

Endovascular Treatment over Standard Medical Therapy in Acute Ischemic Stroke: A Meta-Analysis of Randomized Controlled Trials

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Abstract

Background: Endovascular treatment plays a continuously expanding role in the treatment of acute ischemic stroke. Several randomized controlled clinical trials evaluating possible benefits of endovascular therapy were conducted. From these trials emerged conflicting results. The aim of this study was to evaluate the efficacy of endovascular treatment over standard therapy in acute ischemic stroke.

Methods: We searched in PubMed and EMBASE databases from the date of inception until 2015/07/31. The primary outcome was the functional neurological outcome at 90 days measured with modified Rankin Score ≤ 2 . Secondary outcomes were partial or complete recanalization, assessed with modified arterial occlusive lesion, thrombolysis in myocardial infarction or thrombolysis in cerebral infarction scores of 2-3 and mortality. Safety outcome was Symptomatic Intracranial Hemorrhage (SICH). Data were pooled in the control and intervention groups, and odds ratios were calculated with 95% interval confidence. Statistical heterogeneity was evaluated with the χ^2 Mantel-Haenszel method and I_2 method. A p value <0.05 was considered statistically significant. Heterogeneity was considered significant for P values <0.10 .

Results: 12 trials were included with 2725 participants. Compared with standard therapy, endovascular treatment significantly improved the outcome at 90 days (OR: 1.77; 95% CI: 1.51-2.08). This result was affected by a significant heterogeneity. After a sensitivity analysis, excluding the trials in which the demonstration of large vessel occlusion was not an inclusion criterion, primary outcome was improved in the intervention group (OR: 2.05 95% CI: 1.70-2.46), with non-significant heterogeneity. The recanalization rate was higher and mortality was lower in the intervention groups, but these differences were not significant. The proportion of SICH was marginally higher in the intervention groups, again without any statistical significance.

Conclusion: Endovascular treatment for acute ischemic stroke ensures a significant increase of patients with favorable outcome compared with standard therapy in the absence of risk. Vascular studies before treatment are mandatory.

Keywords: Endovascular treatment; Acute ischemic stroke treatment; Thrombectomy; Intra-arterial thrombolysis

Introduction

Acute stroke treatment has undergone significant evolution during the past decades. Currently, intravenous thrombolysis using tissue plasminogen activator (IV-tPA) within 4.5 h of symptom onset is the established treatment for ischemic stroke and is associated with improved functional outcome. Despite the introduction of intravenous thrombolysis with tPA in clinical settings has changed dramatically the outcome of patients, there are several limitations related to this treatment. Strict exclusion criteria make only about 25% of patients eligible for intravenous thrombolysis. Further, the narrow time window limits the proportion of patients who are treatable [1]. IV-tPA is associated with early recanalization in only 21% of cases of large intracranial vessel occlusion, and the frequency of re-occlusion is about 12% [2,3]. Intravenous administration of tPA often proves ineffective in dissolving thrombi localized in intracranial large vessels, and this may explain the low rates of recanalization after treatment.

Endovascular techniques, both intra-arterial administration of thrombolytic drugs and thrombectomy with special devices, promote dissolution of intracranial large vessels thrombi.

Advantages of endovascular treatment over intravenous thrombolysis may include a selective lytic action into the occluding thrombus, permitting lower amounts of haemorrhagic complications

related to systemic concentration of thrombolytic agents [4]. Patients out of time window or with contraindications to intravenous thrombolysis, could be eligible for primary endovascular treatment [5]. On the other hand endovascular treatment is not free of complications. The procedure could require general anesthesia, which can increase the risk of in-hospital mortality [6], and can cause catheter-related complications. Another factor to consider is the need for an experienced interventional neuroradiology team, not available in all stroke centers.

Endovascular treatment benefits have been debated in the last years. Several Randomized Controlled Trials (RCT), comparing endovascular treatments versus standard therapy have been conducted, but these studies showed conflicting results. The wide differences between these RCTs and the relatively small samples recruited made impossible to draw conclusions.

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In the meantime, endovascular techniques have been greatly improved with development of modern generation devices, such as the stent-retrievers, and might have contributed to the differences in trial results [7].

In the last years several meta-analysis were conducted in order to determine the real impact of endovascular treatment in acute stroke treatment, but these studies considered only a subset of available RCT's, thus preventing from drawing firm conclusions on the global efficacy of endovascular treatment.

The aim of this study was to evaluate the efficacy of endovascular treatment (intra-arterial thrombolysis and/or thrombectomy) in acute ischemic stroke in the overall population and in specific subsets.

Methods

Inclusion criteria

We searched PubMed and EMBASE databases from the date of inception until 2015/07/31 using the terms "ischemic stroke" and "intra-arterial" and "thrombolysis" or "thrombectomy" or "endovascular treatment". Reference lists of relevant articles, congress presentations and conference abstracts were manually searched. Studies published in foreign national language for which translation was unavailable, were excluded. We selected only Randomized Controlled Trials (RCTs) which compared endovascular treatment (intra-arterial thrombolysis and/or mechanical thrombectomy) alone or associated to intravenous thrombolysis, with standard treatments (standard care or intravenous thrombolysis). We excluded RCTs in which endovascular treatment was directly compared with intravenous thrombolysis. There were no restrictions in study age, included patient age, imaging criteria, or National Institutes of Health Stroke Scale (NIHSS) score. We excluded studies without a control group and trials in which primary outcome data were not available or could not be extracted from study groups. We extracted the following information: age, National Institutes of Health Stroke Scale (NIHSS) score at baseline, principal inclusion and exclusion criteria, requirement of arterial occlusion for randomization, neuroimaging techniques used, administered therapy. Quality of included trials was formally assessed with the Jadad scale.

Outcomes

The primary outcome was the proportion of patients with a modified Rankin Score (mRS) of 0-2 at 90 days after the treatment. Secondary outcomes were partial or complete recanalization, assessed with modified Arterial Occlusive Lesion (mAOL) recanalization score, Thrombolysis in Myocardial Infarction (TIMI) score or thrombolysis in cerebral infarction (TICI) score of 2-3, and mortality. Safety outcome was Symptomatic Intracranial Haemorrhage (SICH).

Statistical analysis

We conducted statistical analysis using SPSS software. We compared outcomes between endovascular treatment and control groups for all RCTs. We used the Mantel-Haenszel (MH) method to calculate the pooled odds ratio and its 95% confidence interval. Statistical heterogeneity was evaluated with the χ^2 Mantel-Haenszel method and with I_2 method. Heterogeneity was considered significant if the P values of χ^2 statistics were <0.10 . We regarded an I_2 of $<40\%$ as minimal heterogeneity, 40% - 75% as modest heterogeneity, and $>75\%$ as substantial heterogeneity.

Some degree of heterogeneity was expected and to identify sources

of heterogeneity, two subgroup meta-analyses were pre-specified on the base of vessel occlusion status (required demonstrated vessel occlusion for randomization or not) for the primary outcome. We also generated other subgroups considering the type of treatment (RCTs comparing intra-arterial thrombolysis with standard therapy and RCTs comparing thrombectomy with standard therapy).

Results

A total 1935 articles were identified. 1759 did not match the eligibility criteria. The remaining 176 articles were pertaining to 18 studies available for full text evaluation. Of these 18 studies, 3 were not randomized controlled trials and were thus excluded. For the purpose of the present study 3 studies were further excluded because they compared directly endovascular treatment with intravenous thrombolysis. The characteristics of excluded studies are reported in Table 1. The remaining 12 randomized controlled trials met all the selection criteria and were included in the meta-analysis.

Study characteristics

The selected trials included in total 2725 participants. Study characteristics are shown in Table 2. Quality of study was high in all cases (Jadad score between 3 to 5).

In four RCTs, patients of the treatment group received exclusively intra-arterial thrombolysis. Intravenous thrombolysis was administered neither in treatment nor in control groups. In the remaining eight studies both intervention groups and control groups received intravenous thrombolysis if recommended, in different proportions (from $<50\%$ of treated patients in MR RESCUE to 100% of treated patients in IMS III, EXTEND-IA, SWIFT PRIME) [8-10]. In these studies, endovascular treatment consisted of mechanic thrombectomy plus, eventually, intra-arterial thrombolysis was used.

Time to inclusion from symptoms onset varied between <3 h in the IMS III trial to <24 h in the AUST trial [11,12]. Patients with an occlusion in an artery of anterior circulation were included in ten studies. Three studies (AUST, IMS III and THRACE) included also strokes with occlusion of an artery of posterior circulation (in THRACE were included only patients with occlusion of the upper third of basilar artery) [13]. All studies but one required imaging of vessel occlusion before inclusion. In the IMS III trial, 284 patients had been randomized before CT angiography.

In ESCAPE, EXTEND-IA, SWIFT PRIME and REVASCAT trials, among the inclusion criteria there was also the evaluation of the ischemic core extension [8,9,14,15]. Ischemic core extension was indirectly measured in ESCAPE trial and REVASCAT trial applying the ASPECTS score on non-enhanced CT imaging. In EXTEND-IA ischemic core's volume, measured with CT or MR perfusional study, should be <70 ml. In SWIFT PRIME perfusional studies were initially used to determine the extension of ischemic core, but after a protocol revision, perfusional imaging was no longer mandatory.

Study	Reason for exclusion
Ducroq et al. [24]	This is not a comparison of intra-arterial thrombolysis versus control, since only the control group is given intravenous thrombolysis
SYNTHESIS PILOT, 2010 [22]	This is a direct comparison of intra-arterial thrombolysis versus intravenous thrombolysis
SYNTHESIS EXPANSION 2013	This is a direct comparison of intra-arterial thrombolysis versus intravenous thrombolysis

Table 1: Characteristics of excluded randomized controlled trials.

Trial	Inclusion criteria	Imaging techniques	Time window	Endovascular treatment	Control group	Recanalization	Clinical outcome	Symptomatic intracranial Hemorrhage
PROACT	MCA occlusion (M1 o M2); NIHSS ≥ 4; age 18-85 yr	angiography	<6 h	6 mg ia pro-UK+iv heparine	iv heparine	TIMI 2-3: 57.7% vs. 14.3% in the control group	Mrs ≤ 1 in 30.8% vs. 21.4% of control group	15.4% vs. 7.1% in the control group
PROACT II	MCA occlusion; NIHSS ≥ 4; age 18-85 yr;	angiography	<6 h	9 mg ia pro-UK+iv heparine	iv heparine	TIMI 2-3: 66% vs. 18% of control group	mRS ≤ 2 in 39.7% vs. 25.4% of control group	10% vs. 2% in the control group
AUST	occlusion in posterior circulation; age 18-85 yr	angiography	<24 h	anticoagulants+ia UK	anticoagulants	ND	mRS ≤ 2 at 6 months in 50% vs. 13% of control group	ND
MELT	Occlusion in the M1 or M2 tract of MCA; NIHSS>5; age 20-75 yr	angiography	<6 h	ia UK	standard therapy	partial recanalization ≥ 50%: 47.4% in intervention group	mRS ≤ 2 in 49.1% vs. 38.6% of control group	9% vs. 2% of control group
IMS III	NIHSS ≥ 10 age 18-82 yr	CTA only in subjects with NIHSS=8-9	<3 h for iv thrombolysis <5 hours for endovascular treatment	iv thrombolysis+ia thrombolysis/thrombectomy	iv thrombolysis	TICI 2-3: 75% TICI 2b-3: 41% (intervention group)	mRS ≤ 2 in 40.8% vs. 38.7% control group	6.2% vs. 5.9% of control group
MR RESCUE	MCA occlusion in M1 e M2 and distal ICA NIHSS 6-29 age 18-85 yr	CTA/MRA or angiography;perfusional CT/MR	<8 h	embolectomy (MERC1 or PENUMBRA)	standard therapy	TICI 2-3: 71.4% vs. 86.7% of control group	mRS ≤ 2 in 12.5% vs. 18.5% of control group	4.7% vs. 3.7% of control group
MR CLEAN	MCA occlusion in M1 o M2 tract, A1 or A2 tract of ACA; NIHSS ≥ 2 age>18 yr	CTA/MRA or angiography	<6 h	ia thrombolysis (rt-PA or UK) and/or thrombectomy (eventually preceded by iv thrombolysis)	standard therapy (also iv thrombolysis)	TICI 2b-3: 58.7% of control group	mRS ≤ 2 in 32.6% vs. 19.1% of control group	7.7% vs. 6.4% of control group
ESCAPE	occlusion in MCA and distal ICA age>18 yr ASPECT>6	CTA; ASPECTS score	<12 h	standard therapy (also iv thrombolysis in 72.7%)+thrombectomy	standard therapy (also iv thrombolysis)	TICI 2b-3: 72.4% vs. AOL: 31.2% in the control group	mRS ≤ 2 in 53.0% vs. 29.3% of control group	3.6% vs. 2.7% of control group
EXTEND-IA	occlusion in MCA and distal ICA age>18 yr	CTA/MRA; perfusional CT/MR (core<70 mL)	<4,5 h for iv thrombolysis <6 h for endovascular treatment	iv thrombolysis+thrombectomy with SOLITAIRE	iv thrombolysis	TIMI 2-3: 94.0% vs. 43.0% in the control group	mRS ≤ 2 in 71.0% vs. 40.0% of control group	0% vs. 6.0% of control group
SWIFT PRIME	occlusion of MCA or distal ICA; age 18-85 yr	CTA or MRA; perfusional CT/MR or ASPECTS score	<6 h	iv thrombolysis+thrombectomy with SOLITAIRE	iv thrombolysis	TICI 2b-3: 88%	mRS ≤ 2 nel 60.2% vs. 34.7% in the control group	0% vs. 3% in the control group
REVASCAT	occlusion of M1 tract of MCA or ICA; NIHSS>6 age 18-80 yr ASPECTS>7	CTA/MRA; ASPECTS score	<8 h	thrombectomy with SOLITAIRE also after iv thrombolysis (68%)	Standard therapy (also iv thrombolysis) (77.7%)	TICI 2-3: 90.2% TICI 2b-3: 65.7%	mRS ≤ 2 in 43.7% vs. 28.2% in the control group	4.9% vs. 1.9% in the control group
THRACE	occlusion of the intracranial ICA, M1 tract of MCA, upper third of BA; NIHSS10-25		<4 h	iv thrombolysis+mechanic thrombectomy	iv thrombolysis		mRS ≤ 2 in 54.2% vs. 42.1% of control group	

Table 2: Characteristics of included trials.

Primary and secondary outcomes

Data concerning the proportion of patients with Mrs ≤ 2 at 90 days was available in all the 11 trials (Figure 1). The proportion of patients with mRS 0-2 after 90 days was 44.6% in the intervention group and 31.4% in the control group. The outcome favored the intervention group with an odds ratio of 1.77 (95% CI: 1.51-2.08). However, the result was affected by a significant heterogeneity ($\chi^2=19.81$; $I_2=50\%$;

$P=0.03$). Figure 2 reports a sensitivity analysis excluding RCTs in which there was not a mandatory use of neuroimaging techniques to identify patients with a large artery occlusion before randomization. The proportion of patients with a good outcome (mRS ≤ 2) was 45.4% in the treatment group and 29.5% in the control group. The outcomes for the intervention groups improved, with an odds ratio of 2.05 (95% CI: 1.70-2.46), without any significant heterogeneity ($\chi^2=9.96$; $I_2=10\%$; $P=0.03$).

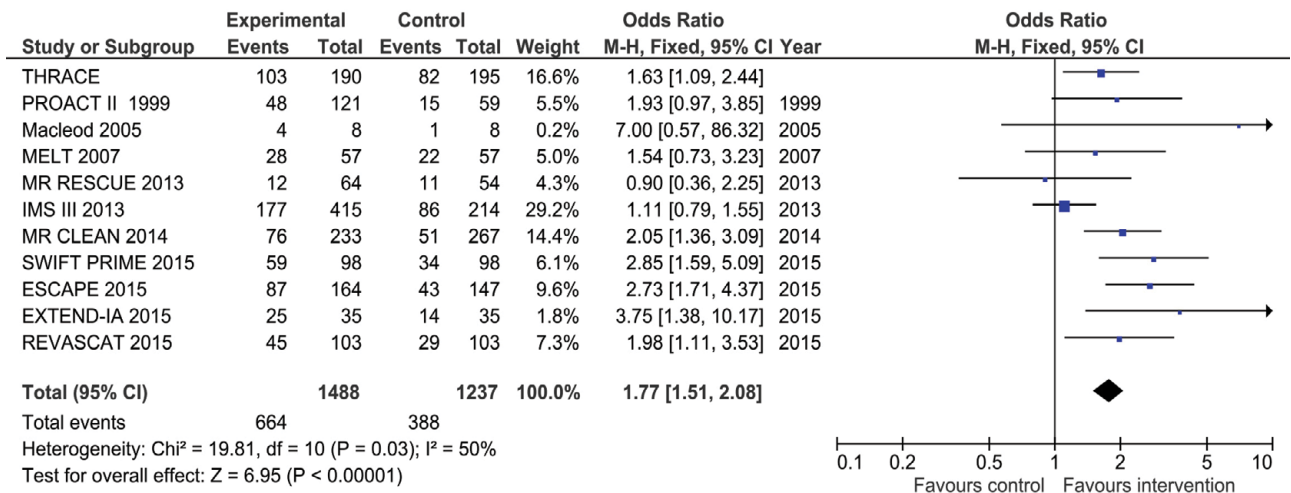


Figure 1: Effectiveness of endovascular treatment on functional independence (modified Rankin Scale [mRS] ≤ 2) at 90 days.

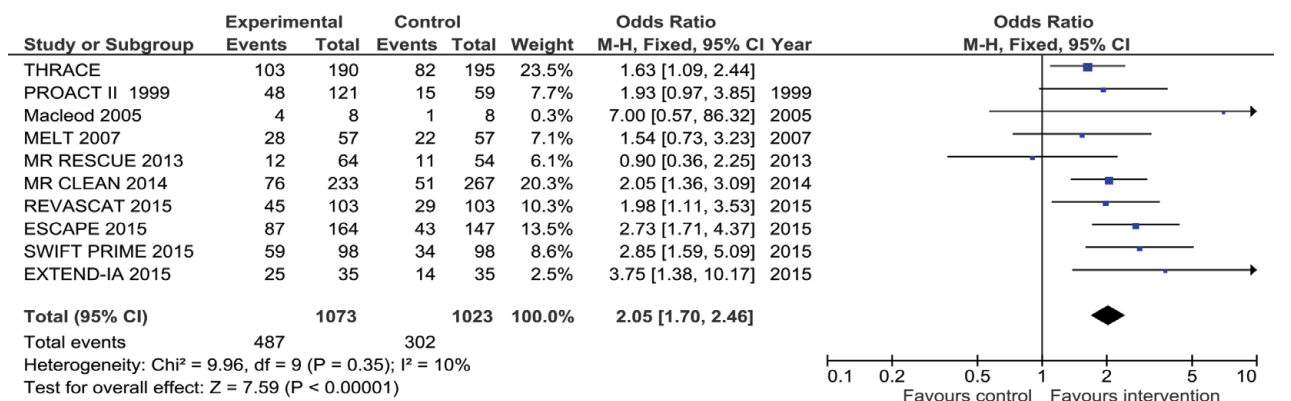


Figure 2: Effectiveness of endovascular treatment on functional independence (modified Rankin Scale [mRS] ≤ 2) at 90 days in in patients with proved Large Vessel Occlusion (LVO).

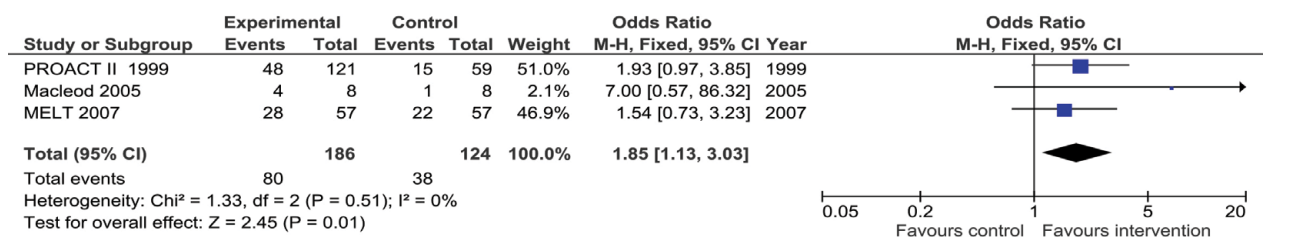


Figure 3: Effectiveness of intra-arterial thrombolysis on functional independence (modified Rankin Scale [mRS] ≤ 2) at 90 days.

We also analyzed the efficacy of intra-arterial thrombolysis and mechanic thrombectomy developing two different subgroups on the base of the type of intervention. In the subgroup of patients treated with intra-arterial thrombolysis (Figure 3) there was a non-significant trend which favored the intervention (OR=1.85; 95% CI: 1.13-3.03; P=0.01). In the subgroup of patients treated with mechanic thrombectomy (Figure 4) a superiority of the intervention groups was observed for the primary outcome (OR=2.17; 95% CI: 1.77-2.67; P<0.00001).

The recanalization rate was higher in the intervention group (Figure 5) with an odds ratio of 4.32 (95% CI: 3.26-5.72; P<0.00001).

There was an increased proportion of patients with symptomatic intracranial hemorrhage in the intervention group (5.9% vs. 4.3%), with an odds ratio of 1.34 (95% CI: 0.92-1.95) but the difference was not statistically significant (Figure 6). Mortality was lower in the intervention (17.8% vs. 20.7%) with an odds ratio of 0.82 (95% CI: 0.66-1.01) than in control groups although the difference did not reach statistical significance (P=0.07) (Figure 7).

Discussion

This meta-analysis evaluated the efficacy of endovascular treatment

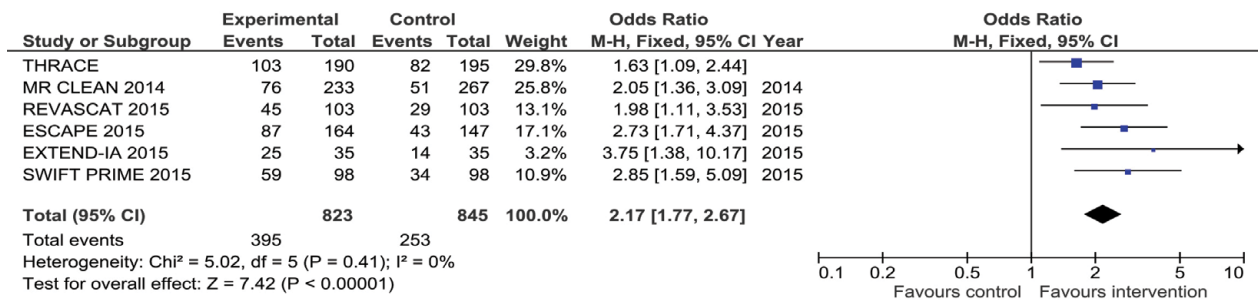


Figure 4: Effectiveness of mechanic thrombectomy on functional independence (modified Rankin Scale [mRS] ≤ 2) at 90 days.

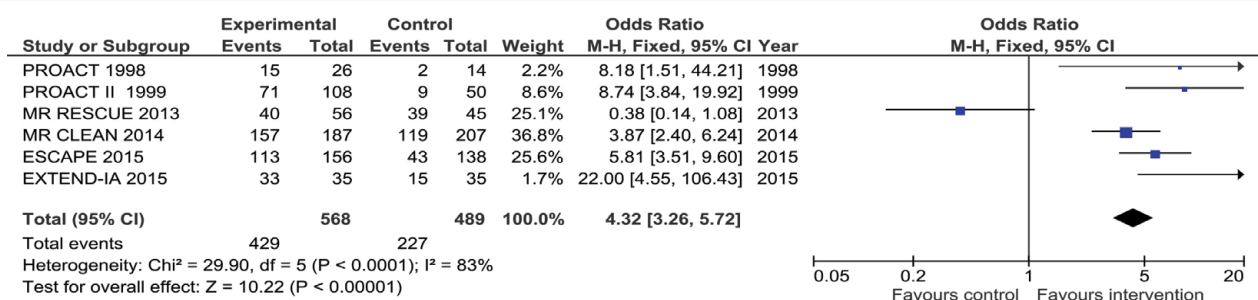


Figure 5: Effectiveness of endovascular treatment on partial or complete recanalization (modified Arterial Occlusive Lesion [mAOL] recanalization score, Thrombolysis in Myocardial Infarction [TIMI] score or Thrombolysis in Cerebral Infarction [TIC1] score of 2-3).

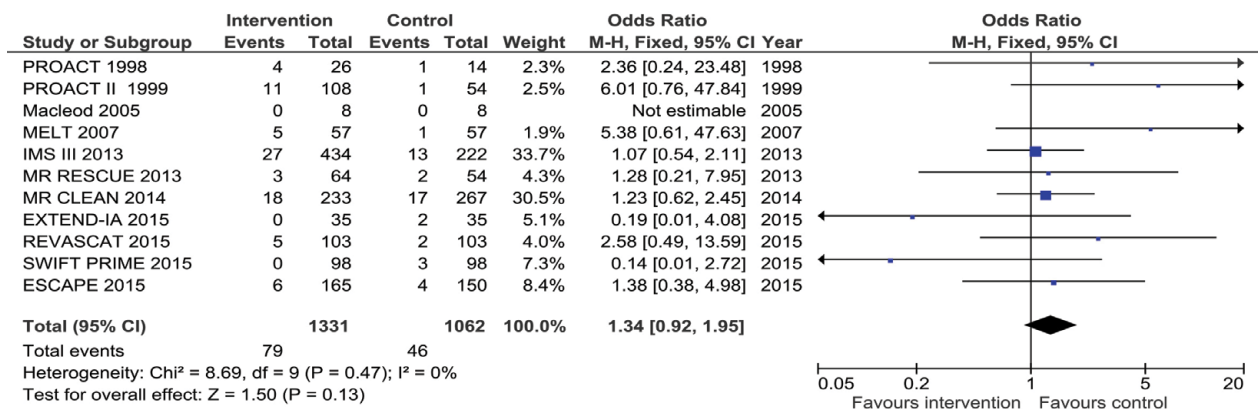


Figure 6: Risk of Symptomatic Intracranial Hemorrhage (SICH) associated with endovascular treatment.

over standard therapy, either including IV thrombolysis or not, in patients with acute ischemic stroke. The results confirmed that endovascular treatment is highly effective in these patients. This result was even sounder considering the high quality of all included trials.

The most important feature of this meta-analysis was the inclusion of virtually all published studies. The main limitation was unavailability of the original single case data that hampered the execution of some important comparisons such as those on the efficacy of endovascular procedures when performed as a primary intervention and on the usefulness of additional studies of ischemic core extension and collateral circle patency.

Some meta-analyses evaluating the efficacy of endovascular treatment have been published during years, showing different results.

A Cochrane Collaboration review published by O' Rourke et al.

[16] in 2010 analyzed the efficacy of intra-arterial thrombolysis over standard therapy, showing a significant improved outcome in the interventional group. In this study only the first RCTs evaluating the efficacy of intra-arterial thrombolysis were included, but there is no evaluation of more recent RCTs using mechanic thrombectomy. Fields et al. [17] in 2011 considered only RCTs applying intra-arterial thrombolysis in patients with an occlusion of middle cerebral artery, confirming the superiority of intra-arterial thrombolysis. Fargen et al. [18] in 2015 published a meta-analysis including RCTs evaluating the efficacy of intra-arterial thrombolysis and mechanic thrombectomy over standard therapy, with an improved outcome in intervention group. Delgado et al. [19] in 2015 included only recent RCTs, in which mechanic thrombectomy was the only treatment administered in the intervention group. The outcome was significantly favored in the intervention group. Chen et al. [20] in 2015 included in their meta-analysis endovascular treatment RCTs from 2013 to 2015, excluding

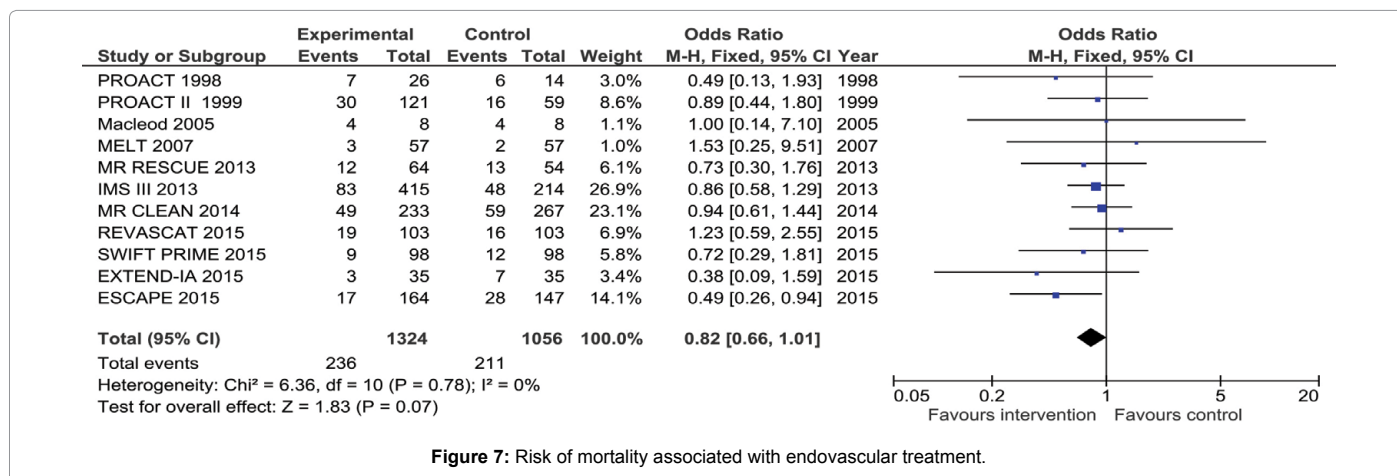


Figure 7: Risk of mortality associated with endovascular treatment.

trials which compared intra-arterial thrombolysis with standard therapy. The authors stratified results by Large Vessel Occlusion (LVO) criteria and by use of stent retriever device. They observed an improved outcome in the intervention group considering RCTs with LVO confirmation and RCTs with the use of stent retrievers in the intervention groups. Hong et al. [21] published a systematic review in 2015, including endovascular treatment RCTs from 1998 to 2015, demonstrating the efficacy of endovascular treatment over standard therapy. Previous meta-analyses underlined the efficacy of mechanic thrombectomy or intra-arterial thrombolysis, focusing only on a subgroup of endovascular techniques. The systematic review published by Hong et al. [21] in 2015 included RCTs which compared intra-arterial thrombolysis and/or thrombectomy with standard therapy. This study included all the main RCTs conducted to evaluate the efficacy of endovascular treatment (intra-arterial thrombolysis and mechanic thrombectomy) over standard therapy but three RCTs (Synthesis Pilot 2010 [22], SYNTHESIS EXPANSION 2013 [23] and Ducroq et al. [24]) did not compare endovascular treatment with standard medical therapy, but with intravenous thrombolysis, that is not administered in the intervention groups [22-24].

Compared with previous studies, our meta-analysis has the advantage of considering both RCTs evaluating intra-arterial thrombolysis [12,25-27] and RCTs evaluating mechanic thrombectomy [8-11,13-15,28] giving a global point of view of the efficacy and safety of endovascular treatment over standard therapy. We did not included RCTs comparing directly endovascular treatment with intravenous thrombolysis. Qualities of data have been formally evaluated. Sensitivity analyses deemed heterogeneity of studies as negligible and allowed definite conclusions on the effectiveness of endovascular treatment in acute ischemic stroke. The efficacy of endovascular treatment was corroborated by clear trends in more frequent recanalization and in reduced mortality. On the other hand the marginally increased risk of symptomatic intracranial hemorrhage was not significant.

Our results showed that endovascular treatment ensures a higher proportion of patients with a mRS ≤ 2 at 90 days compared with standard therapy. However the analysis showed a significant heterogeneity. A sensitivity analysis was done, excluding the RCTs in which intracranial arterial occlusion demonstration on vascular imaging was not an inclusion criterion. Heterogeneity became negligible and the efficacy of endovascular treatment was remarked. The only source of heterogeneity in our study was thus represented by the lack of the demonstration of vascular occlusion before patients' selection. Our results suggest that endovascular treatment should not be performed in patients with acute

ischemic stroke if vascular studies have not detected an intracranial large vessel occlusion or has not been performed.

The negligible heterogeneity that remained after exclusion of trials without vascular studies before randomization indicates that the general result of efficacy of endovascular treatments apply to all studies, irrespective of endovascular techniques that were used and of standard treatment that was used in controls.

The benefit was obvious in the subgroup of patients treated with mechanic thrombectomy but the data were consistent for the subgroup of patients treated with intra-arterial thrombolysis also, although not achieving statistical significance. However, urokinase is no longer available; thus mechanical thrombectomy, either in combination with IA trombolitics or not, should be considered the preferred method.

Higher proportions of recanalization were achieved after endovascular treatment, but the results did not reach statistical significance. However, this result is consistent across all studies and may contribute to explain the greater effectiveness of endovascular treatment over standard therapy.

Our study confirmed a trend toward increased risk of SICH in subjects with endovascular treatment confirming the result of other studies [16-19]. Since we evaluated the effectiveness of endovascular treatment on the top of standard therapy, this finding is not surprising and may be linked to the reperfusion of the ischemic area, in which there is a blood-brain-barrier alteration triggered by ischemia [29]. On the other hand, like in most reperfusion studies in stroke patients, this increased risk did not offset the positive effect of the treatment. Endovascular treatment may thus be considered safe enough to be recommended as a valuable intervention when indicated.

A great proportion of treated cases also had IV thrombolysis. However, we were unable to evaluate the interaction between IV thrombolysis and endovascular treatment because of lack of information in almost all published studies. The SYNTHESIS EXPANSION study directly compared endovascular treatment and systemic thrombolysis, but in this study vascular studies before randomization were not performed and probably very few cases had a true indication to endovascular treatment since very few devices were used. Therefore, whether endovascular treatment should be preceded by systemic thrombolysis, when indicated, or may be used as a primary intervention instead of IV rt-PA remains an unanswered question.

There is a great difference in the design and inclusion criteria of the first generation studies, which tested the efficacy of intra-arterial

thrombolysis and of the last generation studies, which used in almost all cases mechanic thrombectomy. Even in the field of mechanic thrombectomy there can be seen an evolution with gradual replacement of first generation devices with newer ones as stent-retrievers. In RCTs which used mechanic thrombectomy in the intervention groups, there were different proportions of patients treated with stent-retrievers between trials.

The time limit from symptoms onset and groin puncture recommended in the principal international guidelines is 6 hours for anterior circulation strokes and up to 12 h for basilar artery occlusions. However, only four of the clinical trials included in our meta-analysis, randomized patients up to 8 or 12 h from symptoms onset and only AUST, IMS III and THRACE included strokes of the posterior circulation therefore, an analysis of time window and of vascular district could not be performed. Effectiveness, beyond the 6 h time window, even in the posterior circulation has still insufficient support.

The endovascular techniques varied widely across time and studies as well as the devices that have greatly improved with time. It would have been interesting to analyze the impact of these and other aspects on the efficacy of endovascular treatment, but unavailability of data in the published reports prevented these analyses. Still unclear is also the precise role and utility of CTA or MRA diffusion/perfusion

imaging in the selection of patients who will reasonably be responders to endovascular treatment. Lastly, we have to consider that the generalizability of the results is not so obvious, since the included patients differed from those usually seen in a real life setting, because of the strict selection criteria and of the small proportions of admission. Therefore, further studies are needed to address these questions.

In conclusion this meta-analysis showed that patients with an arterial occlusion treated with endovascular treatment showed an improved functional outcome after 3 months from stroke onset compared to patients receiving standard therapy in the absence of significant complications. Vascular studies before treatment are mandatory (Figures 8 and 9).

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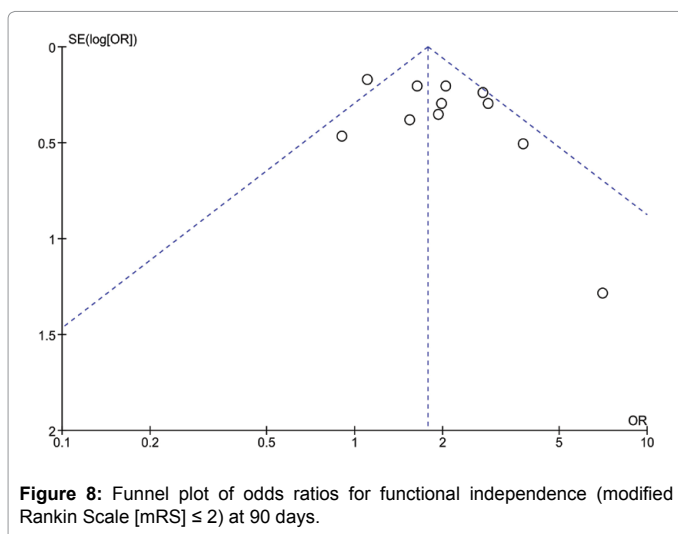


Figure 8: Funnel plot of odds ratios for functional independence (modified Rankin Scale [mRS] ≤ 2) at 90 days.

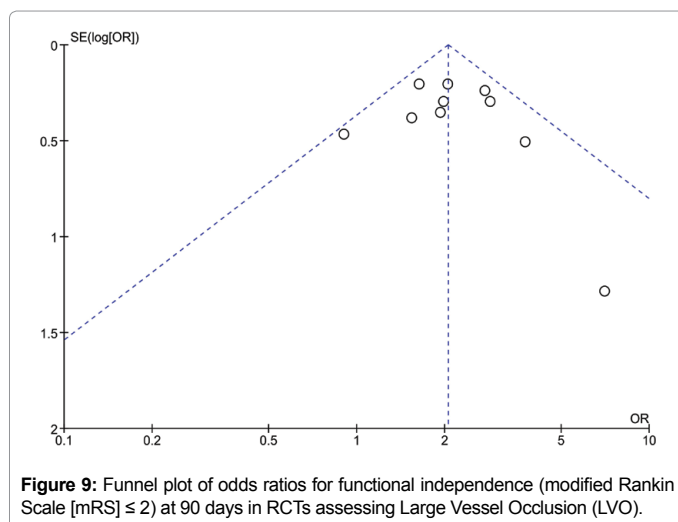


Figure 9: Funnel plot of odds ratios for functional independence (modified Rankin Scale [mRS] ≤ 2) at 90 days in RCTs assessing Large Vessel Occlusion (LVO).

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