ORIGINAL RESEARCH

IMPLICATIONS OF SHORTER DOOR-TO-BALLOON TIMES ON THE OUTCOMES OF PATIENTS WITH ANTERIOR ST-ELEVATION MYOCARDIAL INFARCTION

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ABSTRACT

Cardiovascular disease is still the leading cause of death. In our tertiary care centre, we looked at the change in outcomes for anterior ST-elevation myocardial infarction (STEMI) between January 2017 and December 2021. Over the last five years, 1,658 patients with anterior STEMI who presented to our centre underwent primary percutaneous coronary intervention within 12 hours of their arrival. We gathered demographic, clinical, and mortality data during a five-year period and divided it into four quartiles: 2017-2018 (n=312), 2019 (n=408), 2020 (n=428), and 2021 (n=510).

The average age declined across the four quartiles (64.4, 62, 60.3, and 60 years, respectively, p<0.01). There was a significant increase in the prevalence of smoking, hypertension, and obesity in all groups, but no change in diabetes. The median hospital stay was shorter (6, 4.4, 4.2, and 3.6 days, respectively, p<0.01), as was the median door-to-balloon time (DBT) (217, 194, 135, and 38 minutes, respectively, p<0.01). Thirty-day and one-year mortality rates improved over time (14.4, 11.8, 8.4, and 7.8%) and (20.5, 16.4, 15.9, and 13.9 percent) respectively (p=0.01). In addition, 3-year mortality decreased (25.3, 21.6, 21.3, and 16.5 percent, respectively, p=0.02).Shorter DBT was associated with lower long-term mortality after adjusting for age, gender, co-morbidities, ejection fraction, clinical shock, and mitral regurgitation (compared to DBT <60 minutes; 60-90 minutes HR 1.67, 95 percent CI 0.93-3.00, p=0.084; 90-120 minutes, HR 1.74, 95 percent CI 1.02-2.95, p=0.04; >120 minutes, HR 1.91, 95 percent CI 1.23-2. In conclusion, patients with anterior STEMI have had better long-term results when DBT has been shortened over the last fiveyears.

Keywords: Anterior STEMI, Outcomes, Primary PCI, Ischemic heart disease.

INTRODUCTION

The use of drug-eluting stents, glycoprotein IIB/IIIA inhibitors, mechanical thrombectomy, and new antiplatelets [1–3] have all changed the way STEMI patients are treated in the last two years. Patient risk profiles, on the other hand, have changed as the prevalence of type 2 diabetes and hypertension has increased [4]. More importantly, since the Joint Commission and the Centers for Medicare and Medicaid Services introduced the quality metrics concept in 2002 for the management of patients with myocardial infarction across hospitals in the United States [5,6], there has been a significant reduction in door-to-balloon (DTB) time for STEMI patients [7].The effect of a shortened DTB time on death in these patients has been controversial, with some studies showing improved mortality [8–10] and others reporting no connection [11,12]. The goal of this study was to assess short- and long-term outcome trends in anterior wall STEMI patients receiving primary PCI in our tertiary care centre over the past fiveyears, with a focus on the relationship between these changes and DTB time changes.

METHODS

All patients who underwent PCI at our institution between 5 years were prospectively recruited in our PCI data registry and evaluated for study eligibility. Only patients with anterior STEMI who underwent primary percutaneous coronary intervention (PPCI) were eligible for inclusion, which was determined through a review of the data registry as well as medical records. Only anterior STEMI was included since it is known to be associated with poor outcomes and prognosis, implying the greatest benefit from a shorter DTB time.In addition to rising and fall in cardiac biomarkers and the presence of ischemic symptoms, anterior STEMI was defined as the presence of ≥1 mm ST-segment elevation in two or more contiguous anterior precordial leads (≥2 mm in men and ≥1.5 mm in women for leads V2 and V3), or new-onset left bundle branch block on EKG. Furthermore, PPCI was defined as any percutaneous coronary intervention done in the culprit artery within 12 hours of presentation. Signs of tissue hypoperfusion, low cardiac output/index, or the need for pressor assistance were all considered a cardiogenic shock.Patients were separated into four quartiles. The baseline demographics, comorbidities, clinical state, echocardiographic data, and procedure details were all documented. The start of the patient's observation period was determined as the date of the STEMI presentation and PPCI at our facility.Chart review was used to determine the follow-up, and the dates of incidents were noted. Data on mortality were collected from medical records. All-cause 30-day and 1-year death were the primary endpoints, with 3-year mortality as supplementary outcomes.

Continuous variables are compared using the Studentt-test or analysis of variance (for normally distributed data) or the Mann-Whitney test (for non-normally distributed variables) and represented as mean, ±SD, or median and inter-quartile for skewed distributions. Categorical data are reported as a percentage and compared using the Chi-Square test or Fisher's Exact test, depending on the situation. Cox proportional hazards analysis was used to evaluate independent predictors of outcome (with a p-value cutoff of <0.05 for statistical significance). The researchers estimated and provided hazard ratios (HRs) with 95% confidence intervals. The Kaplan-Meier method was used to calculate the cumulative proportion of occurrences as a function of time for the survival study. We specifically

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performed logistic regression analysis followed by multivariate cox proportional analysis to assess the relationship between mortality and change in DTB time. Statistical analysis was performed using SPSS version22.

RESULTS

The research covered a total of 1,658 patients. There were 312 patients in the first quartile, 408 patients in the second, 428 patients in the third, and 510 patients in the fourth. Table 1 shows the baseline characteristics of the patients in each group, while Table 2 shows the clinical presentations of patients in the four quartiles. The procedure details and complications for the four quartiles have been shown. DBT was considerably shorter in all four quartiles (median DBT 217, 194, 135, and 38 minutes, respectively, p<0.001). Procedural success (defined as post-intervention TIMI III flow) improved over time (89.1, 92.4, 92.3, and 94.8 percent, respectively, p=0.03), while hospital stay decreased (median 6, 4.4, 4.2, and 3.6 days, respectively, p<0.001).The first quartile did not have data on discharge medication; however, prescriptions of guideline drugs following STEMI increased considerably over time in the next three quartiles.

Table 1: Clinical presentations of the study population

Variable	2017-2018	2019	2020	2021	P-value
Heart rate, median (IQR) (bpm)	81(70-93)	80(70-90)	82(70-92)	84(73-97)	**0.001**
Systolic blood pressure, median(IQR)(mmHg)	117(103-134)	116(105-130)	127(111-146)	131(114-148)	**<0.01**
NYHA functional class					
I	93%	91%	74%	79%	**<0.01**
II	3%	2%	13%	10%	
III	1%	1%	6%	7%	
IV	3%	6%	7%	4%	
Shock	14%	10%	14%	12%	**0.1**
Intra-aortic balloon pump	35%	23%	19%	15%	**<0.01**
Ejectionf raction	40.3±12.7	38.4±12.3	37.6±12.6	42.3±12.5	**<0.01**
Ejection fraction<0.4	43%	47%	50%	38%	**0.005**
Anemia(serum hemoglobin <12g/dl)	19%	17%	17%	17%	**0.9**
Creatine Kinase-MB fraction, median(IQR)	**213(82-300.1)**	**136(38-351)**	**124(40-288)**	**118(41-267)**	**0.002**

Table 2: Procedural details, complications, and medications in patients across the four quartiles

Variable	2017-2018	2019	2020	2021	p-value
Door-to-balloon time: median (IQR) (minutes)	217 (135-270)	194 (129-264)	135 (113-232)	38 (25-79)	**<0.01**
No. of narrowed coronary arteries					
1	38%	62%	85%	83%	**<0.01**
2	34%	25%	11.7%	13%	
3	28%	13%	3.5%	3%	
Unprotected Left main or left main equivalent	0.7%	0.5%	1.9%	10%	**<0.01**
Proximal LAD	37%	41%	43%	46%	**0.01**
Graft intervention	4%	2.7%	1.9%	1.2%	**0.08**
Radial access	0%	0.3%	0.5%	19%	**<0.01**
Plain old balloon angioplasty Bare metal stents Drug eluting stents	47% 51% 0%	12% 69% 20%	15% 48% 39%	12% 32% 54%	**<0.01**
Total length stents used: Median (IQR) (mm)	15 (14-17.5)	21 (16-31)	24 (18-36)	23 (16-33)	**<0.01**
Longest treated lesion: Median (IQR) (mm)	8.7 (6-12.1)	14 (10.4-20)	15 (12-20.3)	18 (14-25.7)	**<0.01**
TIMI III at end of procedure	89%	92%	92%	95%	**0.03**
Emergency Coronary artery bypass surgery	5%	1%	1.6%	1.2%	**<0.01**
Heparin	76%	81%	71%	46%	**<0.01**
Glycoprotein IIB/IIIA inhibitors	66%	91%	85%	32%	**<0.01**
Thrombolytic	34%	6%	3%	1%	**<0.01**
Blood transfusion	19%	18%	13%	10%	**<0.01**
Puncture site hematoma	7%	6%	2%	1%	**<0.01**
Retroperitoneal bleed	1.7%	1.3%	1%	0.6%	**0.05**
Arteriovenous fistula	0.4%	0.3%	0.2%	0.3%	**0.9**
Pseudo aneurysm	2%	1%	0.4%	1.1%	**<0.01**
Acute kidney injury	12%	5%	4%	5%	**<0.01**
Length of hospital stay:	6 (4-17)	4.4 (3-8)	4.2 (2.8-7.3)	3.6 (2.8-	**<0.01**

Median (IQR) (days)				7.1)	
Aspirin at discharge	NA	98%	98%	100%	**0.02**
Beta Blockers at discharge	NA	80%	84%	97%	**0.03**
ACE inhibitors at discharge	NA	63%	67%	84%	**0.01**
Statin at discharge	**NA**	**84%**	**87%**	**97%**	**<0.01**

Thirty-day mortality decreased with time (14.4, 11.8, 8.4, and 7.8%, respectively, p<0.01), as did one-year mortality (20.5, 16.4, 15.9, and 13.9 percent, respectively, p=0.01). Three-year mortality improved significantly (25.3, 21.6, 21.3, and 16.5 percent, respectively, p=0.02). The Kaplan-Meier curve for long-term survival in patients in the four quartiles is also seen.

There was no difference in 30-day mortality between the four groups when DTB duration was separated into four groups (<60 minutes, 60-90 minutes, 90-120 minutes, and > 120 minutes) throughout the entire research (log-rank p=0.15). Shorter DTB times, on the other hand, were linked to lower 1-year and 3-year mortality. This study found that shorter DTB times (under 60 minutes) were related to better outcomes than longer DTB times. On multivariate cox analysis, shorter DTB time was still related to significant improvement in long-term mortality after adjusting for age, gender, co-morbidities, mitral regurgitation, clinical shock, and acute kidney injury.

DISCUSSION

Over a five-year period, we show considerable improvement in 30-day, 1-year, and 3-year mortality in patients coming with anterior STEMI to our centre for PPCI. We also found that DBT improved significantly over the same time period, which was linked to lower short- and long-term mortality. Shorter DBT had no effect on 30-day death, but it did improve 1-year and 3-year mortality rates significantly.

In STEMI patients having PPCI [7,9], several studies have demonstrated that shorter DBT improves mortality. In addition to 30-day mortality, there was a significant improvement in long-term mortality up to 5 years in our study, which had not previously been documented. This long-term improvement demonstrates the benefit of the earlier intervention, which results in decreased overall ischemia duration, infarction size reduction, and post-infarction remodeling. Another interesting discovery was that mortality was lower for DBT <60 minutes than for DBT <90 minutes. This reinforces the idea that DBT should not be limited to a set amount of time (e.g., 90 minutes), as most hospitals try to do. Instead, we show that, regardless of the aim, the shorter the DBT, the better the outcomes.A recent study found that shorter DBT had no effect on mortality [12]. This study, however, only looked at in-hospital mortality; it didn't look at 1-year or long-term death, and it didn't account for total ischemia time from the onset of symptoms. Furthermore, anterior STEMI patients made up just half of the study sample, with the balance suffering from inferior STEMI. As a result, the trial may have been underpowered to identify a benefit in anterior STEMI. This is in contrast to our study, which only included individuals with anterior STEMI who had PPCI during the first 12 hours.

In STEMI patients treated with PPCI [13], higher creatinine kinase MB fraction (CK-MB) peak levels have been linked to increased infarct size and higher long-term mortality. Peak levels of CK-MB decreased dramatically in our trial, which could explain some of the better long-term outcomes. The shorter DBT, which would reduce the extent of infarctions, could explain the lower CK-MB peak. Furthermore, the use of drug-eluting stents has been linked to lower long-term mortality and target vessel revascularization in PPCI patients with STEMI [14–16]. According to our findings, the use of DES in coronary procedures grew dramatically after 2018 and had a significant impact on outcomes.In addition, the incidence of retroperitoneal haemorrhage and puncture site complications such as pseudoaneurysm and hematoma formation decreased dramatically with time, according to our findings. When compared to manual compression, the use of vascular closure devices (VCD) is related tofewer puncture site problems and blood transfusions [17]. Increased use of VCDs could explain why there were fewer puncture site problems and blood transfusions in our study. Reduced usage of thrombolytics and increasing use of radial access are two further possibilities. In STEMI patients aged [18–20], radial access has been demonstrated to reduce mortality, puncture site problems, and bleeding issues.Improved outcomes could also be attributed to a lower rate of blood transfusions. Following the publication of a study in late 1999 that demonstrated that restricting blood transfusion with lower criteria (haemoglobin of 7 g/dl) is related to better results, blood transfusion recommendations have switched to a more restricted target. This could explain why the rate of transfusions in our study dropped dramatically. Furthermore, usage of blood products has been linked to considerably worse outcomes in STEMI patients undergoing PPCI [21–23] in multiple trials. The link between blood transfusion and poorer results in PCI patients has been thoroughly investigated.The early assumption was that patients who require blood transfusions are simply at a higher risk of bleeding complications following the intervention, and so are fundamentally linked to poorer outcomes [24,25]. However, independent of bleeding issues, blood transfusion has been shown to worsen outcomes [26–29].

Despite the increased use of high-risk operations such as unprotected left main and proximal LAD interventions, overall procedural success has grown significantly while the rate of complications such as coronary perforation and side branch closure has remained unchanged. Consider that in many circumstances, the intervention would have been aborted if these techniques had not been used.This could also be considered a factor in the improvement of overall outcomes. Finally, we found an increase in the rate of mortality-benefit drugs such beta-blockers, statins, and angiotensin-converting enzyme inhibitors being prescribed at discharge. This is related to the introduction of quality metrics reporting and is another component that contributes to better results.

There are various drawbacks to this study. First, it was an observational study with potentialfor selection bias and limited ability to determine cause rather than association. Second, because this is a single-center study, caution should be exercised when extrapolating findings to other smaller centres or the entire community. Third, certain relevant variables such as DES use and pharmaceutical use were not controlled for in logistic regression. We opted not to include any variables in the model that had more than 10% missing values.

Over the last fiveyears, there has been a dramatic improvement in short- and long-term mortality for patients presenting with anterior STEMI and undergoing PPCI. The observed mortality advantage is linked to a number of parameters, including shorter DBT (even beyond the currently suggested 90-minute threshold) and fewer procedural problems.

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