RESEARCH ARTICLE

Frequency and factors related to not receiving acute reperfusion therapy in patients with ST elevation myocardial infarction; a single specialty cardiac center

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Abstract

Objective: To determine the frequency of no reperfusion therapy, its reasons, hospital management and intermediate-term outcomes of ST-elevation myocardial infarction patients.

Methods: The retrospective ambi-directional observational study was conducted at Tabba Heart Institute, Karachi, and comprised record of ST-elevation myocardial infarction patients without immediate reperfusion therapy with symptom onset time of ≤12 hours who presented between January 2013 and December 2017. Prospective follow-up of all patients was performed till June 2018. Coronary angiography, non-invasive stress tests, medications and late revascularisation were explored. Predictors of hospital mortality and major adverse cardiovascular events at follow-up were analysed. Data was analysed using SPSS 19.

Results: Of the 1977 records evaluated, 218(11%) patients of mean age 60.3±12.4 years did not receive immediate reperfusion therapy. Coronary angiography was done in 163(74.7%) patients of whom 45(27.6%) were taken for immediate procedure. Besides, 26 (11.9%) patients died during hospital stay. Predictors of hospital mortality were no revascularisation (odds ratio: 24.1, 95% confidence interval: 1.3-500), cardiogenic shock (odds ratio: 65, 95% confidence interval: 5.7-745) and tachycardia (odds ratio: 17, 95% confidence interval: 1.2-254.5) at presentation. Predictor of major adverse cardiovascular events was guideline-directed medical therapy (hazard ratio 2.6, 95% confidence interval: 1.16-6.2) at discharge, while revascularisation was not a significant predictor (p>0.05).

Conclusion: A huge number of salvageable ST-elevation myocardial infarction patients failed to receive reperfusion therapy. There is a huge potential of improvement in ST-elevation myocardial infarction care in terms of increasing community awareness, prompt reperfusion therapy and usage of optimal medical therapy.

Keywords: ST elevation myocardial infarction, Stress test, Myocardial reperfusion, Fibrinolytic agent

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Introduction

Reperfusion therapy is the standard of care for all eligible patients with ST-elevation myocardial infarction (STEMI) who reach the hospital within the optimal time window for reperfusion therapy of less than 12 hours, and for most patients up to 24 hours from the onset of symptoms.[1,2] Prompt and myocardial level reperfusion therapy is the major determinant of long- and short-term prognosis in STEMI and accounts for 45% of the overall reduction in hospital mortality of all the currently available therapies.[3,4] The main modes of reperfusion therapy are immediate percutaneous coronary intervention (PCI) and fibrinolysis (FL).[5]

Even in current era, many eligible patients do not receive timely reperfusion therapy despite having no absolute contraindications.[6] The Global Registry of Acute Coronary Events (GRACE) reported that 30% of STEMI patients do not receive reperfusion therapy, and in the Can Rapid risk stratification of Unstable angina patients Suppress Adverse outcomes with Early implementation (CRUSADE) national registry on quality improvement, 7% eligible STEMI patients did not receive any reperfusion therapy.[7] In a registry from India this fraction was 52%.[8] Reasons for not receiving reperfusion therapy are diverse and include perceived older age, female gender, presence of renal disease, resolution of symptoms and prior myocardial infarction (MI).[9] Another study reported that ground for no reperfusion therapy was absence of ischaemia due to

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delayed presentation and unsuitable anatomy.[7] In Pakistan, there are no national level cardiovascular registries and no data on STEMI management patterns. Quantification of magnitude of no reperfusion in eligible STEMI patients and identifying its reasons are the first steps to comprehending the problem and to devise actions required to improve the number of eligible patients that get prompt reperfusion therapy.

The current study was planned to determine the frequency and reasons related to withholding reperfusion therapy in STEMI patients with no absolute contraindication for reperfusion. Also, the plan was to explore hospital management patterns and intermediate-term outcomes of the patient population.

Patients and Methods

The retrospective ambi-directional cohort study was conducted at Tabba Heart institute, Karachi, which is a single specialty, heart only, tertiary care hospital. Patient records were reviewed from January 2013 to December 2017, and prospective follow-up of all patients was performed till June 2018.

Records included related to patients of either gender aged over 18 years presenting to emergency room (ER) with symptom onset time of 12 hours or less and who had received no immediate reperfusion therapy. Non-probability consecutive sampling technique was used. Patients transferred from other health facilities and those coming directly to our institute were also included. Patients with an absolute contraindication for reperfusion therapy (ongoing major gastrointestinal bleeding or history of intracranial bleeding/neoplasm) were excluded After approval from the institutional ethics committee, data on baseline clinical and demographic parameters was drawn from the institute's two separate databases modelled according to the standard United States National Cardiovascular Data Registry (NCDR) Catherisation-percutaneous coronary intervention (Cath-PCI) registry and Acute Coronary Treatment and Intervention Outcomes Network (ACTION) or Acute Coronary Syndrome (ACS) registry.[9] The registry collects data on patient and hospital characteristics, clinical presentation such as Killip class I to IV on admission (to predict risk of 30-day mortality in ACS), treatments, and outcomes associated with ACS patients, their coronary angiography and/or Percutaneous Coronary Intervention (PCIs).

Reasons for not receiving reperfusion therapy were explored form individual file review from treating physician's documentations. Coronary angiography, non-invasive (NIV) stress tests and medications history was derived from hospital records. Revascularisation attempted after the initial STEMI reperfusion therapy time window were also recorded. Revascularisation performed within 4 weeks from STEMI events were counted as index. Follow-up on clinical events were obtained prospectively from clinic record and telephone calls. Frequency of no reperfusion therapy in STEMI patients was noted. Reasons for not receiving reperfusion therapy were also inquired and reported.

Predictors of hospital mortality and intermediate term major adverse cardiovascular events (MACE), which was defined as a composite of all-cause mortality; new MI (positive cardiac biomarkers with or without invasive coronary angiography) and repeat revascularisation with PCI or coronary artery bypass graft (CABG) were noted.

SPSS 19 was used for statistical analysis. Frequencies and percentages were calculated for categorical variables. Mean with standard deviations (SDs) were reported for continuous variables, such as symptom onset-hospital arrival (hours), age (years) and baseline creatinine (mg/dl) if normally distributed (confirmed by constructing Histograms, Shapiro-Wilk's W tests and normal probability plots) or median ± inter-quartile range (IQR) if not normally distributed.

Fisher's exact or chi square test was used as needed for the comparison of in-hospital mortality. Predictors of in-hospital mortality were analysed using logistic regression analysis. Variables with $p<0.25$ in univariate analysis were considered significant for adjusting into multivariable model and $p<0.05$ were considered significant for the final model. Adjusted odds ratios (AOR) were reported with 95% confidence intervals (CIs).The time of follow-up was computed as time to event, lost-to-follow-up or death. For MACE, log rank test was utilised and Hazard Ratio (HR) with 95% CI was calculated. Kaplan Meier survival curves according to the revascularisation status were drawn and log rank p-values were reported.

Results

Of the 2,564 patients presenting with STEMI, 1,971 had symptom duration of less than 12 hours. Of these, 237(12%) did not receive any reperfusion therapy. Of them, 10 (4.21%) patients died before the administration of reperfusion therapy and 9 (3.8%) left against medical

Table-1: Reasons for not delivering reperfusion therapy.

Parameters	n (%)
Missed MI/ no reperfusion offered	74 (31.2)
Anatomy unsuitable	49 (20.7)
Non obstructive CAD	24 (10.1)
Quality of life decision	21 (8.9)
Spontaneous resolution of ischaemia	20 (8.4)
Patient/ family refusal	20 (8.4)
Death before reperfusion therapy	10 (4.2)
LAMA	9 (3.8)
Extreme age	6 (2.5)
Perceived severe bleeding risk	4 (1.7)
Total	237 (100)

Quality of life decisions included 2 patients with malignancy, 4 hypoxic brain injuries, 10 baseline poorfunctional statuses, 5 severe concomitant septicemias.
MI: Myocardial infarction, CAD: Coronary artery disease, LAMA: Left against medical advice

advice (LAMA). The final sample stood at 218 (11%) patients.

Among the 218 patients, there were 134(61.5%) who had presented early to other healthcare centres and had not received reperfusion therapy. Reasons behind lack of immediate reperfusion therapy were noted (Table 1).

Overall, 15(6.9%) patients had left bundle branch block (LBBB) and the rest had ST-segment elevation on electrocardiogram (ECG), and 45(27.6%) underwent immediate CAG.

Also, 24 (11.1%) patients had initial NIV risk stratification and 118(54.1%) had invasive risk stratification during the index admission with the median time to CAG being 1 day (IQR: 1-7 days). Revascularisation was performed in 77(35.3%) patients with median time to revascularisation of 7 days (IQR: 4-13 days). Details of hospital management were separately noted (Figure 1). Besides, 36(16.5%) patients did not undergo invasive or NIV ischaemia work-up. Of these patients, 1(2.7%) died before NIV testing, 21(58%) were felt to have limited one-year survival, extreme age was the cause in 6 (16.7%), 4 (11.12%) had increased risk of bleeding, and 4(11.12%) refused any testing.

During the hospital stay, 26(11.9%) patients died. Among them, 15(58%) belonged to the group which did not undergo any evaluation. Patients who died were more likely to have presentation later than 6 hours (50.0 vs. 29.2%), older age (67.8 vs. 59.4 yrs.),cardiogenic shock (50.0 vs. 5.7%), cardiac arrest (38.7 vs. 6.3%), systolic blood pressure (SBP)<100mmhg (37.5 vs. 7.9%), heart rate (HR)>100bpm (68.0 vs. 30.4%), worse baseline serum creatinine (2.16 vs. 1.36 mg/dl) and likely to present in

Table-2: Clinical characteristics and univariate analysis of non reperfused ST-elevation myocardial infarction (STEMI) patients (n=218).

Parameters	**Overall** (n=218)	**Deceased** n=26 (11.9%)	**Alive** n=192 (88.1%)	**OR** (95%CI)	***p*-value**
Symptom onset-hospital arrival (hrs.)	4.8± 3.8	6.3± 4	4.6± 3.7	1.12 (1.01-1.2)	0.03
> 6hrs from symptom onset	69 (31.7)	13 (50.0)	56 (29.2)	2.4 (1.1-5.6)	0.03
Transferred from other health facility	134 (61.5)	12 (46.2)	122 (63.5)	0.5 (0.2-1.1)	0.07
ER arrival time 8 a.m.- 8 p.m.	129 (59.0)	15 (57.7)	114 (59.4)	0.99 (0.42-2.1)	0.5
Age in years	60.3 ± 12.4	67.8± 12.3	59.4± 12.4	1.04 (1.06-1.1)	0.002
Age less than 50 years	43 (19.7)	1 (3.8)	42 (21.9)	14 (0.02-1.3)	0.03
Males	166 (76.1)	17 (65.4)	149 (77.6)	0.5 (0.2-1.3)	0.17
Smoker	44 (20.2)	2 (7.7)	42 (21.9)	0.3 (0.07-1.3)	0.09
Dyslipidaemia	47 (21.6)	4 (15.4)	43(22.4)	0.6 (0.2-1.9)	0.3
Hypertension	130 (596)	16 (61.5)	114 (59.4)	1.1 (0.47-2.5)	0.5
Family History of Premature CAD	29 (13.3)	1 (3.8)	28 (14.6)	0.2 (0.03-1.8)	0.2
Diabetes Mellitus	91 (41.7)	10 (38.5)	81 (42.2)	0.8 (0.4-1.9)	0.4
Anterior wall MI	80 (37.7)	12 (46.2)	68 (35.4)	1.6 (0.7-3.5)	0.3
Systolic BP<100mmHg	24 (11.2)	9 (37.5)	15 (7.9)	7.0 (2.6-18.8)	0.0002
Heart rate >100bpm	75 (34.7)	17 (68.0)	58 (30.4)	4.9 (1.9-11.9)	0.0003
Killip I or II	175 (80.3)	12 (46.2)	163(84.9)	0.15(0.06-0.37)	<0.001
Cardiogenic shock at presentation	24 (11.0)	13 (50.0)	11 (5.7)	16.4 (6.1-43.4)	<0.001
Cardiac arrest at presentation	22 (10.1)	10 (38.5)	12 (6.3)	9.4 (3.5-25.0)	<0.001
Baseline Creatinine (mg/dl)	1.4 ± 1.2	2.16 ± 1.2	1.36 ± 1.2	1.3 (1.02-1.7)	0.04
Multi-vessel disease (n=163)	105 (64.4)	7 (77.8)	98 (63.6)	2.0 (0.4-9.9)	0.4
LVEF <40%	108 (50.2)	14 (56.0)	94 (59.5)	1.3 (0.5-3.0)	0.5
Angiographic findings (n=163)	(n=163)	(n=9)	(n=154)		
Left main trunk	17 (10.6)	2 (22.2)	15 (9.7)		
2/3VCAD including Proximal LAD	48 (29.4)	2 (22.2)	46 (29.9)		
2/3VCAD excluding proximal LAD	40 (24.5)	3(33.3)	37 (24.0)		0.3
1VCAD including Proximal LAD	28 (17.2)	2 (22.2)	26 (16.9)		
Non obstructive CAD	30 (18.4)	0 (0)	30 (19.5)		

CAD: Coronary artery disease, LVEF: left ventricular ejection fraction, LAD: Left anterior descending coronary artery, OR: Odds ratio, CI: Confidence interval.

Table-3: Medications at discharge.

Medication on discharge	Overall (n=192)	Revascularized (n=75)	Not revascularized (n=117)
Aspirin	169 (88.0)	68 (90.7)	101 (86.3)
Thienopyridines	117 (63.4)	34 (45.3)	83 (70.9)
Statins	167 (87.0)	62 (82.7)	105 (89.7)
Beta blockers (BB)	166 (86.5)	65 (86.7)	101 (86.3)
ACE-I/ ARBs	110 (57.3)	38 (50.7)	72 (61.5)
Aldosterone antagonists	22 (11.5)	9 (12.0)	13 (11.1)
Antiplatelet + Statins + BB + ACE-I or ARBs	92 (47.9)	30 (40.0)	62 (53.0)

ACE: Angiotensin-converting-enzyme, ARB: Angiotensin II receptor blockers

Table-4: Major adverse events at follow up.

Parameters	Overall (n=142)	Revascularized (n=64)	Not revascularized (n=78)	*p*-value
MACE	30 (21.1)	9 (14.1)	22 (26.9)	0.05
Death	18 (12.7)	6 (9.4)	12 (15.4)	0.3
Myocardial infarction	8 (5.6)	3 (4.7)	5 (6.4)	0.6
Need for revascularization	10 (7)	3 (4.7)	7 (9.0)	0.7

MACE: Major adverse cardiovascular events.

Killip I or II (46.2 vs. 84.9%)($p<0.05$ for all). There was no significant difference in angiographic anatomy ($p>0.05$) (Table 2).

On multivariable modelling, mortality was strongly associated with no revascularisation performed (OR: 24.1, 95% CI: 1.3-500), presence of cardiogenic shock at presentation (OR: 65, 95% CI: 5.7-745) and HR>100 at presentation (OR: 17, 95% CI: 1.2-254.5).

Of the 192(88.1%) patients who were discharged alive, 175(91.1%) were prescribed at least one oral antiplatelet therapy (aspirin or clopidogrel) while dual anti-platelet therapy (DAPT) was given to 111(57.8%) patients. More patients in the non-revascularised group were prescribed DAPT compared to revascularized [55 (66.7%) vs. 51 (44%)]. Guideline directed medical therapy (GDMT), consisting of combination of dual anti-platelet, statin, beta blocker (BB) and angiotensin-converting-enzyme (ACE-I) /

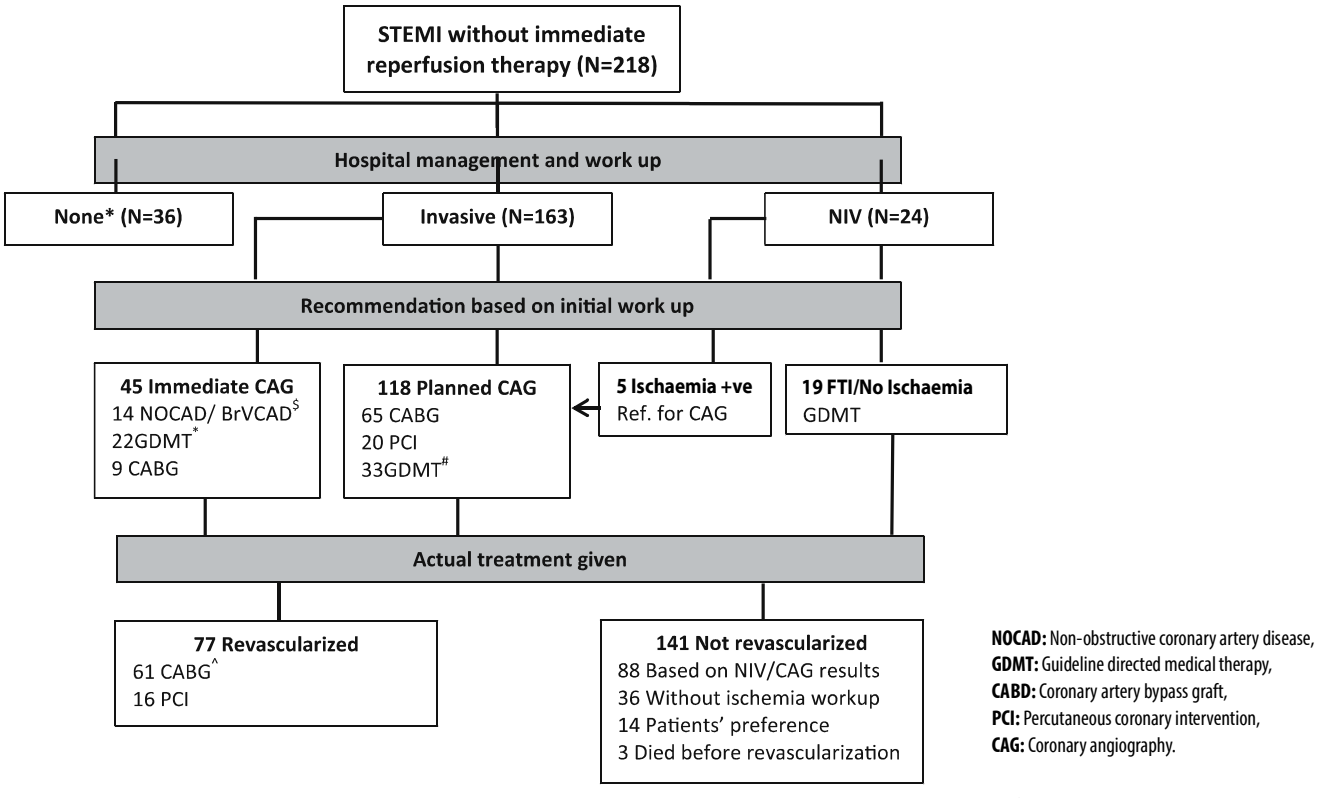

Figure-1: Flow chart of Hospital management and use of invasive coronary angiography (CAG) and non-invasive (NIV) ischaemia evaluation in reperfusion therapy eligible ST-elevation myocardial infarction (STEMI) patients

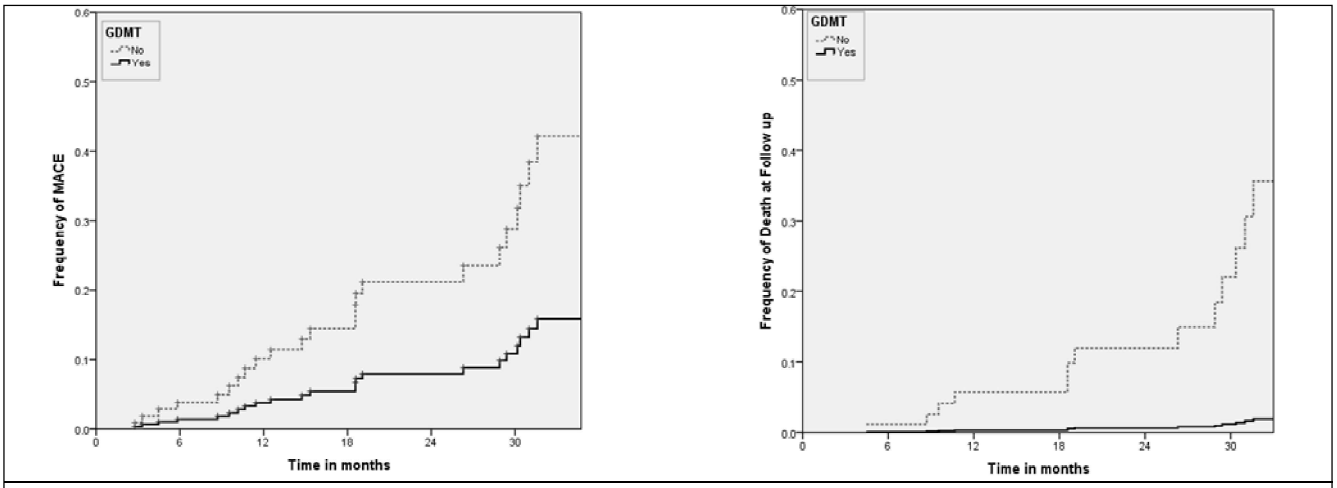

Figure-2 A-B: Major adverse cardiovascular events(MACE) and mortality among patients with and without discharge guideline directed medical therapy (GDMT) (Log Rank p-value 0.004 & 0.0002 resp.)

angiotensin II receptor blockers (ARB) combination was prescribed to 92 (47.9%) of patients discharged alive (Table 3).

MACE was noted on follow-up which was available for 172(84.7%) patients discharged alive with a median follow-up time of 20 (IQR: 10-33) months (Table 4; figure 2A-B). In multivariable analysis, predictors of MACE at follow-up was no GDMT at discharge (HR: 2.6, 95% CI: 1.16-6.2), while the presence of diabetes suggested a trend (HR: 2.0, 95%CI: 0.96-4.2, p=0.06). Revascularisation was not a significant predictor of MACE in multivariable analysis (p>0.05).

Discussion

The current study found that 11.9% patients with STEMI who were eligible for reperfusion therapy did not receive the treatment. The three primary reasons which account for more than half of the patients were misdiagnosis of MI, coronary anatomy considered unsuitable for revascularisation or non-obstructive disease in the main epcardial arteries. More than two-third patients had CAG performed and approximately 35% were revascularized later on with CABG being the major mode of revascularisation. Those who died during index hospitalisation were more likely to be in cardiogenic shock, have tachycardia at presentation and less likely to have undergone revascularisation. However, on follow-up of 20 months, MACE events were not significantly different among those who were revascularized compared to those who were not. GDMT use was related to reduced incidence of MACE and all-cause mortality.

The rates of not receiving reperfusion therapy in our study are similar to that reported in US NCDR of around 12%.[9] In Kerala STEMI registry from India, 52% eligible patients did not receive reperfusion therapy and in another study from Jakarta this rate was 42% despite presenting to a PCI centre.[10,11] No data is available due to absence of collaborative networks for STEMI patients in Pakistan. Devising STEMI network will not only aid in collection of accurate statistics but also improve patients' management and STEMI outcomes. There are examples of customised STEMI network in developing countries such as India and the model can be suitably applied in our population as well.[10,12]

Missed MI is the most common reason in our data which suggests lack of adequate training and failure to recognise STEMI in referring healthcare centres. Possible solutions start from community awareness so patients and family members recognise symptoms of MI and seek immediate medical attention in ER rather than to physicians' office. Also, training and guidance to local physicians and potential supervision and advice using internet for immediate ECG sharing, early recognition of STEMI, prompt reperfusion therapy and, if needed, transfer to nearby facility equipped for FL or primary PCI (PPCI) in a timely fashion. Emergent transfer to PCI facility using equipped ambulance when transfer time is acceptable should also be reinforced. Pharmaco-invasive approach with initial FL and then early transfer to a PCI-capable facility should be considered when transfer time is long.[13]

Unsuitable anatomy for PCI was the other common reason

also reflected in NCDR9 data . In our study, few of these patients underwent CABG later on. In such situations, immediate cardiac surgery consultation with a heart team approach will lead to improved decision-making regarding mode and timing of revascularisation, need for palliative culprit lesion PCI, pharmacological therapy, mechanical circulatory support or emergent CABG.[14] Reasons for withholding reperfusion therapy among prior studies are suggestive that older patients also benefit from acute STEMI reperfusion therapy.[15] In such patients it is recommended that there should be assessment of biological age and use of one of the many objective frailty indices utilising clinical parameters that can be readily applied in the ER.[17]

Our data showed hospital mortality among non-reperfused individuals of 11.9% that was almost similar to US NCDR statistics.[9] We also showed that haemodynamic instability and lack of revascularisation were independent predictors of mortality. As previously reported, cardiogenic shock at presentation is strongly associated with hospital mortality even after adjustment for key clinical parameters.[18] Those who are not revascularised have high risk of hospital mortality.[9] Although management and revascularisation decision in individual patients can be quite complex and in some of our patients who had in-hospital death and did not undergo any evaluation, there was selection bias involved related to other non-cardiac adverse prognostic conditions which led to deferral of further evaluation and probably also contributed to the mortality. We did not find revascularisation to be a significant predictor of MACE at intermediate-term follow up which is contrary to published studies and is because of a small sample size and shorter duration of follow-up.[19]

Less than half of the patients were prescribed GDMT on discharge. This is significantly lower than reported in US STEMI registries, but matches with South Asian data.[11,20] Patients in the revascularized group received less DAPT and GDMT. This finding was mainly driven by absent GDMT in most patients who were discharged after CABG. The finding of protective effect of discharge GDMT on follow-up mortality and MACE further strengthens the recommendations on use of optimal medications in all ACS patients.

Major limitation of our study is its single-centre data. Our data may underestimate proportion of STEMI patients not receiving reperfusion therapy. The reasons may include non-recognition of early STEMI within optimal time window by primary physician, unawareness and lack of specialised cardiac centres resulting in late or no referrals for timely reperfusion therapy. The reasons for no reperfusion therapy were derived from retrospectively collected data, thus reducing its reliability. On the positive side, this is the first study of its kind from Pakistan and points to many areas of future improvement. Data was derived from standardised data registry modelled after US NCDR[9] and all individual files were reviewed for validation.

Conclusion

A significant number of patients failed to receive reperfusion therapy. Most of these patients would have had an improved outcome if they were risk-stratified in a timely manner and offered early reperfusion therapy. There is a huge potential of improvement in STEMI care, starting from increasing awareness at the community level, recognition of eligible patients, prompt reperfusion therapy and usage of optimal medical therapy. STEMI networks and collaboration among local healthcare centres is recommended to have an organised approach to this crucial problem.

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References

1. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, De Lemos JA, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 61: e78-140.
2. banez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2017; 39: 119-77.
3. Hanssen M, Cottin Y, Khalife K, Hammer L, Goldstein P, Puymirat E, et al. French registry on acute ST-elevation and non ST-elevation myocardial infarction 2010. FAST-MI 2010. Heart 2012; 98: 699-705.
4. Gibson CM, Pride YB, Frederick PD, Pollack CV, Canto JG, Tiefenbrunn AJ, et al. Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and in-hospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J 2008; 156: 1035-44.

5. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003; 361: 13-20.
6. Fox KA, Goodman SG, Klein W, Brieger D, Steg PG, Dabbous O, et al. Management of acute coronary syndromes. Variations in practice and outcome. Findings from the Global Registry of Acute Coronary Events (GRACE). Eur Heart J 2002; 23: 1177-89.
7. Gharacholou SM, Alexander KP, Chen AY, Wang TY, Melloni C, Gibler WB, et al. Implications and reasons for the lack of use of reperfusion therapy in patients with ST-segment elevation myocardial infarction: Findings from the CRUSADE initiative. Am Heart J 2010; 159: 757-63.
8. Xavier D, Pais P, Devereaux P, Xie C, Prabhakaran D, Reddy KS, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet 2008; 371: 1435-42.
9. Dasari TW, Hamilton S, Chen AY, Wang TY, Peterson ED, De Lemos JA, et al. Non-eligibility for reperfusion therapy in patients presenting with ST-segment elevation myocardial infarction: contemporary insights from the National Cardiovascular Data Registry (NCDR). Am Heart J 2016; 172: 1-8.
10. Dharma S, Andriantoro H, Purnawan I, Dakota I, Basalamah F, Hartono B, et al. Characteristics, treatment and in-hospital outcomes of patients with STEMI in a metropolitan area of a developing country: an initial report of the extended Jakarta Acute Coronary Syndrome registry. BMJ Open 2016; 6: e012193.
11. Mohanan PP, Mathew R, Harikrishnan S, Krishnan MN, Zachariah G, Joseph J, et al. Presentation, management, and outcomes of 25 748 acute coronary syndrome admissions in Kerala, India: results from the Kerala ACS Registry. Eur Heart J 2012; 34: 121-9.
12. Alexander T, Mullasari AS, Kaifoszova Z, Khot UN, Nallamothu B, Ramana RG, et al. Framework for a National STEMI Program: consensus document developed by STEMI INDIA, Cardiological Society of India and Association Physicians of India. Indian Heart J 2015; 67: 497-502.
13. Pinto DS, Frederick PD, Chakrabarti AK, Kirtane AJ, Ullman E, Dejam A, et al. Benefit of transferring ST-segment-elevation myocardial infarction patients for percutaneous coronary intervention compared with administration of onsite fibrinolytic declines as delays increase. Circulation 2011; 124: 2512-21.
14. Holmes DR, Rich JB, Zoghbi WA, Mack MJ. The heart team of cardiovascular care. J Am Coll Cardiol 2013; 61: 903-7.
15. Zaman MJ, Stirling S, Shepstone L, Ryding A, Flather M, Bachmann M, et al. The association between older age and receipt of care and outcomes in patients with acute coronary syndromes: a cohort study of the Myocardial Ischaemia National Audit Project (MINAP). Eur Heart J 2014; 35: 1551-8.
16. Kang L, Zhang SY, Zhu WL, Pang HY, Zhang L, Zhu ML, et al. Is frailty associated with short-term outcomes for elderly patients with acute coronary syndrome? J Geriatr Cardiol 2015; 12: 662-7.
17. Singh M, Stewart R, White H. Importance of frailty in patients with cardiovascular disease. Eur Heart J 2014; 35: 1726-31.
18. Kolte D, Khera S, Aronow WS, Mujib M, Palaniswamy C, Sule S, et al. Trends in Incidence, management, and outcomes of cardiogenic shock complicating ST?elevation myocardial infarction in the United S tates. J Am Heart Assoc 2014; 3: e000590.
19. Szummer K, Wallentin L, Lindhagen L, Alfredsson J, Erlinge D, Held C, et al. Improved outcomes in patients with ST-elevation myocardial infarction during the last 20?years are related to implementation of evidence-based treatments: experiences from the SWEDEHEART registry 1995-2014. Euro Heart J 2017; 38: 3056-65.
20. McManus DD, Gore J, Yarzebski J, Spencer F, Lessard D, Goldberg RJ. Recent trends in the incidence, treatment, and outcomes of patients with ST and non-ST-segment acutemyocardial infarction. Am J Med 2011; 124: 40-7.