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BANGLADESH SOCIETY OF CARDIOVASCULAR INTERVENTION (BSCI)**



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State-of-the-Art PCI of Left Main Coronary Artery Disease

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Cantonment, Dhaka, Bangladesh*

The left main coronary artery is the primary source of blood flow to the left ventricle. It supplies over 70% of the myocardium. Significant left main coronary artery disease is associated with high morbidity and mortality.

Diseases affecting the left main, by it self or in combination with multivessel disease, place the patient at significant risk for life-threatening cardiovascular events. Treatment requires an understanding of all available tools, devices and techniques, like those employed in invasive imaging and functional assessment, as well as taking into account underlying comorbidities such as diabetes.

With remarkable advances in percutaneous coronary intervention, including stent technology, antithrombotic agents and evolving procedural techniques, percutaneous coronary intervention has become an important treatment option in clinical practice guidelines for the revascularization of left main coronary artery disease.

In contemporary clinical practice, a heart-team approach to shared decision-making, considering clinical and anatomic factors along with patient preferences, is emphasized for patients with significant left main coronary artery disease requiring myocardial revascularization. Furthermore, recent progress in PCI procedures combined with intravascular imaging or functional guidance has resulted in significant improvements in percutaneous coronary intervention outcomes, especially for complex lesions, including left main coronary artery disease. Nevertheless, owing to

inherent anatomic complexities and frequent multivessel involvement, several unmet issues remain regarding the determination of the appropriate treatment approach for significant left main coronary artery disease, for which further clinical research is required.

When balancing procedural risks and post procedural outcomes, intracoronary imaging guidance by IVUS or OCT is recommended for performing percutaneous coronary intervention on anatomically complex lesions, in particular left main stem, true bifurcations and long lesions. Class IA recommendation by ESC 2024 CCS guideline.

In CCS patients with significant left main coronary stenosis of low complexity (SYNTAX score ≤ 22), in whom percutaneous coronary intervention can provide equivalent completeness of revascularization to that of CABG, percutaneous coronary intervention is recommended as an alternative to CABG, given its lower invasiveness and non-inferior survival. Class IA recommendation by ESC 2024 CCS guideline.

In CCS patients with significant left main coronary stenosis of intermediate complexity (SYNTAX score 23-32), in whom PCI can provide equivalent completeness of revascularization to that of CABG. PCI should be considered, given its lower invasiveness and non-inferior survival. Class IIaA recommendation by ESC 2024 CCS guideline.

In CCS patients with significant left main coronary stenosis and multivessel disease, at high surgical risk, PCI may be considered over medical therapy alone. Class IIbB recommendation by ESC 2024 CCS guideline. There is no Class III recommendation in ESC 2024 CCS guideline.

In LM with multivessel disease, anatomic suitable lesion for PCI, PCI is preferred. FFR and IVUS are strongly recommended, all ischemic lesions must be treated. Lesion

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with diameter stenosis $\geq 80\%$ and reference vessel diameter ≥ 2.25 mm must be treated.

In case LM bifurcation disease, if LCX normal or small diameter (< 2.5 mm diameter) one stent strategy and if true bifurcation disease means large LCX (> 2.5 mm diameter) two stent strategy should be followed. Post stent minimal stent area 6mm^2 for LCX, 8mm^2 for LAD and 12mm^2 for LM must be achieved following LM bifurcation PCI. So, target lesion revascularization rate is $< 5\%$ in 5 years. So isolated LM bifurcation disease, if suitable anatomy for PCI, PCI is preferred in almost all cases.

In ostial shaft LM disease, we place a stent in every case.

LM with multivessel disease with high anatomic complexity and LM with extensive CAD (3 VD) with low LVEF $< 40\%$, CABG is preferred. If those patients with multiple comorbidities (prior stroke, lung disease, frailty), PCI may be preferred.

New advancement in stent, development in PCI procedure, imaging in PCI, operator experiences and clinical trials shift treatment strategy of LM disease from CABG to PCI.

Prevalence of Depression and its Associated Factors among Postgraduate Cardiology Students

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Abstract

Background: Depression is common, being one of the three most common causes of morbidity worldwide, and anticipated to be the most common cause by the year 2030. Depression in physicians not only affects their own personal and family lives but also may have impacts on the health behavior of the community in general. Furthermore, depression may seriously affect physicians' professional function. Among all physicians, postgraduate cardiology students have an exceptional position. Cardiology training is a stressful course that entails frequent encounters with severely ill patients, emergency handling and lengthy work hours, etc. These factors make them vulnerable to depression. Several studies have been done to assess the prevalence of depression among medical students and post-graduate doctors and the factors associated with it. The purpose of this study was to assess the prevalence of depression and its associated factors among post-graduate cardiology students.

Methods: A cross-sectional study was conducted among the students of the Department of Cardiology of Dhaka Medical College Hospital, Bangabandhu Sheikh Mujib Medical University, National Institute of Cardiovascular Disease, National Heart Foundation Hospital and Research Institute and Sir Salimullah Medical College and Mitford Hospital, Dhaka from July 2019 to June 2020. Students were enrolled by purposive sampling after fulfilling the inclusion and exclusion criteria. The enrolled students were screened with HADS Questionnaire and depression was diagnosed by DSM-V diagnostic criteria. The subjects with depression were enrolled as Group I and the subjects without depression in Group II. The subjects of Group I are further classified into Group IA and Group IB. Group IA includes subjects with clinical depression and group IB includes subjects with borderline depression. Subjects who had HADS scores more than 10 were confirmed as having clinical depression by DMS-5 diagnostic criteria. A self-administered questionnaire was used to find out variables associated with depression.

Results: The mean age of this study population was 35.27 ± 5.64 years with 32.5% belonging to the 30-34 years age group. Males were predominant (90% vs 10%). Regarding the presence of depression among the post-graduate cardiology students, 82% of subjects had normal scores. Borderline clinical depression was found in 10% of subjects and clinical depression was found in 8% of subjects. Overall about one-fifth of the Cardiology students were suffering from different levels of depression. It was also found that factors that are associated with depression include younger age, sleep deprivation, inadequate colleague support, lower monthly income, and having no children.

Conclusion: The study results revealed that over one-fifth of the cardiology students are suffering from variable levels of depression. It is often unrecognized, underestimated, and not properly addressed. This issue should be properly addressed because of its possible impact on the quality of healthcare services in teaching hospitals and on training outcomes.

Keywords: Depression, Postgraduate, Cardiology

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Introduction

Depression is the leading cause of disability worldwide and is a major contributor to the overall global burden of disease. Globally an estimated 350 million people of all ages suffer from depression. It can cause the affected person to suffer greatly and function poorly at work and in the family.¹ Study in medical college can act as a contributing factor in developing depression in medical students which may have possible negative academic and professional consequences. A study was performed among undergraduate medical students of Armed Forces Medical College, Dhaka Cantonment which showed that 40.8% were reported as having mild to moderate depressive symptoms.² A study was conducted at Dhaka Medical College to find out stress and depression among undergraduate medical students, which revealed that only 1% of respondents were free from any sort of psychological stress.³ Postgraduate medical studies in particular carry a lot of stress. It affects the mental well-being of these students. A study was performed in Haryana, India to assess the prevalence of depression among postgraduate residents in a tertiary healthcare institute. It showed prevalence of depression among postgraduate resident doctors was 17%.¹ Another study conducted in January 2014 in different medical colleges in Indore, India concluded that depression, stress, and anxiety are the major growing mental problems among medical postgraduate aspirant students.⁴ Another different study carried out in India showed that postgraduate medical studies carry a lot of stress which can result in personal tragedies, poorer patient care, and overall loss to society.⁵ Common stressors include heavy workload, sleep deprivation, critical patients, poor learning environments, financial concerns, information overload, and career planning. These stressors often exert negative effects on student's and residents' academic performance, physical health, and psychological well-being making them more susceptible to depression. A similar study was done in Nepal to see the level of depression among medical students which showed overall prevalence of depression among the students was 29.78%.⁶ A systematic review and meta-analysis of the prevalence of depressive symptoms among resident physicians shows the overall pooled prevalence of depression was 28.8%.⁷ Another systematic review shows the prevalence of depression in resident physicians is higher than that of the general population.⁸ A similar study in Istanbul shows the prevalence of depression among the residents was 16%.⁹ Variables such as being junior, long duty hours, no job satisfaction, residents of clinical branches, no recreational

facilities, and staying at a hostel are significantly associated with depression among postgraduate students.⁵ A study conducted in China among physicians to assess the prevalence of depression shows that 28.13% had depressive symptoms.¹⁰ It shows depressive symptoms were associated with poor self-reported physical health, frequent workplace violence, lengthy working hours, frequent night shifts, etc. In our country, there is limited study on the prevalence of depression and associated factors on postgraduate and particularly cardiology students. Cardiology courses carry a lot of stress including prolonged emergency handling, long duty hours, lack of study time, etc. Depression in doctors negatively affects the quality of the service they provide and causes problems in their work environment. In addition, psychiatric problems have negative impacts on learning and academic success in a profession where postgraduate education is highly important. So we designed the study to estimate prevalence and correlate factors associated with depression among cardiology students.

Methods

This cross-section analytical study was conducted at the Cardiology of Dhaka Medical College Hospital (DMCH), Dhaka between July 2019 to July 2020. The study protocol was approved by the Ethical Review Committee of Dhaka Medical College and Hospital, Dhaka. A total of 100 Postgraduate Cardiology course students (MD Residency-Phase A & Phase B & MD non-residency, Diploma cardiology and FCPS cardiology) of the following institutes within the study period: Dhaka Medical College Hospital (DMCH), National Institute of Cardiovascular Diseases (NICVD), Bangabandhu Sheikh Mujib Medical University (BSMMU), National Heart Foundation Hospital & Research Institute (NHFRI), Sir Salimullah Medical College & Mitford Hospital (SSMCH) fulfilling the inclusion and exclusion criteria were enrolled in this study by convenient purposive sampling. Study subjects who denied giving consent for participation were previously diagnosed as psychiatric patients, taking anti-depressant medications and having any severe co-morbidity (cardiac, renal, hepatic and respiratory diseases) were excluded from the study. Informed written consent was taken from each participant. The enrolled participants were screened for the presence and severity of depressive symptoms by using the HADS questionnaire. Depression was diagnosed by DSM-5 diagnostic criteria and factors associated with depression were assessed by a preformed questionnaire. The subjects with depression were enrolled as Group I and the subjects

without depression in Group II. The subjects of Group I were further classified into Group IA and Group IB. Group IA includes subjects with clinical depression and group IB includes subjects with borderline depression. Subjects who had HADS scores more than 10 were confirmed as having clinical depression by DSM-5 diagnostic criteria. The process of assessment of depressive symptoms by this tool was evaluated and approved by the Department of Psychiatry of Dhaka Medical College Hospital. Interviews of the participants were conducted personally and face to face in the institutes mentioned above to diagnose depression and to ascertain socio-demographic and other variables such as work-related risk factors and post-graduate training-related variables. All the information was recorded properly in the preformed data collection sheet. After compiling data from all participants, statistical analysis was done. All statistical analysis was performed using the statistical package for social science (SPSS) program, version 22 for Windows.

Results

Table I illustrates that the subjects of MD Phase B have the highest number of clinical depression compared to other subjects of other post-graduation cardiology courses while subjects of the MD thesis part have the lowest number of clinical depression compared to other subjects.

Table-I: Distribution of the study subjects according to post-graduation course type(n=100):

Variables	Group I		Group II		Total		p-value
	No	%	No	%	No	%	
MD Thesispart	5	13.5	32	86.5	37	37	0.7 ^{ns}
MD Phase A	3	13.6	19	86.4	22	22	
MDPhaseB	6	33.3	12	66.7	18	18	
Diploma in Cardiology	3	16.7	15	83.3	18	18	
FCPS in Cardiology	1	20	4	80	5	5	

Group I= subjects with depression, GroupII= subjects without depression,

Chi-square test was done for qualitative data

ns = not significant (p>0.05)

The minimum age of the respondents was 27 years and the maximum was 49 years. A major proportion (31%) was in the 30- 34 years age group; whereas only a few (5%) had aged more than 44 years. The mean age of the total population was 35.27 ± 5.64 years. The mean age difference was not statistically significant between the two groups (33.23 ± 5.13 years. vs. 35.78 ± 6.03 years; p=0.07).

Table-II: Distribution of the study subjects by age (n = 100)

Age group (years)	Group I(n=18)		GroupII (n=82)		Total (n=100)		p-value
	No.	%	No.	%	No.	%	
25-29	4	22.2%	13	15.8%	17	17%	0.72 ^{ns}
30-34	8	44.4%	23	28%	31	31%	0.22 ^{ns}
35-39	3	16.7%	21	25.6%	24	24%	0.09 ^{ns}
40-44	2	11.1%	21	25.6%	23	23%	0.12 ^{ns}
45-49	1	5.5%	4	4.9%	5	5%	0.15 ^{ns}
Meanage±SD	33.23±5.13		35.78±6.03		35.27±5.64		0.07 ^{ns}

GroupI= subjects with depression, GroupII= subjects with out depression.

Chi-square test for qualitative data and an unpairedt-test for quantitative data were done.

ns = not significant (p>0.05)

Figure 1 shows that, among 100 study subjects, 90 (90%) were males and 10 (10%) were females. The male and female ratio was 9:1.

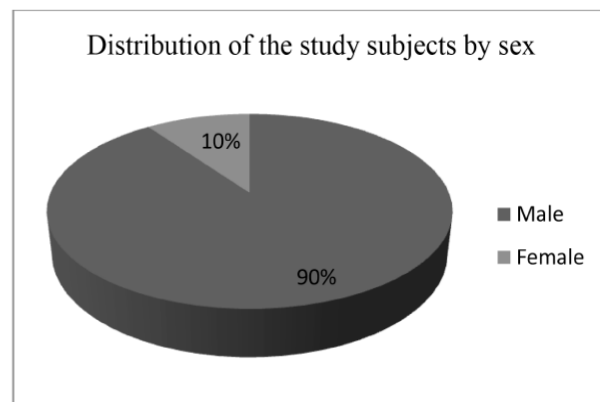


Fig.1: Pie chart of the distribution of study subjects by sex (n= 100)

Table III shows that, in the depressed group about one-fifth (22.2%) was female, whereas in the non-depressed group, less than 10% was female.

Table-III: Relation of Gender with presence of depression (n=100)

Sex	Group I (n=18)		GroupII (n=82)		p-value
	No.	%	No.	%	
Male	14	77.8%	76	92.7%	0.05 ^{ns}
Female	4	22.2%	6	7.3%	

GroupI= subjects with depression, GroupII= subjects without depression

Chi-square test was done for qualitative data

ns=notsignificant(p>0.05)

Table IV shows the distribution of the study subjects according to socio-demographic variables. Around 61 to 78% of the study subjects in both groups are married. A statistically insignificant association was seen between marital status and depression among the study groups ($p=0.13$). Around 63.6% of the subjects without any children had depression, whereas only about 36.4% of the subjects with children had depression. The association between having no children and with prevalence of depression is also statistically significant ($p=0.01$). About 78% of the subjects in group I had monthly incomes $\leq$ 50000 taka; whereas, about 59% of the subjects in group II had monthly incomes $>$ 50000 taka. The association between lower monthly income with depression between groups I and II is statistically significant ($p=0.005$). The table also shows that about 72 to 80% of the subjects in both groups are non-smokers. The association between smoking and depression in both groups is insignificant statistically (p -value: 0.5).

Table-IV: Distribution of the study subjects according to socio-demographic variables ($n = 100$)

Variables	Group I ($n=18$)	Group II ($n=82$)	p-value
Relationship status			
Married	11(61.1%)	64(78.1 %)	0.13 ^{ns}
Unmarried	7(38.9%)	18(21.9%)	
Having children			
Yes	4(36.4%)	48(75%)	0.01 ^s
No	7(63.6%)	16(25%)	
Monthly income(<50,000 TK)			
Yes	14(77.7%)	34(41.5%)	0.005 ^s
No	4(22.3%)	48(58.5%)	
Smoking Habit			
Yes	5(27.8%)	17(20.7%)	0.5 ^{ns}
No	13(72.2%)	65(79.3%)	

Group I= subjects with depression, Group II= Subjects without depression

=Chi-square test was done for qualitative data

=s = significant ($p<0.05$) and ns = not significant ($p>0.05$)

About 67 to 72% of the subjects in both groups reported that their working hours are more than 48 hours per week (Table V). Around 55 to 67% in both groups had night duties of less

than 6 in number per month. However, the association between this variable and depression is not significant statistically (p -value 0.3). Table V also illustrates that about 67 to 72% of the subjects in both groups had inadequate time for study. Sleep deprivation is significantly associated with depression among the subjects of group I. About 61 to 73% of subjects in both groups reported that they do not have adequate recreational facilities.

Table-V: Distribution of the study subjects according to work-related variables ($n = 100$)

Variables	Group I ($n=18$)	Group II ($n=82$)	p-value
Hospital working hours (> 48 hours per week)			
Yes	13(72.2%)	55(67.1%)	0.7 ^{ns}
No	5 (27.8)	27(32.9%)	
No. of night shifts > 6 per month			
Yes	8(44.4%)	27(32.9%)	0.3 ^{ns}
No	10(55.5%)	55(67.1%)	
Inadequate study time			
Yes	13(72.2%)	55(67.1%)	0.7 ^{ns}
No	5(27.8%)	27(32.9%)	
Sleep deprivation			
Yes	13(72.2%)	27(32.9%)	0.002 ^s
No	5(27.8%)	55(67.1%)	
Adequate recreational facilities			
Yes	7(38.9%)	22(26.8%)	0.3 ^{ns}
No	11(61.1%)	60(73.2%)	

Group I= subjects with depression, Group II= Subjects without depression

Chi-square test was done for qualitative data

s = significant ($p<0.05$) and ns = not significant ($p>0.05$)

Table VI shows that about 73 to 78% of subjects in both groups have no training satisfaction. The majority of the subjects in both groups reported their frequency of rotation during the training period was not too much. About 56% of the subjects in group I reported no adequate supervisor's support, whereas, about 60% of the subjects in group II had adequate supervisor's support, although the association between this variable with depression is not significant statistically. There is a statistically significant association between depression and inadequate support from colleagues among the study groups. The majority of the subjects in both groups (73-77%) had stressors outside the work. About 72 to 79% of the subjects in both groups reported no strictness of training.

**Table-VI:** Distribution of the study subjects according to post-graduate training-related variables (n = 100)

Variables	Group I (n=18)	Group II (n=82)	p-value
Having training satisfaction			
Yes	4(22.2%)	22(26.8%)	0.7 ^{ns}
No	14(77.8%)	60(73.2%)	
Frequent rotation			
Yes	4(22.2%)	33(40.2%)	0.15 ^{ns}
No	14(77.8%)	49(59.8%)	
Adequate supervisors support			
Yes	8(44.4%)	49(59.7%)	0.24 ^{ns}
No	10(55.5%)	33(40.2%)	
Adequate colleagues support			
Yes	7(38.9%)	72(87.8%)	0.00001 ^s
No	11(61.1%)	10(12.2%)	
Stressors outside the work			
Yes	14(77.7%)	60(73.1%)	0.8 ^{ns}
No	4(22.2%)	22(26.8%)	
Strictness of training			
Yes	5(27.8%)	17(20.7%)	0.3 ^{ns}
No	13(72.2%)	65(79.3%)	

Group I= subjects with depression, Group II= Subjects without depression

Chi-square test was done for qualitative data

s = significant (p<0.05) and ns = not significant (p>0.05)

Table VII illustrates that a higher number of the subjects in group IA have an age ≤34 years. The association between younger age with depression between group IA and IB is statistically not significant (p=0.06). Table VII also illustrates that a higher number of the subjects in group IA (about 88%) had monthly income ≤ 50000 taka, whereas, about 30% of the subjects in group IB had monthly income > 50000 taka. The association between lower monthly income with depression between groups IA and IB is statistically not significant (p=0.38).

Table-VII: Distribution of the Subjects with depression according to socio-demographic variable (n=18):

Variables	Group IA		Group IB		p-value
	No	%	No	%	
Age (≤35 years)					
Yes	6	75%	3	30%	0.06 ^{ns}
No	2	25%	7	70%	
Monthly income ≤ 50000 taka					
Yes	7	87.5%	7	70%	0.38 ^{ns}
No	1	12.5%	3	30%	

Group IA= subjects with clinical depression, Group IB=subjects with borderline depression

Chi-Square test was done for qualitative data

ns = not significant (p>0.05)

Table VIII illustrates that a higher number of the subjects in group IA do not have any children, whereas, about 15% of the subjects in group IB have children. The association between having children with depression between group IA and IB is statistically significant (p=0.04).

Table-VIII: Distribution of the Subjects with depression according to socio-demographic variable (n=11):

Variables	Group IA		Group IB		p-value
	No	%	No	%	
Having Children					
Yes	1	25%	6	85.71%	0.04 ^s
No	3	75%	1	14.29%	

Group IA= subjects with clinical depression, Group IB=subjects with borderline depression

Chi-Square test was done for qualitative data

s = significant (p<0.05)

Table IX also shows that a higher number of the subjects in both groups had sleep deprivation. However, the association between sleep deprivation and depression is not statistically significant (p=0.1).

Table-IX: Distribution of the Subjects with depression according to a work-related variable (n=18):

Variables	Group IA		Group IB		p-value
	No	%	No	%	
Sleep deprivation					
Yes	7	87.5%	6	60%	0.1 ^{ns}
No	1	12.5%	4	40%	

Group IA= subjects with clinical depression, Group IB=subjects with borderline depression

Chi-Square test was done for qualitative data

ns = not significant (p>0.05)

Table X shows a statistically significant association between adequate colleagues' support and depression among subjects with clinical and borderline depression.



Table-X: Distribution of the Subjects with depression according to post-graduation training-related variable (n=18):

Variables	Group IA No	Group IB No	p-value
Adequate Colleagues' support			
Yes	112.5%	60%	0.005*
No	787.5%	40%	

Group IA= subjects with clinical depression, Group IB=subjects with borderline depression

Chi-Square test was done for qualitative data

s = significant ($p < 0.05$)

Discussions

The mean age of the study population was 35.27 ± 5.64 years. This is slightly more than a study conducted by Sadiq, et al. (2019) where the mean age of the subjects was 32.6 ± 4 years.¹¹ Male subjects were predominant in the study population (90% vs. 10%) which is similar to a study conducted among post-graduate residents of India (Shashikantha and Sheethal, 2016).¹ Regarding the presence of depression among the post-graduate cardiology students, 82% had normal scores. Borderline clinical depression was found in 10% of subjects (Group IB) and clinical depression was found in 8% of subjects (IA). Overall about 18% of students were suffering from different levels of depression. Younger subjects (≤ 34 years) were predominant in group I. However, no significant association has been seen between younger age and depression among subjects of group IA and group IB.

According to WHO, risk factors for depression in the general population are female sex, separation or divorce, family history of depression, early parental loss, negative stressful events, chronic stress, lack of social support, and living in urban areas. In another study (Zaman, et al., 2014), it was found that long working hours, low monthly income, and smoking habits appeared as significant risk factors for depression.¹² Besides these, married male trainees who live away from family suffer from depression more frequently. One important reason might be that, due to our social context, the husband has to take responsibility for the family, so they are more stressed in a similar context than a female and suffer from depression more commonly. In this study, we aimed to evaluate the association of some factors (socio-economic, work-related, and post-graduation training-related) with depression among cardiology students. So, some socio-economic factors, work-related risk factors, and

post-graduation-related risk factors were evaluated by a preformed questionnaire and from particulars of the cardiology students.

Among the socioeconomic factors, it has been found that students who have children suffer from depression less than students having no children. It has also been found that the majority of the subjects in both groups are married and no significant association has been seen between marital status and depression. Another finding is that lower monthly income is significantly associated with depression between the study groups. The majority of the subjects of both groups are non-smokers and no significant association has been seen between smoking and depression among the study groups. Shashikantha and Sheethal (2016), found in their study that, marital status and history of smoking had significant associations with depression.¹ This difference may be due to the smaller sample size and inclusion of multicenter postgraduate cardiology students in this study.

The majority of the subjects in both groups reported that they had to do more than 48 hours of duty per month; however, they had to do less than 6-night duties per month. It has been seen that most of the subjects in both groups had inadequate time for study and no adequate recreational facilities. Sleep deprivation was significantly associated with depression among the subjects of group I. However, no statistically significant association has been seen between above mentioned other work-related variables (like long working hours, number of night shifts per month, inadequate time for study) and depression. Sadiq, et al. (2019) found in their study that long working hours and sleep deprivation are associated with depression among postgraduate medical residents.¹¹ This difference may be due to variations in the sample size and post-graduation course type. Sadiq, et al. (2019) included 200 postgraduate residents of both Medicine and Surgery Faculties as the sample population in their study.¹¹

In this study, it has been seen that, among the post-graduation course types, a higher percentage of the subjects in MD phase B (33.3%) are suffering from depression followed by FCPS cardiology students (20%). Among other post-graduation courses, like diploma cardiology, MD thesis part and MD phase A, a lower percentage of the subjects are suffering from depression. However, there was no statistically significant association between post-graduation course type and depression.

Among other post-graduation variables, inadequate

colleagues' support was associated with depression among the study groups. Most of the subjects in both groups reported no adequate training satisfaction and they had stressors outside the work. However, the majority of them reported that their frequency of rotation during the training period was not too much and they had no strictness of training. 60% of the subjects in Group I reported no adequate supervisor's support and 60% of the subjects in Group II had adequate supervisor's support. In a cross-sectional study in Bangladesh by Zaman, et al. (2014), it was found that depression was present in 39.6% of the subjects and depression was more common among married, male trainees who used to live away from family and who did not get adequate colleague's support.¹² Long working hours, low monthly income, and smoking habits appeared as significant risk factors for depression.

Although statistically not associated with depression significantly, some other variables have been observed to be important in both group I and group II subjects which reflect the overall problems among the cardiology students. Most of the subjects in both groups had to do more than 48 hours of duties per week; they had inadequate recreational facilities, had insufficient time for study, had no training satisfaction, and had stressors outside the work.

This study also reveals that a higher number of the subjects in group IA had no children and had inadequate colleagues' support. However, no significant association has been seen between lower monthly income and depression among subjects of group IA and IB. There was also no significant association between sleep deprivation and depression among the subjects of group IA and group IB.

The result of this study has demonstrated that, overall about one-fifth of the Cardiology students suffer from variable levels of depression. To ensure the patient's safety and well-being, it is very essential to focus on the mental health of the cardiology students. Both modifications of associated factors for depression and psychological support are very much necessary to improve the overall academic performance of cardiology students as well as patient care.

Conclusion

The study results revealed that overall about one-fifth of the postgraduate cardiology students are suffering from depression and among them 10% have borderline depression and 8% have clinical depression. This depression is often unrecognized, underestimated, and not properly addressed.

This issue should be taken care of because of its possible impact on the quality of healthcare services in teaching hospitals and on training outcomes. Further study is needed to identify effective strategies for preventing depression among cardiology students.

Limitations of the study

There were several limitations of the study which included: purposive sampling was done in this study instead of random sampling. Therefore, the results of the study may not reflect the exact picture of the country. A limited number of students responded over a short period. Some other variables like recent life events and seasonal variation were not considered. The sample size was small compared to the calculated size, which does not allow generalization of the findings. Some students did not agree to participate in the study even though they were informed about the study procedure, objectives, anonymity of data, and their right to withdraw from the study at any time, particularly those residents who had imminent exams and were reluctant to participate in the interview done for data collection.

Recommendations

There may be support groups with counseling facilities (student counseling units) within postgraduate cardiology institutes. There may be routine screening for depression among postgraduate cardiology students with subsequent appropriate management. The study also recommends the need for interventions like social and psychological support to improve the quality of life of postgraduate cardiology students. Student advisors should be provided who will train students about stress management.

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Association of C-Reactive Protein to Albumin Ratio with Angiographic Severity of Coronary Artery Disease in Patients with Chronic Coronary Syndrome

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Abstract

Background: The number of coronary artery disease (CAD) patients is increasing day by day in Bangladesh. Chronic coronary syndrome (CCS) increases the risk of having serious cardiovascular events (CVEs) by two times. Predicting the occurrence of these CVEs or CAD severity by low- cost noninvasive or hematological test is an area of interest now a days. Several studies have postulated CRP/albumin ratio (CAR) as a predictive factor of CAD severity. This study was conducted to determine the association of CAR with angiographic severity of CAD in patient with CCS.

Methods: This cross-sectional analytical study was conducted at the Department of Cardiology, Dhaka Medical College & Hospital, for a period of 12 months following ethical clearance. A total of 112 admitted patients undergoing elective coronary angiography due to chronic coronary syndrome were included in this study after taking informed written consent. Patients were divided into two groups according to SYNTAX Score I: non-severe CAD group (SYNTAX Score I ≤ 22 , n=56) and severe CAD group (SYNTAX Score I > 22 , n=56). Socio-demographic characteristics, clinical presentation, investigation findings, CRP/Albumin ratio and angiographic severity by SYNTAX Score I were reported. Data were collected in separated case-record form and analyzed by SPSS 26.

Results: The mean age of severe CAD group was significantly higher than non-severe CAD group (57.25 ± 9.34 vs 52.27 ± 10.41 years respectively, $p=0.009$). severe CAD group had significantly higher frequency of having DM (46.4% vs 26.8%, $p=0.03$), hypertension (60.7% vs 41.1%, $p=0.04$) and dyslipidaemia (55.4% vs 33.9%, $p=0.23$) than non- severe CAD group. Fasting blood sugar, total cholesterol and serum LDL were significantly higher in severe CAD group. The mean CAR was significantly higher in severe CAD group (12.35 ± 6.12) than non-severe CAD (4.51 ± 1.59) ($p<0.001$). CAR had significant moderate positive linear association with angiographic severity by SYNTAX Score I ($r = +0.55$, p value <0.001). A cut-off value of $CAR > 6.3$ showed sensitivity, specificity, PPV, NPV and accuracy 82.14%, 83.93%, 83.64%, 82.46% and 83.04%, respectively to correctly predict severe CAD cases. Multivariate logistic regression analysis found that $CAR > 6.3$ a important predictors of severe CAD in chronic coronary syndrome patients (AOR=25.58, 95%CI: 7.72-84.70, $p<0.0001$).

Conclusion: CRP/albumin ratio had significant positive association with angiographic severity of coronary artery disease in patients with chronic coronary syndrome.

Keywords: Chronic coronary syndrome, SYNTAX Score I, CRP to Albumin Ratio

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Introduction

Coronary artery disease (CAD) is the most common type of cardiovascular diseases (CVDs). CVDs is the leading cause of death globally, taking an estimated 17.9 million lives each year, representing 32% of all global deaths. More than three-quarters of cardiovascular disease deaths occur in low and middle-income countries. It has been predicted that cardiovascular mortality will rise from 18.1 million in 2010 to 24.2 million by 2030.¹ Because of rapid urbanization and globalization in lower and middle-income countries (LMIC), disease-related mortality and disabilities have shifted away from infectious diseases and toward non-communicable diseases such as IHD, which is a concern.^{2,3} It was estimated that globally, IHD affects around 126 million individuals (1,655 per 100,000), which is approximately 1.72% of the world's population.⁴ The exact prevalence of CAD in Bangladesh is not known. Only limited numbers of small-scale epidemiological studies are available. More recent data indicates CAD prevalence is between 1.85% and 3.4% in rural areas. CAD prevalence in urban working population is 19.6%.^{5,6,7} Despite significant disparities in values, CAD appears to be on the rise in Bangladesh.

Angina pectoris, a clinical condition characterized by chest, neck, or left arm discomfort, is the first symptom in almost half of all individuals with coronary artery disease (CAD).^{8,9,10} When symptoms persist for at least two months without changing in severity, character, or triggering situations, chronic stable angina is identified.¹¹ Chronic angina almost doubles the chances of having a severe cardiovascular event (CVEs).⁸ Chronic stable angina is now coined as chronic coronary syndrome.

Atherosclerosis is the primary cause of coronary artery disease. By causing arterial inflammation, plaque rupture, and subsequent thrombosis, inflammation plays an important role in the progression and destabilization of atherosclerosis, as well as the initiation of acute coronary syndrome (ACS).^{12,13,14} To assess the inflammatory process and determine cardiovascular risk, many standard laboratory markers have been used. Increased neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), platelet to lymphocyte ratio (PLR), uric acid, monocyte to high density cholesterol (HDL-C) ratio, and mean platelet volume to lymphocyte ratio (MPVLR) in patients with CAD have all been associated with poor outcomes.^{15,16,17,18,19,20} C-reactive protein (CRP) and albumin are two markers that are associated with the presence of CAD, its severity, and

cardiovascular consequences.²¹ Serum albumin possesses a number of anti-inflammatory, antioxidant, and antiplatelet activities. It plays a crucial function in fluid exchange across the vessel's wall.²² Serum albumin level was independently related to the progress of various damaging conditions such as coronary artery disease, heart failure, atrial fibrillation and stroke.²³ C-reactive protein (CRP) and albumin have also been linked to the presence of both stable and unstable CAD, CAD severity, peripheral artery disease, stroke, and poor cardiovascular outcomes in recent research.^{12,13,24} Recently, a new parameter known as the C-reactive protein to albumin (CAR) ratio has been proposed as being more useful than either CRP or albumin alone in predicting inflammatory status and prognosis in a variety of clinical contexts.^{25,26,27} To the best of our knowledge, there are very few data on the association between CAR and the severity of CAD.^{28,29,30}

Diagnosis of CAD depends on a series of investigation including electrocardiogram (ECG), exercise tolerance test, stress echocardiography, radio-isotope myocardial perfusion scanning, computed tomography scan (CT scan), coronary angiography (CAG), magnetic resonance imaging (MRI), certain cardiac markers like troponin-I, creatinine kinase, AST, LDH, myoglobin etc. The gold standard investigation to diagnose CAD is the coronary angiography.³¹ It also aids in determining the severity of CAD. The SYNTAX Score I is an angiographic tool used in grading the complexity of CAD. This SYNTAX Score I provides important information with respect to favor revascularization strategy and the prognostic significance of CAD.³²

Methods

This cross-sectional analytical study was conducted at the Department of Cardiology, Dhaka Medical College & Hospital, from July 2022 to June 2023 following ethical clearance. A total of 112 admitted patients undergoing elective coronary angiography due to chronic coronary syndrome were included in this study by convenient purposive sampling after fulfilling the inclusion and exclusion criteria. Patients with previous history of ACS, PCI / CABG, active infection, malignancies, chronic renal diseases, connective tissue disorders and pregnancy were excluded from the study. Informed written consent was taken from each participant. Socio-demographic characteristics, clinical presentation, investigation findings, and CRP/Albumin ratio were reported. Coronary angiography was performed by Shimadzu Bransist Alexa-C-12 (Ceiling mounted angiographic

machine) by percutaneous femoral or radial approach. Views were obtained for each coronary vessel in ≥ 2 projections. Analyses of the coronary angiograms were performed visually by an experienced cardiologist. The severity of the CAD was assessed by SYNTAX Score I using (<http://syntaxscore.org/>) by an experienced cardiologist. Patients were divided into two groups according to SYNTAX Score I: non-severe CAD group (SYNTAX Score I ≤ 22 , $n=56$) and severe CAD group (SYNTAX Score I >22 , $n=56$). Data were collected in separated case-record form and analyzed by SPSS 26.

Results

Table-I: Age and gender distribution of study participants ($n=112$)

Variables	Non-severe CAD ($n=56$) N(%)	Severe CAD ($n=56$) N(%)	All ($n=112$) N(%)	p-value
Age (in years)				
<40	5 (8.9)	1 (1.8)	6 (5.4)	0.09 ^a
40-49	17 (30.4)	10 (17.9)	27 (24.1)	0.10 ^a
50-59	20 (35.7)	19 (33.9)	39 (34.8)	0.84 ^a
60-69	9 (16.1)	20 (35.7)	29 (25.9)	0.02 ^a
≥ 70	5 (8.9)	6 (10.7)	11 (9.8)	0.75 ^a
Mean $\pm$ SD	52.27 $\pm$ 10.41	57.25 $\pm$ 9.34	54.76 $\pm$ 10.16	0.009 ^b
Gender				0.68 ^a
Male	40 (71.4)	38 (67.9)	78 (69.6)	
Female	16 (28.6)	18 (32.1)	34 (30.4)	

p-values were obtained by α Pearson Chi-square test and β Independent Sample T test
p-value <0.05 =significant result

Mean age of severe CAD group was significantly higher than non-severe CAD group (57.25 $\pm$ 9.34 vs 52.27 $\pm$ 10.41 years respectively, $p=0.009$).

Table-II: Body mass index of the study participants ($n=112$)

Variables	Non-severe CAD ($n=56$) N(%)	Severe CAD ($n=56$) N(%)	All ($n=112$) N(%)	p-value
BMI (in Kg/m ²)				
Underweight	8 (14.3)	4 (7.1)	12 (10.7)	0.22 ^a
Normal	17 (30.4)	14 (25.0)	31 (27.7)	0.53 ^a
Overweight	21 (37.5)	18 (32.1)	39 (34.8)	0.55 ^a
Obese	10 (17.9)	20 (35.7)	30 (26.8)	0.03 ^a
Mean $\pm$ SD	23.94 $\pm$ 4.06	26.96 $\pm$ 6.72	25.45 $\pm$ 5.73	0.005 ^b

p-values were obtained by α Pearson Chi-square test, and β Independent Sample T test
p-value <0.05 =significant result

Mean BMI of severe CAD group was significantly higher than non-severe CAD group (26.96 $\pm$ 6.72 vs 23.94 $\pm$ 4.06 kg/m² respectively, $p=0.005$). Rate of obesity was significantly higher in severe CAD (35.7% vs 17.9% in non-severe CAD, $p=0.03$).

Table-III: Distribution of risk factors among study patients ($n=112$)

Variables	Non-severe CAD ($n=56$) N(%)	Severe CAD ($n=56$) N(%)	All ($n=112$) N(%)	p-value ^a
DM	15 (26.8)	26 (46.4)	41 (36.6)	0.03
HTN	23 (41.1)	34 (60.7)	57 (50.9)	0.04
Dyslipidaemia	19 (33.9)	31 (55.4)	50 (44.6)	0.023
Smoking	28 (50.0)	21 (37.5)	49 (43.8)	0.18
Family history of CAD	14 (25.0)	13 (23.2)	27 (24.1)	0.83

p-values were obtained by α Pearson Chi-square test
p-value <0.05 =significant result

Severe CAD group had significantly higher frequency of having DM (46.4% vs 26.8%, $p=0.03$), hypertension (60.7% vs 41.1%, $p=0.04$) and dyslipidaemia (55.4% vs 33.9%, $p=0.23$) than non-severe CAD group.

Table-IV: Types of anginas among study patients ($n=112$)

Variables	Non-severe CAD ($n=56$) N(%)	Severe CAD ($n=56$) N(%)	All ($n=112$) N(%)	p-value ^a
Type of angina				
Typical	39 (69.6)	34 (60.4)	73 (65.2)	0.32
Atypical	17 (30.4)	22 (39.3)	39 (34.8)	

p-values were obtained by α Pearson chi-square test.
p-value <0.05 =significant result

Maximum study patients from both groups had typical angina (69.6% in non-severe CAD and 60.4% in severe CAD group, $p=0.32$).

Table-V: Investigation findings of the study patients (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value ^β
Haemoglobin (g/dL)	13.03±1.57	12.54±1.54	12.78±1.57	0.10
C-reactive protein (mg/dL)	0.18±0.07	0.45±0.23	0.31±0.22	<0.0001
Serum albumin (g/dL)	3.89±0.59	3.65±0.60	3.77±0.60	0.027
S. Creatinine (mg/dL)	1.03±0.28	1.05±0.27	1.04±0.27	0.66
FBS (mmol/L)	6.81±2.62	8.52±2.76	7.66±2.81	0.001
Total Cholesterol (mg/dL)	151.07±45.76	203.67±42.14	177.37±51.14	<0.0001
LDL (mg/dL)	101.92±32.90	122.29±33.22	112.11±34.47	0.001
HDL (mg/dL)	39.71±12.48	36.72±8.80	38.21±10.86	0.15
Triglyceride (mg/dL)	166.46±83.83	159.71±89.15	163.09±86.21	0.68
Ejection fraction (%)	57.07±7.76	55.84±3.87	56.46±6.13	0.29

p-values were obtained by β Independent Sample T test
p-value <0.05=significant result

Table-V illustrated the investigation findings of study patients. C-reactive protein, fasting blood sugar, total cholesterol and serum LDL were significantly higher in severe CAD group. Serum albumin was significantly lower in severe CAD group.

Table-VI: Coronary angiography findings of the study patients (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value
Vessel score				
Single	19 (33.9)	2 (3.6)	21 (18.8)	<0.0001 ^α
Double	33 (58.9)	8 (14.3)	41 (36.6)	<0.0001 ^α
Triple	4 (7.1)	46 (82.1)	50 (44.6)	<0.0001 ^α
SYNTAX Score I	11.10±6.32	30.59±6.25	20.85±11.62	<0.0001 ^β

p-values were obtained by α Pearson Chi-square test, β Independent Sample T test
p-value <0.05=significant result

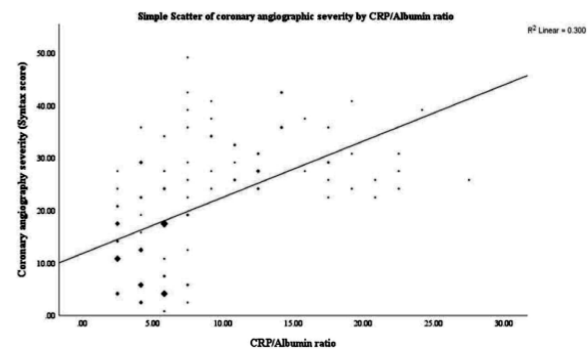
Maximum severe CAD patients had triple vessel involvement (82.1%), while maximum non- severe CAD patients had double vessel disease (58.9%) (p<0.0001).

Table-VII: CRP/Albumin ratio according to angiographic severity (n=112)

Measurements	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value ^β
Mean±SD	4.51±1.59	12.35±6.12	8.43±5.94	
Median	4.55	11.75	6.25	

p-values were obtained by β Independent Sample T test
P-value<0.05=significant result

Mean CRP/Albumin ratio was significantly higher in severe CAD group (12.35±6.12) than non- severe CAD (4.51±1.59) (p<0.001).

**Figure 1:** Correlation between CRP/Albumin ratio and SYNTAX Score I in study patients using scatter plot diagram (n=112)

Pearson correlation model showed that CRP/Albumin ratio had significant moderate positive linear association with angiographic severity by SYNTAX Score I (r = +0.55, p value <0.001).

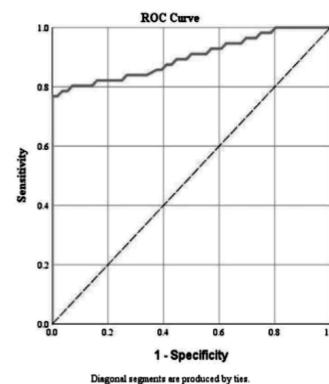
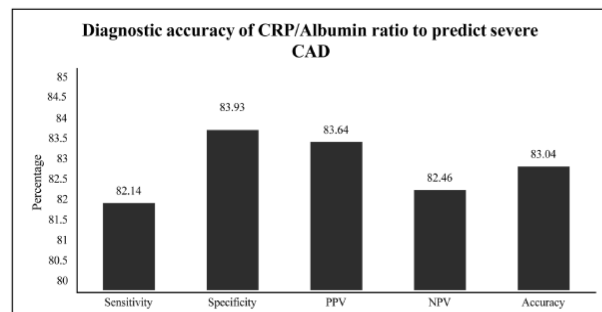
**Figure 2:** Receiver operator characteristic curve of CRP/Albumin ratio to predict severe CAD (SYNTAX Score I > 22). (n=112)

Table-VIII: Result of ROC curve.

AUC	Cut-Off value	95% CI of AUC		P-value
		Lower	Upper	
0.90	6.3	0.84	0.96	<0.001

p-value <0.05=significant result

ROC analysis of CRP/Albumin ratio in predicting severe CAD found AUC of 0.90 (95% CI 0.84-0.96) which was statistically significant ($p<0.001$). CRP/Albumin ratio >6.3 recognized as the best cut-off for severe CAD (SYNTAX Score I >22).

**Figure 3:** Diagnostic accuracy of CRP/Albumin ratio to predict severe CAD. (n=112)

A cut-off value of CRP/Albumin ratio >6.3 showed sensitivity, specificity, PPV, NPV and accuracy 82.14%, 83.93%, 83.64%, 82.46% and 83.04%, respectively to correctly predict severe CAD cases.

Table-IX: Association of CRP/Albumin ratio status with angiographic severity (n=112)

	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value
CRP/Albumin ratio cut off				<0.0001 ^a
>6.3	9 (16.1)	46 (82.1)	55 (49.1)	
≤6.3	47 (83.9)	10 (17.9)	57 (50.9)	

p-values were obtained by α Pearson Chi-square test
p-value <0.05=significant result

Maximum severe CAD patients had significantly higher rate of having CRP/Albumin ratio >6.3 in comparison to non-severe CAD group (82.1% vs 16.1% respectively, $p<0.0001$).

Table-X: Univariate logistic regression to detect odds ratio of variables for predicting severe CAD (n=112)

Predictor	COR	95% CI		p-value
		Lower	Upper	
Age ≥60 years	2.6	1.17	5.79	0.019
Obesity	2.56	1.07	6.13	0.036
Diabetes mellitus	2.37	1.07	5.23	0.033
Hypertension	2.22	1.04	4.72	0.04
Dyslipidaemia	2.42	1.13	5.18	0.024
CRP/Albumin ratio >6.3	24.02	8.94	64.52	<0.0001

p-value <0.05=significant result

Univariate logistic regression analysis shows that age ≥60 years, diabetes mellitus, hypertension, dyslipidaemia, obesity, and CRP/Albumin ratio >6.3 had significant odds ratio for predicting severe CAD in chronic stable angina patients (p value <0.05).

Table-XI: Multivariate logistic regression to detect odds ratio of variables for predicting severe CAD (n=112)

Predictor	AOR	95% CI		p-value
		Lower	Upper	
Age ≥60 years	2.56	0.77	8.52	0.13
Obesity	2.64	0.72	9.64	0.14
Diabetes mellitus	8.31	1.93	35.71	0.004
Hypertension	3.70	0.94	14.58	0.06
Dyslipidaemia	6.72	1.83	24.65	0.004
CRP/Albumin ratio >6.3	25.58	7.72	84.70	<0.0001

p-value <0.05=significant result

Multivariate logistic regression analysis showed that diabetes mellitus, dyslipidaemia, and CRP/Albumin ratio >6.3 were the significant important predictors of severe CAD in chronic stable angina patients after adjusting the confounding variables. Of all these three independent predictors, CRP/Albumin ratio >6.3 had the highest odds ratio (25.58) with highly statistical significance ($p<0.0001$).

Discussion:

In this study, the mean CRP/Albumin ratio was significantly higher in severe CAD group (12.35 ± 6.12) than non-severe CAD (4.51 ± 1.59) ($p<0.001$). CRP/Albumin ratio had significant moderate positive linear association with angiographic severity by SYNTAX Score I ($r = +0.55$, p value <0.001). Likewise, Nasr Ads et al. (2020) also found significantly higher mean of CAR (median 12.7 vs 5.6,

$p < 0.001$) in high-intermediate than low SYNTAX Score I group. They also reported a significant positive correlation between CAR and SYNTAX Score I ($r = +0.662$, $p < 0.001$).³⁰ Besides, Ghaleb, et al. (2021) also found a significant positive correlation between CAR and SYNTAX Score I ($r = +0.76$, $p < 0.0001$).²⁸ Similarly, Kalyoncuoglu and Durmus, (2020) also found that CAR had significant moderate correlation with SYNTAX Score I ($r = 0.517$, $P < 0.001$).³³ Karabag, et al. (2018) reported that patients having stable angina pectoris, for whom a diagnostic coronary angiography was done for suspected CAD, have a high significant difference regarding CAR between the high and low SYNTAX Score I groups (median 5.4 vs 2.7; $p < .001$).²⁹ In accordance with our study findings, Hasnat, et al. (2010) and Ahmed, et al. (2012) found a significant positive correlation between CRP and angiographic severity.^{34,35}

In this research project, a cut-off value of CRP/Albumin ratio > 6.3 showed sensitivity, specificity, PPV, NPV and accuracy 82.14%, 83.93%, 83.64%, 82.46% and 83.04%, respectively to correctly predict severe CAD cases. Similarly, Karabag, et al. (2018) also reported that CAR > 6.3 had 86.8% sensitivity and 43.4% specificity to correctly predict SYNTAX Score I > 22 in stable angina patients.²⁹ Nasr Ads, et al. (2020) found a cut-off value of CRP/Albumin ratio > 7.2 had 93% sensitivity and 85% specificity.³⁰

In our study, multivariate logistic regression analysis found that CRP/Albumin ratio > 6.3 was the significant independent predictors of severe CAD in chronic coronary syndrome patients (AOR=25.58, 95%CI: 7.72-84.70, $p < 0.0001$). Similarly, Karabag, et al. (2018) also observed that CAR (AOR 1.29; 95% CI: 1.128- 1.475; $p < .001$) was found to be independently associated with high SYNTAX Score I after potential confounding factors were adjusted.²⁹ According to the study by Ghaleb, et al. (2021), multivariate regression analysis revealed that CAR was an independent predictor of intermediate-high SS group (AOR 3.36; 95% CI: 1.143- 7.90; $p = 0.005$).²⁸ Moreover, multivariate regression analysis from the study of Nasr, Ads et al. (2020) also revealed that CAR was an independent predictor of intermediate-high SS group (AOR 3.7; 95% CI: 1.92- 7.13; $p < 0.001$).³⁰ These findings are also supported by Kalyoncuoglu and Durmus, (2020).³³

In the present study, the mean age of severe CAD group was significantly higher than non-severe CAD group (57.25 ± 9.34 vs 52.27 ± 10.41 years respectively, $p = 0.009$). Similarly, Karabag, et al. (2018) also noticed that patients with

intermediate-high SYNTAX Score I (> 22) group were older than patients having SYNTAX Score I ≤ 22 .²⁹ Several previous studies also reported that angiographic severity had significant association with increased age.^{28,33} Aging is associated with cellular oxidative stress, inflammation, and shifts in gene expression that contribute to increased vascular stiffness, endothelial dysfunction, and thrombogenicity, and hence aging is the important non- modifiable risk factors of coronary artery diseases and also a predictor of poor outcomes.³⁶

In this study, the mean BMI of severe CAD group was also significantly higher than non- severe CAD group (26.96 ± 6.72 vs 23.94 ± 4.06 kg/m² respectively, $p = 0.005$). Rate of obesity was significantly higher in severe CAD (35.7% vs 17.9% in non-severe CAD, $p = 0.03$). Studies have indicated that adipocytokines and their pro-inflammatory cytokines have significantly affected the development of cardiovascular disease in obese subjects.³⁷

In this study, severe CAD group had significantly higher frequency of having DM (46.4% vs 26.8%, $p = 0.03$), hypertension (60.7% vs 41.1%, $p = 0.04$) and dyslipidaemia (55.4% vs 33.9%, $p = 0.23$) than non-severe CAD group. Fasting blood sugar, total cholesterol and serum LDL were significantly higher in severe CAD group. Besides, multivariate logistic regression analysis found diabetes mellitus and dyslipidaemia as the significant independent predictors of severe CAD in chronic stable angina patients. Similarly, Ghaleb, et al. (2021) also found that high-intermediate SYNTAX Score I group had significantly higher frequency of having DM (52% vs 32%, $p = 0.04$) and hypertension (68% vs 38%, $p = 0.003$), as well as higher mean of fasting blood sugar, total cholesterol and serum LDL in high-intermediate SYNTAX Score I group than low SYNTAX Score I group.²⁸ Similarly, Karabag, et al. (2018) also noticed that patients with intermediate-high SYNTAX Score I (> 22) group had a higher prevalence of hypertension and diabetes mellitus and higher mean of LDL cholesterol and triglyceride level compared to low SYNTAX Score I group. They also found that dyslipidaemia was significantly associated with high SYNTAX Score I after potential confounding factors were adjusted in multivariate logistic regression.²⁹ Several other previous studies also determine the significant relationship between hypertension, dyslipidaemia and CAD severity.^{30,38,39}

The observations of the present study compared with those



of the several other investigators from home and abroad discussed above, expresses the CAR as significantly associated with angiographic severity of CAD assessed by SYNTAX Score I in chronic coronary syndrome patients. The identification of high risk CAD patients might be useful in clinical practice leading to more intensive treatment of modifiable cardiovascular risk factors and early coronary angiogram.

Conclusion:

The results of this study showed a significant moderate positive linear association of CRP/Albumin ratio with angiographic severity by SYNTAX Score I in patients with chronic coronary syndrome. $CAR > 6.3$ was found to be best cut-off to correctly predict severe CAD cases. Additionally, CAR, diabetes mellitus and dyslipidaemia were the important predictors for severe CAD.

Limitations:

All samples were collected from a single site. Coronary angiography was assessed by visual observation, intravascular ultrasonography was not used, so there was every chance of inter observer variation.

Recommendations:

Further multicenter studies with larger sample size and more generalized sample population are recommended. CRP/Albumin ration can be useful to predict a group of chronic coronary syndrome patients, who are likely to have severe CAD and hence needs early CAG and intervention.

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Association of Platelet Lymphocyte Ratio with Angiographic Severity of Coronary Artery Disease in Patients with Chronic Coronary Syndrome

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Abstract

Background: The number of coronary artery disease (CAD) patients is increasing day by day in Bangladesh. Chronic coronary syndrome (CCS) increases the risk of having serious cardiovascular events (CVEs) by two times. Predicting the occurrence of these CVEs or CAD severity by low- cost noninvasive or hematological test is an area of interest now a days. Several studies have postulated platelet-to-lymphocyte ratio as a predictive factor of CAD severity. This study was conducted to determine the association of platelet lymphocyte ratio with angiographic severity of CAD in patient with CCS.

Methods: This cross-sectional analytical study was conducted at the Department of Cardiology, Dhaka Medical College & Hospital, for a period of 12 months following ethical clearance. A total of 112 admitted patients undergoing elective coronary angiography due to chronic coronary syndrome were included in this study after taking informed written consent. Patients were divided into two groups according to SYNTAX score I: non-severe CAD group (SYNTAX Score I ≤ 22 , n=56) and severe CAD group (SYNTAX Score I >22 , n=56). Socio-demographic characteristics, clinical presentation, investigation findings, platelet lymphocyte ratio and angiographic severity by SYNTAX Score I were reported. Data were collected in separated case-record form and analyzed by SPSS 26.

Results: The mean age of severe CAD group was significantly higher than non-severe CAD group (57.25 ± 9.34 vs 52.27 ± 10.41 years respectively, $p=0.009$). Severe CAD group had significantly higher frequency of having DM (46.4% vs 26.8%, $p=0.03$), hypertension (60.7% vs 41.1%, $p=0.04$) and dyslipidaemia (55.4% vs 33.9%, $p=0.23$) than non- severe CAD group. Fasting blood sugar, total cholesterol and serum LDL were significantly higher in severe CAD group. The mean PLR was significantly higher in severe CAD group (167.13 ± 41.95) than non-severe CAD (105.77 ± 22.49) ($p<0.001$). PLR had significant moderate positive linear association with angiographic severity by SYNTAX Score I ($r=+0.53$, $p\text{-value} <0.001$). A cut-off value of $\text{PLR} > 119$ showed sensitivity, specificity, PPV, NPV and accuracy 83.93%, 69.64%, 73.44%, 81.25% and 76.79%, respectively to correctly predict severe CAD cases. Multivariate logistic regression analysis found that $\text{PLR} > 119$ was an important predictor of severe CAD in chronic coronary syndrome patients (AOR=16.73, 95%CI: 4.32-64.80, $p<0.001$).

Conclusion: Platelet/lymphocyte ratio had significant positive association with angiographic severity of coronary artery disease in patients with chronic coronary syndrome. However, further larger study is recommended.

Keywords: Chronic coronary syndrome, SYNTAX score I, Platelet Lymphocyte Ratio.

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Introduction

Chronic stable angina is a common manifestation of coronary artery disease (CAD), which is the leading cause of death worldwide.¹ When symptoms like chest, neck, or left arm discomfort persist for at least two months without changing in character, severity, or triggering situations, chronic stable angina is identified.² Chronic stable angina is now coined as chronic coronary syndrome. It almost doubles the chances of having a severe cardiovascular event (CVEs).³ It has been projected that cardiovascular mortality will increase from 18.1 million in 2010 to 24.2 million by year 2030.⁴

South Asians that are individuals originally from India, Pakistan, Nepal, Sri Lanka and Bangladesh, have a high prevalence of CAD and associated risk factors. The exact prevalence of CAD in Bangladesh is not known. Only limited number of small-scale epidemiological studies is available. Probably the prevalence of CAD was first reported in 1976, which was 0.33%.⁵ More recent data indicates CAD prevalence between 1.85%⁶ and 3.4% in rural and 19.6% in urban sample of working professionals.^{7,8} Despite marked disparity in values, there seems to be a rising prevalence of CAD in Bangladesh.

Previous studies demonstrated an association between major adverse cardiovascular outcomes and higher platelet and lower lymphocyte counts.⁹ The platelet to-lymphocyte ratio (PLR) has recently been investigated as a new inflammatory marker and predictor of major adverse outcomes in various cardiovascular diseases.^{10,11,12} PLR is a significant independent predictor of long-term mortality after non-ST elevated acute coronary syndrome (NSTEMI).¹³ In a recently published study, high pre-procedural PLRs were found to be significant and independent predictors of no reflow in patients with ST elevated acute coronary syndrome (STEMI).⁹ Because it is well known that inflammatory response is closely associated with the pathogenesis of coronary atherosclerosis, we aimed to investigate the usefulness of PLR in predicting severity and complexity of coronary atherosclerosis as assessed by the Syntax score in patients with ACS who underwent urgent coronary angiography (CA).

Previously, an association was found between high circulating platelet count and major adverse cardiovascular outcomes in patients with coronary artery disease (CAD) and also in healthy adults.^{14,15,16} Platelet to-lymphocyte ratio (PLR) is a new prognostic marker that integrates the risk prediction of these 2 parameters into 1. It gives an idea about both the aggregation and inflammation pathways, and it may be more valuable than either platelet or lymphocyte count alone in

the prediction of coronary atherosclerotic burden. PLR was found to be useful in predicting poor prognosis in cancer population^{17,18,19} and in predicting critical limb ischemia in peripheral artery disease¹¹ previously. Moreover, higher PLR value emerged as a significant independent predictor of long-term survival in patients presented with acute coronary syndrome and as an independent predictor of no-reflow development in patients undergoing primary PCI.¹³ In line with these findings, a high PLR tertile of a recent study population that presented with STEMI showed poorer outcomes compared to the low PLR group, and PLR was found to be an independent predictor of in-hospital mortality in patients with STEMI.²⁰

The SYNTAX score is an angiographic tool used in grading the complexity of CAD. This SYNTAX score provides important information with respect to favour revascularization strategy and the prognostic significance of CAD.²¹ It is an angiographic index used in grading the complexity of CAD. Each coronary lesion with a diameter stenosis of at least 50%, in vessels at least 1.5 mm, was scored. The online latest updated version (2.1) was used for the calculation of the SYNTAX scores ([www.syntaxscore.com](http://syntaxscore.com)).²²

Methods

This cross-sectional analytical study was conducted at the Department of Cardiology, Dhaka Medical College & Hospital, from July 2022 to June 2023 following ethical clearance. A total of 112 admitted patients undergoing elective coronary angiography due to chronic coronary syndrome were included in this study by convenient purposive sampling after fulfilling the inclusion and exclusion criteria. Patients with previous history of ACS, PCI / CABG, congestive heart failure, chronic obstructive pulmonary disease, active infection, haematopoietic stem cell disorders, malignancies, chronic renal disease, chronic liver disease, connective tissue disorders and pregnancy were excluded from the study. Informed written consent was taken from each participant. Socio-demographic characteristics, clinical presentation, investigation findings, and platelet lymphocyte ratio were reported. Coronary angiography was performed by Shimadzu Bransist Alexa-C-12 (Ceiling mounted angiographic machine) by percutaneous femoral or radial approach. Views were obtained for each coronary vessel in ≥ 2 projections. Analysis of the coronary angiograms were performed visually by an experienced cardiologist. The severity of the CAD was assessed by SYNTAX Score I using (<http://syntaxscore.org/>)



by an experienced cardiologist. Patients were divided into two groups according to SYNTAX Score I: non-severe CAD group (SYNTAX Score I ≤ 22 , n=56) and severe CAD group (SYNTAX Score I > 22 , n=56). Data were collected in separated case-record form and analyzed by SPSS 26.

Results:

Table-I: Age and gender distribution of study participants (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value
Age group (in years)				
<40	5 (8.9)	1 (1.8)	6 (5.4)	0.09 ^a
40-49	17 (30.4)	10 (17.9)	27 (24.1)	0.10 ^a
50-59	20 (35.7)	19 (33.9)	39 (34.8)	0.84 ^a
60-69	9 (16.1)	20 (35.7)	29 (25.9)	0.02 ^a
≥ 70	5 (8.9)	6 (10.7)	11 (9.8)	0.75 ^a
Mean $\pm$ SD	52.27 $\pm$ 10.41	57.25 $\pm$ 9.34	54.76 $\pm$ 10.16	0.009 ^b
Gender				
Male	40 (71.4)	38 (67.9)	78 (69.6)	0.68 ^a
Female	16 (28.6)	18 (32.1)	34 (30.4)	

P value < 0.05 is significant

p-values were obtained by α Pearson Chi-square test and β Independent Sample T test

Mean age of the study patients was 54.76 $\pm$ 10.16 years with male predominance in both groups (71.4% in non-severe CAD and 67.9% in severe CAD group, p=0.68). Mean age of severe CAD group was significantly higher than non-severe CAD group (57.25 $\pm$ 9.34 vs 52.27 $\pm$ 10.41 years respectively, p=0.009).

Table-II: Body mass index of the study participants (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value
BMI (in Kg/m²)				
Underweight	8 (14.3)	4 (7.1)	12 (10.7)	0.22 ^a
Normal	17 (30.4)	14 (25.0)	31 (27.7)	0.53 ^a
Overweight	21 (37.5)	18 (32.1)	39 (34.8)	0.55 ^a
Obese	10 (17.9)	20 (35.7)	30 (26.8)	0.03 ^a
Mean $\pm$ SD	23.94 $\pm$ 4.06	26.96 $\pm$ 6.72	25.45 $\pm$ 5.73	0.005 ^b

P value < 0.05 is significant

p-values were obtained by α Pearson Chi-square test, and β Independent Sample T test

Mean BMI of severe CAD group was significantly higher than non-severe CAD group (26.96 $\pm$ 6.72 vs 23.94 $\pm$ 4.06 kg/m² respectively, p=0.005). Rate of obesity was significantly higher in severe CAD (35.7% vs 17.9% in non-severe CAD, p=0.03)

Table-III: Distribution of risk factors among study patients (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value ^a
DM	15 (26.8)	26 (46.4)	41 (36.6)	0.03
HTN	23 (41.1)	34 (60.7)	57 (50.9)	0.04
Dyslipidaemia	19 (33.9)	31 (55.4)	50 (44.6)	0.023
Smoking	28 (50.0)	21 (37.5)	49 (43.8)	0.18
Family history of CAD	14 (25.0)	13 (23.2)	27 (24.1)	0.83

P value < 0.05 is significant

p-values were obtained by α Pearson Chi-square test.

Severe CAD group had significantly higher frequency of DM (46.4% vs 26.8%, p=0.03), hypertension (60.7% vs 41.1%, p=0.04) and dyslipidaemia (55.4% vs 33.9%, p=0.23) than non-severe CAD group. However, smoking history and family history of CAD had no significant association with angiographic severity of CAD (p>0.05).

Table-IV: Types of anginas among study patients (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value ^a
Type of angina				
Typical	39 (69.6)	34 (60.4)	73 (65.2)	0.32
Atypical	17 (30.4)	22 (39.3)	39 (34.8)	

P value < 0.05 is significant

p-values were obtained by α Pearson chi-square test.

Maximum study patients from both groups had typical angina (69.6% in non-severe CAD & 60.4% in severe CAD group, p=0.32).

Table-V: Haematological findings of the study patients (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value ^b
Haemoglobin (g/dL)	13.03 $\pm$ 1.57	12.54 $\pm$ 1.54	12.78 $\pm$ 1.57	0.10
Total WBC count (x10 ⁹ /L)	10.52 $\pm$ 3.69	11.99 $\pm$ 4.08	11.256 $\pm$ 3.94	0.048
Platelet count (x10 ⁹ /L)	218.86 $\pm$ 79.69	250.21 $\pm$ 69.40	234.54 $\pm$ 76.03	0.028
Absolute neutrophil count (x10 ⁹ /L)	8.05 $\pm$ 3.65	9.92 $\pm$ 3.82	8.99 $\pm$ 3.84	0.009
Absolute lymphocyte count (x10 ⁹ /L)	2.05 $\pm$ 0.51	1.54 $\pm$ 0.39	1.80 $\pm$ 0.52	<0.0001

P value < 0.05 is significant

p-values were obtained by β Independent Sample T test

Table-V showed that the total WBC count, platelet count, and absolute neutrophil count were significantly higher in severe CAD group. Absolute lymphocyte count was significantly lower in severe CAD group.

Table-VI: Biochemical and echocardiography findings of the study patients (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value β
S. Creatinine (mg/dL)	1.03 $\pm$ 0.28	1.05 $\pm$ 0.27	1.04 $\pm$ 0.27	0.66
FBS (mmol/L)	6.81 $\pm$ 2.62	8.52 $\pm$ 2.76	7.66 $\pm$ 2.81	0.001
Total Cholesterol (mg/dL)	151.07 $\pm$ 45.76	203.67 $\pm$ 42.14	177.37 $\pm$ 51.14	<0.0001
LDL (mg/dL)	101.92 $\pm$ 32.90	122.29 $\pm$ 33.22	112.11 $\pm$ 34.47	0.001
HDL (mg/dL)	39.71 $\pm$ 12.48	36.72 $\pm$ 8.80	38.21 $\pm$ 10.86	0.15
Triglyceride (mg/dL)	166.46 $\pm$ 83.83	159.71 $\pm$ 89.15	163.09 $\pm$ 86.21	0.68
Ejection fraction (%)	57.07 $\pm$ 7.76	55.84 $\pm$ 3.87	56.46 $\pm$ 6.13	0.29 β

p-value < 0.05 is significant

p-values were obtained by β Independent Sample T test

Table-VI showed that the fasting blood sugar, total cholesterol and serum LDL were significantly higher in severe CAD group. However, other investigation markers were statistically similar in both groups as p>0.05.

Table-VII: Coronary angiography findings of the study patients (n=112)

Variables	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value
Vesselscore				
Single	19(33.9)	2(3.6)	21(18.8)	<0.0001 α
Double	33(58.9)	8(14.3)	41(36.6)	<0.0001 α
Triple	4(7.1)	46(82.1)	50(44.6)	<0.0001 α
SYNTAX Scoreβ	11.10 $\pm$ 6.32	30.59 $\pm$ 6.25	20.85 $\pm$ 11.62	<0.0001 β

p-values were obtained by α Pearson Chi-square test, β

Independent Sample T test

p-value<0.05 = significant result

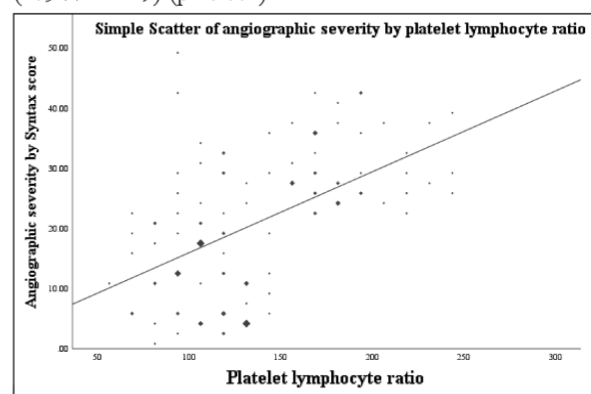
Maximum severe CAD patient had triple vessel involvement (82.1%), while maximum non-severe CAD patients had double vessel disease (58.9%) (p<0.0001).

Table-VIII: Platelet lymphocyte ratio according to angiographic severity (n=112)

Measurements	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value β
Mean $\pm$ SD	105.77 $\pm$ 22.49	167.13 $\pm$ 41.95	136.45 $\pm$ 45.52	<0.0001
Median	107	170	126	

p-values were obtained by β Independent Sample T test
P value < 0.05 is significant

Mean platelet lymphocyte ratio was significantly higher in severe CAD group (167.13 $\pm$ 41.95) than non-severe CAD (105.77 $\pm$ 22.49) (p<0.001).

**Fig. 1:** Correlation between platelet lymphocyte ratio and Syntax score in study patients using scatter plot diagram (n=112)

Pearson correlation model showed that platelet lymphocyte ratio had significant moderate positive linear association with angiographic severity by Syntax score ($r=+0.53$, p value <0.001).

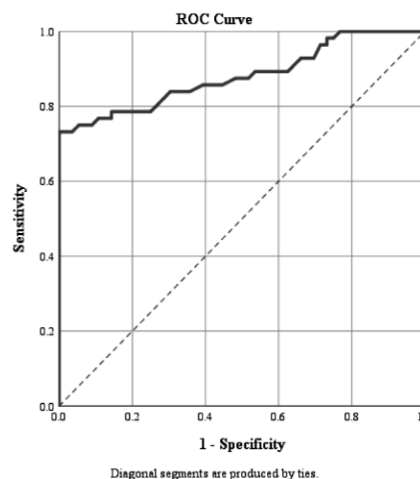
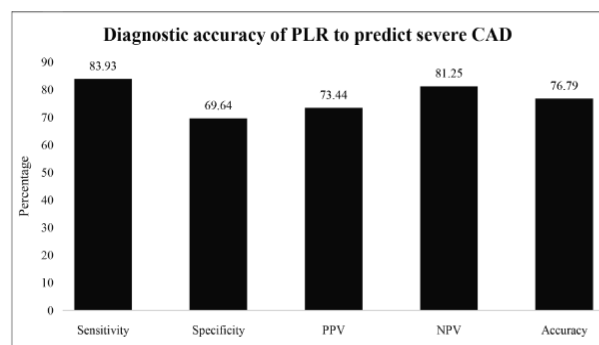
**Fig. 2:** Receiver operator curve of platelet lymphocyte ratio to predict severe CAD (SYNTAX score $\geq$ 23). (n=112)

**Table-IX:** Result of ROC curve

AUC	Cut-Off value	95% CI of AUC		P-value
		Lower	Upper	
0.881	119	0.82	0.95	<0.001

P value < 0.05 is significant

ROC analysis of platelet lymphocyte ratio in predicting severe CAD found AUC of 0.881 (95% CI 0.82-0.95) which was statistically significant ($p < 0.001$). Platelet lymphocyte ratio >119 recognized as the best cut-off for severe CAD (SYNTAX score ≥ 23).

**Fig. 3:** Diagnostic accuracy of platelet lymphocyte ratio to predict severe CAD. (n=112)

A cut-off value of platelet lymphocyte ratio >119 showed sensitivity, specificity, PPV, NPV and accuracy 83.93%, 69.64%, 73.44%, 81.25% and 76.79%, respectively to correctly predict severe CAD cases.

Table-X: Association of PLR status with angiographic severity (n=112)

	Non-severe CAD (n=56) N(%)	Severe CAD (n=56) N(%)	All (n=112) N(%)	p-value
PLR cut off				<0.0001 ^a
>119	17 (30.4)	47 (83.9)	64 (57.1)	
≤119	39 (69.6)	9 (16.1)	48 (42.9)	

p-value < 0.05 is significant

p-values were obtained by α Pearson Chi-square test

Maximum severe CAD patients had significantly higher rate of having platelet lymphocyte ratio >119 in comparison to non-severe CAD group (83.9% vs 30.4% respectively, $p < 0.0001$).

Table-XI: Univariate logistic regression to detect odds ratio of variables for predicting severe CAD (n=112)

Predictor	COR	95% CI		p-value
		Lower	Upper	
Age ≥ 60 years	2.6	1.17	5.79	0.019
Obesity	2.56	1.07	6.13	0.036
Diabetes mellitus	2.37	1.07	5.23	0.033
Hypertension	2.22	1.04	4.72	0.04
Dyslipidaemia	2.42	1.13	5.18	0.024
PLR > 119	11.98	4.81	29.84	<0.0001

p-value < 0.05 = significant result

Univariate logistic regression analysis shows that age ≥ 60 years, diabetes mellitus, hypertension, dyslipidaemia, obesity, and PLR >119 had significant odds ratio for predicting severe CAD in chronic stable angina patients (p value < 0.05).

Table-XII: Multivariate logistic regression to detect odds ratio of variables for predicting severe CAD (n=112)

Predictor	AOR	95% CI		p-value
		Lower	Upper	
Age ≥ 60 years	2.28	0.80	6.46	0.12
Obesity	1.03	0.34	3.10	0.96
Diabetes mellitus	8.25	3.97	28.89	0.01
Hypertension	4.24	1.08	16.67	0.039
Dyslipidaemia	3.59	1.56	11.13	0.027
PLR > 119	16.73	4.32	64.80	<0.0001

P value < 0.05 is significant

AOR=Adjusted odds ratio, CI= confidence interval, EF=ejection fraction

Multivariate logistic regression analysis showed that diabetes mellitus, hypertension, dyslipidaemia and PLR >119 were the significant independent predictors of severe CAD in chronic stable angina patients after adjusting the confounding variables. Of all these three independent predictors, PLR >119 had the highest odds ratio (16.73) with highly statistical significance ($p < 0.0001$).

Discussion

The Syntax score is an anatomic scoring system based on coronary angiogram that quantifies lesion severity and

complexity and predicts poor cardiovascular outcomes, including mortality.^{23,24} Previous studies have demonstrated that higher platelet and lower lymphocyte counts are associated with poor clinical outcomes in various cardiovascular diseases.^{14,25} In recent years, PLR has been investigated as a simple a feasible new prognostic inflammatory marker for adverse cardiovascular outcomes in many types of cardiovascular diseases.^{10,12,13} This study aimed to determine the association of platelet lymphocyte ratio with angiographic severity of coronary artery disease (CAD) in chronic coronary syndrome patients. A total of 112 admitted chronic coronary syndrome patients undergoing elective coronary angiography were included in this study, and equally divided into two groups according to Syntax score: non-severe CAD (Syntax score ≤ 22) and severe CAD (Syntax score >22), as previous studies demonstrated that Syntax score >22 was associated with a higher in-hospital mortality rate.⁹

In our current study, mean age of severe CAD group was significantly higher than non-severe CAD group (57.25 ± 9.34 vs 52.27 ± 10.41 years respectively, $p=0.009$). Similarly, Karabag et al. (2018) also noticed that patients with intermediate-high syntax score (>22) group were older than patients having syntax score <22 .²⁶ Similarly, Abd Elaal et al. (2021) also observed that patients with intermediate-high syntax score (>22) had significantly older than patients having syntax score <22 (59.72 ± 3.43 vs 55.12 ± 3.49 years, $p=0.0003$).²⁷ Several previous studies also reported that angiographic severity had significant association with increased age.^{9,28,29} Aging is associated with cellular oxidative stress, inflammation, and shifts in gene expression that contribute to increased vascular stiffness, endothelial dysfunction, and thrombogenicity, and hence aging is the important non-modifiable risk factors of coronary artery diseases and also a predictor of poor outcomes.³⁰

In this study, severe CAD group had significantly higher frequency of having DM (46.4% vs 26.8%, $p=0.03$), hypertension (60.7% vs 41.1%, $p=0.04$) and dyslipidaemia (55.4% vs 33.9%, $p=0.23$) than non-severe CAD group. Fasting blood sugar, total cholesterol and serum LDL were significantly higher in severe CAD group. Besides, multivariate logistic regression analysis found diabetes mellitus, hypertension, and dyslipidaemia as the significant independent predictors of severe CAD in chronic stable angina patients. Likewise, Nasr Ads et al. (2020) also found that high-intermediate Syntax score group had significantly higher frequency of having DM (54% vs 32%, $p=0.03$) and hypertension (66% vs 40%, $p<0.01$) than low Syntax score

group. They also found significantly higher mean of total cholesterol (205.24 ± 40.04 vs 184 ± 35.28 mg/dL, $p<0.006$) and serum LDL (110.7 ± 36.6 vs 92.12 ± 16.82 mg/dL, $p<0.001$) in high-intermediate than low Syntax score group.³¹ Furthermore, Karabag et al. (2018) also noticed that patients with intermediate-high syntax score (>22) group had a higher prevalence of hypertension and diabetes mellitus and higher mean of LDL cholesterol and triglyceride level compared to low syntax score group. They also found that hypertension and dyslipidaemia were found to be associated with high syntax score after potential confounding factors were adjusted in multivariate logistic regression.²⁶ Several other previous studies also determine the significant relationship between hypertension, dyslipidaemia, and CAD severity.^{27,32,33,34}

In our research project, the mean platelet lymphocyte ratio was significantly higher in severe CAD group (167.13 ± 41.95) than non-severe CAD (105.77 ± 22.49) ($p<0.001$). Pearson correlation model showed that platelet lymphocyte ratio had significant moderate positive linear association with angiographic severity by Syntax score ($r = +0.53$, p value <0.001). Similarly, Kurtul et al. (2014) also found significantly higher mean of PLR in severe CAD than non-severe CAD group (172 ± 93 vs 104 ± 43 , $p<0.001$). They also reported a significant positive correlation between PLR and Syntax score ($r=+0.422$, $p<0.001$).⁹ The mechanisms of the relation between PLR and Syntax score are not clear. One of the possible mechanisms may be an increased inflammatory response. This study found a higher mean of CRP level and neutrophil count in severe CAD group. Besides, higher platelet counts may also reflect underlying inflammation, as several inflammatory mediators stimulate megakaryocytic proliferation and produce relative thrombocytosis. On the other side, lymphocytes represent a quiescent and controlling inflammatory pathway. Consequently, in our study population, higher PLR may indicate increased inflammatory response, which is related to the extent and complexity of coronary atherosclerosis. In addition, the underlying mechanism may also be associated with excess thrombotic status. The presence of thrombi in the coronary arteries increases Syntax scores in patients with chronic coronary syndrome. It has been speculated that a higher platelet count is a marker of prothrombotic status.³⁵ In addition, high platelet counts may represent higher propensity to form platelet-rich thrombi on atherosclerotic plaques, leading to worse outcomes. Elevated PLR may indicate excess thrombotic status, which contributes to higher Syntax score.



In this study, a cut-off value of platelet lymphocyte ratio >119 showed sensitivity, specificity, PPV, NPV and accuracy 83.93%, 69.64%, 73.44%, 81.25% and 76.79%, respectively to correctly predict severe CAD cases. Besides, multivariate logistic regression analysis showed that PLR >119 was the significant independent predictors of severe CAD in chronic stable angina patients with an odds ratio of 16.73. Similarly, Kurtul et al. (2014) also reported that PLR >116 had 71% sensitivity and 66% specificity to correctly predict severe CAD. They also observed that PLR (AOR 1.018; 95% CI: 1.01- 1.02; $p < .001$) was independently associated with high Syntax score after potential confounding factors were adjusted.⁹ Besides, Ayca et al. (2015) found a cut-off value of PLR >137 had 61% sensitivity and 52% specificity. In their study, multivariate regression analysis also revealed that PLR was an independent predictor of severe CAD (AOR 2.94; 95% CI: 1.65- 5.26; $p < 0.001$).²⁹

Conclusion

The study results showed that Platelet/lymphocyte ratio had significant positive association with angiographic severity of coronary artery disease in patients with chronic stable angina. Chronic stable angina with PLR >119 was found to be best cut-off to correctly predict severe CAD cases. PLR, hypertension, diabetes mellitus and dyslipidaemia are the independent predictors for severe CAD. Platelet/lymphocyte ratio measurement is a cheap and simple test. Hence, it can be a useful tool for early risk stratification in patients with chronic stable angina. Patients with chronic stable angina with PLR > 119 warrant more attention by physicians and cardiologist in terms of more aggressive medical and interventional management.

Limitations

Because of the single-center non-randomized design, the study findings could not be generalized. Coronary angiography was assessed by visual observation, intravascular ultrasonography was not used, so there was every chance of interobserver variation. Only one entity of coronary artery disease has been included in this study, other entities need to be evaluated. PLR was based on a single measurement. It would be interesting to know if the PLR changes over time and if the PLR on subsequent tests remains a predictor of the severity of coronary disease.

Recommendations

Further multicenter based prospective study needed to assess the causal association between PLR and severity of coronary artery disease in chronic stable angina.

Platelet/lymphocyte ratio can be used for risk stratification in patients with chronic stable angina. Platelet/lymphocyte ratio predict severity of coronary artery disease which help to identify individual at high risk of severe coronary artery disease and guide physician, cardiologist to follow and making decision regarding aggressive medical and interventional management.

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Drug Eluting Technology in Drug Eluting Coronary Stent - Review Article

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Abstract

Drug eluting technics used in drug eluting stent includes drug with polymer and drug without polymer. Polymer may be durable or biodegradable. Developing bioresorbable polymers to improve biocompatibility and facilitate the endothelialization process. Conformal coating stent has larger area of polymer compared to abluminal coating stent. Abluminal thin coating stent allows targeting release of the drug to coronary vessel wall, lower drug dosage can achieve similar tissue concentration and less drug enables fast healing and potentially brings more safety of the device. Polymers used in stents can be avoided by eliminating the polymer coating completely and releasing the antiproliferative drug directly from the stent surface. To address this issue, stent manufacturers have adopted different approaches to decrease the elution rate. These approaches can be roughly separated into five categories: smooth surface, macroporous, microporous, nanoporous and drug-filled stents. Drug-filled stents are a new and promising technology that allows the drug to be eluted from inside the stent through holes laser drilled on the abluminal side. Unique groove-based technology, the stent offers targeted drug delivery directly to lesion sites, minimizing systemic exposure and enhancing patient safety, this innovative stent may significantly reduce restenosis rates, ensuring superior long-term outcomes need further investigation.

Introduction

Drug-eluting stents (DES) are the standard of care in the percutaneous treatment of ischemic coronary artery disease (CAD)^{1,2}. The promises of improved safety and efficacy of DES with biodegradable-compared to durable-polymer coatings have not born out in the short term. Failure of durable-polymer DES occurs over time and has been characterized by delayed vessel healing, neoatherosclerosis formation, and associated late repeat revascularization and late and very late stent thrombosis³⁻⁵. Whether modifying the drug/biodegradable-polymer kinetics of a DES can improve clinical outcomes in the long term is controversial⁶⁻⁹.

A drug-eluting stent is an implantable device that releases bioactive agents into blood vessels to limit the growth of abnormal tissue and improve long-term outcomes for restenosis in coronary arteries.

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Drug eluting technics in drug eluting stent includes drug with polymer and drug without polymer. Polymer may be durable or biodegradable. Conformal coating stent has larger area of polymer compared to abluminal coating stent. Abluminal thin coating stent allows targeting release of the drug to coronary vessel wall, lower drug dosage can achieve similar tissue concentration and less drug enables fast healing and potentially brings more safety of the device. Polymers used in stents can be avoided by eliminating the polymer coating completely and releasing the antiproliferative drug directly from the stent surface. To address this issue, stent manufacturers have adopted different approaches to decrease the elution rate. These approaches can be roughly separated into five categories: smooth surface, microporous, microporous, nanoporous and drug-filled stents. Drug-filled stents are a new and promising technology that allows the drug to be eluted from inside the stent through holes laser drilled on the abluminal side. Unique groove-based technology, the stent offers targeted drug delivery directly to lesion sites, minimizing systemic exposure and enhancing patient safety, this innovative stent significantly reduces restenosis rates, ensuring superior long-term outcomes.

Components of DES

Drug-eluting stents (DESs) use a combination of a drug and a polymer carrier to prevent restenosis and other

complications. The drug is designed to inhibit the proliferation of smooth muscle cells, which can lead to restenosis. Some examples of drugs used in DESs include sirolimus and paclitaxel.

The polymer carrier controls the release of the drug into the surrounding tissue. The polymer is crucial for ensuring that the drug is released in a sustained manner to match the kinetics of restenosis.

The stent platform prevents recoil and fibrous constrictive remodeling. DESs are typically made from metal alloys, such as stainless steel or cobalt-chromium.

The first FDA-approved DESs were Cypher and Taxus, which were released in 2002 and 2003. DESs have been shown to outperform bare-metal stents (BMSs) in terms of restenosis and target lesion revascularization (TLR) rates, particularly in the first year after implantation.

However, there are still some shortcomings with DESs, and new approaches are needed to improve their safety and efficacy. Some of these approaches include:

Developing bioresorbable polymers to improve biocompatibility and facilitate the endothelialization process. Using polymer-free stents where the drug is directly coated on the stent or contained in reservoirs within the stent.

Ideal drug eluting stent

The ideal DES should incorporate a number of newer and improved materials and delivery systems to enhance safety, efficacy and cost-efficiency. The ideal system should include:¹⁰

- A very low-profile stent delivery system
- High flexibility and conformability due to a hybrid open-cell design
- Thinner struts
- Adequate radiopacity and radial strength
- A high-pressure balloon that is suitable for direct stenting
- Minimal late loss (≤ 0.2 mm)
- A-limus drug.
- Drug-elution for 60-90 days, followed by complete absence of drug release
- Stimulation of early re-endothelialisation
- A thrombus-resistant luminal surface
- A very thin surface of durable or biodegradable polymer coating
- A minimal duration of DAPT

Bioresorbable stent

The biodegradable stents made from materials that dissolve over time in the body. They are also known as bioresorbable stents (BRS). BRS technology is considered important revolution in interventional cardiology.

Benefits of BRS include:

Reduced risk of thrombosis: BRS technology can significantly reduce the risk of early and late thrombosis.

Scaffolding: BRS scaffolds prevent acute vessel closure or recoil.

Antiproliferative drugs: BRS elute antiproliferative drugs to inhibit neointimal hyperplasia and constrictive remodeling.

However, some concerns about BRS include:

Strut thickness

Thicker struts can increase the risk of subacute thrombosis and delay full neointimal coverage.

Long-term results

While there is no evidence to doubt the benefits of BRS technology, long-term data is still pending.

Drug Delivery Vehicles

Drug delivery vehicles are the coating polymer which act as a drug carrier in DES.

Coating:

Coating consists with drug and polymer. Polymer may be bioabsorbable polymer or durable polymer.

Biodegradable polymers:

Biodegradable polymers in stents have several advantages over durable polymer in traditional stents, including:

- Reduced risk of late complications
- Biodegradable polymers dissolve over time, eliminating the need for stent removal and reducing the risk of late complications like thrombosis.
- Reduced inflammatory response
- Biodegradable polymers allow for complete elution of drugs, which can reduce the inflammatory response.
- No need for long-term antiplatelet therapy
- Once the polymer has completely disappeared, long-term antiplatelet therapy is no longer required.
- Improved imaging
- The absence of a permanent metal implant makes imaging easier during follow-up evaluations.
- Potential for shorter DAPT duration

Biodegradable polymers are commonly made from polylactic acid (PLA), polyglycolide, and poly (D,L-lactic-co-glycolic acid) (PLGA). They facilitate drug delivery to the vessel wall and are fully resorbed by hydrolysis after drug release without causing any long-term sequelae.¹¹

Whether stents with biodegradable polymers require shorter double antiplatelet therapy (DAPT) than stents with durable polymers have yet to be properly assessed in randomized studies.¹²

Polymer-free Drug Eluting Stent

Inflammatory issues caused by the polymers used in stents can be avoided by eliminating the polymer coating completely and releasing the antiproliferative drug directly from the stent surface. Without a polymer coating, it would be expected that the elution rate would increase, which might affect the stent's therapeutic efficacy.¹³ To address this issue, stent manufacturers have adopted different approaches to decrease the elution rate. These approaches can be roughly separated into five categories: smooth surface, macroporous, microporous, nanoporous and drug-filled stents.¹⁴ Perhaps the simplest polymer-free design is where the drug is coated directly onto the relatively unmodified smooth surface of the metal stent. With no polymer or pores to control drug release, the release rate is determined solely by the solubility and diffusion coefficient of the drug in the release medium and by the thickness of the coating. In macro-, micro- and nanoporous techniques, the surface of the stent is roughened. The drug is put into holes or slits in the body of macroporous stents. Pits and holes (in the order of microns) are made on the surface of microporous stents by a sandblasting or microabrasion process. The rough surface is then coated with the drug, resulting in the micropores being filled and a nominal layer covering the stent surface. The micropores act as a reservoir for the drug and aid adhesion to the stent surface. The nanopores of nanoporous stents are created by electrochemical treatments or sputter-coating techniques. These stents allow for a higher drug-loading capacity. Finally, drug-filled stents are a new and promising technology that allows the drug to be eluted from inside the stent through holes laser drilled on the abluminal side.¹⁵

Drug filled stent technology offers polymer free drug delivery stent. Essentially a BMS surface. So, avoid polymer biocompatibility, inflammation upon polymer degradation, surface coating durability.



Figure 1: Drug filled stent technology.

Umirolimus has been specifically developed for local delivery to the coronary arteries. It is the most lipophilic of the common -limus drugs (around 10 times greater than sirolimus), which is why a low dose is used in free-polymer stents.¹⁵ Novolimus is an active metabolite of sirolimus and has been shown to be a potent inhibitor of smooth muscle cells in *in vitro* studies.¹⁶

In the near future, the use of different drugs or combinations of drugs with different actions may address not only intimal proliferation but also thrombosis and, in the long term, in-stent neoatherosclerosis.

Drug eluting technology progression

From conformal biostable polymer to abluminal bioabsorbable polymer concept developed to improved better DES. Drug only released to artery wall. Metallic surface with minimal drug, enables fast endothelialization. Thin abluminal coating minimized drug and polymer dosage, also ensure drug release to coronary vessel wall. It also stimulates early re-endothelialisation. Thinner struts can decrease the risk of subacute thrombosis and early full neointimal coverage. Minimal duration of DAPT needed. Developing bioresorbable polymers to improve biocompatibility and facilitate the endothelialization process. Essentially DES having a BMS luminal surface.

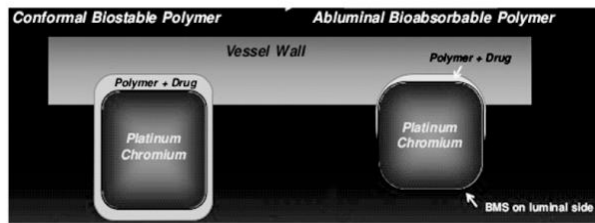


Figure 2: Drug eluting technology progression, from conformal biostable polymer to abluminal bioabsorbable polymer.



Figure 3: Conformal multidirectional Eluting of drug. The drug used might inhibit both smooth muscle cell (SMC) and endothelial cell (EC). The drug not only released to artery wall, but also to blood.

Target Eluting Technology-Abluminal groove design

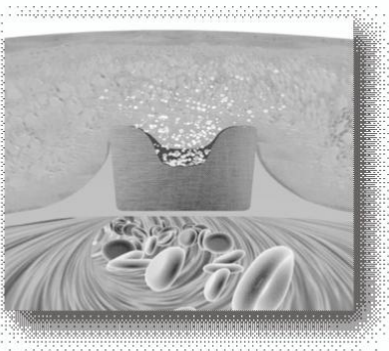


Figure 4: Unique groove-based technology, the stent offers targeted drug delivery directly to lesion sites.

In this technology drug only released to artery wall. Metallic surface on luminal area with minimal drug, enables fast endothelialization. Abluminal Groove design also minimized drug and polymer dosage. It gives coating protection. The grooves designed on the outer surface of the stent allows

targeting release of the drug to coronary vessel wall. The depth of groove is about 1/3 of the strut, and the thickness of coating stored in the groove is about 10 microns.

Unique groove-based technology, the stent offers targeted drug delivery directly to lesion sites, minimizing systemic exposure and enhancing patient safety, this innovative stent may reduce restenosis rates, ensuring superior long-term outcomes, need further investigation.

Lower drug dosage can achieve similar tissue concentration. Less drug enables fast healing and potentially brings more safety of the device. A novel technology of an abluminal groove-filled biodegradable polymer low dose sirolimus-eluting stent, polymer and drug are really protected by its in-grooved design. Outcomes in the long term is controversial⁶⁻⁹.

The abluminal groove design stent is a thin-strut cobalt-chromium platform with a biodegradable, sirolimus-eluting polymer (BP-SES) that is applied to recessed grooves on the stent surface to minimize the inflammatory vascular response¹⁶⁻²⁰. The TARGET-ALL Comers (TARGET-AC) study confirmed the safety and efficacy of this low-dose BP-SES by demonstrating non-inferiority for the primary endpoint of target lesion failure (TLF) at 12 months compared with the benchmark durable-polymer everolimus-eluting stent (DP-EES) in randomized all-comers patient population. The long-term results for this BP-SES compared to the DP-EES are not known.

Conclusion

Continuous newer technology adapted to develop better drug eluting stent in respect to drug delivery to vessel wall. Biodegradable polymer coating newer generation stent with thin coating on abluminal surface may build up new hope. Also developed DES without polymer and abluminal groove design biodegradable polymer coating DES.

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Congenitally corrected transposition of the great arteries with severe tricuspid regurgitation and systemic right ventricular dysfunction: a case report in Bangladesh

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Abstract

Congenitally corrected transposition of great arteries (ccTGA) is a complex congenital heart disease. It may remain asymptomatic in first few decades of life; therefore, diagnosis can be incidental. Symptoms arise when there is any complication or associated anomaly.

We report the case of a 35-year-old man, presented with shortness of breath in Cardiology department in Chittagong Medical College Hospital. The man had progressive breathlessness for 2 months with previous episodes of similar kind of illness over the last 2.5 years. Examination revealed a pansystolic murmur (loudest at the left lower parasternal area), apex beat was diffuse, thrusting in nature, just lateral to the midclavicular line in the left fifth intercostal space. Transthoracic echocardiography (TTE) confirmed the anatomy of ccTGA with tricuspid regurgitation.

Background:

Congenitally corrected transposition of the great arteries (ccTGA) is a rare congenital heart disease; with an estimated prevalence of 1 per 33,000 live births. (1,2) The disease is characterized by atrioventricular and ventriculo-arterial discordance. (1-4) The condition can be associated with interventricular communications (70%~80%), obstructions of the outlet from the morphologically left ventricle (25%~50%), pulmonary stenosis, AV block and anomalies of the tricuspid valve (70%). (2-9) Generally by the fourth decade, systemic right ventricle (RV) dysfunction is clinically apparent. (1,3) Systemic RV dysfunction is the main cause of mortality and morbidity in adults with ccTGA. (9)

We present the case of a 35-years old patient with ccTGA with severe tricuspid regurgitation, who took repeated medical consultation for his progressive breathlessness. In our centre, the medical management was given and referred for valve replacement.

Case presentation

A 35-year-old male, normotensive, nondiabetic patient came with complain of progressive dyspnea on moderate to severe exertion. He had to take admission in hospital for two times in the last one month.

2.5 years back, he was diagnosed to have severe mitral valve regurgitation, due to mitral valve prolapse, and was advised for mitral valve replacement/repair. He decided to take

second opinion/consultation from the specialized heart center both in Bangladesh and India. Then he was diagnosed as a case of ccTGA with moderate left atrioventricular valve regurgitation with normal biventricular function. He was advised regular medications and routine follow-up. His last TTE was done 7 months ago. But his condition deteriorated in the last two months before the current admission. Examination revealed a 3/6 holosystolic murmur in the left lower parasternal area. Other positive findings included palpable P2, left parasternal heave, epigastric pulsation.

Chest radiograph showed cardiomegaly, splaying of carina, vascular pedicle appears abnormally straight (since there is an abnormal relationship of the great arteries).

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Fig 1: Chest radiograph shows cardiomegaly, splaying of carina, straightening of vascular pedicle.

The ECG showed sinus rhythm, rate around 80/min, absence of Q waves in V4-6 (physiologic Qwaves in this lead often referred to as "Septal Q waves"), (5) S in V1+R in V6 > 35 mm.

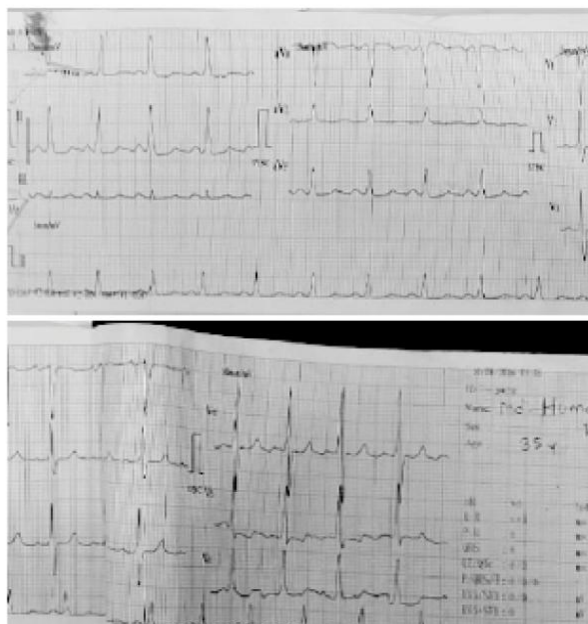


Fig 2: 12-lead ECG shows LVH, absence of septal q wave in V4-V6.

Echocardiography showed the aorta arising from the morphological right ventricle (RV), which was identified by

the three leaflet tricuspid valve that inserted more apically than the mitral valve. The pulmonary trunk, identified by its bifurcation, arose from the morphological left ventricle (LV). The systemic RV was dilated.

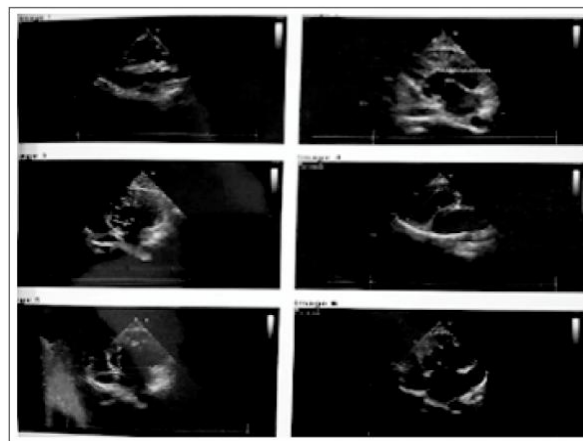


Fig 3: 2D Transthoracic echocardiography depicts ccTGA

The primary management with beta blockers and diuretics was given in the department. Then the patient was consulted accordingly and referred to specialized centre for valve replacement.

Discussion

CCTGA comprises both atrioventricular and ventriculoarterial discordance; the right atrium enters the morphological LV, which gives rise to the pulmonary artery, whereas the left atrium enters the morphological RV, which gives rise to the aorta. (7) This defect occurs due to abnormal cardiac development during the third gestational week where left looping (L-loop) of the heart tube instead right looping occurs. (4) Patients without associated intracardiac lesions are usually asymptomatic early in life. Later on, patients may present with ventricular dysfunction. (3,7) The 80% of patients with CCTGA have associated lesions (e.g., ventricular septal defect, pulmonary stenosis, Ebstein anomaly of tricuspid valve, and abnormalities of the conduction system) and they develop symptoms earlier. (1-7) Abnormalities of the tricuspid valve are found in up to 70% of patients with ccTGA. Ebstein-like anomaly in tricuspid valve in ccTGA represents a variable spectrum of disease. (8) Tethering and apical displacement of the leaflet hinge points, maximally at the commissure between the posterior and septal leaflets is observed. (8)

The RV, normally supporting the low-pressure pulmonary circulation, when in the systemic position has to pump high-



pressure systemic blood. (7,9) RV undergoes various adaptive mechanisms to enable itself to sustain the systemic load. (7) High systolic pressures inside the RV lead to eccentric hypertrophy of its free wall, dilation of the RV, increased ventricular wall stress and dysfunction of the trabecular component.(9)

In complete TGA/d-loop TGA, tricuspid regurgitation is secondary to annular dilatation and RV dysfunction, and thus tricuspid valve replacement is not warranted. On the other hand, choice of intervention in CCTGA is addressing intrinsic abnormalities of tricuspid valve itself. Therefore, tricuspid replacement (repair is usually not gratifying) is ideal in ccTGA to preserve SRV function. (7)

Conclusion:

We presented the case of ccTGA that came in fourth decade of life with severe tricuspid regurgitation and systemic RV dysfunction. The age of presentation and the ongoing complications are consistent with existing literatures on ccTGA. In spite of regular medication for 2.5 years, the condition of the patient worsened. The final decision was made to refer the patient for valve replacement.

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