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Manual Thrombus Aspiration Is Not Associated With Reduced Mortality in Patients Treated With Primary Percutaneous Coronary Intervention

An Observational Study of 10,929 Patients With ST-Segment Elevation Myocardial Infarction From the London Heart Attack Group

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ABSTRACT

OBJECTIVES This study aimed to assess the impact of thrombus aspiration on mortality in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention (PCI).

BACKGROUND The clinical effect of routine intracoronary thrombus aspiration before primary PCI in patients with ST-segment elevation myocardial infarction is uncertain.

METHODS We undertook an observational cohort study of 10,929 ST-segment elevation myocardial infarction patients from January 2005 to July 2011 at 8 centers across London, United Kingdom. Patients' details were recorded at the time of the procedure into local databases using the British Cardiac Intervention Society PCI dataset. Primary outcome was all-cause mortality at a median follow-up of 3.0 years (interquartile range: 1.2 to 4.6 years).

RESULTS In our cohort, 3,572 patients (32.7%) underwent thrombus aspiration during primary PCI. Patients who had thrombus aspiration were younger, had lower rates of previous myocardial infarction but were more likely to have poor left ventricular function. Procedural success rates were higher (90.9% vs. 89.2%; $p = 0.005$) and in-hospital major adverse cardiac event rates were lower (4.4% vs. 5.5%; $p = 0.012$) in patients undergoing thrombus aspiration. However, Kaplan-Meier analysis demonstrated no significant difference in mortality rates between patients with and without thrombus aspiration (14.8% aspiration vs. 15.3% PCI only; $p = 0.737$) during the follow-up period. After multivariate Cox analysis (hazard ratio [HR]: 0.89, 95% confidence interval [CI]: 0.65 to 1.23) and the addition of propensity matching (HR: 0.85 95% CI: 0.60 to 1.20) thrombus aspiration was still not associated with decreased mortality.

CONCLUSIONS In this cohort of nearly 11,000 patients, routine thrombus aspiration was not associated with a reduction in long-term mortality in patients undergoing primary PCI, although procedural success and in-hospital major adverse cardiac event rates were improved. (J Am Coll Cardiol Intv 2015;8:575–84) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

BCIS = British Cardiovascular Intervention Society

CI = confidence interval

HR = hazard ratio

MACE = major adverse cardiac events

PCI = percutaneous coronary intervention

PPCI = primary percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

Mechanical reperfusion with primary percutaneous coronary intervention (PPCI) is the optimal treatment strategy for patients with ST-segment elevation myocardial infarction (STEMI) (1). During PPCI, embolization of thrombus and plaque fragments into the distal coronary artery bed may lead to microvascular obstruction and reduced flow associated with failure to achieve restoration of microvascular perfusion, and this has been associated with an increase in mortality (2,3). Removing the thrombus prior to PCI, with the use of thrombectomy devices could prevent distal embolization, improve microvascular perfusion, and improve outcomes after STEMI treated with PPCI. Both the European Society of Cardiology and American College of Cardiology/American Heart Association guidelines recommend that coronary artery thrombus aspiration should be considered as an adjunctive therapy during PPCI for STEMI (4,5).

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These recommendations (IIa) are mainly based on a single study, the TAPAS (Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction Study). This was a single-center trial involving 1,071 patients, which demonstrated not only an improvement in the primary outcome of myocardial blush grade but a nearly 50% reduction in mortality at 1 year (6,7). However, since TAPAS, the evidence supporting the benefit of thrombus aspiration on clinical outcomes is less clear (3,8-10). The recent publication of the largest randomized trial of thrombus aspiration, TASTE (Thrombus Aspiration During ST-Segment Elevation Myocardial Infarction), which randomized over 7,000 patients to thrombus aspiration or PCI alone, suggested that routine aspiration does not reduce either 30-day or 1-year mortality in patients undergoing PPCI (11,12).

The aim of this study was to describe the impact of thrombus aspiration on post-procedural outcomes, post-PPCI TIMI (Thrombolysis In Myocardial Infarction) flow grade and long-term mortality in a large regional network of heart attack centers.

METHODS

This was an observational cohort study to investigate the relationship between thrombectomy use and outcome after PPCI for STEMI. We merged the databases of the 8 London Heart Attack Centres who collect data based on the British Cardiac Intervention Society (BCIS) dataset, with the analysis comparing thrombectomy and no thrombectomy pre-specified. The BCIS audit is part of a national mandatory audit that all UK PCI centers participate in.

STUDY DATABASE. The UK BCIS audit collects data from all hospitals in the United Kingdom that perform PCI, recording information about every procedure performed (13). PCI is defined as the use of any coronary device to approach, probe, or cross 1 or more coronary lesions, with the intention of performing a coronary intervention (13). The database is part of the suite of datasets collected under the auspices of the National Institute for Cardiovascular Outcomes Research and is compliant with UK data protection legislation. Data are collected prospectively at each hospital, electronically encrypted, and transferred online to a central database. Each patient entry offers details of the patient journey, including the method and timing of admission, inpatient investigations, results, treatment, and outcomes. Patients' survival data are obtained by linkage of patients' National Health Service numbers to the Office of National Statistics, which records live status and the date of death for all deceased patients.

POPULATION STUDY AND DESIGN. We examined an observational cohort of consecutive patients with STEMI treated with PPCI between January 2005 and July 2011 at all 8 tertiary cardiac centers in London, United Kingdom. There are no other centers in London that undertake PPCI. Patient and procedural details were recorded at the time of the procedure and during the admission into each center's local BCIS database. Anonymous datasets with linked mortality data from the Office of National Statistics

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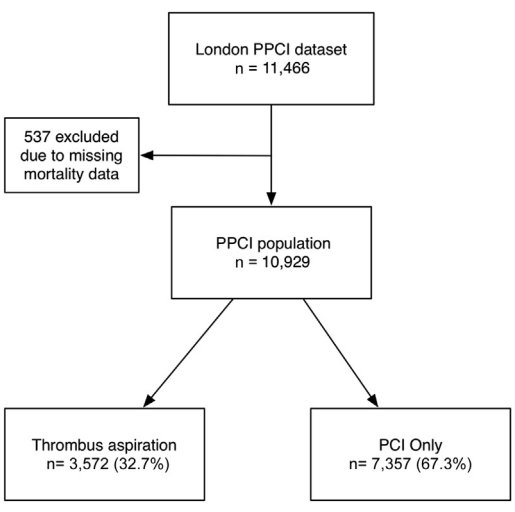
were merged for analysis from the 8 centers. During the study period, 11,466 patients underwent PPCI. Of these, 95.3% had complete datasets and National Health Service numbers and were included in the analysis (Figure 1).

All patients with onset of symptoms of <12 h and at least 1-mm ST-segment elevation in 2 or more contiguous limb leads or at least 2 mm in 2 or more contiguous precordial leads or left bundle branch block were considered for PPCI. Coronary angiography was performed via the radial or femoral artery. The culprit lesion was identified and crossed with an angioplasty guidewire. Manual thrombus aspiration was performed at the discretion of the operator followed by conventional PCI to the culprit vessel.

THROMBUS ASPIRATION PROCEDURE. Patients were classified into thrombus aspiration or non-thrombus aspiration groups. The thrombus aspiration group included all patients in whom thrombus aspiration was attempted. All thrombus aspiration was performed manually using the following devices: Export (Medtronic, Minneapolis, Minnesota) in 67.4%; X-Sizer (ev3, Plymouth, Minnesota) in 3.9%; Pronto (Vascular Solutions, Minneapolis, Minnesota) in 2.9%; TEC (Boston Scientific, Natick, Massachusetts) in 6.4%; and others including Hunter (Innovative Health Technologies), QuickCat (Spectranetics, Colorado Springs, Colorado), Eliminate (Terumo, Somerset, New Jersey), and Rescue (Boston Scientific) in 19.4%. No mechanical devices were included in the analysis.

FIGURE 1 Flow Diagram of Study Patients



Flow diagram of study patients describing patient exclusions and makeup of study population. PPCI = primary percutaneous coronary intervention.

CLINICAL OUTCOMES. Patient clinical and demographic data, procedural characteristics, bleeding complications, procedural complications, all-cause in-hospital mortality, nonfatal MI, reintervention, and stroke were recorded during the admission. In-hospital major adverse cardiac events (MACE) were defined as death, myocardial infarction (new pathologic Q waves in the distribution of the treated coronary artery with an increase of creatine kinase-myocardial band to ≥2× the reference value or significant rise in troponin biomarkers, stroke, and target vessel revascularization. Procedural complications recorded included MI, emergency coronary artery bypass graft, arterial complications, aortic/coronary dissection, side branch occlusion, and arrhythmia. Following discharge, long-term all-cause mortality was obtained by linkage to the Office of National Statistics. Successful primary PCI result was defined as final TIMI flow grade 3 and residual stenosis <20% in the infarct-related artery at the end of the procedure.

ETHICS. The data was collected as part of a national cardiac audit and all patient identifiable fields were removed prior to analysis. The local ethics committee advised us that formal ethical approval was not required.

STATISTICAL ANALYSIS. Clinical characteristics of thrombus aspiration versus PCI-only treated patients were compared using the Pearson chi-square test for categorical variables and Student *t* test for continuous variables. Normality of distribution was assessed using the Shapiro-Wilks test. We calculated Kaplan-Meier product limits for cumulative probability of reaching an endpoint and used the log-rank test for evidence of a statistically significant difference between the groups. Time was measured from the first admission for a procedure to outcome (all-cause mortality). Cox regression analysis was used to estimate hazard ratios for the effect of thrombus aspiration in age-adjusted and fully adjusted models, based on covariates ($p < 0.05$) associated with the outcome. The proportional hazards assumption was evaluated by examining log(-log) survival curves and additionally was tested with Schoenfeld residuals. The proportional hazard assumption was satisfied for all outcomes evaluated.

A propensity score analysis was carried out using a nonparsimonious logistic regression model comparing thrombus aspiration and PCI-only patients. Multiple variables were included in the model,

including age, sex, diabetes, hypertension, hypercholesterolemia, previous coronary artery bypass graft, previous PCI, previous MI, multivessel disease, chronic renal failure, pre-procedure TIMI flow, ejection fraction, procedural success, and glycoprotein IIb/IIIa use. The C-score was 0.78, indicating good discrimination. After ranking propensity score in an ascending order, a nearest neighbor 1:1 matching algorithm was used with calipers of 0.2 SD of the logit of the propensity score. Each thrombectomy and PCI-only patient was used in at most 1 matched pair to create a matched sample with similar distribution of baseline characteristics between observed groups. Based on the matched samples, the Cox proportional hazard model was used to determine the impact of thrombectomy on mortality over follow-up. STATA (version 10, StataCorp, College Station, Texas) was used for all analysis.

RESULTS

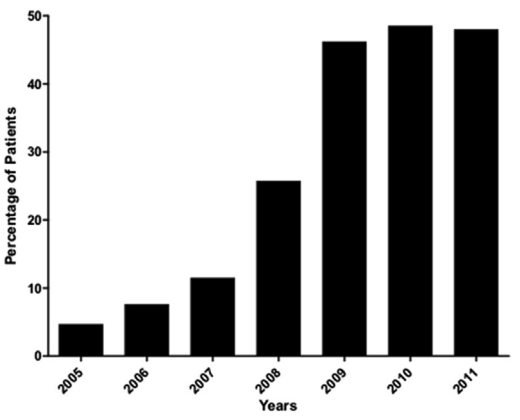
We included 10,929 patients in the study population with a mean age of 62.25 years; 22.5% of the patients were women. A total of 39.1% of the patients had hypertension, 41.5% had dyslipidemia, 55.9% were active or ex-smokers, and 15.2% had diabetes. In our cohort, 6.4% of patients had poor left ventricular function with 6.0% of patients presenting with cardiogenic shock. The overwhelming majority of PCI procedures were performed through the femoral route, being the access route of choice for each study year and accounting for 76.5% of procedures throughout the study period. However, radial procedures did increase from <10% in 2005 to approximately 40% in 2011. In our cohort, 41.4% of patients received a drug-eluting stent and 69.9% received a glycoprotein IIb/IIIa inhibitor.

In our cohort, 3,572 patients (32.7%) underwent thrombus aspiration during their PPCI (thrombus aspiration group) and 7,357 (67.3%) did not (PCI-only group). The percentage of patients who underwent thrombectomy use quadrupled over the course of the study period, from 7.6% in the first year to 48.5% in the last year (Figure 2).

PATIENT CHARACTERISTICS. Overall, the thrombus aspiration group was younger, more likely to be male and have poor left ventricular function compared with the PCI-only group (Table 1). Higher rates of previous MI, hypercholesterolemia, diabetes, and renal failure were seen in the PCI-only group. No differences were seen in the incidence of shock.

PROCEDURAL CHARACTERISTICS AND OUTCOMES. There were no differences in the rates of multivessel disease or multivessel intervention between the groups (Table 2). There were higher rates of drug-eluting stent and glycoprotein IIb/IIIa inhibitor use in the thrombus aspiration group than in the PCI-only group. Thrombus aspiration patients had significantly higher rates of infarct-related artery TIMI flow grade 0 (68.5% vs. 42.7%, $p < 0.0001$) and lower rates of infarct-related artery TIMI flow grade 3 (6.7% vs. 13.6%; $p > 0.0001$) at presentation compared with those treated with PCI alone. Procedural success rates defined as rates of post-procedural TIMI flow grade 3 (thrombus aspiration 90.9% vs. PCI only 89.2%; $p = 0.005$) were higher in the thrombus aspiration group than in the PCI-only group.

FIGURE 2 Percentage of Patients Undergoing Thrombectomy Before PPCI From 2005 to 2011



The bar graph shows the percentage of patients undergoing thrombectomy before PPCI from 2005 to 2011. PPCI = primary percutaneous coronary intervention.

IN-HOSPITAL OUTCOME. In-hospital MACE rates were lower in the thrombus aspiration group than in the PCI-only group (4.4% vs. 5.5%; $p = 0.012$). There was no difference in the incidence of cerebrovascular accident between the 2 groups (Table 3).

LONG-TERM OUTCOME. Patients were followed-up for a median of 3.0 years (interquartile range: 1.2 to 4.6 years). Kaplan-Meier analysis demonstrated that there was no statistically significant difference in mortality rates between the 2 groups (14.8% aspiration vs. 15.3% PCI-only; $p = 0.737$) (Figure 3).

PREDICTORS OF ALL-CAUSE MORTALITY. Age-adjusted Cox analysis revealed that the use of thrombectomy in PPCI was not associated with all-cause mortality (hazard ratio [HR]: 0.77, 95% confidence interval [CI]: 0.65 to 1.10) (Figure 4). This did not change after

multivariate adjustment (HR: 0.89, 95% CI: 0.70 to 1.23) (Figure 5). The variables that showed independent association with mortality were age, chronic kidney disease, severe systolic left ventricular impairment, cardiogenic shock, multivessel disease, and call-to-balloon time (Figure 4). Radial artery access, TIMI flow grade 3 in the infarct-related artery prior to PPCI, procedural success, and use of a glycoprotein IIb/IIa inhibitor were independently associated with 3-year survival.

The preceding Cox proportional hazard model was repeated with the year of procedure included as a categorical variable to allow for improvements in PCI technique and technology over the long study period. This confirmed no association between thrombectomy use and mortality (HR: 0.85, 95% CI: 0.63 to 1.12).

PROPENSITY SCORE. To further account for confounding variables and bias, propensity score matching was performed to adjust for differences in demographic and procedural variables producing a total of 6,912 patients (3,456 in the thrombus aspiration group and 3,456 in the PCI-alone group). Following matching, the baseline demographics and procedural variables were well balanced in the 2 propensity-matched cohorts. In the propensity-matched cohorts, Cox regression analysis revealed that the use of thrombectomy during PPCI was not a predictor of all-cause mortality (HR: 0.82, 95% CI: 0.60 to 1.13).

TABLE 1 Baseline Characteristics According to Thrombus Aspiration or PCI-Only Group

	Thrombus Aspiration (n = 3,572)	PCI Only (n = 7,357)	p Value	Data Completeness, % (n) (n = 10,929)
Age, yrs	60.80 ± 13.17	62.96 ± 13.25	<0.0001	100 (10,929)
Female	758 (21.2)	1,698 (23.1)	0.026	99.8 (10,905)
Previous MI	426 (11.9)	1315 (17.9)	<0.0001	91.8 (10,030)
Previous CABG	92 (2.6)	236 (3.2)	0.057	95.5 (10,432)
Previous PCI	454 (12.7)	864 (11.7)	0.246	95.1 (10,390)
Hypercholesterolemia	1,454 (40.7)	3,081 (41.9)	0.039	94.6 (10,344)
Diabetes mellitus	502 (14.1)	1,159 (15.8)	0.005	94.0 (10,273)
Hypertension	1,383 (38.7)	2,894 (39.3)	0.143	94.6 (10,344)
Smoking history	2,135 (59.8)	3,974 (54.0)	0.030	85.9 (9,393)
PVD	55 (1.5)	138 (1.9)	0.190	94.6 (10,344)
CKD (Creat >200), μmol/l	22 (0.6)	75 (1.0)	0.018	88.9 (9,715)
Previous CVA	68 (1.9)	140 (1.9)	0.938	94.6 (10,344)
Left ventricular function			<0.0001	39.8 (4,347)
Good	604 (16.9)	2,179 (29.6)		
Fair	406 (11.4)	456 (6.2)		
Poor	288 (8.1)	414 (5.6)		
Cardiogenic shock	234 (6.6)	422 (5.7)	0.100	98.3 (10,748)
Direct transfer	2,316 (64.8)	4,080 (55.5)	<0.0001	91.2 (9,971)
Call-to-balloon time, min	115 (92, 165)	125 (98, 170)	0.057	61.0 (6,161)
Door-to-balloon time, min	45 (26, 120)	48 (26, 118)	0.191	

Values are mean ± SD, n (%), or median (interquartile range).

CABG = coronary artery bypass graft; CKD = chronic kidney disease; Creat = creatinine concentration; CVA = cardiovascular accident; MI = myocardial infarction; PCI = percutaneous coronary intervention; PVD = pulmonary vascular disease.

DISCUSSION

In this large observational study of 10,929 patients undergoing PPCI for STEMI, 32.7% of patients underwent thrombus aspiration during PPCI. Despite a greater rate of procedural success and lower in-hospital MACE, in-hospital mortality and long-term survival were similar for the patients who underwent thrombus aspiration to those who received PCI only. Our data suggest that in our cohort routine thrombus aspiration during PPCI, compared with not receiving therapy, does not appear to be associated with a reduction in mortality rates. This is the largest cohort of PPCI-treated STEMI patients to have demonstrated no association between thrombus aspiration and reduced mortality.

Studies assessing the use of thrombectomy and outcome have demonstrated varied results. Current European Society of Cardiology and American College of Cardiology/American Heart Association guidelines recommend thrombus aspiration as an adjunctive therapy during PPCI (4,5). These IIa recommendations are based predominately on the TAPAS study, which demonstrated an approximately 50% reduction in mortality at 1 year (6,7). However, the TAPAS trial (6,7) is the only randomized trial to have demonstrated a significant beneficial effect on mortality, and TAPAS was not designed or powered for the primary endpoint of mortality with subsequent data from observational studies also suggesting benefit (3). Although our results may be consistent with more recent interventional studies such as TASTE (11,12) (that imply that routine thrombectomy use may not be associated with an improvement in mortality), we feel that at present there is insufficient data to exclude thrombectomy as a potentially effective therapy during PPCI, even after considering our observational data. To date, most studies have been underpowered, not selective enough in recruitment or have not included sensitive enough endpoints to detect a clinically meaningful benefit. Although the TASTE study was a large multicenter, prospective, randomized controlled trial that randomized 7,244 patients undergoing PPCI to either manual thrombus aspiration or no aspiration, the study does have limitations. This was a novel trial design using an established national registry. The study had a primary endpoint of mortality but did not reliably collect TIMI

TABLE 2 Procedural Characteristics According to Thrombus Aspiration or PCI-Only Group

	Thrombus Aspiration (n = 3,572)	PCI Only (n = 7,357)	p Value	Data Completeness (n = 10,929)
Access				98.2 (10,728)
Femoral	2,425 (67.9)	5,931 (80.6)	<0.0001	
Radial	1,148 (32.1)	1,303 (17.7)	<0.0001	
No. of diseased vessels				94.4 (10,313)
Single-vessel	1,593 (68.0)	3,493 (63.0)	0.320	
Multivessel	1,685 (47.2)	3,542 (48.1)	0.320	
Mean vessels	1.67 ± 1.0	1.68 ± 1.0	0.721	
Target vessel				100% (10,929)
Right coronary artery	1,557 (43.6)	2,889 (39.3)	<0.0001	
Left main coronary artery	50 (1.4)	137 (1.9)	0.086	
Left anterior descending	661 (18.5)	1831 (24.9)	<0.0001	
Left circumflex coronary	467 (13.1)	1,293 (17.6)	<0.0001	
Saphenous vein graft	68 (1.9)	122 (1.7)	0.351	
Multivessel intervention	1,979 (55.4)	3,864 (52.5)	0.320	94.4% (10,313)
Vessel diameter	3.92 ± 7.6	3.89 ± 26.68	0.712	86.7% (9,473)
Vessel length	21.95 ± 9.3	22.91 ± 11.55	<0.0001	86.7% (9,473)
TIMI Pre-angiography			<0.0001	84.8% (9,266)
TIMI flow grade 0	2,447 (68.5)	3,141 (42.7)		
TIMI flow grade 3	239 (6.7)	1,001 (13.6)		
DES	1,687 (47.2)	2,841 (38.6)	<0.0001	95.5% (10,433)
GP IIb/IIIa inhibitor	2,836 (79.4)	4,806 (65.3)	<0.0001	95.5% (10,433)
Procedural success	3,247 (90.9)	6,560 (89.2)	0.005	84.8% (9,266)

Values are n (%), mean ± SD, or % (n).

DES = drug-eluting stent(s); GP = glycoprotein; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

flow grade, myocardial blush, and ST-segment resolution, which may be related to improved clinical outcomes. In addition, other potentially important endpoints such as heart failure or recurrent MI were either not collected or reliably captured as would have occurred in a conventional randomized controlled trial. Also, approximately 7% of patients were not randomized because the clinicians felt thrombus aspiration was required and the expected event rate (30-day mortality) was significantly lower (3%) than had been estimated (6.3%) for the power calculation, implying the study was underpowered. Perhaps not surprisingly, therefore, the TASTE study demonstrated no significant difference in either 30-day or more recently 1-year mortality between the 2 groups (11,12).

TABLE 3 In-Hospital Outcomes and Complications Post-PCI According to Thrombus Aspiration or PCI-Only Group

	Thrombus Aspiration (n = 3,572)	PCI Only (n = 7,357)	p Value	Data Completeness (n = 10,929)
In-hospital				96.5% (10,545)
MACE	157 (4.4)	408 (5.5)	0.012	
Death	93 (2.6)	219 (3.0)	0.423	
Q wave MI	54 (1.5)	140 (1.9)	0.216	
Reintervention PCI	11 (0.3)	40 (0.5)	0.135	
CVA	14 (0.4)	14 (0.2)	0.065	
Emergency CABG	6 (0.2)	30 (0.4)	0.055	
Arterial complications	28 (0.8)	58 (0.7)	0.914	88.3% (9,648)

Values are n (%) or % (n).

MACE = major adverse cardiac events; other abbreviations as in Table 1.

Other studies such as the INFUSE-AMI (Intracoronary Abciximab and Aspiration Thrombectomy in Patients with Large Anterior Myocardial Infarction) randomized trial (14) have come to similar conclusions as thrombus aspiration was not effective in reducing infarct size. These trials are consistent with meta-analyses (9,15) that again suggest no mortality benefit with thrombectomy. Although our data appear to support the conclusion that aspiration thrombectomy does not improve mortality, we feel that our results merely support the conclusion at present that there have been insufficiently powered or appropriately designed trials to detect or exclude clinically important benefits.

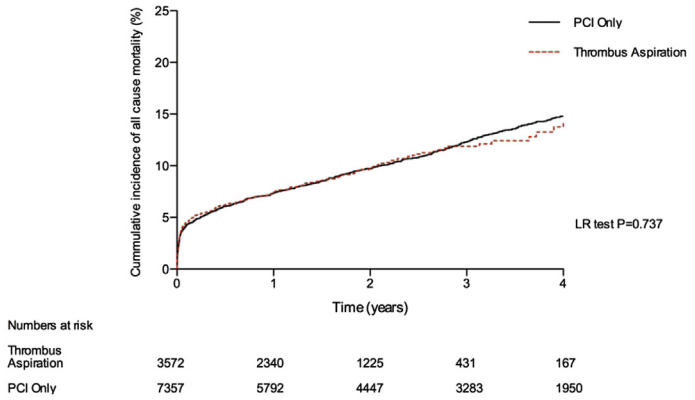
Thrombectomy use in our cohort was shown to increase over the study period with a sharp increase following the publication of TAPAS in 2008. However, none of the participating centers in our cohort had local guidelines dictating when to use a thrombus aspiration catheter and, therefore, there was likely to be a heterogeneous mix of cases. As thrombus characteristics and composition vary according to the type of acute coronary syndromes and time to presentation, it is likely that different subsets of acute coronary syndrome patients may respond differently to thrombus aspiration. As our database does not have detailed morphological characterization of lesion and thrombus morphology or thrombus burden, we are unable to explore whether there are subsets of patients who may respond better than others to aspiration. In addition, it has been suggested that thrombus aspiration may not be a risk-free procedure. Systemic embolization may occur, and in a recent meta-analysis, thrombus aspiration was associated with a trend toward an increased rate of stroke (p = 0.06) (10). Although in our cohort, there was no significant difference between the groups in the rates of stroke and neurological complications, it is possible that some subsets of patients (perhaps with established organized thrombus) may not only not benefit from aspiration but could be harmed by the risk of embolization, either into the distal coronary bed or indeed systemically.

We found that thrombus aspiration was less likely to be performed in older patients perhaps due to a

higher incidence of features known to reduce the likelihood of successful delivery of the thrombectomy catheter (16), including greater vessel tortuosity and calcification. In addition, we found patients with pre-PPCI TIMI flow grade 2 or 3 were less likely to undergo thrombus aspiration. This is probably due to a lower visible thrombus burden in these patients compared with those with pre-PPCI TIMI flow grade 0 or 1 and may be appropriate. However, this variation in use of thrombus extraction in different settings of PPCI may well hide an important benefit that is only seen in certain subsets of patients. Although we did not find a significant interaction between pre-PPCI TIMI flow grade and the impact of thrombectomy on mortality, by analyzing these subsets, we are further decreasing the power to detect a potentially important signal and so this data should be interpreted with caution.

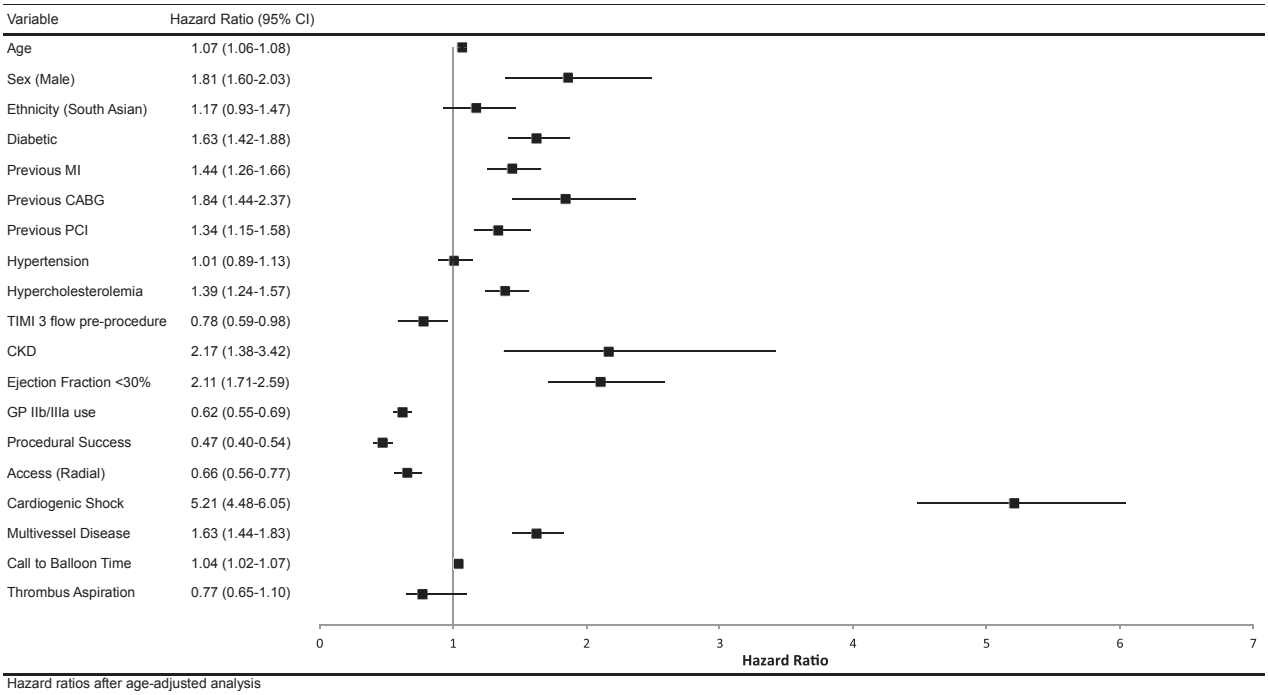
It is generally accepted that distal embolization plays a pivotal role in causing microvascular injury after PPCI (2,17) with a high thrombus burden associated with increased incidence of distal embolization and higher frequency of adverse outcomes (MACE and mortality) (18). Thrombectomy devices were introduced to reduce thrombus burden and prevent distal embolization, thereby increasing microvascular flow with a hope to improve outcomes, which intuitively is a good intervention to undertake (19,20).

FIGURE 3 Kaplan-Meier Curves Showing All-Cause Mortality After PCI



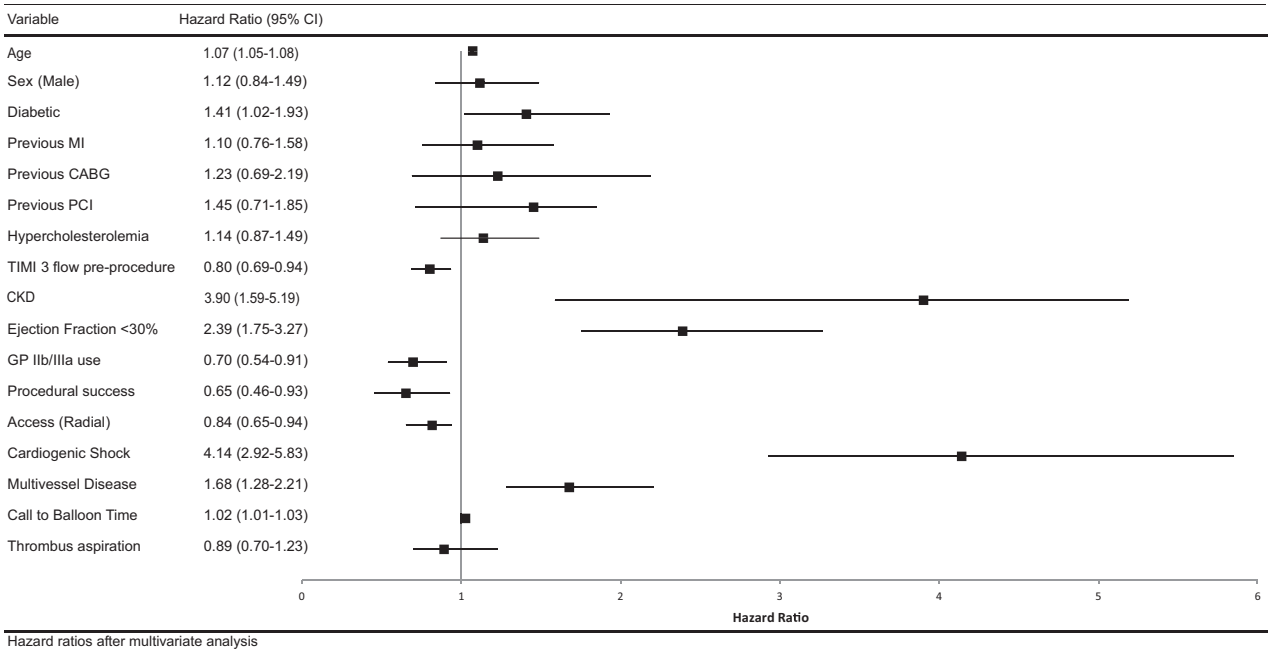
Kaplan-Meier curves showing cumulative probability of all-cause mortality after PCI according to group. LR = log-rank; PCI = percutaneous coronary intervention.

FIGURE 4 Age-Adjusted Cox Regression Analysis for Hazard of All-Cause Mortality After PPCI



Age-adjusted Cox regression analysis for hazard of all-cause mortality after PPCI. CABG = coronary artery bypass graft; CKD = chronic kidney disease; CI = confidence interval; GP = glycoprotein; MI = myocardial infarction; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Figures 1 and 3.

FIGURE 5 Multivariate Cox Regression Analysis for Hazard of All-Cause Mortality After PPCI



Multivariate Cox regression analysis for hazard of all-cause mortality after PPCI. Abbreviations as in Figures 1, 3, and 4.

Theoretically, thrombectomy appears to be a valuable approach to improve outcomes after PPCI. In this study, improved procedural outcomes and in-hospital MACE rates with manual thrombectomy were seen; however, these improvements were not associated with a long-term mortality benefit. Similar benefits on surrogate markers of reperfusion and clinical outcomes with thrombectomy use have been demonstrated in many randomized trials (21-24) and meta-analyses (8,10,25,26). However, these have often not translated into improved hard endpoints such as mortality, and in the largest randomized controlled trial performed to date (TASTE), thrombus aspiration did not result in improved clinical outcomes (11,12).

Our conclusion is that to date there has been no sufficiently powered trial to answer this important question. Despite our large cohort, we do not feel it is sufficiently large to make a clear statement about the lack of association of thrombus aspiration on mortality. The TOTAL (A Randomized Trial of Routine Aspiration Thrombectomy With PCI Versus PCI Alone in Patients With STEMI Undergoing Primary PCI) study is now recruiting, and this study will recruit 10,000 patients and has a combined endpoint of cardiovascular death, MI, shock, and heart failure. This study is also powered assuming a 5% to 7% crossover rate and hence is more effectively designed to establish the clinical efficacy of aspiration catheters in PPCI.

STRENGTHS AND LIMITATIONS OF THIS STUDY. The strength of this study is that it includes patients from 8 different centers in a large metropolitan city with a diverse ethnic and social makeup. The study includes patients with cardiogenic shock, previous bypass surgery, and other comorbidities and is thus representative of the broad range of patients encountered in day-to-day clinical practice. Whereas inclusion of such patients may result in bias, the baseline characteristics were similar and any differences were adjusted for in the multivariate analyses. To further account for confounding variables and bias, propensity analyses were performed, which were in agreement with findings from other cohort analyses. Mortality tracking in England is particularly robust based on official UK Office of National Statistics data and hence our mortality endpoint is reliable. The multivariate analyses highlight the quality of the data with well-recognized predictors of mortality associated with adverse outcomes in our dataset.

However, our study also has limitations. First, our study only applies to patients with STEMI who received PPCI. In addition, this study has all the limitations of a registry and all the potential bias and unmeasured confounding associated with nonrandomized studies. In addition, we cannot exclude the possibility of under-reporting of complications, although the tracking of mortality is robust and we only included the 95.3% of patients who had definitive mortality data in our study cohort. Despite the very large size of our population studied, our cohort does not have the power to detect a small but important difference in mortality related to thrombectomy use. While awaiting the results of the TOTAL trial and the meta-analyses that will follow, it would be useful to have data from large national level registries that may have the power to describe potentially important association of thrombus aspiration with clinical benefits. This will include identifying high-risk individuals such as those with high thrombus burden who remain more likely to benefit from thrombectomy use.

CONCLUSIONS

In this large registry of nearly 11,000 patients, routine thrombus aspiration does not appear to be associated with reduced long-term mortality in patients undergoing PPCI, although procedural success and in-hospital MACE were improved.

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PERSPECTIVES

Device-based removal of thrombus from the infarct-related artery (adjunctive thrombectomy) during PPCI for STEMI has been the object of increasing interest, but it is currently unclear whether a survival benefit is associated with the therapy. We found that despite greater rates of procedural success and lower rates of in-hospital MACE, in-hospital mortality and long-term survival were similar for the patients who underwent thrombus aspiration to those who received PCI only. Our data suggest that in our cohort routine thrombus aspiration during PPCI, compared with not receiving therapy, does not appear to be associated with a reduction in mortality rates. We feel that our results support the conclusion that to date there have been insufficiently powered or few appropriately designed trials to detect or exclude clinically important benefits of thrombus aspiration and that there is an increasing need for these studies.

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