Original Article
Manual vs mechanical thrombectomy during PCI for STEMI: a comprehensive direct and adjusted indirect meta-analysis of randomized trials

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Abstract: Thrombus removal by manual thrombectomy improves coronary flow and myocardial perfusion after percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI); growing interest is on mechanical devices for thrombectomy which may allow a larger thrombus removal as compared to manual devices. We aimed to perform the first direct and adjusted indirect meta-analysis of studies on manual and mechanical thrombectomy in PCI for STEMI. Methods: The literature was scanned for direct and indirect randomized comparisons between manual and/or mechanical thrombectomy and/or placebo by formal searches of electronic databases from November 1994 to June 2013. Clinical and procedural endpoints were selected. Results: Three studies directly comparing (2 RCTs and 1 non-randomized; N = 513) and 21 RCTs (N = 4514) indirectly comparing the two strategies were included in the meta-analysis. The direct meta-analysis showed comparable rates of survival (p = 0.88), re-infarction (MI) (p = 0.84) and procedural outcomes between the two strategies; direct evidence was however limited in number of enrolled patients. The indirect meta-analysis showed a superior reduction in mortality with manual thrombectomy compared to mechanical thrombectomy in the overall analysis (p = 0.01); by excluding trials with low percentage of patients with intracoronary thrombus (< 50%) at baseline, the two strategies were comparable in survival, but mechanical thrombectomy was associated with a significant reduction in re-MI (p < 0.001) and stroke (p = 0.04). Conclusions: This meta-analysis lends support to mechanical thrombectomy in the population with high thrombus burden only where, compared to manual thrombectomy, it is likely to provide higher benefits in reduction of re-MI and stroke.

Keywords: Mechanical thrombectomy, manual thrombectomy, meta-analysis

Introduction

Primary percutaneous coronary intervention (PCI) remains the most effective treatment strategy for patients presenting with STEMI [1]; however, despite the efficacy in achieving epicardial reperfusion in STEMI, this strategy is often limited by distal atherothrombotic embolization, leading to a suboptimal reperfusion and resulting in unfavorable short and long-term outcomes [2, 3]. In the last years thrombectomy has emerged as a useful tool to further enhance the benefit of reperfusion during primary PCI by preventing distal embolization of infarct-related thrombus. Various adjunctive thrombectomy devices have been developed allowing manual or mechanical removal of intracoronary thrombus. To date the evidence from randomized controlled trials (RCTs) directly comparing these two types of thrombectomy is however limited; in this regard, a direct and indirect inference on the data coming from the studies comparing these two strategies could significantly increase the understanding of their comparative efficacy. The aim of this report was therefore to perform a comprehensive direct and adjusted indirect meta-analysis of studies on manual vs mechanical thrombectomy during PCI for STEMI.
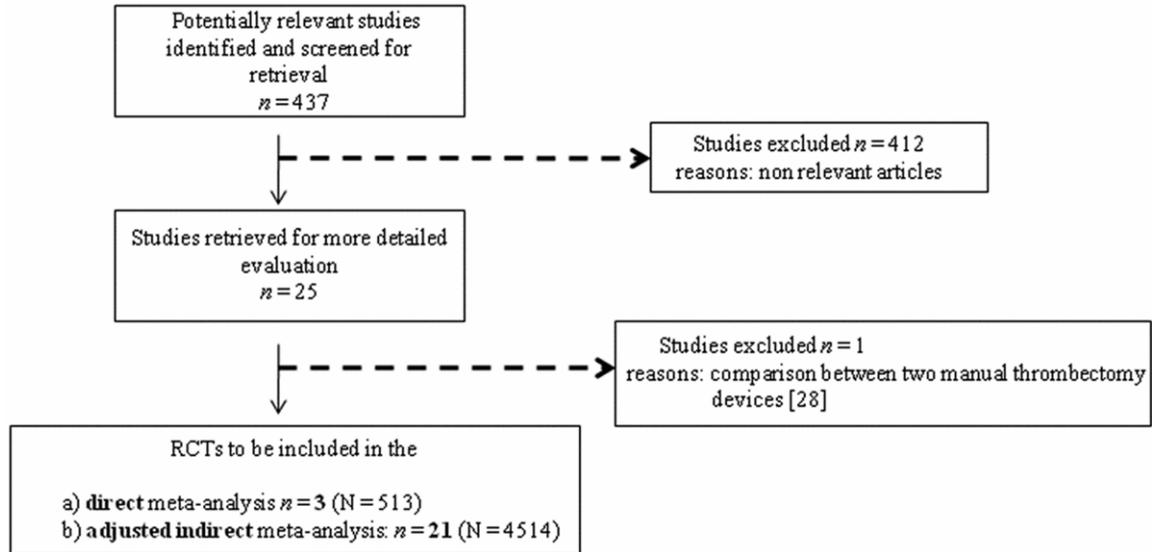
Figure 1. Flow chart of the systematic search for the direct and indirect meta-analysis.

Methods

A search covering the period from November 1994 to June 2013 was conducted by two independent investigators (EPN and GT) using MEDLINE/CENTRAL and Google Scholar databases, and conference proceedings from the American College of Cardiology, American Heart Association, European Society of Cardiology, Transcatheter Cardiovascular Therapeutics and EuroPCR scientific sessions. The following keywords were applied: randomized trial, myocardial infarction, reperfusion, primary angioplasty, rescue angioplasty, thrombectomy, thrombus aspiration, manual thrombectomy, mechanical thrombectomy, rheolytic thrombectomy, Diver catheter, Pronto catheter, Export catheter, Thrombus Vacuum Aspiration Catheter, Angiojet, Rescue, and X-sizer. Inclusion criteria were: 1) studies (RCTs or non-randomized studies) comparing directly manual vs mechanical thrombectomy AND/OR RCTs separately investigating manual vs mechanical thrombectomy in PCI for STEMI; 2) availability of complete clinical data, whereas exclusion criteria were i) follow-up data in less than 90% of patients and ii) ongoing studies or irretrievable data. References of retrieved studies were searched manually for additional trials. No language restrictions were applied. Data were abstracted on pre-specified forms by two independent investigators, neither involved in any of the studies retrieved; divergences were resolved by discussion with a third investigator.

Outcomes measures

Clinical endpoints were mortality, re-infarction (MI) and stroke at 30-day follow-up for the indirect meta-analysis. The same endpoints with the available follow-up were used for the direct meta-analysis.

Procedural endpoints were postprocedural epicardial flow, as evaluated by postprocedural Thrombolysis in Myocardial Infarction (TIMI-3), and myocardial perfusion, as evaluated by complete ST-segment resolution.

Data analysis

Data were analyzed according to the intention-to-treat principle. Odds ratio (OR) and 95% Confidence intervals (95% CI) were used as summary statistics. Heterogeneity was assessed by Cochran's Q test. The statistical inconsistency test (I2) $\{((Q\text{-}df)/Q) \times 100\%$, where Q is the chi-squared statistic and df its degrees of freedom$\}$ was also employed to overcome the low statistical power of Cochran's Q test.

For the direct meta-analysis, pooled ORs were calculated using a fixed effect model with the Mantel-Haenszel method. The DerSimonian and Laird random effects model was used in

Table 1. Main characteristics of the the studies included in the direct and indirect meta-analysis

Study	Year of Publication	Design	Thrombectomy	Devices	Publication status	Patients	Thrombus T (%)	Thrombus C (%)	GP IIb/ IIIa T (%)	GP IIb/ IIIa C (%)
SMART [9]	abstract	Randomized	manual vs mechanical	NR	Abstract	80	100	100	NR	NR
Tarsia et al. [7]	2010	Retrospective	manual vs mechanical	Export/Diver-Angiojet	Full paper	232	100	100	90.8	95.9
TREAT-MI [8]	2011	Randomized	manual vs mechanical	Export-X-sizer	Full paper	204	201	100	100	100
REMEDIA [17]	2005	Randomized	Manual vs NO	Diver	Full paper	96	58	55	68	63
De Luca et al. [21]	2006	Randomized	Manual vs NO	Diver	Full paper	76	100	100	100	100
PIHRATE [25]	2010	Randomized	Manual vs NO	Export	Full paper	196	70	70	62	63
Noel et al. [18]	abstract	Randomized	Manual vs NO	Export	Abstract	45	NR	NR	NR	NR
Sardella et al. [27]	2009	Randomized	Manual vs NO	Export	Full paper	175	100	100	100	100
Chao et al. [26]	2008	Randomized	Manual vs NO	Export	Full paper	74	NR	NR	19	32
Chevalier et al. [30]	2008	Randomized	Manual vs NO	Export	Full paper	249	NR	NR	66	70
TAPAS [28]	2008	Randomized	Manual vs NO	Export	Full paper	1060	49	44	93	90
Lipiecki et al. [29]	2009	Randomized	Manual vs NO	Export	Full paper	81	NR	NR	74	30
Liistro et al. [23]	2009	Randomized	Manual vs NO	Export	Full paper	111	NR	NR	100	100
DEAR-MI [20]	2006	Randomized	Manual vs NO	Pronto	Full paper	148	NR	NR	100	100
Dudek et al. [12]	2004	Randomized	Mechanical vs NO	Rescue	Full paper	41	100	100	0	0
Kaltoft et al. [19]	2006	Randomized	Mechanical vs NO	Rescue	Full paper	215	69	79	96	93
VAMPIRE [24]	2008	Randomized	Mechanical vs NO	TVAC	Full paper	349	NR	NR	0	0
Beran et al. [10]	2002	Randomized	Mechanical vs NO	X-sizer	Full paper	66	100	100	73	68
Napodano et al. [11]	2003	Randomized	Mechanical vs NO	Rescue	Full paper	92	100	100	43	41
Lefevre et al. [15]	2005	Randomized	Mechanical vs NO	X-sizer	Full paper	201	100	100	55	65
Antoniucci et al. [13]	2004	Randomized	Mechanical vs NO	Angiojet	Full paper	100	NR	NR	98	98
AIMI [16]	2006	Randomized	Mechanical vs NO	Angiojet	Full paper	480	49	44	95	94
JETSTENT [22]	2010	Randomized	Mechanical vs NO	Angiojet	Full paper	501	98.6	98.6	97	98
Kuni et al. [14]	2004	Randomized	Mechanical vs NO	Rescue	Abstract	258	NR	NR	NR	NR

T = treatment group, C = control group, no = no thrombectomy, NR = not reported.
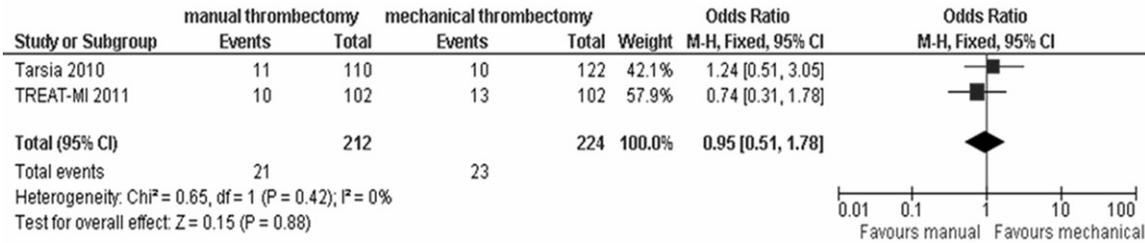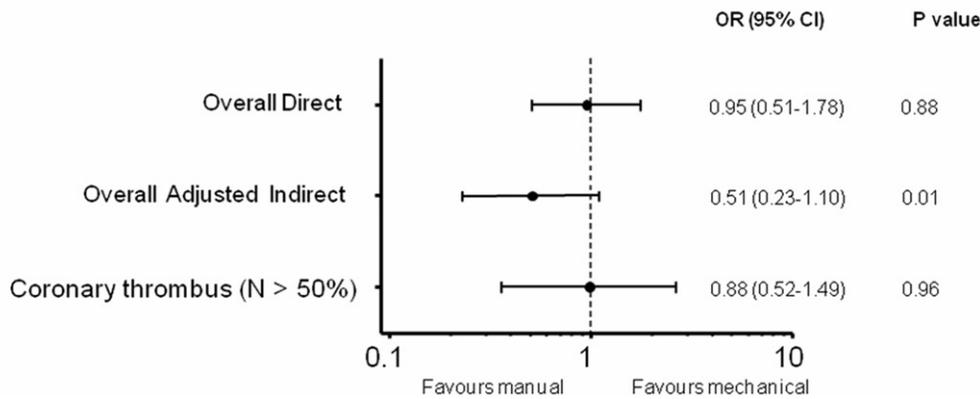
Figure 2. Odds ratios (ORs) with 95% confidence intervals (CIs) for mortality after manual vs mechanical thrombectomy in the direct meta-analysis (Panel A), overall direct and indirect meta-analysis and in the meta-analysis without TAPAS and AIMI trial, enrolling < 50% patients with intracoronary thrombus at baseline (Panel B). N = patients with visible coronary thrombus.

case of significant heterogeneity and/or moderate or significant inconsistency (> 50%) across studies.

Adjusted indirect comparisons is a relatively novel methodology which allows to compare two different treatments not directly compared in the studies (treatment A = mechanical thrombectomy and C = manual thrombectomy) but which have a common comparator (treatment B = no thrombectomy); the use of statistical adjustment constructed from two trials that have a common comparator (comparison of manual versus mechanical thrombectomy using trials comparing A versus B and B versus C) has the advantage to maintain the randomization design of the comparison mechanical vs manual. We used the Bucher method [4] for indirect comparisons using a common comparator, which is a statistical method for estimating OR and corresponding uncertainty. Adjusted indirect comparisons of pooled estimates were then performed according to Song et al. [5].

The method is well validated and recommended as a preferred method for indirect comparison, superior to other methods, as it preserves the randomization and retains the methodological properties of the RCTs.

In detail, we generated from OR comparing manual or mechanical thrombectomy vs. placebo interaction OR for manual or mechanical thrombectomy, with pertinent 95% CI and Z scores for 2-tailed hypothesis testing (p significant if < 0.05); specifically, these interaction OR are calculated according to the following formula: $\ln(OR_{manual\ vs.\ mechanical}) = \ln(OR_{manual\ vs.\ no\ thrombectomy}) - \ln(OR_{mechanical\ vs.\ no\ thrombectomy})$, and var $(\ln(OR_{manual\ vs.\ mechanical})) = var(\ln(OR_{manual\ vs.\ no\ thrombectomy})) + var(\ln(OR_{mechanical\ vs.\ no\ thrombectomy}))$, where ln is the natural logarithm, and var is the variance. Trial inconsistency was assessed with I2.

Separate indirect meta-analyses comparing the two strategies in the overall population and excluding trials enrolling < 50% patients with
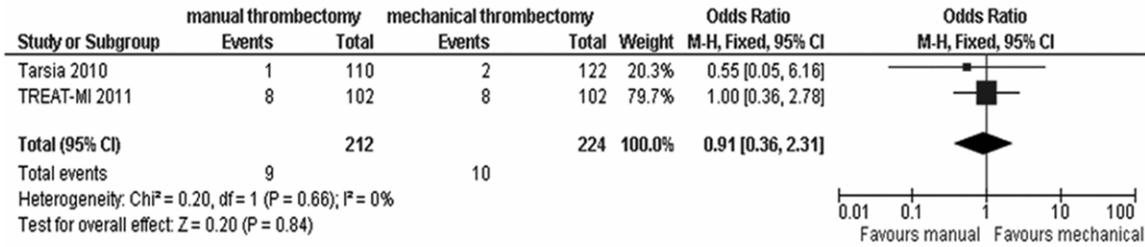
Figure 3. Odds ratios (ORs) with 95% confidence intervals (CIs) for MI after manual vs mechanical thrombectomy in the direct (Panel A), overall direct and indirect meta-analysis and in the meta-analysis without TAPAS and AIMI studies enrolling < 50% patients with intracoronary thrombus at baseline (Panel B). N = patients with visible coronary thrombus.

intracoronary thrombus at baseline angiography were planned and carried out.

Results

Eligible studies

Among the 436 potentially relevant publications, a total of 3 studies (two randomized and one non-randomized) directly comparing manual vs mechanical thrombectomy and 21 RCTs separately comparing these two strategies were initially identified (**Figure 1**). One trial was excluded because of comparison between two manual thrombectomy devices [6]. Therefore, 3 studies for the direct meta-analysis [7-9] with a total of 513 patients (249 allocated to manual vs 264 to mechanical thrombectomy) and 21 trials for the adjusted indirect meta-analysis [10-31] with a total of 4514 patients (2270 allocated to thrombectomy and a total number of 2244 patients without thrombectomy) were finally included. One trial was excluded because of comparison between two manual thrombec-

tomy devices [28]. Trial characteristics are shown in **Table 1**.

Clinical endpoints

Mortality: Direct meta-analysis: no significant difference in mortality outcome was observed between the two strategies; 21 patients out of 212 and 23 patients out of 224 died in the manual and in the mechanical thrombectomy groups, respectively: (OR (95% CI) = 0.95 (0.51-1.78), p = 0.88) (**Figure 2A**).

Indirect meta-analysis: Data on 30-day mortality were available in 4449 patients. Results of the adjusted indirect meta-analysis showed reduced mortality in the manual vs mechanical thrombectomy group (OR (95% CI) = 0.51 (0.23-1.10), p = 0.01) (**Figure 2B**); when discarding the TAPAS trial in the manual thrombectomy group and the AIMI trial in the mechanical thrombectomy group, both reporting an overall low percentage of patients with intracoronary

Stroke

	OR (95% CI)	P value
Overall Adjusted Indirect	1.57 (0.23-10.35)	0.07
Coronary thrombus (N > 50%)	1.58 (0.21-11.80)	0.04

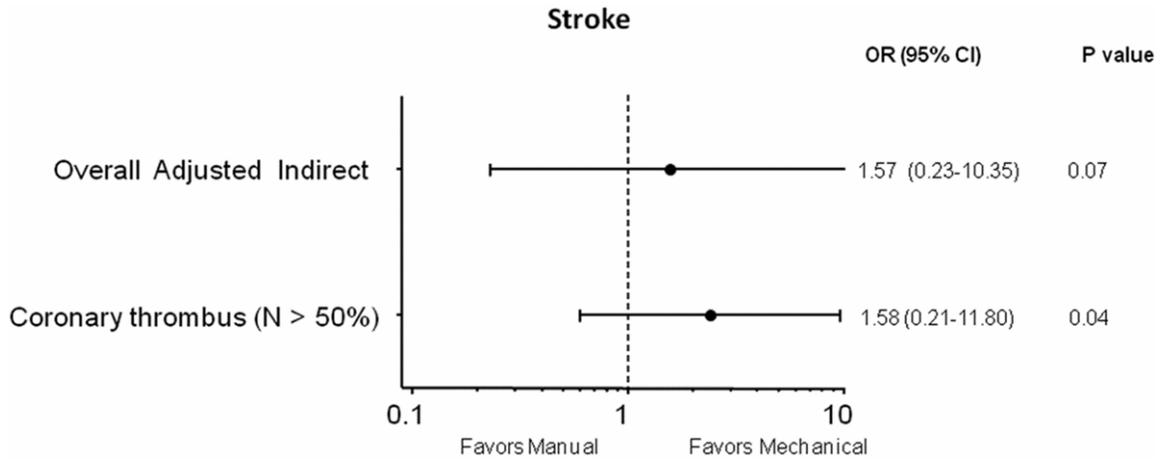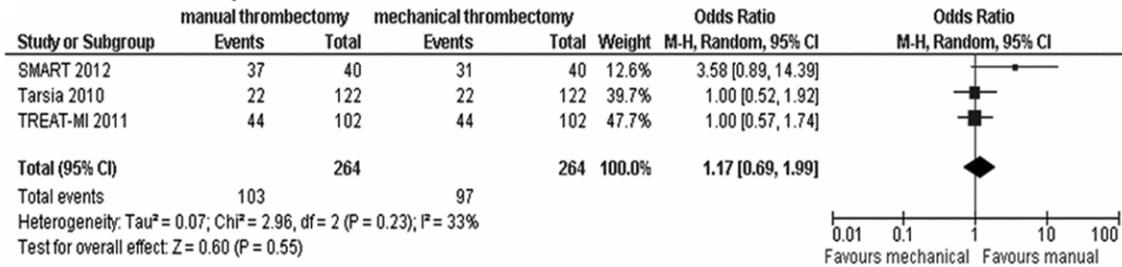0.1   1   10
Favors Manual   Favors Mechanical

Figure 4. Odds ratios (ORs) with 95% confidence intervals (CIs) for stroke after manual vs mechanical thrombectomy in the overall indirect meta-analysis and in the meta-analysis without TAPAS and AIMI studies enrolling < 50% patients with intracoronary thrombus at baseline. N = patients with visible coronary thrombus.

ST- Resolution

A Direct meta-analysis

Study or Subgroup	manual thrombectomy Events	Total	mechanical thrombectomy Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% CI
SMART 2012	37	40	31	40	12.6%	3.58 [0.89, 14.39]	
Tarsia 2010	22	122	22	122	39.7%	1.00 [0.52, 1.92]	
TREAT-MI 2011	44	102	44	102	47.7%	1.00 [0.57, 1.74]	
Total (95% CI)		264		264	100.0%	1.17 [0.69, 1.99]	
Total events	103		97				

Heterogeneity: Tau² = 0.07; Chi² = 2.96, df = 2 (P = 0.23); I² = 33%
Test for overall effect: Z = 0.60 (P = 0.55)

0.01   0.1   1   10   100
Favours mechanical   Favours manual

B Direct and Indirect meta-analysis

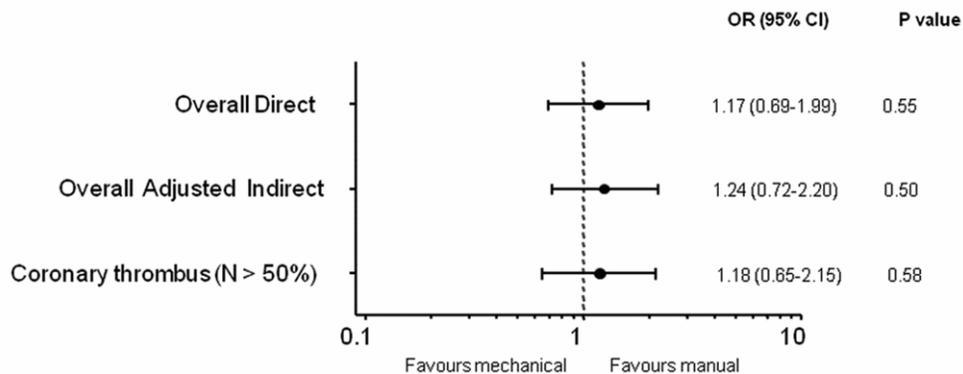|	OR (95% CI)	P value
Overall Direct	1.17 (0.69-1.99)	0.55
Overall Adjusted Indirect	1.24 (0.72-2.20)	0.50
Coronary thrombus (N > 50%)	1.18 (0.65-2.15)	0.58

0.1   1   10
Favours mechanical   Favours manual

Figure 5. Odds ratios (ORs) with 95% confidence intervals (CIs) for ST-resolution after manual vs mechanical thrombectomy in the direct meta-analysis (Panel A), overall direct and indirect meta-analysis and in the meta-analysis without TAPAS and AIMI studies enrolling < 50% patients with intracoronary thrombus at baseline (Panel B). N = patients with visible coronary thrombus.
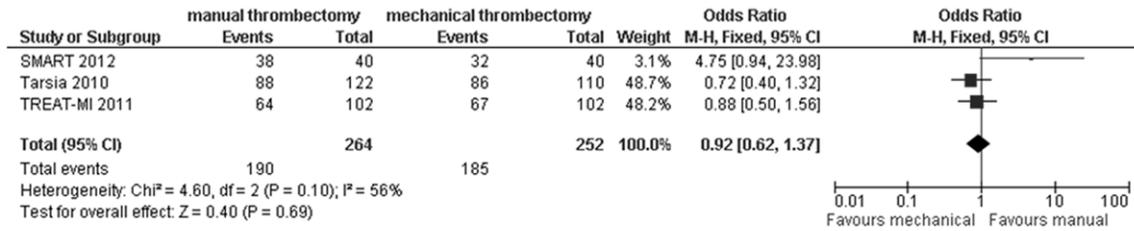
thrombus at baseline, the effect on survival was comparable between the two strategies: OR (95% CI) = 0.88 (0.52-1.49), p = 0.96 (**Figure 2B**).

TIMI-3 flow

A Direct meta-analysis

Study or Subgroup	manual thrombectomy Events	Total	mechanical thrombectomy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
SMART 2012	38	40	32	40	3.1%	4.75 [0.94, 23.98]
Tarsia 2010	88	122	86	110	48.7%	0.72 [0.40, 1.32]
TREAT-MI 2011	64	102	67	102	48.2%	0.88 [0.50, 1.56]
Total (95% CI)		264		252	100.0%	0.92 [0.62, 1.37]
Total events	190		185			

Heterogeneity: Chi² = 4.60, df = 2 (P = 0.10); I² = 56%
Test for overall effect: Z = 0.40 (P = 0.69)

Odds Ratio M-H, Fixed, 95% CI — scale from 0.01 to 100. Favours mechanical / Favours manual

B Direct and Indirect meta-analysis

	OR (95% CI)	P value
Overall Direct	0.92 (0.62-1.37)	0.69
Overall Adjusted Indirect	1.68 (0.96 -2.94)	0.08
Coronary thrombus (N > 50%)	1.50 (0.88-2.54)	0.15

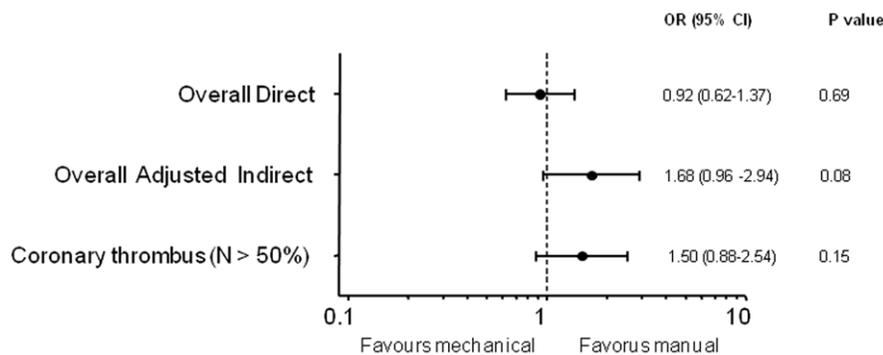Scale from 0.1 to 10. Favours mechanical / Favorus manual

Figure 6. Odds ratios (ORs) with 95% confidence intervals (CIs) for TIMI-3 flow after manual vs mechanical thrombectomy in the direct meta-analysis (Panel A), overall indirect meta-analysis and in the meta-analysis without TAPAS and AIMI studies enrolling < 50 % patients with intracoronary thrombus at baseline (Panel B). N = patients with visible coronary thrombus.

Re-infarction: Direct meta-analysis: re-MI rates were comparable between the two strategies: OR (95% CI) = 0.91 (0.36-2.31), p = 0.84 (**Figure 3A**).

Indirect meta-analysis: data were available in 4056 (89.8%) patients. The overall indirect meta-analysis showed a non-significant trend in less re-MI rates in the mechanical thrombectomy group as compared to the manual thrombectomy arm: OR (95% CI)= 1.47 (0.42-5.0), p = 0.09 (**Figure 3B**); on the other hand, this trend in favor of mechanical thrombectomy turned out to be strongly significant when removing the TAPAS and AIMI trial with reported low percentage of patients with intracoronary thrombus at baseline: OR (95% CI) = 2.41 (0.60-9.63), p < 0.001 (**Figure 3B**).

Stroke: Data on stroke were consistently available for indirect meta-analysis only; they were available in 3859 (85.5%) patients. The overall

indirect meta-analysis showed not significant increased rates of stroke in the manual vs mechanical thrombectomy arm: OR (95% CI) = 1.57 (0.23-10.35), p = 0.07 (**Figure 4**); when discarding TAPAS and AIMI studies, a higher risk of stroke was observed with manual thrombectomy: OR (95% CI) = 1.58 (0.21-11.80), p = 0.04 (**Figure 4**).

Procedural endpoints

ST-segment resolution: Direct meta-analysis: no difference in the resolutions of ST-segment was found between manual and mechanical thrombectomy, although a significant heterogeneity and inconsistency was observed between the two RCTs: OR (95% CI) = 1.17 (0.69-1.99), p = 0.55 (**Figure 5A**).

Indirect meta-analysis: data on complete ST-segment resolution were available in 3974 patients (89.3%). Comparable favorable results

in normalizing ST-segment were observed in patients treated either with manual or mechanical thrombectomy in the overall adjusted indirect meta-analysis: OR (95% CI) = 1.24 (0.72-2.20), p = 0.50 (**Figure 5B**); when removing the TAPAS and AIMI studies, these findings persisted: OR (95% CI) = 1.18 (0.65-2.15), p = 0.58 (**Figure 5B**).

TIMI-3 coronary flow: Direct meta-analysis: manual and mechanical thrombectomy yielded similar TIMI-3 angiographic post-procedural results: OR (95% CI) = 0.92 (0.62-1.37), p = 0.69 (**Figure 6A**).

Indirect meta-analysis: data on postprocedural TIMI-3 flow were available in 4192 (94.2%) patients. Non-significant higher rates of TIMI-3 flow restoration were noted in the manual thrombectomy group: OR (95% CI) 1.68 (0.96-2.94), p = 0.08 (**Figure 6B**); this trend however disappeared in the analysis by discarding TAPAS and AIMI trials where the two strategies provided comparable TIMI 3 flow rates: OR (95% CI) = 1.50 (0.88-2.54), p = 0.15 (**Figure 6B**).

Discussion

This is the first meta-analysis comparing to date manual vs mechanical thrombectomy in a systematic fashion; direct and indirect evidence were used to provide the most comprehensive source of evidence available to date; the main findings of this report are that 1) no clear clinical benefits emerged from mechanical thrombectomy in both the direct and overall indirect meta-analysis; in the meta-analysis without the inclusion of the TAPAS and AIMI trials, reporting low percentage (< 50%) of patients with intracoronary thrombus at baseline, 2) mechanical thrombectomy yielded a significant reduction of re-MI and stroke rates as compared to a manual strategy.

Several RCTs and a large meta-analysis have shown that primary PCI provides mortality benefits in comparison with thrombolysis, mainly due to better and sustained optimal epicardial perfusion; however, despite epicardial recanalization with angiographic TIMI-3 flow, suboptimal myocardial perfusion may occur in up to 20-40% of patients, affecting significantly the long-term survival.

Indeed, the patency of epicardial infarct related coronary artery after reperfusion is not a guarantee for adequate microvascular perfusion. Therefore, optimizing tissue-level reperfusion is a therapeutic goal in the setting of primary PCI. Distal embolization of material from coronary thrombus is a known predictor of coronary no-reflow and impaired tissue perfusion; the larger is the thrombus, the higher to chance to foster distal embolization.

In several studies thrombectomy has emerged as an important tool to reduce thrombus burden, counteracting distal embolization; In the Long-Term Clinical Efficacy of Thrombectomy Devices in Acute ST-Elevation Myocardial Infarction (ATTEMPT) meta-analysis [31], patient-level data were pooled, including 2686 patients from 11 trials. At a median of 1-year follow-up, all-cause mortality, death and MI, and major cardiovascular adverse events were significantly reduced with thrombectomy. As expected from results of individual trials, the survival benefit observed in this meta-analysis was confined to patients who were treated with manual thrombectomy, However, the investigators failed to obtain data from six eligible trials comprising approximately 1000 patients, which may have biased their results. Subsequently, updated meta-analyses have been performed incorporating more trials showing that thrombectomy was able to improve surrogate markers of reperfusion but not reinfarction and 30-day mortality.

Mechanical thrombectomy has emerged as a new promising tool which appears to be more effective in removing thrombus as compared to manual thrombectomy.

The recently published CompariSon of Manual Aspiration with Rheolytic Thrombectomy in Acute Myocardial Infarction: the (SMART) Primary PCI Trial [9], compared by optical coherence tomography the efficacy of mechanical thrombectomy vs manual thrombectomy in thrombus removal before infarct artery stenting in patients with STEMI; the study, while underpowered to assess clinical outcome, showed that mechanical thrombectomy as compared to manual thrombectomy, is more effective in thrombus removal and is associated with a better myocardial reperfusion. In the A Randomized Comparison of Manual Versus Mechanical Thrombus Removal in Primary Percutaneous Coronary Intervention in the Treatment of ST-Segment Elevation Myocardial

Infarction (TREAT-MI) study [8], a single center study, mechanical thrombectomy failed to provide any further procedural or clinical improvement as compared to manual thrombectomy.

It must be noted that, however, the TREAT-MI trial was flawed by several biases: 1) paucity of clinical and angiographic data on the patients enrolled in the study; indeed, their hemodynamic condition, the size of the myocardial infarction, the extent of coronary disease in other major epicardial vessels, left ventricular function, presence of angiographic collaterals toward the infarct-related artery, all are not reported; 2) lack of adequate thrombus measurement precluded an adequate assessment of thrombus which was classified as absent in at least 16% of the patients receiving mechanical thrombectomy and 13% of the patients allocated to manual thrombectomy. Accordingly, a meta-analysis providing the results coming from a direct but also indirect evidence on manual and mechanical thrombectomy appears timely; despite the limited evidence available from direct meta-analysis, the adjusted indirect meta-analysis showed in a large population of 4514 patients that mechanical thrombectomy strongly reduced the incidence of re-MI when discarding from the analysis the two trials with lower thrombus burden.

High thrombus burden is in fact known to be associated with an increased incidence of distal embolization, a significant pathogenetic component of no-reflow, and may limit reperfusion at tissue level and is associated with a higher frequency of major adverse clinical events; moreover, stenting in the presence of high thrombus burden may hence increase the risk of late stent malposition when, days after, the thrombus is completely dissolved and which constitutes and important risk factor for stent thrombosis and re-MI.

Mechanical catheters, while more bulky, may provide more consistent advantages in removal of thrombus because of their intrinsic properties; for example within ANJOJET catheter there is a high-velocity saline jets which creates a strong negative pressure (Bernoulli effect) that entrains the thrombus to the catheter inflow windows where it is captured, fragmented, and evacuated through the outflow lumen; this may ultimately result in a larger thrombus removal when compared to manual aspiration.

This meta-analysis made clear the limited evidence of studies directly comparing manual vs mechanical thrombectomy; despite this, the findings coming from the large populations of indirect analysis have been useful to give new insights on this debated issue.

According to the present report, indeed the benefits from mechanical thrombectomy over manual thrombectomy are mainly related to the thrombus burden, which therefore should be assessed before starting the invasive procedure and might guide the choice of the proper thrombus removal device; the present study showed that patients presenting with visible thrombus experienced lower rates of re-MI after mechanical thrombectomy as compared to those treated with manual thrombectomy; conversely the benefits in the immediate procedural characteristics such as TIMI-3 flow and ST-segment resolutions were comparable between the two strategies; these findings reflect the efficacy of manual aspiration in improving coronary flow velocities and restoring coronary flow by removing part of the thrombus; the higher the thrombus however, the higher the possibility not to completely remove it with a manual passing of the device; conversely, the manual passage itself may favor in case of large thrombus burden microembolization and increase the possibility of re-MI.

Future powered head to head randomized comparisons in a population with large thrombus burden are certainly needed to definitively clarify the benefits of mechanical thrombectomy in reducing the rate of ischemic outcomes such as re-MI and stroke.

Limitations

The evidence from this meta-analysis is mainly derived by indirect comparisons; clearly, there are a number of constraints and limitations related to the method used for an indirect comparison analysis, but when performed according to established methods, it represents a reasonable and well validated statistical tool to qualify a comparison of effects especially when there is a limited direct evidence available. Therefore, indirect estimates obtained with adjusted methods which preserve randomization design appear informative to this purpose. Studies investigating mechanical thrombectomy used two essentially different catheters such as ANGIOJET and X-SIZER catheters; on

the other hand, the stability of the results by performing separate analyses based on the mechanical catheter used provided similar results to those obtained in the overall analyses, suggesting the robustness of the overall estimates.

Conclusions

Mechanical thrombectomy, as compared to manual thrombectomy, provides higher benefits in reduction of re-MI and stroke in the population with high thrombus burden only. Large powered head-to-head comparisons in patients with high thrombus burden are warranted to definitively confirm the clinical benefits of mechanical thrombectomy.

Acknowledgments

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