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Outcomes From Selective Use of Thrombectomy in Patients Undergoing Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction

An Analysis of the British Cardiovascular Intervention Society/National Institute for Cardiovascular Outcomes Research (BCIS-NICOR) Registry, 2006–2013

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ABSTRACT

OBJECTIVES This study used a large national cohort to examine patterns of thrombectomy use in ST-segment elevation myocardial infarction (STEMI) and the relationship to mortality.

BACKGROUND The impact of coronary thrombectomy on mortality in STEMI has not been definitively established. Published trial data have been insufficiently powered to address this.

METHODS The U.K. national registry was used to study 98,176 patients treated with primary percutaneous coronary intervention (PCI), between January 1, 2006, and December 31, 2013. Patients were grouped on the basis of whether they received thrombectomy or not; subgroups of simple (manual aspiration) and complex (mechanical) thrombectomy were also evaluated. The primary endpoint was 30-day mortality. The principal adjusted analysis used propensity score matching (PSM). A sensitivity analysis was performed using logistic regression controlled for the propensity score.

RESULTS Thrombectomy use markedly increased in the United Kingdom between 2008 and 2010 but plateaued thereafter at slightly below 50% of all primary PCI cases. No significant mortality difference was seen, in adjusted analyses, between the overall thrombectomy group and the no thrombectomy group, at 30 days or 1 year (at 30 days, PSM average treatment effect [ATE] coefficient 0.0028, 95% confidence interval: −0.0048 to 0.0104; $p = 0.47$). Likewise, no difference was seen between the simple (manual) thrombectomy versus no thrombectomy, at either time point (at 30 days, PSM ATE coefficient 0.0007, 95% confidence interval: −0.0049 to 0.0063; $p = 0.80$). By contrast, the complex (mechanical) thrombectomy group demonstrated a significantly higher mortality than the no thrombectomy group at 1-year follow-up (PSM ATE coefficient 0.0434, 95% confidence interval: 0.0081 to 0.0786; $p = 0.017$).

CONCLUSIONS Coronary thrombectomy was not associated with lower mortality in primary PCI for STEMI when used in our large all-comer cohort in a selective manner on the basis of physician judgment. These findings are consistent with other negative clinical outcomes in recent large randomized controlled trials studying routine manual thrombectomy in primary PCI. (J Am Coll Cardiol Intv 2016;9:126–34) © 2016 by the American College of Cardiology Foundation.

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Primary percutaneous coronary intervention (PPCI) has become the treatment of choice for ST-segment elevation myocardial infarction (STEMI). Attempts to minimize distal embolization of thrombus led to the development of thrombectomy devices for use before angioplasty or stenting. These devices are broadly classified into simple (manual aspiration) or complex (mechanical aspiration, with or without prior fragmentation), with the former most widely used in clinical practice. Small early trials with various aspiration catheters yielded encouraging results but were underpowered to study major adverse cardiovascular events (1,2). The larger TAPAS (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study) found an unanticipated, sizeable mortality advantage at 1 year from manual aspiration thrombectomy (3), and a subsequent meta-analysis in 2013 continued to support this notion of reduced mortality with thrombectomy use

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(4). Since then, results from the randomized TASTE (Thrombus Aspiration in Myocardial Infarction) trial have cast doubt over the value of routine manual thrombectomy in STEMI (5,6). However, the much lower-than-anticipated event rate represents a major caveat in interpreting mortality findings from the TASTE trial (7). The TOTAL (A Trial of Routine Aspiration Thrombectomy With Percutaneous Coronary Intervention [PCI] Versus PCI Alone in Patients With ST-Segment Elevation Myocardial Infarction [STEMI] Undergoing Primary PC) study (with event-driven trial completion) has now also shown no significant improvement in any hard clinical endpoints (including death) by 180 days with routine thrombectomy use (8). There was a trend towards reduction in cardiovascular mortality at 30 days favoring thrombectomy use (hazard ratio: 0.83, 95% confidence interval: 0.65 to 1.06), but this did not achieve statistical significance. As the TOTAL authors had recognized in advance, a trial with adequate power to conclusively demonstrate (or refute) an impact on all-cause mortality with thrombectomy would have required in excess of 30,000 patients and was therefore judged to be impractical (9). Hence, larger randomized controlled trials (RCTs) with adequate power to detect a mortality benefit from thrombectomy use are unlikely, and an alternative approach is warranted. Such information could influence clinical practice, because thrombectomy use is by no means "the norm" worldwide—for example, it was utilized in only around 20% of PPCI cases in a survey of >1,000 hospitals in the United States during 2009 to 2010 (10). Its use appears set to decline further in the light of results from the TOTAL study.

The U.K.-British Cardiovascular Intervention Society (BCIS) cohort has several major strengths, making the information it can provide complementary to that gained from recent RCTs on thrombectomy. First, very large patient numbers confer statistical power to specifically study the unresolved question about a mortality benefit associated with thrombectomy use. Second, as a registry, it naturally includes higher-risk patients who are frequently excluded from RCTs—this is relevant because one explicit limitation in the TOTAL study was the lack of screening log records, making generalizability of the study's outcomes to all-comers somewhat harder to ascertain. Third, another inherent limitation in TOTAL was the mandated use of thrombectomy in the active treatment arm—thereby removing the potential impact of physician judgment to direct its use to cases where it might be of greatest benefit and to avoid its use where there was greatest risk of harm. By contrast, our work provides insight into the impact of selective use of thrombectomy on clinical outcomes in an all-comer primary PPCI population, and it is therefore highly pertinent to real-world practice.

ABBREVIATIONS AND ACRONYMS

BCIS = British Cardiovascular Intervention Society

CABG = coronary artery bypass grafting

NICOR = National Institute of Cardiovascular Outcomes Research

PCI = percutaneous coronary intervention

PPCI = primary percutaneous coronary intervention

RCT = randomized controlled trial

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

METHODS

U.K. NATIONAL PCI DATABASE. U.K. PCI data are collected by the BCIS and overseen by the National Institute of Cardiovascular Outcomes Research (NICOR). The dataset records PCI procedures performed in any hospital within the United Kingdom. Further detailed information regarding data collection processes, data validation, and handling of missing data has been published previously (11).

The BCIS-NICOR database records clinical, procedural, and outcome information with a total of 113 variables. The Medical Research Information Service collects mortality information by linking patients'

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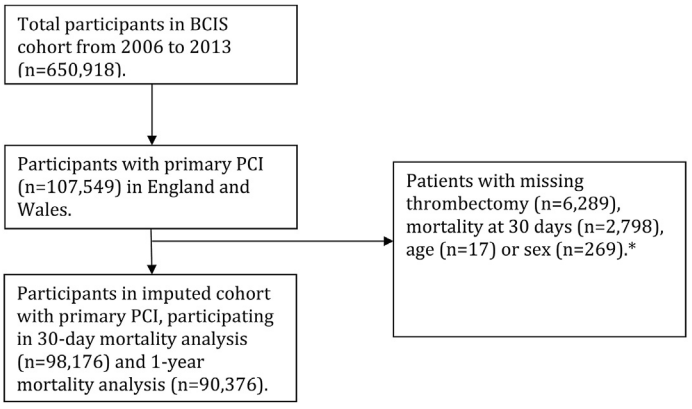
FIGURE 1 Participant Flow Diagram



An indication of the numbers of patients involved in the study and reasons for patient exclusion are shown. See text for further details. *Missingness across variables is not mutually exclusive (e.g., sex and age might be missing for a case). BCIS = British Cardiovascular Intervention Society; PCI = percutaneous coronary intervention.

unique National Health Service numbers to government mortality records for patients in England and Wales. Mortality tracking is not currently performed for patients from Scotland or Northern Ireland.

STUDY POPULATION. Study subjects were those patients on the database who underwent a primary PCI procedure for STEMI in England and Wales between January 1, 2006, and December 31, 2013. This time period was chosen to commence after the publication of small positive clinical trials on thrombectomy but before publication of the TAPAS study. It extends forward to include the most recent available BCIS-NICOR validated data.

OUTCOME MEASURES. The primary outcome measure for this study was 30-day mortality. The secondary endpoint was 1-year mortality. These were selected on the basis of the predicted time frame of benefit from the active intervention (thrombectomy) and the design and findings of foregoing RCTs. Other secondary endpoints were in-hospital incidence of reinfarction and of stroke.

STUDY GROUPING. Patients were divided into 2 groups, on the basis of use of a thrombectomy catheter during the PPCI, versus no such use, as indicated on the registry. Where a thrombectomy catheter is passed into the coronary artery, its use is recorded on the database, regardless of whether the culprit lesion was successfully reached and of the amount of thrombus retrieved from the device—hence coding is on an intention-to-treat basis. The thrombectomy group was further subclassified as simple or complex. Simple (manual) thrombectomy procedures were those that involved any of the following (aspiration) devices: Pronto (Vascular Solutions Inc., Minneapolis, Minnesota), Hunter (IHT Cordynamic, Barcelona, Spain), Eliminate (Terumo Europe, Leuven, Belgium), Export (Medtronic, Minneapolis, Minnesota), Quickcat (Spectranetics Inc., Colorado Springs, Colorado), Thrombcat (Kensay Nash Corp., Exton, Pennsylvania), and Diver (Invatec, Roncadelle, Italy). Procedures were coded as complex thrombectomy if they used any of the following devices: X-sizer (eV3 Endovascular Inc., Plymouth, Minnesota), Angiojet (Boston Scientific Inc., Marlborough, Massachusetts), Acolysis (Vascular Solutions Inc., Minneapolis, Minnesota), and TEC (Interventional Technologies, Inc., San Diego, California).

STATISTICAL ANALYSIS. Statistical analysis was performed using Stata v13.1 (College Station, Texas). Patients who did not have PPCI or did not have their procedure in England or Wales or had missing information regarding critical variables for the analysis (thrombectomy use, mortality at 30 days, age, or sex) were excluded.

Descriptive statistics. For basic analyses of demographics, procedural details, and unadjusted outcomes, continuous variables were evaluated as mean ± SD. Means, SDs, and percentages quoted for unadjusted data refer to numbers within the cohort for which data were available. Chi-square tests were used to assess the significance of differences in proportions between groups for categorical variables. One-way analysis of variance was used for continuous variables. All statistical tests were 2-tailed, and an alpha of 5% (for significance) was used throughout.

Multiple imputation for missing data. To reduce potential bias created by missing data, multiple imputation methods were used, through the mi impute procedure on Stata. Chained equations were used to impute data for all variables with missing information and also included complete variables (age, sex, year of procedure, thrombectomy type) to generate 10 datasets for use in the analyses.

Variables included in modeling. Variables of interest were selected to encompass known or potential predictors of 30-day mortality, and thus involved: age, sex, diabetes, hypertension, hyperlipidemia, smoking status, cerebrovascular disease (previous stroke), peripheral vascular disease, renal impairment (defined here as serum creatinine>200 μmol/l or on dialysis), cardiogenic shock, previous MI, previous PCI, previous coronary artery bypass grafting (CABG), pre-procedural Thrombolysis In Myocardial Infarction (TIMI) flow grade, and procedural details (year of procedure, route of vascular access, use of aspirin/clopidogrel/prasugrel/ticagrelor, use of

glycoprotein IIb/IIIa inhibitor, type of thrombectomy device, that is, simple aspiration or complex mechanical, use of embolic protection device, use of circulatory support including intra-aortic balloon pump) and requirement for ventilator support. Stent type (drug-eluting vs. bare-metal) was also included because it may be considered as a surrogate marker for unrecorded comorbidities, and its use as a covariate within the model should help to mitigate the influence of unmeasured confounders.

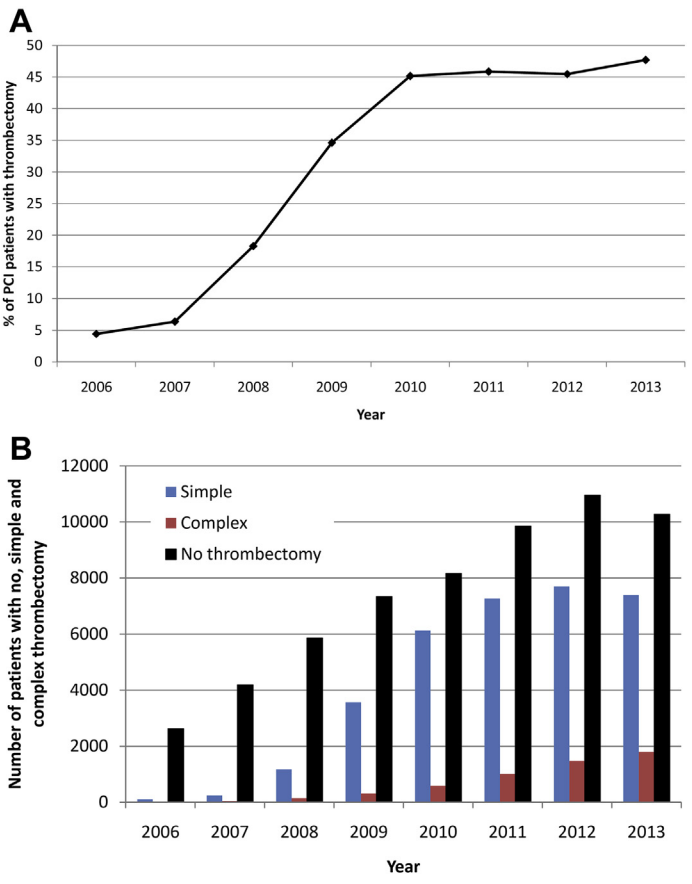
Propensity score–based analyses. To better control for the baseline differences across the groups, multiple imputation propensity score matching (mi estimate: teffects psmatch on Stata) was used to estimate the average treatment effect. The method used all the predictors previously mentioned in 3 separate multiple imputation logistic regression models (thrombectomy vs. none; simple vs. none; complex vs. none), calculating propensity scores for group membership. Standard settings for the matching algorithm were used. A minimum of 1 neighbor was requested, and all observations were considered as potential matches regardless of how dissimilar their propensity scores were. Tolerance for the overlap assumptions was set to 10^{-5}. Simple logistic regression models were run (the only predictor being group membership) to obtain the average treatment effect.

Sensitivity analyses were performed with fully adjusted (multiple) logistic regression. Multiple imputation logistic regressions (mi estimate: logistic on Stata), which included the propensity score as a covariate, were used to calculate adjusted odds of 30-day mortality for overall thrombectomy use versus none, simple thrombectomy versus none, and complex thrombectomy versus none. We performed 2 additional sensitivity analyses, the first limited to patients with left ventricular ejection fraction data and controlled for them, the second considering only participants with the left anterior descending coronary artery as the infarct-related artery.

RESULTS

Figure 1 provides a flowchart indicating exclusions and hence the numbers available for unadjusted and adjusted statistical analyses. A total of 107,549 patients underwent primary PCI from 2005 to 2013 in England and Wales, and 98,176 were included in the analysis. Although multiple imputation was used to obtain a cohort that was as complete as possible, there were lower patient numbers in the adjusted analyses because cases in which critical variables (see the preceding text) were missing were excluded.

FIGURE 2 Temporal Patterns in Thrombectomy Use



(A) Changes in use of thrombectomy over time in percutaneous coronary intervention (PCI). The increase in thrombectomy use in primary PCI in the United Kingdom in recent years is shown. Possible reasons are discussed further in the text. **(B)** Annual figures for use of simple (manual) and complex (mechanical) thrombectomy devices. It is seen that simple (aspiration) thrombectomy accounts for the majority of thrombectomy used. By contrast, the overall number of cases of complex thrombectomy remains small although it has increased.

Figure 2A demonstrates the changing pattern of thrombectomy use in PPCI over the study period. Thrombectomy was used in <5% of cases in 2006. A rapid uptake of the technique was seen between 2008 and 2010, with a relative plateauing of overall thrombectomy numbers (i.e., proportional use in primary PCI) thereafter, at slightly below 50%. Figure 2B demonstrates that simple aspiration tools accounted for the majority of devices used, although there has been a steady year-on-year increase in the use of complex devices from 2007 until 2012.

Baseline demographics and procedural details for patients who did and did not receive thrombectomy are shown in Table 1. Missing data are summarized in Online Table 1. It is seen that imbalances exist between the 2 groups in terms of these baseline characteristics,

TABLE 1 Baseline Patient Demographics, Procedural Details, and Unadjusted Outcomes

	No Thrombectomy (n = 59,228)	Thrombectomy (n = 38,948)	p Value
Age, yrs	65 ± 13	62 ± 13	<0.001
Male	43,291 (73)	29,595 (76)	<0.001
Smoking status			<0.001
Never	17,804 (34)	11,389 (32)	
Ex-smoker	14,305 (27)	9,394 (26)	
Current	20,207 (39)	15,100 (42)	
Diabetes mellitus	8,349 (15)	4,780 (13)	<0.001
Hypertension	24,012 (42)	14,845 (38)	<0.001
Hypercholesterolemia	22,940 (40)	14,827 (38)	<0.001
Peripheral vascular disease	2,019 (4)	1,075 (3)	<0.001
Renal disease	1,091 (2)	538 (1)	<0.001
Previous myocardial infarction	7,931 (14)	4,089 (11)	<0.001
Previous stroke	2,220 (4)	1,331 (3)	0.001
Previous percutaneous coronary intervention	5,283 (9)	3,376 (9)	0.061
Previous coronary artery bypass graft	16,040 (27)	14,055 (36)	<0.001
Left ventricular ejection fraction			<0.001
≥50%	11,486 (57)	6,162 (53)	
31%–49%	6,152 (31)	4,126 (36)	
≤30%	2,513 (12)	1,306 (11)	
Pre-procedure TIMI flow grade			<0.001
TIMI 0	31,905 (64)	27,744 (82)	
TIMI 1	4,829 (10)	1,949 (6)	
TIMI 2	5,892 (12)	2,128 (6)	
TIMI 3	7,537 (15)	1,816 (5)	
Cardiogenic shock	4,112 (7)	2,757 (7)	0.585
Ventilatory support	2,159 (4)	1,313 (4)	0.304
Circulatory support	2,830 (5)	2,037 (5)	<0.001
Glycoprotein IIb/IIIa inhibitors	27,778 (49)	20,280 (55)	<0.001
Antiplatelet therapy			<0.001
Clopidogrel	33,664 (78)	17,180 (64)	
Prasugrel	7,220 (17)	6,616 (25)	
Ticagrelor	2,408 (6)	3,104 (12)	
Bivalirudin	5,025 (9)	6,991 (19)	<0.001
Embolic protection device	213 (0.4)	294 (0.8)	<0.001
Stent			<0.001
None	4,898 (8)	2,373 (6)	
Bare-metal	29,104 (50)	14,917 (39)	
Drug-eluting	24,661 (42)	21,426 (55)	
Radial access	27,179 (47)	24,868 (64)	<0.001
Vessel attempted			
Venous or arterial graft	1,143 (2)	666 (2)	0.011
Left main stem artery	1,499 (3)	749 (2)	<0.001
Left anterior descending artery	26,361 (45)	16,387 (42)	<0.001
Left circumflex artery	10,229 (17)	5,420 (14)	<0.001
Right coronary artery	24,134 (41)	17,482 (45)	<0.001

Continued on the next page

although no consistent direction of bias is evident. For example, patients who did not receive thrombectomy tended to be slightly older, more likely to be female, and have diabetes, hypertension, hypercholesterolemia, peripheral vascular disease, or previous MI. Patients who did receive thrombectomy were more likely to be current smokers, have had prior CABG, to present with pre-procedural TIMI flow grade 0, and to need circulatory support (with inotropes or intra-aortic balloon pumping). In terms of $P2Y_{12}$ receptor antagonists, clopidogrel was the most commonly used agent in both groups, but both prasugrel and ticagrelor were used to a greater extent in those patients who received thrombectomy. Additionally, glycoprotein IIb/IIIa inhibitors, bivalirudin, and drug-eluting stents were used more often in patients with thrombectomy. Patients in the thrombectomy group also had a shorter mean symptom-to-balloon time. Crude mortality at both 30 days and 1 year was seen to be significantly lower in those who received thrombectomy compared with those who did not. There were no differences between groups in reinfarction or incident stroke rates. Online Table 2 shows a comparison of demographics and procedural variables according to no thrombectomy versus simple thrombectomy versus complex thrombectomy.

Table 2 shows the propensity score-matched results comparing use of thrombectomy and no thrombectomy. It was seen that, when comparison between matched pairs was undertaken, no significant difference in all-cause mortality (at 30 days or at 1 year) remained between the 2 groups (thrombectomy vs. no thrombectomy). **Table 2** shows a subgroup analysis of simple thrombectomy compared with no thrombectomy. Simple (manual) thrombectomy was not associated with any significant difference in mortality at either time point. However, with complex thrombectomy, no mortality difference was observed at 30 days, but there was a significant increase in mortality by 1 year ($p = 0.017$) (Online Table 3). The area under the receiver operator curves for these analyses are shown in **Table 2**. The balance diagnostics for this propensity matching model and the quality of matching are presented in Online Table 4.

This relationship was explored further through sensitivity analysis incorporating the propensity score as a covariate in a fully adjusted multiple logistic regression (**Table 3**). This showed similar findings to the propensity score-matched results, namely complex thrombectomy being associated with a trend to higher mortality (compared with no thrombectomy) by 30 days ($p = 0.063$) and a significant difference at the 1-year time point ($p = 0.026$). None of the other comparisons between groups in the sensitivity analysis showed statistically significant differences.

We performed additional analyses with adjustments for left ventricular ejection fraction and only considering participants that had the left anterior descending coronary artery as the infarct-related artery. These results are shown in Online Tables 5

and 6, respectively, and the results are similar to those of previous analyses.

DISCUSSION

The role of coronary thrombectomy in PPCI for STEMI has been controversial. An appealing biological rationale, coupled with encouraging early trial results, fueled its uptake over the early part of the last decade. Now, in the wake of 2 large RCTs that failed to show any important clinical benefits, its place in our therapeutic armamentarium is unclear. This uncertainty is intensified by safety concerns with thrombectomy, particularly in relation to increased risk of stroke (8,12). However, one central unanswered question, notwithstanding results from the TASTE and TOTAL studies, is whether there may yet be a relevant impact on mortality that these RCTs were not able to identify. This is certainly plausible, given the size of studies required to demonstrate the survival benefits of other STEMI therapies such as aspirin and thrombolysis (more than 17,000 patients in the ISIS-2 study (Second International Study of Infarct Survival) to show a relative risk reduction of 20% to 25%) (13). A smaller (but still clinically meaningful) effect with thrombectomy may require a much larger sample size than that to be detectable. Our BCIS cohort comprised over 98,000 STEMI cases (compared with around 7,000 in the TASTE study and around 10,700 in the TOTAL study), yielding more statistical power to study the association between thrombectomy use and mortality—albeit within the constraints of observational data and in the context of selective, rather than routine, thrombectomy use. Our data represent by far the largest published series addressing this issue.

PATTERNS OF PRACTICE. Our data illustrate the temporal patterns in thrombectomy use in the United Kingdom. Some of the sharp increase in uptake seen after 2008 may relate to the high-profile publication of findings from the TAPAS trial, possibly persuading previously skeptical operators. However, a leveling out of uptake is seen after 2010, with proportionate use running at slightly <50% of all PPCI cases. The explanation for this observed plateau may relate to physician judgments on both efficacy and safety of thrombectomy in individual cases. Regarding efficacy, operator decisions may incorporate the angiographically visible thrombus burden (with thrombectomy being omitted in cases with less marked thrombus, if gains are perceived to be limited). Thrombus burden is not coded as a field on the BCIS-NICOR dataset, so the decision to use thrombectomy could not be correlated to this index. Surprising findings from the TOTAL study suggest that high TIMI thrombus grade might not in fact delineate a group in which thrombectomy is of particular benefit; however, because the study was not powered for this subgroup analysis, this finding should be considered as hypothesis generating.

Other potential limitations to thrombectomy uptake relate to individualized safety concerns—for example, when coronary anatomic factors suggest

TABLE 1 Continued

	No Thrombectomy (n = 59,228)	Thrombectomy (n = 38,948)	p Value
Post-procedure TIMI flow grade			<0.001
TIMI 0	3,854 (8)	955 (3)	
TIMI 1	747 (1)	349 (1)	
TIMI 2	2,474 (5)	1,855 (5)	
TIMI 3	43,333 (86)	30,810 (91)	
Symptom to balloon time, h	4.6 ± 3.9	4.2 ± 3.5	<0.001
Year			<0.001
2006	2,621 (4)	122 (0.3)	
2007	4,185 (7)	285 (0.7)	
2008	5,862 (10)	1,310 (3)	
2009	7,334 (12)	3,880 (10)	
2010	8,162 (14)	6,719 (17)	
2011	9,845 (17)	8,280 (21)	
2012	10,951 (18)	9,176 (24)	
2013	10,268 (17)	9,176 (24)	
Reinfarction (during index admission)	108 (0.2)	57 (0.2)	0.197
Stroke (during index admission)	157 (0.3)	116 (0.3)	0.303
30-Day mortality	3,863 (7)	2,142 (6)	<0.001
1-Year mortality	6,123 (11)	3,289 (9)	<0.001

Values are mean ± SD for age and for symptom-to-balloon time; for remaining variables, values are n(%), where n denotes absolute number of cases and % indicates this as a percentage of all cases for which data was available for that variable.

TIMI = Thrombolysis In Myocardial Infarction.

TABLE 2 Propensity Score Matching Analysis on 10 Imputed Datasets, Reporting ATE, and Area Under ROC Curve*

	N	Coefficient	95% Confidence Interval		p Value
Any vs. no thrombectomy†					
30-day mortality	98,176	0.0028	−0.0048	0.0104	0.465
1-yr mortality	90,376	0.0057	−0.0027	0.0140	0.181
Simple vs. no thrombectomy†					
30-day mortality	92,793	0.0007	−0.0049	0.0063	0.802
1-yr mortality	85,675	0.0023	−0.0072	0.0118	0.628

	Any vs. No Thrombectomy	Simple vs. No Thrombectomy
Average ROC curve‡	0.746	0.749

*Adjusted for age, sex, smoking status, year of PCI, previous PCI, previous CABG, previous myocardial infarction, diabetes, hypercholesterolemia, hypertension, peripheral vascular disease, previous stroke, renal disease, cardiogenic shock, receipt of ventilation, circulatory support, use of glycoprotein IIb/IIIa inhibitors, use of bivalirudin, antiplatelet use, radial access site, embolic protection device, left main stem disease, graft disease, type of stent, pre-procedure TIMI flow, balloon time, in-hospital reinfarction, and in-hospital stroke. †Each case was matched to at least 1 control patient, and each control patient was matched to at least 1 case (matching with replacement). ‡Across the 10 imputed datasets.

ATE = average treatment effects; ROC = receiver-operating characteristic.

TABLE 3 Sensitivity Analysis, by Multiple Logistic Regression Incorporating the Propensity Score as a Covariate in the Model

Adjusted by Propensity Score*	N	Odds Ratio (95% Confidence Interval)	p Value
30-day mortality			
Thrombectomy vs. no thrombectomy	98,176	1.02 (0.96–1.08)	0.608
1-yr mortality			
Thrombectomy vs. no thrombectomy	90,376	1.02 (0.97–1.07)	0.452
30-day mortality			
Simple vs. no thrombectomy	92,793	1.00 (0.93–1.06)	0.889
1-yr mortality			
Simple vs. no thrombectomy	85,675	1.00 (0.95–1.05)	0.955

*Adjusted for age, sex, smoking status, year of percutaneous coronary intervention (PCI), previous PCI, previous coronary artery bypass grafting, previous myocardial infarction, diabetes, hypercholesterolemia, hypertension, peripheral vascular disease, previous stroke, renal disease, cardiogenic shock, receipt of ventilation, circulatory support, use of glycoprotein IIb/IIIa inhibitors, use of bivalirudin, antiplatelet use, radial access site, embolic protection device, left main stem disease, graft disease, type of stent, pre-procedure Thrombolysis In Myocardial Infarction flow grade, balloon time, in-hospital reinfarction, and in-hospital stroke.

likely difficulties with thrombectomy use—this could include upstream coronary disease, calcified or highly tortuous vessels, and small caliber or distally located culprit-lesion locations. All of these situations can potentially prevent delivery of the device to the culprit lesion and create concomitant risks of vessel wall injury. These relative contraindications were, in effect, already factored into the TASTE trial, where randomization was undertaken after angiographic results were known, and hence patients with significant anatomic complexities were very likely to have been excluded. This caveat does not apply to the TOTAL trial. However, in real-life practice, many operators will be highly reluctant to use thrombectomy in cases of unfavorable anatomy. For these reasons, clinical outcomes from cases where physicians voluntarily performed thrombectomy (rather than being mandated to perform it by a trial protocol) are of great practical relevance.

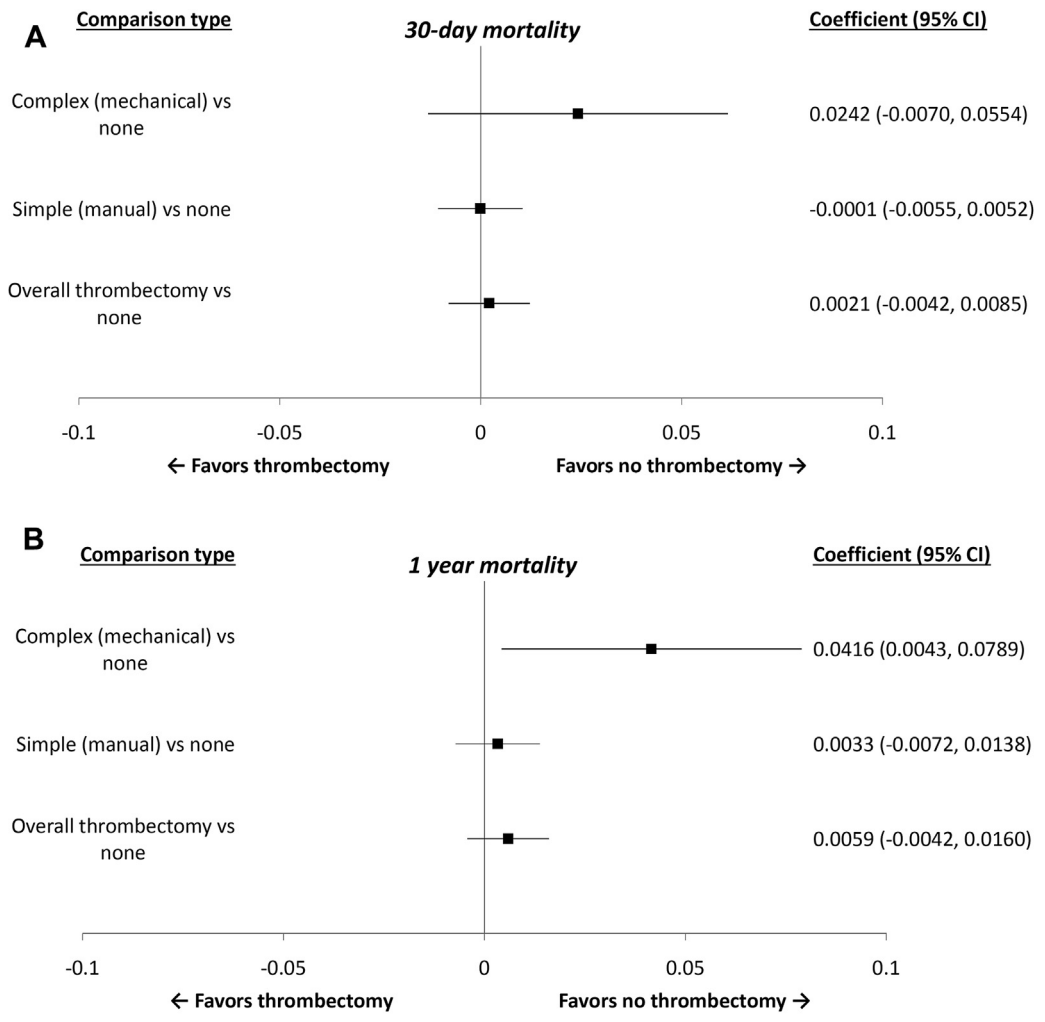
KEY FINDINGS FROM THE BCIS-NICOR REGISTRY. Our unadjusted (raw) data demonstrated a lower mortality in the thrombectomy group, but nonrandom treatment allocation severely limits any conclusions from this. Hence, propensity-based adjustment was used to balance groups—our principal analysis (by matching) and the sensitivity analysis concurred in finding no significant evidence of lower mortality with selective use of thrombectomy at either 30 days or 1 year. This held true for both the overall thrombectomy group and for the simple (manual aspiration) group. (**Central Illustration**). Furthermore, no advantage to thrombectomy emerged even when only patients with a left anterior descending coronary artery culprit lesion were studied. Our findings are thus consistent with the message emerging from the routine manual thrombectomy approach tested in the TASTE and TOTAL studies. It appears that, even when used more selectively in an all-comer STEMI population, manual thrombectomy was not associated with a survival advantage.

The group of patients who received complex (mechanical) thrombectomy deserve additional consideration. They were seen to have higher mortality in both of our adjusted analyses. Review of their baseline characteristics (Online Table 2) does not suggest a group who were more unwell at baseline compared with other subjects. The indication for choosing complex (mechanical) thrombectomy is not captured on our database and hence to comment is speculative. However, it is plausible that use of mechanical thrombectomy might be more likely in cases with massive or recalcitrant thrombus, or where preceding efforts during the case had failed to obtain a good result in terms of restoring flow. Hence, these patients may not have been more unwell by virtue of database-captured baseline indices but may nevertheless have been at higher risk on the basis of angiographic appearances or the response to initial treatment. These factors might therefore underlie the higher mortality found in this group. An alternative explanation could involve a higher risk of complications specifically related to the mechanical thrombectomy device; however, this would run contrary to the findings of the larger RCTs in which such complex devices have been studied.

STUDY LIMITATIONS. First, the U.K. national PCI database does not currently record the reasons underlying the use (or nonuse) of thrombectomy devices, and hence, it is not possible to distinguish between those on the basis specific culprit lesion factors (e.g., heavy thrombus load), other anatomic factors (e.g., calcific tortuous vessels), or simply physicians' default preferences. These possible underlying reasons (some of which may potentially influence both treatment allocation and clinical outcome) therefore represent unmeasured confounders in this work. Similarly, reasons behind the choice between manual aspiration versus complex mechanical thrombectomy are not captured, and the same confounders may be present.

Second, there were many patients with missing data regarding left ventricular ejection fraction, which is an important determinant of survival (14). This has been addressed in part by exclusion of this variable from the

CENTRAL ILLUSTRATION Plots of Overall Thrombectomy, Simple Thrombectomy, and Complex Thrombectomy, Each Compared to No Thrombectomy, With Regard to Mortality



Sirker, A. et al. J Am Coll Cardiol Intv. 2016; 9(2):126–34.

Average treatment effects calculated from our principal analysis (propensity score matching) are indicated. Mortality at 30-day and 1-year time points is shown in the **upper and lower**, respectively. CI = confidence interval.

principal analysis and by use of a sensitivity analysis in which left ventricular ejection fraction was included, with similar outcomes recorded. Third, we do not have data on the specific complication of stent thrombosis, although this is relevant in examining the possible value of thrombectomy.

CONCLUSIONS

Our large observational study does not provide evidence to support the hypothesis that selective thrombectomy in primary PCI is associated with lower mortality. Our findings are in keeping with other negative clinical outcomes from 2 recent large RCTs studying routine thrombectomy use in STEMI.

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PERSPECTIVES

WHAT IS KNOWN? Coronary thrombectomy has been frequently used in primary PCI for STEMI. However, recent large randomized trials have shown no significant advantages in clinical outcome measures with its use, but increased risks, particularly stroke. However, these trials were not adequately powered to examine an influence on mortality. Additionally, the potential benefit of using thrombectomy in a more selective manner (on the basis of physician choice), rather than routinely, remains unclear.

WHAT IS NEW? This study examined mortality in over 98,000 patients treated with PPCI for STEMI in the United Kingdom between 2006 and 2013. The findings indicate no evidence of improved survival (at 30 days or 1 year) in patients treated with thrombectomy, at physician discretion, for STEMI. These results are consistent with a lack of improvement in other clinical indices in recent large RCTs of routine aspiration thrombectomy in STEMI.

WHAT IS NEXT? Future work should focus on alternative strategies to minimize reperfusion injury and microvascular dysfunction during and after primary PCI for STEMI.

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KEY WORDS aspiration, mortality, myocardial infarction, thrombectomy

APPENDIX For supplemental tables, please see the online version of this article.