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Effect of Early Door to Balloon Time on Treatment with Adjunctive Therapy and Resultant Procedural Success in STEMI

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Abstract

Objectives: We studied whether earlier door-to-balloon (DTB) times affected use of standard adjunct medications (Rx), and the effect of differential Rx on PCI success.

Background: Striving for earlier DTB times in STEMI is important, but rushing may negatively impact pt management. We studied whether earlier DTB times negatively affected use of standard adjunct Rx, pre-PCI chest x-ray (CXR), and the effect on PCI success.

Methods: 227 pts diagnosed with STEMI were taken directly for angiography. Rx use between 3 grps were compared: Grp A=DTB>90 (n=156), Grp B=DTB<90 (n=71), Grp C =DTB<60 (n=12). Differential Rx patterns were evaluated for effect on PCI success. Optimal PCI result was defined as post-PCI TIMI 3 flow and stenosis <50% in the infarct vessel.

Results: Fewer pts received all Rx pre-PCI in Grp B than in Grp A, 1.4% vs. 9.6% (p=0.02), including B-blk, 53.5% vs. 67.3% (p=0.01) heparin infusion (GTT), 19.7% vs. 46.8% (p<0.001), and IIb/IIIa GTT, 12.6 vs. 28.2% (p<0.01). Shorter DTB reduced duration of pre-PCI heparin and IIb/IIIa Rx (p<0.01), and performance of CXR, grps A/B/C at 89.7%/ 61.2%/ 41.7% (p<0.0001). When adjusted for other variables, DTB<90 was a significant predictor of less heparin GTT use, OR 0.3 ([0.17-0.55], p<0.0001). Pts in Q4 (>66min) of heparin pretreatment had more optimal PCI result (65.0%), vs. Q1 (0-30min) (41.0%) (p=0.02). Pts receiving heparin GTT had optimal results 66.2% vs. 50.0% (p=0.02), and higher TIMI 3 flow (69.8% vs. 53.2%, p=0.02). In this cohort, there was no significant difference in mortality based on DTB group, though use of B-blk and IIb/IIIa medications improved mortality and cardiac mortality, respectively.

Conclusion: In this cohort, earlier DTB times led to less complete adjunctive Rx and omission of diagnostic steps. Shorter pretreatment with heparin, and omission of heparin GTT, predicted less favorable procedural outcomes.

Abbreviations: STEMI: ST-Elevation Myocardial Infarction; DTB: Door-To-Balloon; PCI: Percutaneous Coronary Intervention; TIMI: Thrombolysis In Myocardial Infarction; IRA: Infarct Related Artery; ED: Emergency Department; ECG: Electrocardiogram

Background

Timely reperfusion in ST-elevation MI (STEMI) has consistently been shown to improve outcomes [1-3]. The AHA/ACC/SCAI guidelines currently establish a goal of 90 minutes from door to balloon (DTB) in primary percutaneous intervention (PCI) [4], and some sources suggest that DTB goals should be reduced even further [3]. The achievement of this goal in 75% of cases is considered a primary quality indicator by Get with the Guidelines [5]. In addition, a number of medications have indications for use as early adjunctive therapy, including aspirin, heparin (all Class I indications), and less strongly emphasized, the use of beta-blockers (Class I to be given "promptly to those without contraindication" per 2004 guidelines, now stated as within 24 hours), and ADP inhibitors and GPIIb/IIa inhibitors (Class IIa for upstream use during the study period, now IIb) [4,6].

Whether the time pressure to routinely achieve a 90 minute DTB goal could result in withholding or delay of administering adjunctive medical treatments, and how this might affect procedural outcomes, is not known. Thus, we investigated the effect of progressively earlier DTB times on the administration of adjunctive medications, and whether differential use of these medications had any effect on markers for procedural success, including post-PCI TIMI flow in the infarct related artery (IRA), post-PCI thrombus burden, no-reflow phenomenon, and residual stenosis. Because we were primarily interested in the affect of time constraints on physician behavior and process, we also investigated whether lower DTB times lead to less thorough diagnostic evaluation, using pre-PCI chest x-ray as a marker, and the impact of the ECG pattern on these decisions.

Methods

Subjects

We analyzed a cohort of consecutive patients presenting to a single active urban center with presumed STEMI over a 6 year period during which decreasing the DTB time was a significant medical and administrative focus. Patients were identified as having an acute

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STEMI via records of the cardiac catheterization laboratory as well as discharge coding documents. Included were patients presenting with chest pain within the prior 12 hours and ST-elevation by ECG of > 1mm in at least 2 leads, or new left bundle branch block, transferred directly from the emergency department (ED) to the catheterization laboratory for emergent angiography and primary PCI. Excluded were patients with STEMI who were not first seen within the ED, patients who were transferred from other institutions for primary PCI, and patients who were treated with fibrinolysis before planned PCI, a total of 28 patients during the study period, leaving a cohort of 227 patients. All patients in this cohort were included in the analysis of the timing and administration of adjunctive medications before PCI. One hundred ninety-six patients ultimately received PCI, and these patients comprised the procedural study group. Patients who did not have coronary angiographic findings consistent with STEMI on catheterization, or in whom PCI was not performed due to technical or logistical reasons, were excluded from the procedural outcome analysis (n=31). The institutional IRB reviewed and approved the study of these subjects.

Study protocol

In the analysis of adjunctive medication administration, subjects were divided into three groups based on DTB times: Group A included patients with DTB>90 minutes (n=156), Group B patients with DTB<90 (n=71), and Group C a subgroup of Group B in whom DTB<60 (n=12). Door-to-balloon time was defined as the difference between the time of balloon inflation within the IRA and the time of first medical contact. If the patient did not receive a revascularization attempt with a balloon or other interventional device, he/she was grouped based on [door-to-sheath time + 15 minutes] as a surrogate for DTB (n=54). Adjunctive medications studied included aspirin, heparin, heparin infusion, GPIIb/IIIa inhibitor bolus and infusion, and beta-blocker. ADP inhibitors were not routinely administered in this institution prior to PCI, nor were direct thrombin inhibitors. The use and timing of administration of the adjunctive medications included in the analysis was determined by the treating team, which consisted of the ED attending physician and attending cardiologist. Standard dosing regimens were used for heparin boluses and infusions. The use of abciximab and eptifibatide were both categorized as GPIIb/IIIa, with standard dosing regimens used for boluses and infusion, unless adjusted for renal function or age. The timing of medications was obtained from review of electronic ED and catheterization laboratory records. "Duration of treatment" prior to PCI for each of heparin and IIb/IIIa medications was defined as the time between bolus injection and the placement of arterial sheath. Patient demographics, laboratory results, and procedural data were obtained from the hospital electronic medical records.

All patients receiving PCI were included in the procedural outcomes analysis. The decision to intervene and the technical aspects of primary PCI were at the discretion of the operating interventional cardiologist. All catheterization films were reviewed by a single observer. TIMI flow categories were characterized as previously defined [7]. Slow or no-reflow phenomenon was determined based on TIMI flow and time to distal opacification in the IRA after definitive management, e.g., angioplasty or stent placement, in each case [8]. Residual thrombus was defined as visible angiographic filling defect >5mm dimension within the IRA at the conclusion of the procedure. One year mortality data was taken from the electronic medical record, as possible, as well as from public records, and could be obtained for all but 2 patients. Mortality findings are reported as they pertain to all patients with true STEMI.

Endpoints

The endpoints of the medication administration analysis included categorical use of each individual adjunct, cumulative use of all adjuncts, and duration of pretreatment with each anticoagulant (heparin, IIB/IIA) before PCI. The endpoints of the procedural outcome analysis included TIMI flow in the IRA, no-reflow phenomenon, presence of residual thrombus, and optimal procedural result, which was defined as TIMI 3 flow in the IRA with residual stenosis <50% post-PCI, as previously described [9]. One year mortality, and cardiac mortality, are included as secondary endpoints.

Statistical analysis

Values are expressed as percentages, mean ± standard deviation or median and range. Categorical variables were analyzed using chi-square or Fisher Exact analysis when appropriate. Continuous variables were analyzed using student's t-test; ordinal variables were analyzed via Mann-Whitney test. Backward stepwise logistic regression and forward stepwise linear regression analyses were performed to examine the combined effect of multiple patient characteristics on the reception of the study medications, including DTB group, age, gender, history of CAD, admission during off-hours, STEMI location, and shock at admission. A p-value of <0.05 was considered to be significant. All analyses were performed with SPSS software (release 18.0, IBM-SPSS, Chicago).

Results

Demographics

The mean age of the population was 59+/-14 years, 79.7% of which were male. Standard risk factors were widely present in the population, including 71.4% of subjects with hypertension, 51.1% with dyslipidemia, and 36.6% current smokers. Overall, there were no significant differences between the DTB cohorts with respect to baseline demographics (Table 1). Median door-to-balloon times improved throughout the study period, at 150.3 +/-65.2 minutes at year one to 90 +/- 29.86 minutes at year six. Overall, there were a total of 20 deaths (8.8%), including 13 cardiac deaths (5.7%) at 1 year. There was no statistical difference in 1-year mortality or cardiac mortality between the 3 DTB groups.

The effect of presentation during off-hours on DTB times was evaluated. Groups A/B/C arrived during off hours (5pm-7am) at 49.4%/ 22.5%/25.0% (p<0.001), redemonstrating that patients with earlier DTB times were more likely to have arrived during normal working hours [10]. Males tended to have earlier DTB times compared to females (mean 119.5+/-60.8 vs. 148.5+/-80.1, p<0.01). There was no difference in mean DTB times when comparing weekend vs. weekday presenters.

ECG findings were evaluated in detail. In this cohort, inferior/posterior MI, and the presence of reciprocal depression, were significantly more frequent in groups B and C, with the OR to achieve DTB<90 at 2.38 and 3.00 respectively, both highly significant. Notably, heparin infusion was more likely to be given in lateral MI or LBBB (p<0.01), but no other significant medication discrepancies were found based on ECG characteristics. Performance of a chest x-ray in the emergency department receives a class I indication in the STEMI guidelines (providing time-to-reperfusion is not delayed). In our cohort, 89.7% of patients in Group A received x-rays, 61.2% in Group B (p<0.0001), and 41.7% in group C (p<0.0001).

Variable	DTB>90 MIN (N=156)	DTB<90 MIN (N=71)	DTB<60 MIN (N=12)
Age	59±15	60±14	62±9
Age >75	23 (14.7%)	8 (11.3%)	1 (8.33%)
Male*	121 (77.6%)	60 (84.5%)	11 (91.7%)
Tobacco	58 (35.2%)	25 (35.2%)	4 (33.3%)
Diabetes	43 (27.6%)	21 (29.6%)	3 (25.0%)
Hypertension	107 (68.6%)	55 (77.5%)	10 (83.3%)
Hyperlipidemia	78 (50.0%)	38 (53.5%)	8 (75.0%)
History of CAD	42 (26.9%)	20 (28.2%)	4 (33.3%)
History of CABG	5 (3.20%)	3 (4.22%)	1 (8.33%)
History of PCI	31 (19.9%)	14 (19.7%)	2 (16.7%)
BMI	28.2 +/-5.7	28.9 +/-7.8	32.1 +/-12.3
False alarm	15 (9.62%)	5 (7.04%)	0 (0.00%)
Weekend presentation	48 (30.8%)	14 (19.7%)	2 (16.7%)
Off hours presentation*	77 (49.4%)	16 (22.5%)*	3 (25.0%)
Mean DTB time*	151.3 +/-64.0	70 +/-15.2*	46.9 +/-8.5*
Home Medications			
Aspirin	31 (55.4%)	23 (32.4%)	5 (41.7%)
Beta blockers	36 (23.1%)	19 (26.8%)	5 (41.7%)
Statins	36 (23.1%)	19 (26.8%)	5 (41.7%)
Plavix	12 (7.69%)	6 (8.45%)	1 (8.33%)
ACEI	34 (21.8%)	14 (19.7%)	3 (25.0%)
1-year Mortality	14 (8.97%)	5 (7.04%)	1 (8.33%)

Table 1: Clinical characteristics (n=227). Baseline characteristics of the three door-to-balloon cohorts. *asterisk indicates statistically significant in comparison with group dtb>90.

Variable	Received Heparin Infusion	
	Odds Ratio	p-Value
*DTB<90 min	0.30 [0.17-0.55]	<0.0001
Age >75	1.02 [0.99-1.04]	0.08
Male Sex	0.85 [0.41-1.77]	0.67
Off hours	0.98 [0.54-1.78]	0.94
*Inferior STEMI	1.65 [1.11-2.46]	0.01
Hx CAD	0.77 [0.40-1.52]	0.46
Shock	0.99 [0.48-2.06]	0.99

Table 2: Effect of separate variables on administration of heparin drip. Multivariate logistic regression analysis of combined effect of multiple factors on administration of heparin infusion.

Medication administration

The percentage of patients cumulatively receiving all study medications in Groups B and C were compared with Group A. Fewer patients received all therapies prior to PCI in Group B (DTB<90) than in Group A (DTB>90), 1.4% vs. 9.6% (p=0.02). None of the patients (0%) in Group C (DTB<60) received all of the study medications. The percentage of patients cumulatively receiving the indicated Class I medications in groups A/B/C was 64.7%/57.7%/41.7% (p-value for trend <0.001). The mean number of study medications received by group A patients was 4.24+/-1.09, which was higher than both of the other groups, group B at 3.81 +/-1.03 (p=0.0055), Group C at 3.58 +/-0.79 (p=0.04) (Figure 1). Patients arriving during off hours were actually likely to receive a higher number of study medications (p=0.036).

Each medication was also evaluated separately. Nearly all of the patients received aspirin, 218/227 (96.0%), prior to PCI. Comparing Group B (DTB<90) with Group A (DTB>90), fewer received the heparin infusion, 19.7% vs. 46.8% (p<0.001), fewer received the GPIIb/IIIa infusion, 12.6 vs. 28.2% (p<0.01) and fewer received beta blocker 53.5 vs. 67.3% (p=0.01). An even smaller percentage of group C received the heparin infusion (8.3%, p<0.01), the GPIIb/IIIa infusion (0%, p=0.03), and beta blocker (50.0%, p=0.38) (Figure 2). Patients not treated with heparin infusion generally were found to have received bolus dosing of heparin during the PCI procedure, and the majority (82.1%) of true STEMI patients not receiving upstream IIB/IIIA infusion received it during the procedure. IIB/IIIA medications were overall less likely to be given in females or patients >75 years old (p=0.036)

Shorter DTB time also had a significant effect on duration of pre-PCI heparin and IIb/IIIa. Significant decrement in pre-PCI duration of these medications was noted with shorter DTB times (Figure 3). When evaluated by quartile of heparin duration, 59.6% of Group A were in either quartile 3 (>45-66 minutes) or 4 (>66 minutes), while only 11.3% of Group B were in quartile 3 or 4 (p<0.001).

When adjusted for multiple other variables, DTB<90 remained the single strongest significant predictor for failure to give heparin infusion, OR=0.30 [0.17-0.55] (p<0.0001). Inferior MI predicted a higher likelihood to administer heparin infusion, OR 1.65 [1.11-2.46] (p<0.01), and age>75 years demonstrated a slight trend towards increased heparin infusion. Male sex, off-hours presentation, history of CAD, and presentation with shock had no significant effect (Table 2). After adjustment, DTB<90 also remained a significant predictor for overall reduced medications given, mean 3.86 +/-1.07 versus 4.24 +/-1.09 in DTB>90 group (p=0.004).

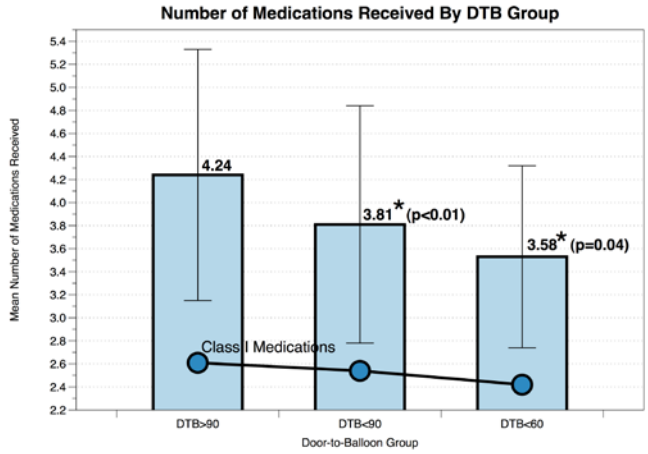

Figure 1: Number of medications received by dtb group. Overall use of medications, and Class I medications, segregated by door-to-balloon group. Bars with confidence intervals are inclusive of all study medications, dots represent only medications with Class I indication. *Asterisk indicates statistically significant in comparison with group DTB>90.

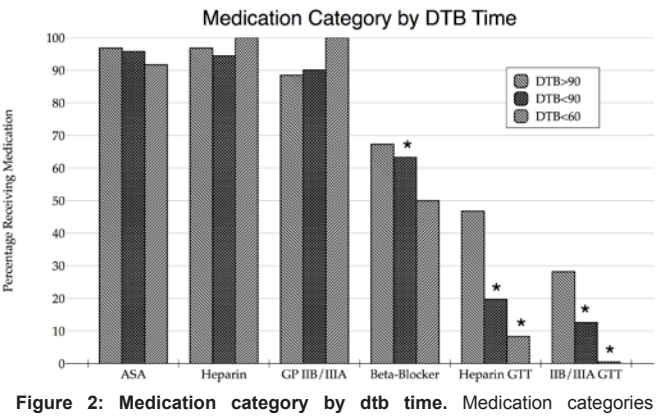

Figure 2: Medication category by dtb time. Medication categories considered separately with respect to door-to-balloon group. *Asterisk indicates statistically significant at (p<0.05) in comparison with group DTB>90.

Procedural outcomes

Overall, 196 patients received a PCI attempt, of whom 158 (80.6%) had a stent placed. Of patients receiving PCI, 93.4% had post-PCI TIMI flow ≥2, with 16.8% of which requiring pharmacologic intervention prior to the conclusion of the case for slow/no-reflow. Higher post-PCI TIMI flow demonstrated trends towards improved outcomes, with 1 year mortality for TIMI 3/2/1/0 at 6.56%/ 11.6%/ 14.3%/ and 22.2%, with TIMI 3 versus TIMI 0 flow not quite reaching statistical signficance (p=0.058). While as noted above, improvements in yearly median DTB times were observed over the study period, this was not mirrored in achievement of post-PCI TIMI 3 flow, nor optimal procedural results. The nadir for both TIMI 3 flow (42.6%) and optimal procedural result (29.8%) came at year 5 (2008), which corresponded to the year with the lowest median DTB time (89.5 +/- 48 minutes) and highest achievement of DTB<90 (46.8%) (Figure 4).

Categorical use of IIb/IIIa, at any time, was associated with a higher mean post-PCI TIMI flow, 2.54+/-0.67 versus 2.13 +/-1.19 in those not receiving IIb/IIIa (p=0.035). There was no significant difference in post-PCI TIMI flow based on categorical use of heparin, though the number of patients not receiving heparin was small (n=6).

Of patients receiving neither anticoagulant prior to PCI (n=4), an optimal procedural result was obtained in 0%, compared to patients who received both (n=180) in whom an optimal procedural result was obtained in 57.8% (p=0.02). Patients not receiving anti-coagulants also demonstrated more thrombus at the conclusion of the case 100% vs. 35.1% (p<0.01).

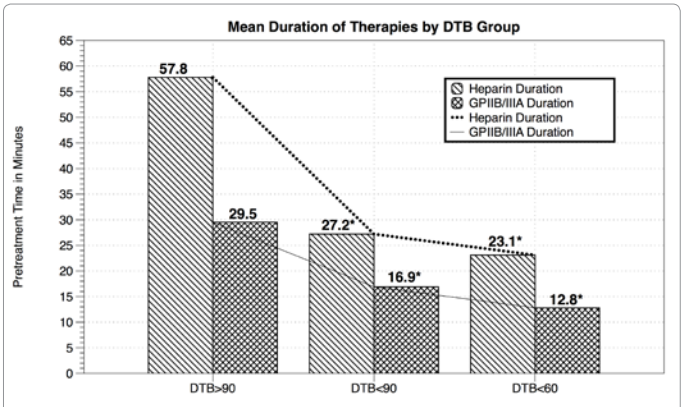

Figure 3: Mean duration of therapies by dtb group. Duration of anticoagulant therapies prior to PCI, segregated by door-to-balloon groups. *Indicates statistically significant at p<0.05 in comparison with group DTB>90.

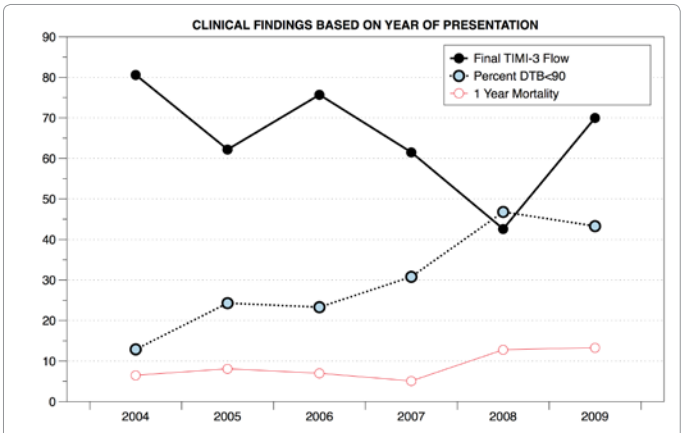

Figure 4: Clinical findings stratified by year of presentation. Final TIMI-3 flow (solid line with black dots), percent door-to-balloon <90 minutes (dotted line with blue dots), and 1 year mortality (red line with open red dots), in each of the years included in the study.

Procedural outcomes were analyzed within quartiles of pretreatment time for both heparin and IIa/IIIa, as well as categorically with respect to use of the use heparin and IIb/IIIa *infusions* pre-PCI, as these patterns were the most discrepant between groups DTB>90 and DTB<90 as above. An optimal procedural result was more frequent in quartile 4 (Q4, >66min) of heparin pretreatment at 65.0%, compared to quartile 1 (Q1,0-30min) at 41.0% (p=0.02). Furthermore, patients receiving heparin infusion also had significantly higher optimal procedural results, 66.2% vs. 50.0 % in those without heparin infusion (p=0.02), as well as higher TIMI 3 flow (69.8% vs. 53.2%, p=0.018), (Figure 5) and less slow/no reflow prior to the conclusion of the case (9.4% vs. 21.3%, p=0.018). In patients receiving heparin infusion, mean post-PCI TIMI flow was 2.63 (+/-0.65), compared to patients without heparin infusion, mean TIMI 2.39 (+/-0.78) (p=0.027). Interestingly, there were no significant differences in TIMI flow, no-reflow, or procedural success stratified by quartile of GPIIb/IIIa pretreatment, or use of GPIIb/IIIa infusion.

Within the DTB<90 group, pretreatment with heparin and use of heparin infusion were evaluated with respect to procedural outcomes, to determine if the observed differences in medication use had an effect. When evaluated solely within Group DTB<90 min (the guideline mandated value), the use of heparin infusion demonstrated a trend toward higher percentage TIMI 3 flow (76% vs. 60.3%, p=0.27), and optimal procedural result (76% vs. 52.8%, p=0.11). Patients not meeting the 90 min DTB goal, but receiving more complete heparin treatment (i.e., falling into the highest quartile of heparin pretreatment, and receiving heparin infusion), demonstrated higher optimal procedural result (66.7%) than those meeting the 90 min DTB goal but receiving less complete heparin treatment (i.e. not receiving heparin infusion and falling into the lowest quartile of pretreatment), optimal procedural result (35.9%), (p=0.013).

One year mortality was determined based on the use of the study medications. Use of beta-blockers was associated with 5.71%/ 5.0% overall/cardiac mortality vs 16.4%/ 9.0% if not used (p=0.02 for mortality, 0.44 for cardiac mortality). Subjects in whom IIb/IIIb inhibitors were used demonstrated 1 year mortality of 7.94%, versus not used 22.2% (p=0.08), though cardiac mortality was better with IIb/IIIa use at 4.8% vs 22.2% (p=0.02). Use of heparin was associated with 9.0% mortality versus 16.7% (p=0.53), though the number of patients not receiving heparin as above was small (n=6).

Discussion

Current guidelines place appropriate emphasis on striving for shorter door-to-balloon times, given the incremental improvement in in-hospital (2) and 30 day (1) mortality outcomes with more rapid reperfusion. However, the early hospital course of the STEMI patient is chaotic and rushed, involving multiple physicians and specialties, and a host of early diagnostic tests. A patient triaged into a direct ED-to-catheterization laboratory track is acutely ill, often unstable, and requires continual monitoring. In this milieu, it is not difficult to envision inadvertently delayed and/or withheld adjunctive medications. Furthermore, the anticoagulants approved for use in STEMI, even if

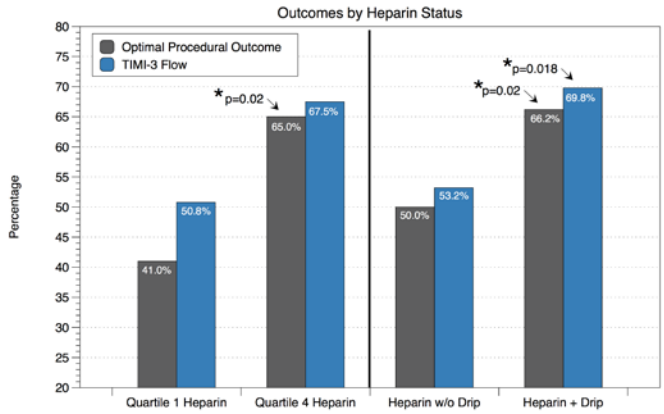

Figure 5: Outcomes by heparin status. Procedural outcomes, including TIMI-3 flow, and optimal procedural outcome, by heparin treatment status. Left pane compares Quartile 1 (0-30 minutes) of heparin pretreatment with Quartile 4 (>66 minutes) with respect to achievement of TIMI-3 flow (blue bars) and optimal procedural result (gray bars). Right pane compares patients receiving bolus dosing of heparin only with those receiving bolus and infusion.

rapid in onset, require a finite lead-time in order to be of utility during the PCI procedure itself. It is conceivable that cases can arise in which the time pressure to perform PCI within the 90 minute goal, a process indicator which is widely considered the quintessential quality of care indicator, leads to failure to give appropriate adjuncts.

The most important finding of this study is that earlier DTB times were significantly associated with less frequent use of beta-blockers, adjunctive IIb/IIIa infusion, and heparin infusion prior to the procedure. In the total cohort, shorter pretreatment time with heparin, and failure to use heparin infusion, were significantly associated with less often achieving an optimal procedural result, including less frequent achievement of TIMI 3 flow, and increased no-reflow; which was mirrored by the trend within the smaller group whose DTB time was less than the 90-minute guideline mandated value, also significant if stratified by heparin quartile and receipt of heparin infusion. Further, omission of B-blk and IIb/IIIa, in this cohort, had significant effect on mortality and cardiac mortality, respectively.

Notably, while median DTB times and the achievement of DTB<90 minutes demonstrated improvements over the course of the study period, a period during which the institution had an active DTB quality improvement initiative in place, this positive trend was not mirrored in improved 1 year mortality nor achievement of post-PCI TIMI 3 flow. Interestingly, the year in which the DTB time was overall the lowest was also the nadir for achievement of TIMI 3 flow and procedural success, and highest mortality, conceivably due in part to less complete adjunctive therapies.

TIMI 3 flow is of particular importance, as this subset of patients has the lowest overall mortality in STEMI, significantly lower than the TIMI 2 subset [11]. The no-reflow phenomenon is a poor prognostic sign, associated with less procedural success, larger enzymatic infarct, and higher long term mortality [12]. In this study, failure to use heparin infusion, which was highly correlated with shorter DTB times, was found to be a significant predictor of the no reflow phenomenon.

The optimal timing of anticoagulant administration remains under robust debate. In the case of IIb/IIIa inhibitors, the guidelines have recently changed the "upstream" indication from IIA to IIB, with more stress on use of oral thienopyridines "as soon as possible" [13,14]. This is in contrast to earlier data that seemed to suggest improvement in procedural outcomes and a trend towards lower mortality with pre-PCI use of IIb/IIIa [15,16]. The data in this study seem to confirm the current guidelines, as upstream versus procedural use had no significant effect on PCI outcomes or 1-year mortality. Use of upstream heparin is less controversial, as it is widely accepted as a relatively benign and inexpensive treatment. Prior studies have shown improvement in procedural outcomes [17] and even mortality with earlier use of heparin [9]. Our findings tend to confirm this observation, as longer pre-treatment and use of pre-PCI infusion had measurable effects on PCI success and TIMI 3 flow.

Para clinical evaluation in STEMI may be more of an art than a science. Knowledge of a patient's heart failure status in the setting of STEMI has prognostic [18] as well as treatment implications [19], but whether this should mandate performance of chest x-ray in the ED during STEMI is not clear. In our cohort, shorter DTB times had an association with a lower percentage of subjects receiving pre-cath lab chest x-rays. While it might be concluded that omitting this step can streamline the emergency room visit and facilitate faster transfer to the lab, caution should always be advised when "cutting corners" in the workup in this population. For instance, in this cohort, there were 17 patients (7.5%) whose ECG's were misinterpreted as STEMI, which could have had alternative diagnoses evident by x-ray, e.g. aortic dissection, pericardial effusion, etc. Ultimately, a pre-PCI chest x-ray should probably be considered, and omitted on a case by case basis. Another interesting finding is that certain ECG patterns translated into achievement of earlier DTB time, namely the presence of inferior/posterior MI, reciprocal depression, and maximum ST-elevation >3mm. This suggests that treating physicians may be applying an incorrect and possibly rushed heuristic when interpreting the presenting ECG, as findings known to be specific (and eye-catching), though not sensitive [20,21] predicted earlier DTB times. Arguably, anterior MI, which is also less likely to demonstrate reciprocal depression, benefits more from earlier reperfusion.

Some study has been put forth on the issue of protocol-driven, or critical-pathway driven, medication use in STEMI. The ACC Guidelines Applied in Practice (GAP) program, put into action at 10 hospitals, improved the use of medications including ASA and B-blk through the use of standardized order sets and pocket cards [22]. In the unique environment of the VA system, use of critical pathway and computerized order sets resulted in improvement in utilization of adjunct medications, in MI patients upon admission [23]. An interesting correlary to this study would be to evaluate the effect of such a protocol in this institution on peri-PCI medication use, PCI outcomes, and mortality.

Implications of the Study

Achieving a DTB goal of <90 minutes is paramount to achieving excellent STEMI outcomes within an institution, including reduced mortality. We do not in any way suggest that this goal should be overlooked or relaxed in order to assure administration of adjunctive medications indicated by the existing guidelines. Moreover, we believe that achieving all of the guideline-mandated goals is not only possible, but arguably very important for the highest procedural success. In certain scenarios, one could envision the treatment team trading certain measures, such as expedited heparin administration, clinical exam, or performance of chest films, in order to achieve the mandate. This does not need to be the case. We hypothesize that a certain threshold of hurried management may exist, beyond which care of individual

patients can suffer. Future recommendations pushing DTB goals ever shorter (particularly if a specific lower time-limit is ascribed, such as 60 or 30 minutes) should not overlook the reality of human error.

Limitations

A number of important limitations are present in this retrospective, single center study. As a retrospective cohort analysis, this study suffers from all biases and confounders that are inherent to such analyses. Of particular note is that the patients were treated by a number of different emergency room and cardiology physicians, whose own preferences for medication use, and technical operation, may have impacted both the medication and procedural analysis. The time period overlaps a period during which the literature and guidelines were in flux, particularly with respect to use of beta-blockers and IIb/IIIa medications as an upstream adjunct, which may have had an effect on how these medications were used. Use of IIb/IIIa upstream has been de-emphasized in favor of the use of oral thienopyridines and also procedural bivalirudin, which have become the standard of care in many institutions. Attempts to apply the above findings to these other medication categories would only be conjecture. In the present study, final TIMI 3 flow percentages were slightly lower than has been described in similarly sized randomized trials [17,24], though final TIMI 2 or 3 percentages were nearly identical, at >90%. Finally, this study was neither conceived nor designed to compare outcomes across varied DTB times, as this is a widely accepted arbiter of of outcomes; rather it was designed to evaluate the effects of attempting to achieve rapid DTB times on the processes of triage and treatment. While no mortality benefit was noted based on DTB times in this study, it was not powered to do so. In this way, it can be viewed as hypothesis generating only.

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