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ORIGINAL ARTICLE

Assessment of Coronary Collaterals Among Patients With ST-segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention and its Impact on In-hospital and 30-day Mortality: A Prospective Observational Study

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Abstract

Objectives: **This study aimed to determine the distribution of coronary collaterals (CC) as per the Rentrop Collateral Score (RCS) among patients with ST-segment elevation myocardial infarction (STEMI) and its impact on in-hospital and 30-day mortality after primary percutaneous coronary intervention (PCI).**

Methods: **In this study, a selected sample of consecutive STEMI patients was assessed for the development of CC as per the RCS classification. An RCS grade of 2 or 3 was taken as the presence of CC with either partial or complete filling of the infarct-related artery (IRA). Patients were followed during the hospital stay and up to 30 days, and the incidence of major adverse cardiovascular events (MACE) was recorded, which included mortality, re-infarction, stroke, and hospitalization due to heart failure.**

Results: **This study was conducted on a sample of 347 patients; 81.6% (283) were male, and the mean age was 56.2 ± 10.3 years. CC was not visible (RCS-0) in 206 (59.4%) patients, visible but without filling of the IRA (RCS-1) in 39 (11.2%) patients, and visible with partial (RCS-2) and complete (RCS-3) filling of the IRA in 72 (20.7%) and 30 (8.6%) patients, respectively. No significant differences were observed in the incidence of in-hospital mortality and short-term MACE between patients with and without CC, with an in-hospital mortality rate of 2% vs. 4.9% ($p = 0.248$) and a MACE rate of 7% vs. 6.4% ($p = 0.850$), respectively.**

Conclusion: **Good CC with either partial or complete filling of the IRA was observed in more than one-fourth of the patients with STEMI. However, no significant benefits of good CC were observed.**

Keywords: STEMI, Primary PCI, Coronary collaterals, Rentrop collateral score

1. Introduction

ST-elevation myocardial infarction (STEMI), which results from the total occlusion of an infarct-related artery (IRA), is a life-threatening and time-sensitive emergency [1]. Primary percutaneous coronary intervention (PCI) with a short door-to-balloon time is the preferred coronary revascularization strategy for patients with STEMI [2]. Coronary collateral circulation provides a natural bypass to the same coronary artery or other coronary arteries when the blood supply to a particular territory is compromised. These conduits serve as an essential part of circulation for

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blood supply to severely narrowed or totally occluded arteries when the myocardium is jeopardized due to myocardial ischemia [3,4]. The imbalance between supply and demand leads to myocardial ischemia, which progressively results in myocyte necrosis, but factors like the development of coronary collaterals can mitigate this [5].

The coronary collaterals, based on Rentrop classification, are reported to be present in up to 23.6% of the patients with STEMI undergoing primary PCI [4]. In the current era of primary PCI for patients with acute STEMI, the impact of coronary collateral appearance has significantly reduced coronary artery disease mortality, recurrence of myocardial infarction, and cardiovascular mortality [6]. The knowledge and information about coronary collateral development play an important role in delineating future therapeutic methods to promote collateral growth and functionality to overcome the global burden of coronary artery disease [7]. However, in the recent era of coronary revascularization, clinical outcomes associated with coronary collaterals have shown conflicting results in trials. Previous meta-analyses concluded that coronary collaterals have reduced both in-hospital and long-term mortality in patients with coronary artery disease [8].

The development of human coronary collaterals is often neglected even though it is an important prognostic factor and could play a vital role in cardiac vulnerability by adding more time to the limited golden hours from the onset of STEMI to coronary revascularization. Recently, gene therapy has shown encouraging results for developing coronary collaterals in coronary artery disease by administering angiogenic growth factors [9].

Thus, the aims of this study are to determine the distribution of coronary collaterals as per the Rentrop Collateral Score (RCS), their temporal association, and their impact on in-hospital and 30-day mortality among patients with STEMI undergoing primary PCI. To the best of our knowledge, no local study has been conducted in Pakistan; international studies have conflicting data. Despite conflicting outcomes in recent trials, understanding the role of coronary collaterals is crucial in optimizing patient outcomes within the limited golden hours from STEMI onset to coronary revascularization. Moreover, the study will contribute valuable insights into the prognostic impact of coronary collaterals and explore their potential as a target for therapeutic interventions, including emerging gene therapy approaches involving angiogenic growth factors.

Abbreviations

STEMI	ST-elevation myocardial infarction
IRA	infarct-related artery
PCI	Primary percutaneous coronary intervention
RCS	Rentrop Collateral Score
NICVD	National Institute of Cardiovascular Disease
TMI	thrombolysis in myocardial infarction
MACE	major adverse cardiovascular events
CAD	coronary artery diseases
NLR	neutrophil to lymphocyte ratio

2. Materials and methods

2.1. Study setting

This was a prospective observational study conducted at the cardiac catheterization laboratory of the National Institute of Cardiovascular Disease (NICVD), Karachi, Pakistan, between July 2021 and December 2021. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki. The study was initiated after approval from the institutional review board (ERC-01/2020), and all participants' consent was obtained.

2.2. Study population

The study was conducted on a selected sample of consecutive patients who presented to the emergency department with typical chest pain and were diagnosed with STEMI as per the fourth universal definition of myocardial infarction. Inclusion criteria were STEMI patients between 18 and 80 years of age and undergoing primary PCI for complete occlusion of the infarct-related artery (IRA). The angiographic evidence of thrombolysis in myocardial infarction (TIMI) grade 0 was taken as complete occlusion. However, this study did not include patients with a prior history of any cardiac-related surgery or intervention. To ensure a representative sample, all eligible patients presenting within the study period were screened for inclusion. Patients who met the criteria were enrolled consecutively, meaning each eligible and consented patient was included in the study without any selective bias.

The sample size for the study was calculated based on the 23.6% expected frequency of coronary collaterals among patients with STEMI at a 95% confidence level and 5% margin of error; the sample size of 278 was calculated [4]. A total of 347 patients were recruited, with an expected 30-day loss to follow-up rate of 25%.

2.3. Data collection

Routine clinical and angiographic data points were collected using a structured proforma that included demographic variables, risk factors, hemodynamic status at presentation (Killip class), duration between the development of symptoms and indication of procedure, angiographic variables, and in-hospital and 30-day outcomes. Additionally, coronary collateral flow in the IRA was assessed as per the Rentrop Collateral Score (RCS).

2.4. Procedure and outcomes

All the primary PCI procedures were performed in accordance with current clinical practice guidelines. Each of the angiographies was assessed by three independent interventional cardiologists for the assessment of coronary collateral in accordance with RCS and categorized as 0, 1, 2, and 3, indicating "no visible coronary collaterals," "coronary collaterals without IRA filling," "coronary collaterals with partial IRA filling," and "collaterals with complete IRA filling," respectively. Patients were followed during the hospital stay and up to 30 days (either physically during clinical visits or telephonic), and the incidence of major adverse cardiovascular events (MACE) was recorded, which included mortality, re-infarction, stroke, and hospitalization due to heart failure.

2.5. Statistical analysis

For the comparative analysis, patients were categorized into two groups based on RCS grade 0 or 1 as group one and RCS grade 2 or 3 as group two. The angiographic and clinical variables and outcomes between the two groups were compared using appropriate statistical tests such as the t-test, Chi-square test, Log-likelihood test, or Fisher Exact test. Furthermore, the temporal analysis with respect to symptom onset to the angiographic appearance of collaterals was also performed by categorizing time as 0–3 h, 3–6 h, 6–9 h, and more than 9 h. All the analyses were performed with the help of IBM SPSS version 21, and the significance criterion was a p-value <0.05.

3. Results

This study was conducted on a sample of 347 patients; 81.6% (283) were male, and the mean age was 56.2 ± 10.3 years. Coronary collaterals were not visible (RCS-0) in 206 (59.4%), visible but without filling of IRA (RCS-1) in 39 (11.2%), visible with partial filling of in the IRA (RCS-2) in 72 (20.7%), and visible with complete filling of in the IRA (RCS-3) was observed in 30 (8.6%) patients. Coronary collaterals with either partial or complete filling of the IRA were found to be associated with longer ischemic time and ongoing angina pectoris (Table 1).

A relatively higher tendency of coronary collaterals development was observed in patients with multi-vessel disease, with the distribution of 32.4% vs. 23.7% with and without coronary collaterals among patients with three-vessel disease and 35.3% vs. 31.8% with and without coronary collaterals among patients with two-vessel disease, respectively (Table 2). However, no significant differences were observed in the in-hospital course of patients with and without coronary collaterals; in-hospital mortality was 2% vs. 4.9%; $p = 0.248$ among patients with and without coronary collaterals (Table 2).

However, no significant differences were observed in the incidence of short-term MACE between patients with and without coronary collaterals with a MACE rate of 7% vs. 6.4%; $p = 0.850$, respectively (Table 3).

The development of coronary collaterals was observed to be positively associated ($p < 0.05$) with the ischemic time; the longer the ischemic time, the higher the frequency of coronary collaterals with either partial or complete filling of the IRA (Fig. 1). Good collaterals (RCS-2 or 3) were observed in 7.7%, 25.3%, 31.5%, 33.9%, and 39.7% among patients with ischemic time duration of 0–3 h, 3–6 h, 6–9 h, 9–12 h, and 12–24 h, respectively.

4. Discussion

The coronary collaterals, at least on theoretical grounds, play a vital role in maintaining blood supply to severely narrowed or totally occluded arteries when the myocardium is jeopardized due to myocardial ischemia [3,4]. The clinical and prognostic benefit of collateralized flow in patients with stable coronary artery diseases (CAD) is well established; however, we have conflicting observations regarding the beneficial role of collateralized flow in acute myocardial infarction settings [4,10]. Therefore, in this prospective observational study, we included a sample of 347 patients with STEMI undergoing primary PCI for complete occlusion of IRA, and coronary collaterals were assessed in accordance with RCS. It was observed that a good coronary collaterals flow with either partial or complete filling of the IRA was present in more than 29% of the patients. The presence of good coronary collaterals was found to be positively associated with longer ischemic time and the presence of

Table 1. Distribution of clinical and demographic characteristics stratified by the status of the coronary collateral at the time of intervention among patients with ST-segment elevation myocardial infarction.

Characteristics	Total	Rentrop Collateral Classification		P-value
		RCS 0 to 1	RCS 2 to 3	
Total (N)	**347**	**245 (70.6%)**	**102 (29.4%)**	–
Male	81.6% (283)	82.4% (202)	79.4% (81)	0.506[a]
Mean age ± SD (years)	56.2 ± 10.3	55.9 ± 10.4	56.9 ± 10.2	0.397[d]
≤40 y	7.5% (26)	8.2% (20)	5.9% (6)	0.256[a]
41 to 65 y	77.5% (269)	78.8% (193)	74.5% (76)	
>65 years	15% (52)	13.1% (32)	19.6% (20)	
Timing of collateral assessment				
0–3 h	11.2% (39)	14.7% (36)	2.9% (3)	0.007[a]
>3–6 h	25.1% (87)	26.5% (65)	21.6% (22)	
>6–9 h	25.6% (89)	24.9% (61)	27.5% (28)	
>9–12 h	17% (59)	15.9% (39)	19.6% (20)	
>12–24 h	21% (73)	18% (44)	28.4% (29)	
Killip class				
I	81.6% (283)	81.2% (199)	82.4% (84)	0.128[b]
II	9.5% (33)	9.8% (24)	8.8% (9)	
III	6.9% (24)	6.1% (15)	8.8% (9)	
IV	2% (7)	2.9% (7)	0% (0)	
Co-morbid conditions				
Hypertension	53.3% (185)	53.9% (132)	52% (53)	0.744[a]
Diabetes mellitus	32.3% (112)	29.8% (73)	38.2% (39)	0.126[a]
Smoking	31.4% (109)	32.7% (80)	28.4% (29)	0.440[a]
Family history of IHD	5.2% (18)	4.5% (11)	6.9% (7)	0.364[a]
Obesity	13.8% (48)	15.1% (37)	10.8% (11)	0.289[a]
Type of myocardial infarction				
Anterior	53.6% (186)	55.1% (135)	50% (51)	0.373[b]
Inferior	32% (111)	29.8% (73)	37.3% (38)	
Lateral	3.2% (11)	2.9% (7)	3.9% (4)	
Posterior	0.9% (3)	1.2% (3)	0% (0)	
Inferior, posterior	10.4% (36)	11% (27)	8.8% (9)	
Ongoing angina	43.2% (150)	33.1% (81)	67.6% (69)	<0.001[a]

SD = standard deviation, IHD = ischemic heart diseases, a = Chi square, b = Loglikelihood test, c = Fisher Exact test, d = t-test, RCS= Rentrop collateral classification.
RCS-0: "indicates no visible coronary collaterals", RCS-1: "coronary collaterals without IRA filling", RCS-2: "coronary collaterals with partial IRA filling", RCS-3: "collaterals with complete IRA filling".

ongoing angina. Additionally, multi-vessel involvement was also found to be associated with a relatively higher presence of good coronary collaterals. However, no significant improvement was observed in the hospital course or the short-term MACE of patients with good coronary collaterals. Theoretically, good collateral circulation can provide an alternative route for blood to the ischemic area of the heart. This collateral circulation may help maintain some level of blood flow even before PCI is performed, potentially reducing the extent of damage to the heart muscle.

Various other clinical studies also support our study findings of the association between good coronary collaterals and prolonged ischemic time. For instance, in a study of 164 late presented non-reperfused patients with acute coronary occlusion, good coronary collators were observed in 54% of the patients, and the poor coronary collaterals were reported to be associated with an increased risk of major adverse outcomes at one-year follow-up [11]. A study by Freund A et al. [12] included patients who presented between 12 and 48 h of symptom onset and reported well-developed coronary collaterals in 35% of the patients. Further, the well-developed collaterals were not only reported to be associated with a reduction of infarct size and microvascular obstruction but also found to be associated with reduced long-term mortality [12].

However, we have a number of studies with contradicting results regarding the beneficial impact of good coronary collaterals on immediate, short- and long-term outcomes. For instance, a study conducted by Hernández-Pérez FJ et al. [13] failed to establish a beneficial role of the presence of good coronary collaterals in long-term clinical outcomes among patients treated with primary angioplasty. A recent study in this regard observed that patients with STEMI with good coronary collaterals tend to have a higher thrombus burden, hence indicating more severe coronary lesions, which may result in an increased burden of adverse events [14]. Chu AA

Table 2. Distribution of angiographic characteristics and hospital course stratified by the status of the coronary collateral at the time of intervention among patients with ST-segment elevation myocardial infarction.

Characteristics	Total	Rentrop Collateral Classification		P-value
		RCS 0 to 1	RCS 2 to 3	
Total (N)	**347**	**245 (70.6%)**	**102 (29.4%)**	-
Access for procedure				
Radial	76.1% (261)	76% (184)	76.2% (77)	0.968[a]
Femoral	23.9% (82)	24% (58)	23.8% (24)	
Number of vessels involved				
Single vessel disease	40.9% (142)	44.5% (109)	32.4% (33)	0.085[a]
Two vessel disease	32.9% (114)	31.8% (78)	35.3% (36)	
Three vessel disease	26.2% (91)	23.7% (58)	32.4% (33)	
Culprit coronary artery				
Left main	0.6% (2)	0.4% (1)	1% (1)	0.655[b]
Left anterior descending artery	53.9% (187)	55.9% (137)	49% (50)	
Right coronary artery	28.8% (100)	28.2% (69)	30.4% (31)	
Left circumflex	15% (52)	13.5% (33)	18.6% (19)	
Diagonal	1.4% (5)	1.6% (4)	1% (1)	
Ramus	0.3% (1)	0.4% (1)	0% (0)	
Pre-procedure LVEF (%)	36.4 ± 8.4	36.5 ± 8.5	36 ± 8.2	0.644[d]
Post-procedure LVEF (%)	38.9 ± 8.5	38.9 ± 8.6	39.1 ± 8.4	0.837[d]
Peri-procedure complications and in-hospital outcomes				
Mortality	4% (14)	4.9% (12)	2% (2)	0.248[c]
Acute kidney injury	5.2% (18)	6.1% (15)	2.9% (3)	0.223[a]
Heart failure	6.6% (23)	6.9% (17)	5.9% (6)	0.719[a]
Cardiogenic shock	4.6% (16)	5.3% (13)	2.9% (3)	0.413[c]
Cardiac arrest	2.6% (9)	3.3% (8)	1% (1)	0.292[c]
Arrhythmia	2% (7)	2.9% (7)	0% (0)	0.110[c]
Sepsis	0.3% (1)	0.4% (1)	0% (0)	>0.999[c]
Major bleeding	1.7% (6)	2% (5)	1% (1)	0.675[c]
Hematoma	1.7% (6)	2.4% (6)	0% (0)	0.186[c]
Invasive ventilation	7.2% (25)	7.8% (19)	5.9% (6)	0.539[a]

LVEF = left ventricular ejection fraction a = Chi square, b = Loglikelihood test, c = Fisher Exact test, d = t-test, RCS= Rentrop collateral classification.
RCS-0: "indicates no visible coronary collaterals", RCS-1: "coronary collaterals without IRA filling", RCS-2: "coronary collaterals with partial IRA filling", RCS-3: "collaterals with complete IRA filling".

et al. [15] also reported no direct beneficial role of good coronary collaterals, but better post-procedure myocardial blush grade and lower cardiogenic shock were reported for the patients with STEMI with well-developed coronary collaterals. Similarly, results from the ACUITY trial also failed to establish the beneficial role of good coronary collaterals; instead, the presence of coronary collaterals was

Table 3. Distribution of short-term outcomes stratified by the status of the coronary collateral at the time of intervention among patients with ST-segment elevation myocardial infarction.

Characteristics	Total	Rentrop Collateral Classification		P-value
		RCS 0 to 1	RCS 2 to 3	
Total (N)	**333**	**191**	**162**	–
Follow-up duration (days)	36.6 ± 25.6	36.2 ± 25.5	37.5 ± 25.9	0.672[d]
Follow-up outcomes				
All-cause death	3.6% (12)	3.9% (9)	3% (3)	>0.999[c]
MI needing intervention	3% (10)	2.1% (5)	5% (5)	0.174[c]
Hospitalization due to HF	2.1% (7)	2.1% (5)	2% (2)	>0.999[c]
Stroke	0.3% (1)	0.4% (1)	0% (0)	>0.999[c]
MACE	6.6% (22)	6.4% (15)	7% (7)	0.850[a]
Functional class				
I	82.9% (276)	85% (198)	78% (78)	0.313[b]
II	14.7% (49)	12.9% (30)	19% (19)	
III	2.4% (8)	2.1% (5)	3% (3)	
IV	0% (0)	0% (0)	0% (0)	

MI = myocardial infarction, HF = heart failure, MACE = major adverse cardiovascular events, a = Chi square, b = Loglikelihood test, c = Fisher Exact test, d = t-test, RCS= Rentrop collateral classification.
RCS-0: "indicates no visible coronary collaterals", RCS-1: "coronary collaterals without IRA filling", RCS-2: "coronary collaterals with partial IRA filling", RCS-3: "collaterals with complete IRA filling".

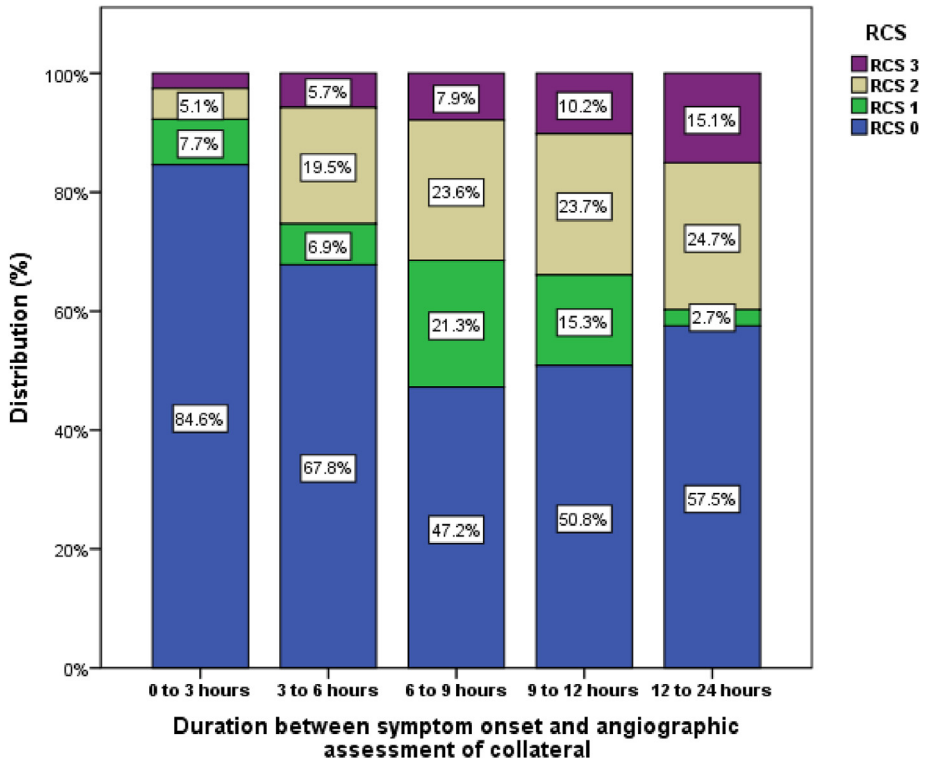

Fig. 1. ***Distribution of Rentrop Collateral Classification (RCS) in relation to the time between symptom onset and angiographic assessment of collaterals.*** *RCS= Rentrop collateral classification. RCS-0: "indicates no visible coronary collaterals", RCS-1: "coronary collaterals without IRA filling", RCS-2: "coronary collaterals with partial IRA filling", RCS-3: "collaterals with complete IRA filling".*

found to be associated with an increased risk of target vessel revascularization and mortality among patients with acute coronary syndrome [16]. On the contrary, a meta-analysis of over ten thousand patients with STEMI by Cui K et al. [4] showed better in-hospital, 30-day, and > 6-month survival among patients with good collateral.

On the other hand, for the patients with chronic total occlusion, a meta-analysis of over three thousand patients by Allahwala UK et al. [10] also confirmed this evidence with the conclusion of no significantly better mortality rate for patients with coronary collaterals. On the contrary, it has been observed that good coronary collaterals have beneficial effects on the long-term outcome of the chronic, totally occluded arteries with post-stenting low FFR but not in patients with post-stenting high FFR [17].

Similar to our finding of a positive association between angina and good coronary collaterals, a study by Chandra S et al. [7] also reported angina prior to STEMI as an independent predictor of good coronary collaterals in addition to age and obstructive sleep apnea [18,19]. Smoking status and diabetes were reported to have an inverse relationship with coronary collaterals [7]. Similarly, the presence of coronary collaterals is reported to be associated with the presence of high-risk features such as impaired renal function, lower left ventricular ejection fraction, older age, and hemodynamic instability at presentation (Killip class $\geq$ II) [20].

There are a number of other clinical parameters that are found to be associated with the presence of good coronary collaterals. For example, good coronary collateral development is reported to be associated with ischemia-modified albumin among patients with chronic total occlusive arteries [21]. The duration of QRS at admission is another important parameter found to be inversely associated with the presence of well-developed collaterals in patients with acute myocardial infarction [22]. Neutrophil and neutrophil-to-lymphocyte ratio (NLR) is another parameter that has been reported to be associated with good collaterals in STEMI patients [23]. A higher red cell distribution width has been reported to be associated with the absence of good coronary collaterals [24].

This systematic review and meta-analysis by Meier P et al. [8] reported benefits of collateral circulation in terms of infarct size and left ventricular remodeling in MI, but its effect on mortality remains debated. The analysis included 12 studies with 6529 participants, showing that patients with high collateralization had a 36% lower mortality risk than those with low collateralization (RR 0.64, 95% CI

0.45–0.91; P = 0.012). The protective effect was most pronounced in stable CAD (RR 0.59), while the impact in acute and subacute MI was less clear [8]. The protective mechanisms of collateral circulation can be stem from the fact that collateral circulation can reduce the extent of myocardial infarction by providing alternative blood flow routes [25]. Hence, patients with collateral circulation are reported to have lower troponin levels, indicating less myocardial damage [25].

Even though this was the first study on the assessment of coronary collaterals among patients with STEMI in our population, certain limitations need to be acknowledged, which include a single center-based study with a small sample size. Further, the association of various laboratory-based parameters and angiographic and echocardiographic parameters, such as infarct size and the left ventricular ejection fraction, with the development of coronary collaterals could not be assessed due to the non-availability of the data. Another limitation of our study is the lack of specific analysis on the role of collateral circulation in STEMI patients presenting for the first time versus those with a history of chronic coronary syndrome or prior angina. Future studies should investigate the impact of collateral circulation in de-novo ACS patients compared to CCS patients, as this distinction may provide further insights into prognosis and management strategies. Therefore, further large-scale studies are warranted, especially to ascertain the clinical role of coronary collaterals in determining the outcomes after primary PCI.

5. Conclusions

In conclusion, coronary collaterals with either partial or complete filling of the IRA were observed in more than 1/4th of the patients with STEMI. The presence of good coronary collaterals was found to be positively associated with prolonged ischemic time and ongoing angina pectoris. However, contrary to popular belief, we observed no significant beneficial impact of good coronary collaterals on the hospital course as well as the incidence of short-term MACE. However, further large-scale studies are warranted to confirm our study findings.

Author contributions

Conception and design of Study: ZI, MNM. Literature review: ZI, TA, BAS, KIB, ASA, TS. Acquisition of data: ZI, TA, RK, KIB. Analysis and interpretation of data: ZI, RK, BA, ASA, TS. Research investigation and analysis: ZI, MNM, TA, BAS, RK, KIB, BA, ASA. Data collection: TA, BAS, KIB, ASA. Drafting of manuscript: ZI, BAS, RK, KIB, BA, ASA. Revising and editing the manuscript critically for important intellectual contents: ZI, MNM, BAS. Data preparation and presentation: ZI, BA. Supervision of the research: MNM, BAS. Research coordination and management: ZI, BA, ASA. Funding for the research: ZI, MNM

Disclaimer

None to declare.

Ethics information

The study protocol conforms to the ethical guidelines of the Declaration of Helsinki. The study was initiated after approval from the institutional review board (ERC-01/2020), and all participants' consent was obtained.

Source of funding

This study did not receive funding from any sources.

Conflict of interest

None to declare.

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