergraduate research committee in Saudi Arabia in providing national and international research opportunities to undergraduate students during the summers of 2010–2013 with significant qualitative (learning) and quantitative (publication) outcomes can be considered as one of the successful examples in this regard.[45]

The role of a mentor in the journey of research is inexplicable. Mentoring can assist mentees in securing research time and resources, facilitating the writing process, improving writing abilities, and assisting in additional publications and research funding as part of their research goals[46]. Mentorship also helps expand academic prospects, and speeds up the development of academic and professional skills for mentees[47].

Professional scientific conferences can be a place to hone the research skills of a researcher. Sharing personal experiences and ideas on research can help anybody to upgrade their skill significantly. The oral, poster presentations and even the feedbacks from the audience can shape the very way of the writing process[48]. Formal training or seminars on time management, stress management, scientific writing, and effective communication would be also beneficial. For example, during scientific writing training, the practice of writing, the requirement of regular literature reading, and instructor comments will help one's writing skills and increase confidence in continuing to write[49].

Adopting an iterative process to enhance the writing quality can be a useful idea whereby a creator creates an outline or first draft and after that refines the draft over time. The layout and ensuing drafts will frequently advantage from talks and input from other individuals of the group.[50]

Undoubtedly, we need to put more emphasis on the quality of published articles, not just the number of publications. Medical and research institutions should come forward to train up new researchers, organizing seminars, symposiums and workshops to produce more skillful research personnel.

Conclusion:

In spite of all the drawbacks many researchers and scholars are still trying to increase the overall quality of medical journals and research articles. Government and other concerned authorities like

Bangladesh Medical & Dental Council, Bangladesh Medical Research Council, Bangladesh Medical Association should come forward in this regard and incorporate policies into their plan to develop the skill of the writers and scholars so that they become efficient to write articles maintaining international standard.

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Epstein-Barr Virus Induced Dilated Cardiomyopathy in Adult: A Rare Aetiology

Umme Kulsum Khadiza Parveen[1], Upul Wickramarachchi[2]

Abstract:

Viral myocarditis has been recognised as a cause of congestive cardiac failure for more than 50 years. Many viruses, most commonly adenoviruses and enteroviruses have been associated with myocarditis and dilated cardiomyopathy. However, worldwide Epstein-Barr virus induced cardiomyopathy is very rare. Here we report a case of a 47-year-old fit and active school teacher who presented with rapidly developing symptoms of congestive cardiac failure due to a dilated cardiomyopathy possibly caused by Epstein-Barr virus infection.

Key Words: Epstein-Barr virus (EBV), Cardiac Magnetic Resonance Imaging (CMR), Endomyocardial biopsy (EMB), congestive cardiac failure (CCF), Dilated cardiomyopathy (DCM).

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Introduction:

The term dilated cardiomyopathy (DCM) is defined as left ventricular (LV) dilation and systolic dysfunction in the absence of coronary artery disease, hypertension, valvular, or congenital heart disease[1]. Although half of the cases aetiology is unknown, viruses causing myocarditis is a known inflammatory insult[2,3]. However, we could locate only 15 cases (9 adults and 6 children) worldwide with recent-onset DCM/myocarditis caused by Epstein-Barr virus[2]. It has important clinical implications due to the high potential for LV recovery[3]. A detailed cardiology work-up with standard clinical examination is mandatory to identify the cause, treatment strategy, and prognostication.

Case Report:

A 47-year-old fit and active lady without any prior medical history presented to the ambulatory medical department complaining of progressive shortness of breath for one month and chest tightness with bipedal oedema for last one week. There was no palpitation, paroxysmal nocturnal dyspnoea. She denied any palpitation, paroxysmal nocturnal dyspnoea. She also denied any fever, cough, sore throat, any other viral or systemic symptoms. She is a primary school teacher working closely with small children. She neither smokes nor drinks alcohol heavily. There was no family history of cardiac disease of note.

Examination revealed a breathless patient with tachypnoea and tachycardia of heart rate 120 beats/min, blood pressure 110/70 mmHg, raised JVP and bilateral pitting oedema on both lower limbs. Cardiovascular system examination revealed soft first heart sound with S3 gallop and a pansystolic murmur in apical radiating to the axilla. Respiratory system examination revealed features of bilateral pleural effusion.

Initially, due to the pandemic, Covid related pneumonia with it's complication was suspected. However, baseline inflammatory markers including Covid-19 screening were normal. Because of the symptoms of breathlessness in a young female, pulmonary embolism was also considered. Moreover, D-dimer was slightly elevated at 1176 ng/ml, admitting medical team organised a CT pulmonary angiogram which ruled out evidence of pulmonary embolism but showed evidence of cardiomegaly, pulmonary congestion with bilateral pleural effusions.

A 12 lead ECG showed normal sinus tachycardia, and poor progression of R wave. Initial chest X-ray demonstrated features of pulmonary congestion.

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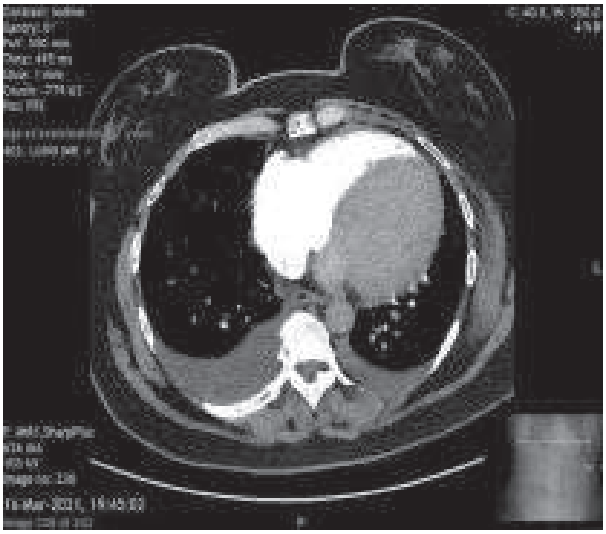


Fig.-1: *CTPA showing cardiomegaly.*

A subsequent transthoracic echocardiogram confirmed the presence of a dilated left ventricle of 6 cm and severely impaired systolic function with ejection fraction of 22% and evidence of pulmonary hypertension (Figure 2).

Later, extensive serology testing was carried out to identify the aetiology of this disease. Her thyroid profile, serum angiotensin converting enzyme, acylcarnitine, ferritin and ceruloplasmin level were within reference range. Both vasculitic and autoimmune screenings were negative.

IgG and IgM antibodies to viral capsid antigen (VCA) of Epstein-Barr virus (EBV) were detected. Likewise, IgG antibodies of Epstein-Barr virus nuclear antigen (EBNA) was also positive. Therefore, confirmed the aetiology of DCM as viral myocarditis.

Troponin I level was mildly positive at 38.5 ng/l (0-15.6). NT-proBNP level was markedly raised at 2656 ng/l (<400).

Later, Coronary angiogram ruled out any obstructive coronary artery disease causing this dilated cardiomyopathy (Figure 3).

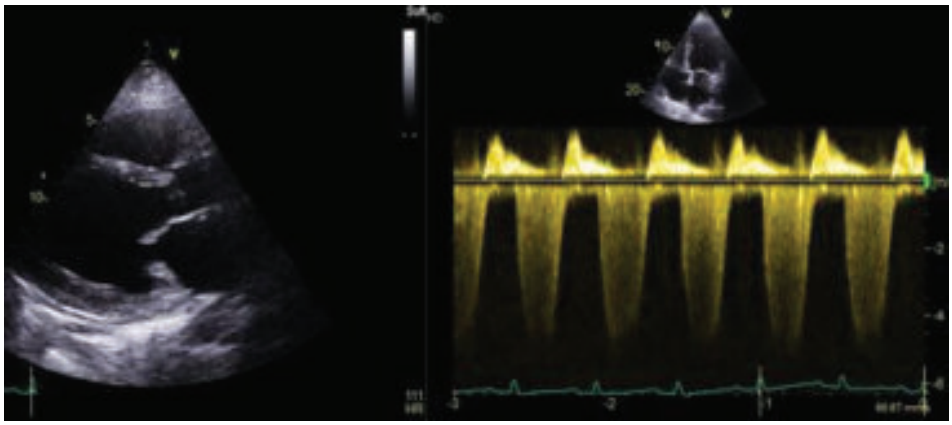


Fig.-2: *Echocardiography shows dilated severely impaired left ventricle (EF-22%) with mild to moderate central mitral regurgitation and LVIDd-6.0 cm.*

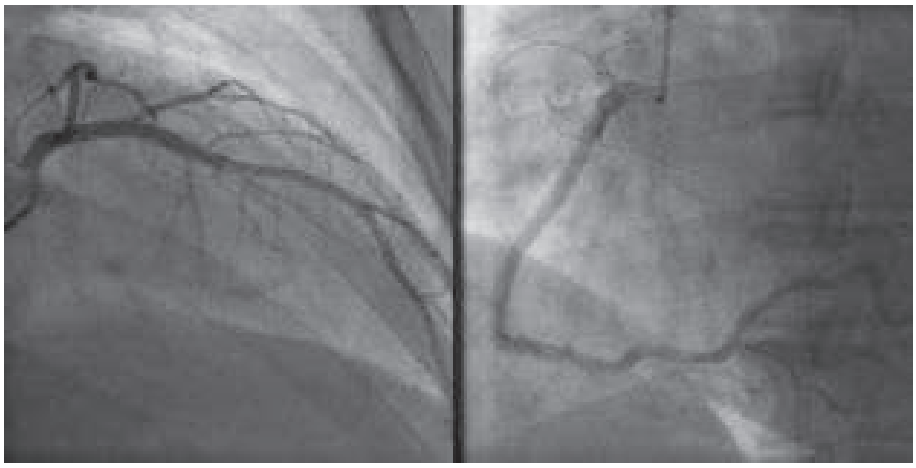


Fig.-3: *Coronary angiogram showing normal arteries*

Cardiac magnetic resonance (CMR) done after two months and reported as an end diastolic volume (EDV) of 290 mL (131 mL/mA^2) and end systolic volume of 225 mL (102 mL/mA^2) with no features of myocardial fibrosis and scarring, therefore established the diagnosis of dilated cardiomyopathy (Figure 4).

With standard heart failure treatment, her discomfort reduced significantly, therefore was discharged with an outpatient follow up plan and a clinical geneticist referral.

After 3 months with medication, she demonstrated an excellent recovery. Her symptoms including shortness of breath and bilateral pedal oedema went down significantly. Biochemical marker (NT-proBNP) reduced from 2656 ng/l to 273ng/l (normal < 400). Repeat echocardiography showed improved ejection fraction from 25% to 37%, LV cavity size reduced by 2 mm and the severity of mitral regurgitation lowered from moderate to mild in nature (Figure 5).

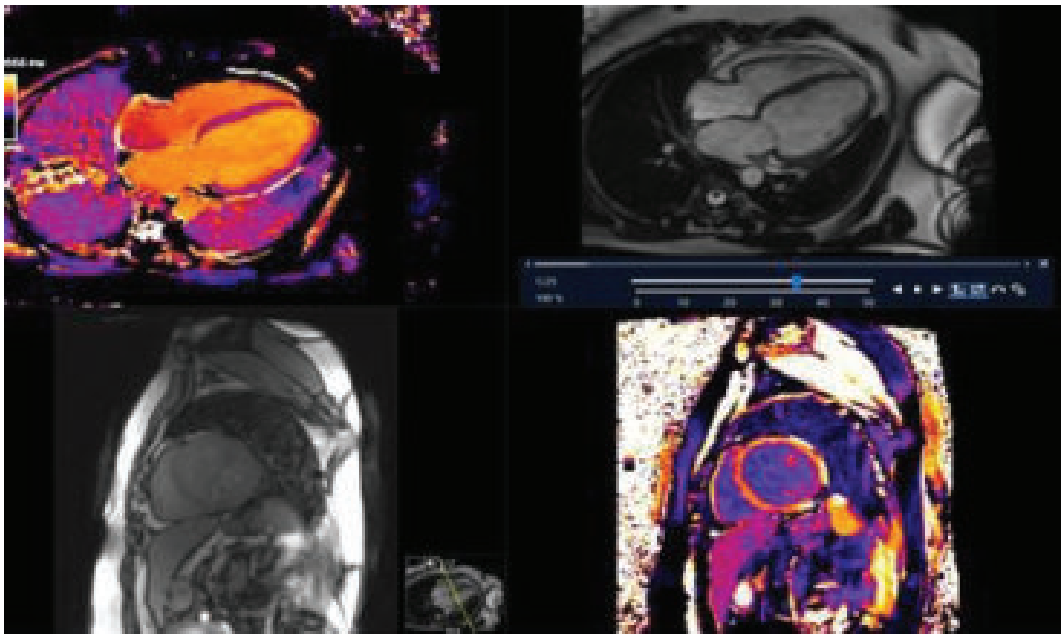


Fig.-4: *Cardiac magnetic resonance imaging showing dilated left ventricle without any features of scarring.*

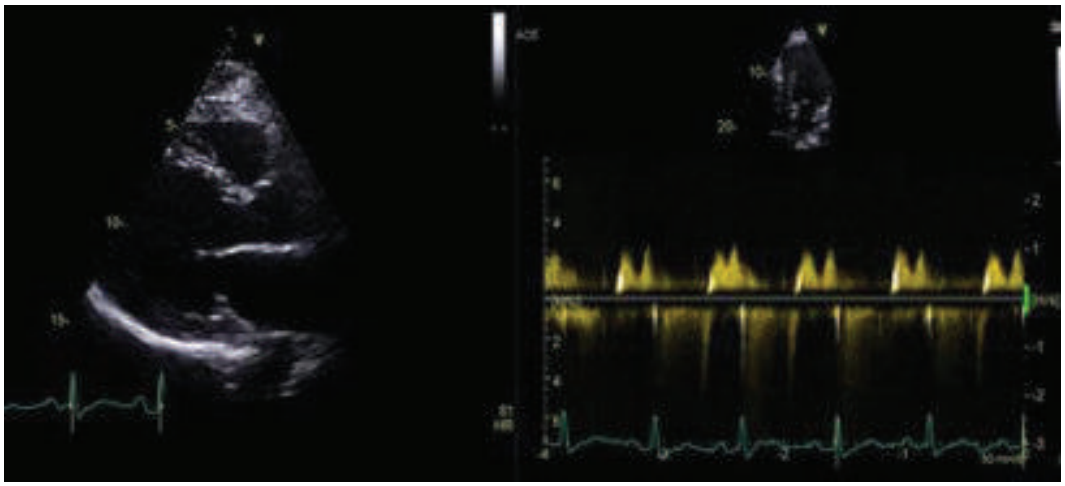


Fig.-5: *Repeat Echocardiography shows improved LV function EF (32-37%) and minimal MR. LVIDd 5.8cm*

Discussion:

Evidence of viral infection as a cause of heart failure dates to many years. Adenovirus, enterovirus, Epstein-Barr, and cytomegalovirus are the most common groups of cardiotropic viruses[4]. Although up to 90% of people will catch one or more of these viruses in their lifetime without any cardiac involvement, why only a selected few develop clinical symptoms remains unclear[5].

About 25–35% of affected individuals have familial forms of the disease, with most mutations affecting genes encoding cytoskeletal proteins, while some affect other proteins involved in contraction,[6]. A recent review, by Caforio and Iliceto, shows that in myocarditis/DCM, cardiac-specific and disease-specific antibodies of IgG class are potential biomarkers for identifying 'at-risk' relatives. Therefore, a certain genetic background, with or without immune alterations, appears to be a requisite to develop clinical symptoms of myocarditis and/or progression to DCM following virus infection in the heart[5].

Although viruses are the most common trigger in Europe and North America, serology is generally unhelpful, partly because of high background seropositivity rates. An acute onset of symptoms, "flu-like" prodrome, or elevated serum troponin/ inflammatory markers may raise suspicion. Myocarditis develop by means of three distinct chronological phases. During the first phase direct cardiomyocyte destruction occurs due to viruses causing damage and dilatation of the heart which might remain unnoticed due to innate immune response. In the second phase, ongoing myocyte harm occurs due to immune dysregulation which culminates in extensive myocyte damage and dilated cardiomyopathy[5].

The first case of EBV induced myocarditis/dilated cardiomyopathy was reported by Miller et al,[7] who reported varied reasons of myo-pericarditis including viruses. One case reported a 7-year-old girl presenting with fever, abdominal pain with raised inflammatory markers and deranged liver function test with normal ECG findings. The echocardiogram showed LV systolic dysfunction[8]. Due to the presence of chest pain and raised troponin the diagnosis was made. Other case reported a 17-years old male presented with generalized fatigue, chest pain, fever, high inflammatory marker, and persistent generalized lymphadenopathy who gradually developed infectious mononucleosis one week later and severe LV dysfunction[9].

EBV is a member of the herpesvirus family and spreads through saliva. It infects more than 90% of the world population causing infectious mononucleosis without any sequel,[10]. However, it has been implicated in causing various malignancies such as Burkitt's lymphoma, Hodgkins's lymphoma and nasopharyngeal carcinoma. The incidence is highest in persons 10 to 19 of age (six to eight cases in 1000 cases) and relatively uncommon in adults, accounting for less than 2 percent of all adults presenting with sore throat[11]. Being a school teacher, our patient was highly exposed to this virus.

Standards set to diagnose myocarditis are called Dallas criteria,[4,5,8]. The first criteria is any one of the symptoms such as chest pain, breathlessness, palpitation, or arrhythmia, plus one diagnostic evidence such as ECG or Holter monitor findings, elevated troponin T or I level, functional or structural cardiac abnormalities on imaging, or tissue characterization by cardiovascular magnetic resonance imaging,[8]. In our case the diagnosis was made by the onset of symptoms of breathlessness and elevated troponin. However, the confirmatory diagnosis was not made as positive serology for EBV is non-specific and biopsy was not done which was also not indicated in such case.

Mono spot rapid latex agglutination test has a specificity of 95% to 100%. It can be falsely positive for some other viruses and has the limitation that low levels of heterophile antibodies can persist for 9 to 12 months after EBV infection[8]. Antibodies to viral capsid antigen (i.e., VCA-IgG and VCA-IgM) are produced slightly earlier than the heterophile antibody and are more specific for EBV infection[11]. However, these essays do not prove presence of virus in the heart due to the high background prevalence,[5], hence they will be useful in selected group of patients who do not undergo endomyocardial biopsy (EMB) for PCR or immunocytochemical analysis.

American Heart Association guidelines support the use of EMB for patients presenting with unexplained new-onset heart failure <2 weeks in duration associated with a normal-sized or dilated left ventricle in addition to haemodynamic compromise[12]. As our patient was hemodynamically stable and improved significantly with conventional treatment, EMB hasn't been carried out.

ECG should always be performed in cases of myocarditis. QRS interval more than 120ms indicates

worse prognosis[13]. Cardiac troponin, a marker of myocardial injury is mainly elevated in patients with acute, early-onset myocarditis, and high levels are associated with marked hemodynamic abnormalities[13,14], this is associated with worse clinical outcomes and higher risk of death[12], whereas the absence of increased levels suggests long-term presence of myocarditis[5]. Small raise of Troponin in our patient suggested less myocardial injury with chronicity of the disease and therefore, better recovery.

The role of echocardiography is paramount in diagnosing fulminant myocarditis, however findings may vary in acute or subacute myocarditis. Newer modalities such as TDI strain may increase the sensitivity, but CMR should always be advised in addition to it[5,13]. Especially, gadolinium late enhancement (LE) and T2-weighted image sequences differentiate between ischaemic and non- ischaemic cardiomyopathy and provides a high diagnostic accuracy and should become gold standard imaging in patients with a suspicion of myocarditis[5,13]. Unfortunately, CMR was done after months of symptoms onset in case of our patient, that's why typical findings like oedema or fibrosis were absent.

Diagnostic coronary angiography is crucial in unexplained DCM especially in adults age more than 35 years even in the absence of anginal symptoms, as 7% patients have evidence of coronary artery disease which is potentially treatable either medically or by revascularisation[13].

Patients with acute myocarditis should limit physical activity, as exercise within 3 to 6 months[13] may increase viral replication and shorten survival[5]. They should also receive standard heart failure treatment such as diuretics[12], b-blockers[15], angiotensin converting enzyme-inhibitors or angiotensin II receptor blockers[12,16], spironolactone12, ARNI (valsartan/ sacubitril)[17].

Individual trials and a meta-analysis suggest that immunosuppression and antivirals therapy is generally not indicated[12,13]. Arrhythmias should be monitored and treated conservatively because they often resolve with resolution of acute inflammation[13]. Mechanical support with intra-aortic balloon pump or LV assist device as a bridge to recovery or heart transplantation may be necessary in severe cases[5].

The long-term prognosis of myocarditis/DCM depends upon the initial clinical presentation, hemodynamic instability, wide QRS complex, high NT-proBNP, Troponin level, and aetiology of the disease[12,18]. With the advancement of standard treatment, the prognosis has improved significantly over 20 years[18].

Conclusion:

This case illustrates the detailed cardiology work up to confirm the aetiology of left ventricular dysfunction in myocarditis/DCM patients.

Learning points:

1. As this is a disease of variable natural history, therefore the diagnostic pathway is extremely difficult as it requires knowledge to recognize phenotypic overlap and sophisticated investigations.
2. Though EBV induced DCM is rare in adults, clinician should have high index of suspicion especially if no aetiology is identified.

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Consent: We are grateful to the patient for her kind written consent for reporting.

Author's contribution:

UKK Parveen: Case taking, record keeping, writing, and editing the manuscript, literature search, compiling and integration of different images.

U Wickramarachchi: Literature search, citing references, critical revision, and final approval.

Conflict of interest: All the authors declared no competing interest.

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