Original Article

Aspiration thrombectomy in ST-Elevation myocardial infarction: Further insights from a network meta-analysis of randomized trials

Rama Dilip Gajulapalli [a, *], Arun Kanmanthareddy [b], Kathir Balakumaran [c], Hwanhee Hong [d], Shari Bolen [e], Meera Kondapaneni [c], Tilak K.R. Pasala [f]

[a] Department of Hospital Medicine, Cleveland Clinic, Cleveland, OH, USA
[b] Division of Cardiology, Creighton University School of Medicine, Omaha, NE, USA
[c] The Heart and Vascular Center, Case Western Reserve University/MetroHealth, Cleveland, OH, USA
[d] Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[e] Center for Health Care Research and Policy, MetroHealth/Case Western Reserve University School of Medicine, Cleveland, OH, USA
[f] Heart and Vascular Center, Hackensack University Medical Center, Hackensack, NJ, USA

A R T I C L E   I N F O

A B S T R A C T

Background: The initial enthusiasm for thrombectomy during percutaneous coronary intervention (PCI) of ST-elevation myocardial infarction (STEMI) patients has given way to restraint. There has been some limited interest whether it is beneficial in a few selected subgroups. Hence, we performed a network meta-analysis to compare conventional PCI (cPCI), Aspiration or manual thrombectomy (AT) and Mechanical thrombectomy (McT) for clarification.
Methods: Electronic databases were searched for randomized studies that compared AT, McT, or cPCI. A network meta-analysis was performed and odd's ratio (OR) with 95% confidence intervals was generated for major adverse cardiac events (MACE), mortality, myocardial infarction (MI), target vessel revascularization (TVR), stent thrombosis (ST), stroke, left ventricular ejection fraction (LVEF), myocardial blush grade (MBG) and ST segment resolution (STR).
Results: A total of 43 randomized trials (n = 26,682) were included. The risk of MACE (OR 0.86 95% CI 0.73–1.00), Mortality (OR 0.85 95% CI 0.73–0.99), MI (OR 0.65, 95% CI: 0.44–0.95) and TVR (OR 0.86, 95% CI: 0.74–1.00) were lower with AT compared to cPCI. The risk of ST and stroke was no different with the use of adjunctive AT. MBG, STR, and LVEF improved with the use of AT while the infarct size was no different in the two groups.
Conclusions: Our comprehensive network meta-analysis suggests conflicting outcomes with AT. While Mortality, MACE, MI seem better, there is a suggestion that, Stroke and ST might be worse. Whether AT can still be pursued in any select cases should be further scrutinized.

1. Introduction

Myocardial infarction with ST segment elevation (STEMI) is characterized by complete occlusion of the epicardial coronary artery due to plaque rupture and subsequent thrombus formation. Conventional percutaneous coronary intervention (cPCI) has been established as an effective method of reperfusion of the occluded coronary artery.[1] However, distal embolization of the plaque debris and subsequent microvascular obstruction is an unfavorable event with cPCI.[2] Therefore, thrombectomy was introduced to decrease the risk of distal embolization of the thrombus burden and thereby preserving microvascular perfusion. A few early randomized controlled trials (RCT) demonstrated that aspiration thrombectomy (AT) was beneficial in the setting of STEMI.[3,4] Based on these studies, the ACC (American college of Cardiology) & AHA (American Heart Association) initially included AT as an adjunct procedure to cPCI[Class IIA indication] in the setting of STEMI.[5,6] However, subsequent RCT's with a larger sample size demonstrated lack of clinical benefit with the use of AT.[7,8] In addition, there was a concern for increased risk of stroke with the use of AT.[7] Based on the above evidence, the ACC/AHA appropriately downgraded the recommendation for routine use of adjunct thrombectomy to a class III indication.[6,9] Given the mixed results of various clinical trials and limited evidence comparing manual or aspiration

* Corresponding author. Cleveland Clinic Foundation, Cleveland, USA.
E-mail address: Gajular@ccf.org (R.D. Gajulapalli).

thrombectomy (AT) vs mechanical thrombectomy (McT), we performed a network meta-analysis of all the RCT's evaluating the efficacy of AT and McT compared to cPCI.

2. Methods

2.1. Study search and selection criteria

We performed a systematic review for RCT's comparing thrombectomy strategies in PCI following the QUOROM (Quality of Reporting of Meta-Analysis) and PRISMA guidelines.[10–12] We electronically searched PubMed, EBSCO, CINAHL and Google Scholar databases using search terms "thrombectomy", "thrombus aspiration", "thromboaspiration", "manual thrombectomy", "mechanical thrombectomy", "aspiration thrombectomy" and "myocardial infarction". Abstract lists and conference proceedings of major cardiology societies including American College of Cardiology, American Heart Association, Transcatheter Cardiovascular Therapeutics, Cardiovascular Research Technologies, European Society of Cardiology and EuroPCR were searched for all published reports, articles, letters, and communications using the above mentioned terms. Clinical trial databases, expert reviews, prior meta-analyses, and the reference citations of selected manuscripts were also manually searched for potential articles. Two researchers (KB, RDG) independently performed title and abstract level screening. Citations screened at abstract level were retrieved if they met the inclusion criteria. Final approval of the study selection was done only after full text review by authors (RDG, TP). Any conflicts between reviewers were resolved by consensus. The search was restricted to studies published in English.

2.2. Inclusion and exclusion criteria

Studies were included when: 1) They were prospective randomized trials; 2) data on outcomes were reported based on treatment strategy, i.e. the type of intervention used; 3) the study compared subjects receiving at least two different interventional strategies; 4) more than 25 patients were included in the study; 5) type of thrombectomy strategy used was clear in the manuscript; 6) included patients were undergoing cPCI for STEMI; and 7) the length of follow-up post cPCI was a minimum of 48 h. Studies published in languages other than English and studies using distal embolic protection devices in conjunction with thrombectomy were excluded.

2.3. Data extraction and quality assessment

Relevant information extracted from articles include the first author, study name, year of publication, study design, number of subjects included, definition of endpoints, baseline characteristics, type of thrombectomy used, anticoagulant characteristics including dose, type of P2Y12 and/or Glycoprotein IIb/IIIainhibitors (GPI) used, type of access used during the cPCI, follow-up length when reported and relevant clinical outcomes. Internal validity of randomized trials was assessed by evaluating allocation concealment, masked adjudication of outcomes, and inclusion of all patients randomly assigned to treatment groups in the analysis per intention-to-treat principle.

2.4. Study endpoints and subgroups

Primary outcomes evaluated in our study include major adverse cardiac events (MACE), all-cause mortality, stent thrombosis (ST), myocardial infarction (MI), target vessel revascularization (TVR) and stroke as provided. These outcomes encompassed both efficacy and safety endpoints. Secondary outcomes evaluated include ST segment resolution (STR), change in left ventricular ejection fraction (LV EF), change in myocardial blush grade (MBG), changes in the infarct size before and after the procedure. Outcomes were also analyzed in the following subgroups from studies which reported these clearly: 1) Trials reported in the last 5 years, 2) Routine use of GPI anticoagulation, 3) Type of P2Y12 inhibitor preloading.

2.5. Statistical analyses

The reference treatment chosen was cPCI against which each treatment (AT and McT) was compared in the primary analysis. We performed network meta-analysis using the frequentist method to estimate the effect of each treatment relative to each other.[13,14] We performed multivariate random-effects meta-analysis for MACE, all-cause mortality, ST, MI, TVR, stroke, STR, and MBG to obtain pairwise pooled odd's ratio (OR) and 95% confidence intervals (CI). We performed weighted mean difference (WMD) and 95% CI to assess changes in EF and infarct size. We performed hierarchical ranking (comparative best treatment strategy) for the clinical outcomes using SUrface under the Cumulative Ranking curve (SUCRA) values (larger the value, better the rank of the treatment). We estimated the contribution of between-studies heterogeneity by I^2 statistic.[14] We tested for inconsistency between direct and indirect evidence using the node-splitting method.[15] We used 'comparison-adjusted' funnel plots for assessing the presence of small-study effects.[16] We performed all analyses using the STATA statistical software (STATA 13, StataCorp LP, College Station, TX, USA).

3. Results

Our initial search yielded 2972 citations and of these 43 studies met our inclusion and exclusion criteria (Supplementary Fig. 1) which were included. Among the 43 studies (Fig. 1), 29 studies compared AT versus cPCI, 14 studies compared McT versus cPCI and 3 studies evaluated AT versus McT. A total of 26,682 patients were included and the study characteristics of the included studies are listed in Tables 1a, 1b, 1c. Trial inclusion criteria, clinical end point definitions, time of follow up are provided in the supplementary tables 1, 2a & 2b. The mean age of patients included in the study was 61.2 years and were predominantly males (77.3%). The number
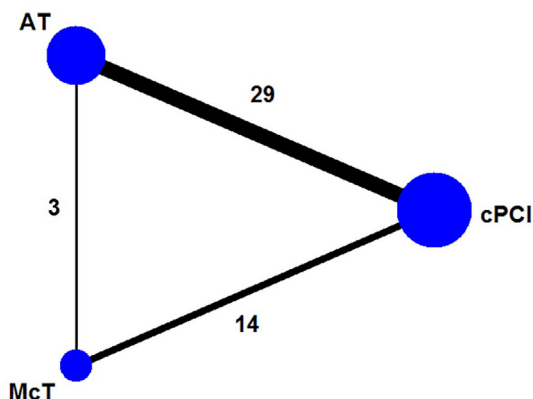

Fig. 1. Network map of procedural comparisons for mortality outcome. *Legend* – Circles represent the number of patients undergoing each procedure. The number represents the number of trials comparing each procedure. **Abbreviations:** cPCI, conventional percutaneous coronary intervention; AT, aspiration or manual thrombectomy; McT, mechanical thrombectomy.

Table 1a
Study Characteristics of Aspiration thrombectomy trials.

Trial/Author	Device	N	Age	Sex (F)	DM	MVD	Mean Ischemic Time	LAD	GP2b3a	TIMI 0/1	P2Y12	Direct stenting	DES
Ahn SG[1]	NA	40	60	20	30	NA	5.4	75	75	90	100	NA	NA
Bulum J[6]	Export	60	56	22	10	NA	4.4	42	90	NA	100	NA	NA
Chao[7]	Export	74	61	15	27	NA	5.8	58	26	99	100	31	NA
Chevalier B[8]	Export	249	60	19	15	NA	5.5	50	68	100	42	NA	NA
COCTAIL II[10]	Thrombuster	128	63	16	18	47	2.9	43	34	60	NA	NA	80
De Luca[11]	Diver	76	66	37	21	21	7.4	99	100	100	NA	49	57
DEAR-MI[12]	Pronto	148	58	20	18	51	3.4	47	100	77	NA	47	NA
Examination[14]	NA	1498	61	18	18	13	NA	42	50	NA	100	56	NA
Expira[15]	Export	175	66	40	21	21	6.2	43	100	100	100	39	58
INFUSE-AMI[17]	Export	452	60	26	11	NA	2.5	100	50	72	66	NA	73
ITTI[18]	Thrombuster	100	59	14	26	59	4.3	51	50	87	100	NA	NA
Liistro[21]	Export	111	65	23	16	42	3.4	42	100	73	100	15	0
Lipiecki[22]	Export	44	59	32	7	57	7.2	41	44	98	100	93	NA
Liu X[23]	Zeek	80	66	NA	NA	NA	NA	NA	50	NA	100	NA	NA
Messas N[24]	Export	239	61	26	17	52	4.7	42	74	87	NA	52	17
Noel[27]	Export	50	61	NA	NA	NA	4.7	44	NA	NA	NA	NA	NA
PATA STEMI[30]	Eliminate	128	59	33	11	65	3.0	41	27	81	NA	NA	NA
PIHRATE[31]	Diver	196	59	19	11	NA	NA	39	9	97	100	40	NA
REMEDIA[32]	Diver	99	61	16	20	38	4.8	45	66	88	100	45	NA
Shehata M[33]	Export	100	60	36	100	NA	1.3	54	100	NA	100	NA	0
Sim DS[34]	Thrombuster	86	62	31	30	NA	2.1	56	38	77	100	NA	86
TAPAS[35]	Export	1071	63	30	12	68	3.1	43	92	57	100	73	0
TASTE[36]	Export/Pronto	7244	66	25	12	43	3.0	45	16	78	100	NA	NA
TOTAL[37]	Export	10732	61	22	18	NA	2.9	NA	38	67	91	30	45
TROFI[39]	Eliminate	141	61	28	11	0	NA	59	55	48	100	NA	100
Wita K[41]	Diver	42	57	25	11	55	4.9	67	100	NA	100	NA	NA
Woo SI[42]	Export	63	54	8	19	29	4.5	64	0	81	100	NA	100

N, number; F, female; DM, diabetes mellitus; MVD, multi-vessel disease; LAD, left anterior descending artery, GP2b3a, glycoprotein 2b 3a inhibitors; TIMI, thrombolysis in myocardial infarction; DES, drug-eluting stent.

Table 1b
Study Characteristics of Mechanical thrombectomy trials.

Trial/Author	Device	N	Age	Sex (F)	DM	MVD	Mean Ischemic Time	LAD	GP2b3a	TIMI 0/1	P2Y12	Direct stenting	DES
Ali A − AIMI[2]	Angiojet	480	60	25	16	NA	2.5	38	95	66	100	NA	NA
Andersen NH[3]	Rescue	215	63	22	6	NA	NA	NA	100	NA	100	NA	NA
Antoniucci D[4]	Angiojet	100	64	20	17	35	NA	40	98	78	NA	88	NA
Beran G[5]	Xsizer	66	55	25	15	46	4.7	31	71	71	100	NA	NA
Ciszweski[9]	Rescue/Diver	137	64	29	14	NA	5.6	36	82	91	72	58	NA
Dudek[13]	Rescue	72	58	25	14	NA	4.1	47	0	74	NA	NA	NA
Hamza MA[16]	Diver	75	53	12	37	NA	5.2	57	33	NA	100	NA	NA
JETSTENT[19]	Angiojet	501	63	21	14	42	2.7	40	97	84	100	50	0
Kaltoft[20]	Rescue	215	64	22	7	50	3.8	45	95	67	100	NA	NA
Napadano M[26]	Xsizer	92	62	22	13	46	3.7	NA	42	NA	NA	45	NA
NONSTOP[28]	Rescue	258	65	20	NA	NA	NA	40	NA	NA	NA	NA	NA
Vampire[40]	TVAC	355	63	21	27	NA	6.7	51	0	75	100	NA	0
X AMINE ST[43]	Xsizer	201	62	26	22	40	4.3	52	60	NA	NA	47	NA

N, number; F, female; DM, diabetes mellitus; MVD, multi-vessel disease; LAD, left anterior descending artery, GP2b3a, glycoprotein 2b 3a inhibitors; TIMI, thrombolysis in myocardial infarction; DES, drug-eluting stent.

Table 1c
Study Characteristics of Aspiration vs Mechanical thrombectomy trials.

Trial/Author	Device	N	Age	Sex (F)	DM	MVD	Mean Ischemic Time	LAD	GP2b3a	TIMI 0/1	P2Y12	Direct stenting	DES
MUSTELA[25]	Export/Angiojet	208	63	23	20	11	3.6	NA	NA	NA	100	62	NA
Parodi G[29]	Angiojet/Export	80	65	22	14	NA	3.4	45	100	82	100	79	100
TREAT MI[38]	Xsizer/Export	201	61	22	15	NA	3.1	NA	100	85	100	NA	NA

N, number; F, female; DM, diabetes mellitus; MVD, multi-vessel disease; LAD, left anterior descending artery, GP2b3a, glycoprotein 2b 3a inhibitors; TIMI, thrombolysis in myocardial infarction; DES, drug-eluting stent.

of studies included in the meta-analysis for each outcome is noted in Fig. 2.

Major adverse cardiovascular events: The OR of MACE was 0.86 (95% CI: 0.73–1.00) between AT and cPCI groups suggesting benefit with the use of AT (Fig. 2). However, the McT group did not benefit significantly compared to the PCI group (OR 0.74, 95% CI: 0.54–1.02). There was no difference in MACE between McT and AT groups (OR 0.87, 95% CI 0.61–1.22).

Mortality: There was a lower risk of mortality with the use of AT compared to cPCI (OR 0.85, 95% CI: 0.73–0.99) (Fig. 2). However, when McT was compared to the cPCI group, there was no benefit with the use of McT (OR 1.12, 95% CI 0.72–1.74). Further, there was
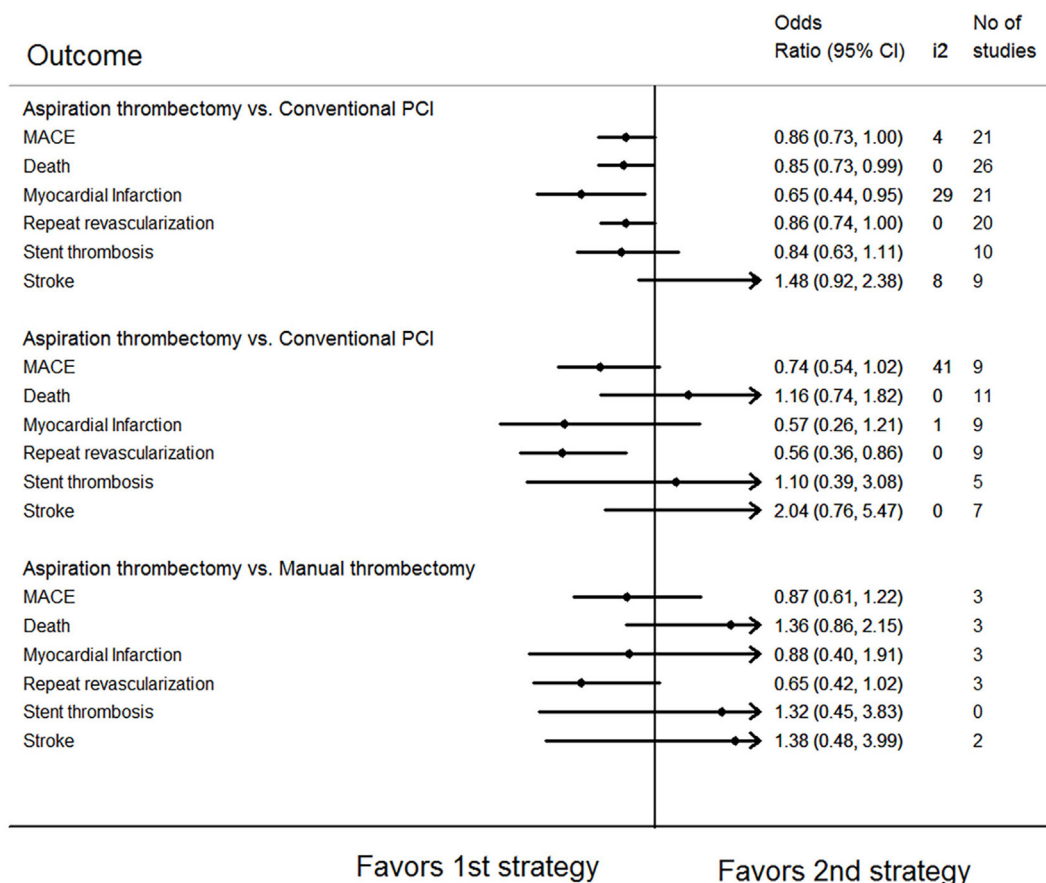
Fig. 2. Forest plot for clinical outcomes; **Abbreviations:** CrI, confidence interval; MACE, major adverse cardiovascular events; PCI, percutaneous coronary intervention; vs., versus.

no difference in the outcome of mortality in the groups comparing McT versus AT (OR 1.31, 95% CI: 0.84—2.05).

Myocardial Infarction: The risk of recurrent MI was lower with the use of AT compared to cPCI (OR 0.65, 95% CI: 0.44—0.95). There was no difference in the outcome of recurrent MI when McT was compared to the cPCI (OR 0.57, 95% CI: 0.26—1.21). There was also no difference between the uses of the two modalities of thrombectomy (OR 0.88, 95% CI: 0.40—1.91).

Target Vessel Revascularization: The risk of TVR was lower with both AT and McT compared to cPCI (OR 0.86, 95% CI: 0.74—1.00 and OR 0.56, 95% CI: 0.36—0.86 respectively) (Fig. 2). There was no difference in the risk of TVR with the use of McT versus AT (OR 0.65, 95% CI: 0.42—1.02).

Stent Thrombosis: AT or McT did not have any benefit with respect to stent thrombosis compared to cPCI (OR 0.84, 95% CI: 0.63—1.11 and OR 1.10, 95% CI: 0.39—3.08 respectively) (Fig. 2). Stent thrombosis risk was also not different between McT and AT (OR 1.32, 95% CI 0.45—3.83).

Stroke: There was no difference in the risk of stroke with AT or McT compared to cPCI (OR 1.48, 95% CI: 0.92—2.38 and OR 2.04, 95% CI 0.76—5.47 respectively), although there was a suggestion of higher odds of stroke with the use of AT and McT (Fig. 2). There was no difference between McT and AT (OR 1.38, 95% CI 0.48—3.99).

ST segment resolution: There was significant resolution of the ST segment after both AT and McT (Fig. 3). The OR of complete ST segment resolution with AT was 1.63 (95% CI: 1.30—2.04) compared to cPCI. McT also increased the odds of complete ST segment resolution (OR 1.83, 95% CI: 1.32—2.55). There was no difference in the

odds of ST segment resolution between McT and AT (OR 1.12, 95% CI: 0.78—1.62).

Myocardial Blush: There was significant improvement of myocardial blush grade (MBG) after both AT and McT (Fig. 3). The odds of achieving myocardial blush grade 2 or more were higher with the use of either AT (OR 2.13, 95% CI: 1.49—3.03) or McT (OR 1.76, 95% CI: 1.08—2.85) compared to cPCI. There was no difference in myocardial blush grade between McT and AT (OR 0.83, 95% CI: 0.47—1.45).

Left ventricular ejection fraction: LVEF was higher in the group that underwent AT compared to cPCI (WMD 2.39, 95% CI: 0.83—3.94) (Fig. 4). There was no difference in the LVEF in the groups that underwent McT versus cPCI (WMD -0.05, 95% CI: −2.23 − 2.14). There was also no difference in the LVEF between the groups undergoing McT or AT (WMD -2.43, 95% CI: −5.12 − 0.25).

Infarct Size: AT did not decrease infarct size compared to cPCI (WMD − 1.65, 95% CI: −5.09 − 1.79) (Fig. 4). The use of McT as an adjunct to cPCI showed similar results (WMD -0.65, 95% CI -4.63 − 3.33). There was no difference in LVEF with the use of AT or McT groups (WMD 1.00, 95% CI -3.96 − 5.97).

3.1. Subgroup analysis

Studies published within 5 years: The risk of MI (OR 0.59, 95% CI 0.36—0.98) and TVR (OR 0.85, 95% CI 0.73—1.00) was lower with the use of AT compared to cPCI (Table 2). The risk of MACE (OR 0.57, 95% CI 0.36—0.91) and TVR (OR 0.41, 95% CI 0.21—0.82) were lower with the use of McT compared to cPCI. The odds of TVR were lower with the use of McT compared to AT (OR 0.48, 95% CI 0.24—0.95).

Outcome   Odds ratio (95% CI)
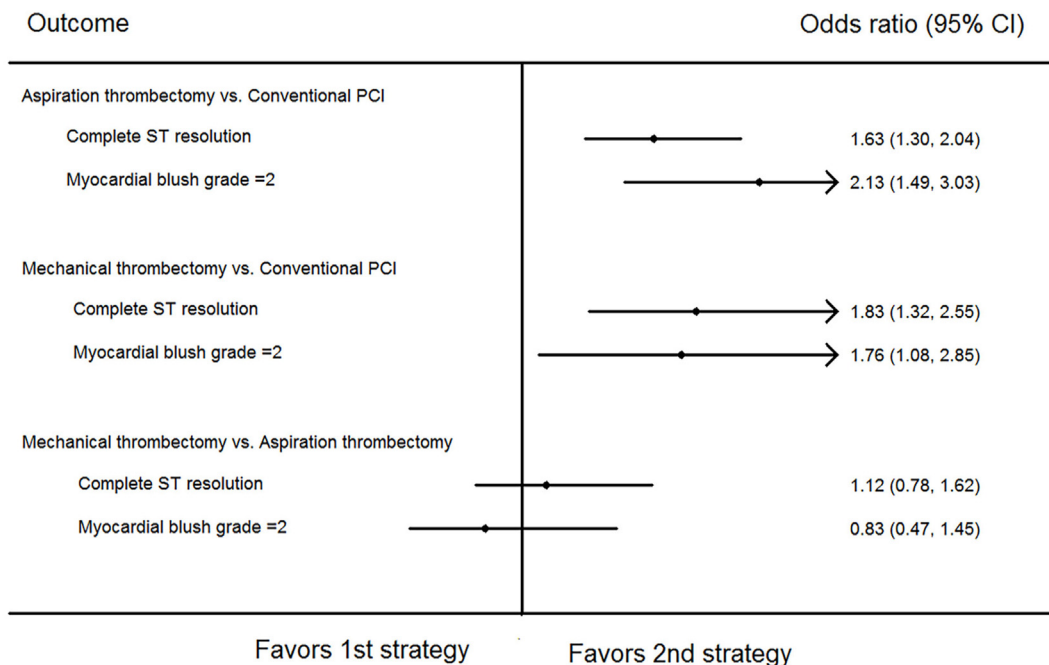

Fig. 3. Forest plot for complete ST-segment resolution and myocardial blush grade. **Legend** – Aspiration thrombectomy and mechanical thrombectomy performed better than conventional PCI in regards to complete ST-segment resolution and myocardial blush grade. **Abbreviations:** CI, confidence interval; PCI, percutaneous coronary intervention; vs., versus.
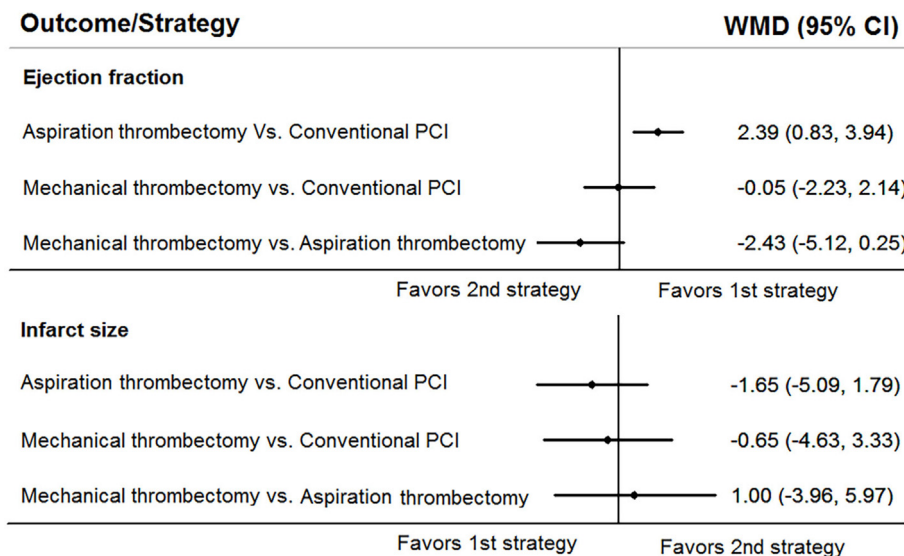

Fig. 4. Forest plot for ejection fraction and infarct size. **Legend**–There was no significant differences in the procedures for ejection fraction and infarct size except for aspiration thrombectomy was associated with slightly higher ejection fraction compared to conventional PCI. **Abbreviations:** CI, confidence interval; PCI, percutaneous coronary intervention; vs., versus.

Routine GpIIb/IIIa inhibitor use: Only the risk of TVR was lower with the use of routine GPI use along with McT (OR 0.49, 95% CI 0.25–0.97). The remainder of the outcomes were not different between AT versus cPCI, McT versus PCI and McT versus AT.

Preloading with P2Y12 Inhibitors: The risk of MI (OR 0.58, 95% CI 0.37–0.91) and TVR (OR 0.85, 95% CI 0.73–0.99) were lower in the group with AT compared to cPCI while MACE, mortality, stroke and stent thrombosis were not different between the two groups. Further, there were no differences in the outcomes for McT versus cPCI group and also no differences between McT and AT groups.

3.2. Hierarchical ranking

AT was the highest in the hierarchical ranking for Death, stent thrombosis, MBG, EF, and infarct size (Fig. 5). McT was the highest in the hierarchical ranking for MACE, MI, TVR and STR. cPCI was the highest for stroke.

3.3. Heterogeneity and inconsistency assessment

There was no significant contribution of between-studies heterogeneity to the meta-analyses (Fig. 2). There was no evidence of

Table 2
Subgroup analysis.

Subgroups/Outcomes	AT vs PPCI OR (95% CrI)	McT vs PPCI OR (95% CrI)	McT vs AT OR (95% CrI)
Studies published <5 years			
MACE	0.89 (0.76–1.03)	**0.57 (0.36–0.91)**	0.65 (0.41–1.02)
Death	0.87 (0.74–1.03)	0.96 (0.53–1.74)	1.11 (0.62–1.99)
Myocardial Infarction	**0.59 (0.36–0.98)**	0.54 (0.18–1.57)	0.90 (0.32–2.57)
Repeat Revascularization	**0.85 (0.73–1.00)**	**0.41 (0.21–0.82)**	**0.48 (0.24–0.95)**
Stent Thrombosis	0.84 (0.63–1.12)	0.71 (0.16–3.23)	0.85 (0.18–3.93)
Stroke	1.39 (0.77–2.48)	1.16 (0.20–6.70)	0.84 (-0.15–4.83)
Routine GP IIb/IIIa inhibitor use			
MACE	0.85 (0.58–1.25)	0.79 (0.46–1.35)	0.93 (0.53–1.62)
Death	0.66 (0.42–1.05)	1.04 (0.59–1.85)	1.57 (0.89–2.78)
Myocardial Infarction	0.57 (0.57–1.02)	0.52 (0.19–1.40)	0.92 (0.35–2.44)
Repeat Revascularization	0.82 (0.57–1.18)	**0.49 (0.25–0.97)**	0.60 (0.31–1.15)
Stent Thrombosis	0.74 (0.22–2.48)	1.13 (0.36–3.60)	1.53 (0.29–8.08)
Stroke	1.51 (0.28–8.05)	1.94 (0.64–5.85)	1.28 (0.23–7.13)
P2Y12 inhibitor pre-loaded			
MACE	0.84 (0.69–1.01)	0.86 (0.56–1.33)	1.03 (0.66–1.62)
Death	0.86 (0.73–1.01)	1.19 (0.68–2.07)	1.38 (0.79–2.42)
Myocardial Infarction	**0.58 (0.37–0.91)**	0.53 (0.20–1.41)	0.90 (0.34–2.39)
Repeat Revascularization	**0.85 (0.73–0.99)**	0.62 (0.31–1.23)	0.73 (0.37–1.44)
Stent Thrombosis	0.83 (0.62–1.10)	1.13 (0.36–3.60)	1.37 (0.42–4.49)
Stroke	1.37 (0.79–2.37)	2.17 (0.64–7.40)	1.59 (0.42–5.94)

AT, aspiration or manual thrombectomy; McT, mechanical thrombectomy; PPCI, primary (conventional) percutaneous coronary intervention; CrI, confidence interval; MACE, major adverse cardiovascular events; GP, glycoprotein; OR, odds ratio; vs, versus.
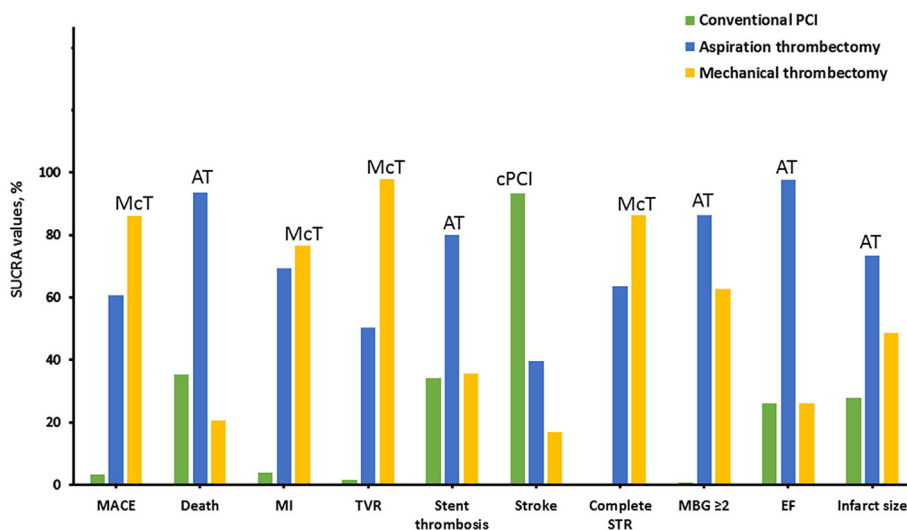

Fig. 5. Hierarchical ranking plot. *Legend* – Higher the SUCRA value, higher is the comparative ranking of the treatment. Outcomes are represented in the *x*-axis.; ***Abbreviations:*** cPCI, conventional percutaneous coronary intervention; AT, aspiration or manual thrombectomy; McT, mechanical thrombectomy; MACE, major adverse cardiovascular events; MI, myocardial infarction; TVR, repeat revascularization; STR, ST-segment resolution; MBG,

statistical inconsistency between direct and indirect estimates for the above outcomes (Supplementary Table 3). There was also no evidence of small-study effect for the outcomes, a representative comparison-adjusted funnel plot for death is shown in supplementary figure 2.

4. Discussion

The key findings of our comprehensive network meta-analysis incorporating 43 randomized studies with a total of 26,682 patients are the following: 1) MACE, MI, Death and TVR were lower with the use of AT compared to cPCI. Even when our analysis was restricted to studies published in the last 5 years or those that pre-loaded with P2Y12 inhibitors, AT was associated with a lower risk

of MI and TVR. 2) Indirect markers of complete revascularization (myocardial blush grade and ST segment resolution) were significantly better with the use of either AT or McT; however, this did not translate to improvement in hard outcomes in the case of McT except with TVR. 3) While there was no statistically significant increase in the risk of stroke with the use of both AT and McT compared to cPCI, there seemed to be a trend towards higher strokes.

The evidence regarding utility of thrombectomy so far has been conflicting.[6] The TAPAS (Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study) trial (n = 1071) showed an improvement in reinfarction and mortality (3.6% vs 6.7%, *p* = 0.02) at 1 year after AT.[3,17] This led to the initial enthusiasm for routine thrombus aspiration in STEMI. However,

subsequent large RCTs trials failed to show improvement in clinical outcomes.[7,8] The TOTAL (Trial of Routine Aspiration Thrombectomy With Percutaneous Coronary Intervention (PCI) Versus cPCI Alone in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary PCI) trial (n = 10,732) showed a lack of mortality benefit with AT (3.1% vs 3.5%, $p = 0.34$ at 180 days and 3.6% vs 3.8%, $p = 0.48$ at 1 year) with an increase in the risk of stroke (0.1% vs 0.5%, $p = 0.003$ at 180 days and 1.2% vs 0.7%, $p = 0.015$ at 1 year).[7,18,19] Similarly, in the TASTE (Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia) trial, AT did not improve clinical outcomes but was not associated with a higher risk of stroke.[8,20] Few possible explanations for this lack of benefit in the newer trials should be explored. First, residual high thrombus burden is shown to be associated with a greater degree of microvascular dysfunction as well as greater extent of myocardial damage.[21] In the OCT (optical coherence tomography) sub study of TOTAL trial, after the initial intervention to restore flow with thrombectomy or balloon angioplasty, no difference in thrombus burden was noted (2.4% vs 2.9%, $p = 0.37$).[22] The recent individual patient level meta-analysis by Jolly et al suggests thrombus aspiration was associated with less cardiac death (170 [2.5%] vs. 205 [3.1%] HR 0.80; 95% CI 0.65–0.98, $p = 0.03$) in the subgroup with high thrombus burden (TIMI thrombus grade ≥3) however with an increased risk of stroke.[23] Hence, the lack of benefit in the recent trials could be due to a small thrombus burden pre-AT or due to an inadequate removal of thrombus by AT.[8] Second, the improvements in cardiovascular care over the last decade with faster times to revascularization, newer anti-platelet agents and aggressive adaptation of secondary prevention strategies, may have attenuated some of the benefits accrued from AT. In our study, the subgroup analyses of trials published <5 years or those with P2Y12 inhibitors showed improvement in MI and TVR with AT. Thus, patient selection may be an important factor to reap the benefits of AT.

The higher incidence of stroke following AT is a cause for concern. In the TOTAL trial, the stroke rates were significantly elevated with AT compared to cPCI (0.7% vs 0.3%; $p = 0.02$) whereas there was no difference in the incidence of stroke in the TASTE (0.5% vs 0.5%) trial.[3,7] Prior Meta analyses have reported varied outcomes primarily due to the difference in the number of studies that were included in those meta-analyses.[24–26] However, in a meta-analysis by Kumbhani el al., which analyzed 11,321 patients across 20 trials, the stroke risk was not significantly different with and without the use of AT during cPCI (0.6% vs 0.6%; RR 1.04, 95% CI: 0.59–1.81, $p = 0.09$).[27] The etiology for stroke could be multifactorial. The varying definitions and adjudication events and tests used to diagnose stroke could be contributing to the heterogeneity in the reporting of stroke incidence. Further, operator technique and experience in using AT may also contribute to the varying risk of stroke. Also, the amount of thrombus burden could be a contributory factor in embolization to the brain. Our analysis which is by far the largest did not show statistically significant increase in the risk of stroke with the use of AT (OR 1.48, 95% CI 0.92–2.38).

Devices using mechanical disruption of the thrombus provide a theoretical advantage of the possibility of removal of even larger thrombus and hence higher chance of restoration of coronary flow. There have been few RCT comparing McT with AT. Parodi et al showed less residual thrombus burden with McT as well as Mustela et al who suggested better surrogate markers with McT.[28,29] However hard clinical outcomes both short and long term seem to be comparable with no clear benefit over AT. In fact a prior meta-analysis by Kumbhani et al which included 7 studies with 1598 subjects, found no clear benefit with McT.[26] Out study which included 17 studies in total involving McT did not find any evidence of benefit with McT over cPCI or AT. The various society guidelines

appropriately do not recommend Mechanical thrombectomy after STEMI.

There has been however some renewed, though limited interest in aspiration thrombectomy. It is thought to better facilitate direct stenting (DS) which during PCI can reduce microvascular obstruction and improve clinical outcomes.[30] This especially becomes relevant given that STEMI patients with greater residual thrombus burden had worse microvascular dysfunction and greater myocardial damage compared to those with smaller residual thrombus burden.[21] Further studies have shown possible subsets of patients who may benefit from AT. Fournier et al showed there was some circadian variance in outcomes with greater myocardial salvage after AT during daylight hours.[31] Jolly et al also suggested a trend towards decreased death after AT in the high thrombus burden group.[32]

The 2015 ACC/AHA/SCAI focused update on primary PCI for patients with STEMI guidelines have revised the indication for routine AT during PCI for STEMI patients from Class IIA recommendation to Class III (No benefit, level of evidence A).[9] The current recommendations are driven mainly by the results of the large RCTs such as TASTE and TOTAL. Results from large multicenter RCTs are usually more persuasive than inferences from any meta-analysis but finer analysis may suggest different options for different subgroups. Our results seem to suggest if this may be the case in regards to utility of AT. The results of our meta-analysis are far from conclusive given the varying study designs (underpowered and single center studies), heterogeneity of the included patients and different endpoints, which could have contributed to our results. We, therefore are of the opinion that while there seems to be some benefit from AT in terms of clinical end points, the risk of stroke should dissuade from wide practice of AT. Review of the United States National Cardiovascular Data Registry (NCDR) CathPCI Registry by Secemsky et al shows that the uptake of AT has appropriately been low in the recent past.[33]

Whether there may still be a role for AT in select patients with STEMI like those with embolic causes, large thrombus burden and certainly as a bail out procedure is an open question. We should focus our efforts on identifying these theoretical subgroups of patients who could likely benefit from AT. This especially is relevant in the new Covid-19 pandemic paradigm with delayed STEMI presentations with a high thrombus burden needing bail out procedures adding to this discussion.[34]

5. Limitations

Our study being a meta-analysis inherits all the fundamental fallacies of every individual included study. Without access to patient level data, we were unable to further adjust the analyses or assess the effect of differing variables such as ischemic time, location of thrombus, individual thrombus grade/burden, and type of thrombectomy device used. We were also unable to assess the effect of type of coronary stent (i.e drug eluting versus bare metal, first versus second generation etc.) on patient outcomes and risk of stent thrombosis and MI. Also, the location of the epicardial coronary artery revascularized and the role of complete versus incomplete aspiration of thrombus could not be assessed in this study. The lack of this data and lack of standardization across studies may obscure the clinical picture and actual risk/benefit of AT. Although we carried out the NMA accounting for the different type of AT method in each study, this assumes proportional hazards throughout the period of study. Individual patient-level data would allow exploration of other assumptions. Although all of the studies included were RCT's, our study may or may not be sufficiently powered to observe difference in clinical outcomes.

6. Conclusion

Our analysis which is the most comprehensive to date analyzing 43 trials and 26,682 patients suggests that AT compared to PCI, but not McT may improve the surrogate endpoints of perfusion, decrease the risk of MACE and mortality. However given a concern for possible increase in the risk of stroke in patients undergoing cPCI for STEMI, a class III indication in the guidelines is probably a prudent current approach. Whether further trials are necessary to identify any subgroups that may benefit from AT is open to discussion.

Declaration of competing interest

All other authors have declared no conflict of interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2021.01.006.

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