Local anaesthesia as a distinct comparator versus conscious sedation and general anaesthesia in endovascular stroke treatment: a systematic review and meta-analysis

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Abbreviations: EVT = Endovascular treatment, AIS = acute ischaemic stroke, LA = local anaesthesia, CS = conscious sedation, GA = general anaesthesia, mRS = modified Rankin Scale, TICI = thrombolysis in cerebral infarction, NIHSS = National Institutes of Health Stroke Scale

ABSTRACT

Background: The optimal anaesthetic modality for endovascular treatment (EVT) in acute ischaemic stroke (AIS) is undetermined. Comparisons of general anaesthesia (GA) with composite non-GA cohorts of conscious sedation (CS) and local anaesthesia (LA) without sedation have provided conflicting results. There has been emerging interest in assessing whether LA alone may be associated with improved outcomes. We conducted a systematic-review and meta-analysis to evaluate clinical and procedural outcomes comparing LA to CS and GA.

Methods: We reviewed the literature for studies reporting outcome variables in LA versus CS and LA versus GA comparisons. The primary outcome was 90-day good functional outcome (modified Rankin Scale (mRS≤2). Secondary outcomes included mortality, symptomatic intracerebral haemorrhage, excellent functional outcome (mRS≤1), successful reperfusion (thrombolysis in cerebral infarction (TICI)>2b), procedural time metrics and procedural complications. Random effects meta-analysis was performed on unadjusted and adjusted data.

Results: Eight non-randomised studies of 7797 patients (2797 LA, 2218 CS, 2782 GA) were identified. In the LA versus GA comparison, no statistical differences were found in unadjusted analyses for 90-day good functional outcome or mortality (OR=1.22, 95%CI 0.84-1.76, p=0.3 and OR=0.83, 95%CI 0.64-1.07, p=0.15 respectively) or in the LA versus CS comparison (OR=1.14, 95%CI 0.76-1.71, p=0.53 and OR=0.88, 95%CI 0.62-1.24, p=0.47 respectively). There was a tendency towards achieving excellent functional outcome (mRS≤1) in the LA group versus GA (OR=1.44, 95%CI 1.00-2.08, p=0.05, I^2=70%).

Analysis of adjusted data demonstrated a tendency towards higher odds of death at 90 days in GA versus LA (OR=1.24, 95%CI 1.00-1.54, p=0.05 I^2=0%).

Conclusion: LA without sedation was not significantly superior to CS or GA in improving outcomes when performing EVT for AIS. However, quality of included studies impairs interpretation and inclusion of a LA arm in future well-designed multi-centre randomised controlled trials is warranted.

INTRODUCTION

Endovascular treatment (EVT) for acute ischaemic stroke (AIS) can be performed on patients by way of three approaches 1) local anaesthesia (LA) at the arterial access site without sedation in awake subjects, 2) administering procedural sedation, commonly referred to as conscious sedation (CS) or 3) general anaesthesia (GA). Observational studies comparing GA with composite non-GA cohorts of awake (LA) and sedated (CS) patients have reported poorer outcomes in patients treated under GA[1–3]. Pooled analysis of individual patient level data from the High Effective Reperfusion Using Multiple Endovascular Devices (HERMES) collaboration similarly supported the avoidance of GA when feasible[4]. By contrast, single-centre randomized trials comparing protocol based GA with CS yielded either no difference or more favourable outcomes in the GA group[5–9]. These opposing results have been acknowledged by current guidelines and the optimal anaesthetic modality for EVT remains undetermined[10,11].

Performing EVT under LA without sedation obviates exposure to the sedative pharmacological agents administered in CS and GA which potentially directly disrupt cerebral haemodynamics and alter cardiorespiratory variables (such as PaO2 and arterial blood pressure) to the detriment of cerebral perfusion[12]. Another important argument to perform EVT under LA is the potential delay in initiation of the EVT procedure under CS and GA due to sedation and/or intubation[4]. These considerations have been recognised by calls to include LA without sedation as a distinct comparator in prospective studies assessing the optimal anaesthetic strategy[13]. To our knowledge, there are no on-going randomised controlled trials with a LA-only arm.

Retrospective data differentiating subjects receiving LA without sedation from CS and GA has recently been published but individual studies have reported conflicting results for the functional outcomes between the LA, CS and GA cohorts[14–21]. Hence, the objective of this systematic and meta-analysis was to assess if LA without sedation resulted in superior procedural and clinical outcomes, compared to CS and GA, in AIS patients following EVT.

METHODS

Search Strategy, study selection and eligibility criteria

The study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[22]. We systematically searched electronic databases up to January 2021, including PubMed/MEDLINE, EMBASE, and Cochrane. The following keywords were used in combination or individually by using the Boolean operators "OR" and "AND": 'thrombectomy', 'endovascular procedures', 'stroke', ‘anaesthesia’, 'local anaesthesia’ , ‘general anaesthesia’ and ‘conscious sedation’. The articles were selected in 2 stages. Firstly, the titles and abstracts were screened for relevant studies, and duplicates excluded. Secondly, the full texts were downloaded and assessed for eligibility. The reference lists of included publications were then hand-searched for additional relevant studies. This process was carried out by three assessors independently (WB, PD, AP). Any differences were resolved by consensus.

Studies evaluating one or more procedural and clinical outcomes of EVT in LA compared to CS or LA compared to GA were included. LA was defined as the use of subcutaneous anaesthetic injection only at the site of the arteriotomy, GA required the need for endotracheal intubation and CS required the need for systemic medication for sedation, without requiring advanced airway protection. Randomized and non-randomized controlled (retrospective and prospective) trials and pre- and post-intervention studies, observational and cohort studies or post-hoc analyses of observational data in trials were included when a control group was reported. The exclusion criteria included studies published before 2010 (prior to the use of modern stent retrievers/aspiration), review articles and meta-analyses, guidelines, technical notes, studies in animals, studies in languages other than English, studies that did not discriminate between CS and LA in the comparator arm and studies that did not report our specified outcome measures. In the event of overlapping patient population, only the series with the largest number of patients or the most detailed data reported were included.

Data Extraction

Variables recorded, if available, were first line choice of anaesthetic technique (LA, CS, GA), study type (retrospective, prospective), study recruitment period, sample size, mean age, number of males, presence of co-morbidities (atrial fibrillation, hypertension, diabetes, coronary artery disease, heart failure, hyperlipidaemia, smoking) anatomical region (anterior/posterior circulation), lateralization of hemispheres (left/right), clot location (ICA, M1, M2, vertebrobasilar, tandem occlusion), baseline National Institutes of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS), prior intravenous tissue plasminogen activator (IV-tPA), Alberta stroke program early CT score (ASPECTS), anaesthesia conversion, the first-line EVT technique used (aspiration, stent-retriever, combined), onset to groin puncture time, groin puncture to reperfusion time, total procedure time, number of passes, successful reperfusion rate and first pass effect [defined as extended or modified thrombolysis in cerebral infarction (TICI) scale of 2b or above], excellent functional outcome defined as modified Rankin score of 1 or lower (mRS≤1) at 90 days, good functional outcome defined as functional independence with a mRS≤2 at 90 days, symptomatic intracranial haemorrhage (sICH) defined as any ICH with an increase of the NIHSS score of 4 or more within 24 hours or death, mortality at 90 days, and procedure related complications, including vessel dissection/perforation, intra-procedural haemorrhage and new or distal emboli.

Outcome measures

The primary outcome was good functional outcome (mRS≤2) at 90 days. The secondary clinical outcomes were excellent functional outcome (mRS≤1), mortality and sICH. The secondary procedural outcomes included successful reperfusion (TICI ≥2b), the first pass effect, procedure related complications, door to groin puncture time, groin puncture to reperfusion time.

Statistical analysis

Study characteristics and extracted variables were summarized using standard descriptive statistics. Continuous variables were expressed as means and SD, and categorical variables were expressed as frequencies or percentages. Meta analyses of binary outcomes were expressed as odds ratio (OR) with a 95% confidence interval (CI), and continuous variables as weighted mean difference (MD) with a 95%CI. A random effects model was used. Tests of heterogeneity were conducted with the Q statistic distributed as a chi-square variate (assumption of homogeneity of effect sizes). The extent of between-study heterogeneity was assessed with the I^2 statistic. Study heterogeneity I^2 values >50% were considered substantial and >75% deemed considerable heterogeneity. Funnel plots and Egger's test were used to assess publication bias for the primary outcome. ROBINS-I[23] tool was used to evaluate the risk of bias of each study. P-values were two-tailed with values <0.05 considered statistically significant.

To account for the between-group heterogeneity in variables due to the inclusion of non-randomized studies, we also performed analyses based on adjusted data for potential confounders (adjusted OR from regression analyses or propensity matching) using the generic inverse variance method. Additionally we conducted sub-group analysis for GA vs non-GA and sub-group analysis for anterior circulation only. Meta-regression was not specifically performed as there were fewer than ten studies included in our meta-analysis[24]. All analyses were implemented using JASP 0.14.1.0 and Review Manager 5.4.1 software.

Ethics

This study is a systematic review and meta-analysis, and no human participant procedure was involved. Informed consent and ethical approval were not essential for this study.

RESULTS

Literature search results

We screened 921 titles and abstracts, from which 20 full-text articles were evaluated (Supplementary Figure 1). Out of those, data was extracted from 8 studies[14–21] that met the inclusion criteria. 913 studies were excluded for not reporting on LA vs GA and/or CS, not reporting the specified outcome measures, lack of full-text or duplicates.

Characteristics of Included Studies

We included 8 studies published between 2010-2020 describing 7797 patients (2797 LA, 2218 CS and 2782 GA) that underwent EVT due to occlusion in the anterior circulation (7004 patients) or posterior circulation (793 patients). Six studies were prospective and 2 were retrospective cohort studies. The largest study cohort had 4429 patients (1131 LA, 1285 CA and 2013 GA), whilst the smallest study had 158 patients (111 LA and 47 CS). The studies are summarised in Table 1. The detailed baseline characteristics are presented in Supplementary Figure 2.

Clinical outcomes

The type of anaesthesia (LA vs GA) was not associated with the odds of achieving good functional outcome (mRS≤2) at 90 days (Figure 1; 6 studies; OR=1.22, 95%CI 0.84-1.76, p=0.3, I^2=82%), mortality at 90 days (5 studies; OR=0.83, 95%CI 0.64-1.07, p=0.15, I^2=82%, Table 2) and sICH (6 studies; OR=1.16, 95%CI 0.88-1.58, p=0.26, I^2=0%, Table 2).

Similarly, there was no statistical difference between LA vs CS with respect to good functional outcome (mRS≤2) at 90 days (Figure 2; 5 studies; OR=1.14, 95%CI 0.76-1.71, p=0.53, I^2=83%), sICH (5 studies; OR=1.18, 95%CI 0.85-1.64, p=0.33, I^2=5%, Table 2) or mortality at 90 days (4 studies; OR=0.88, 95%CI 0.62-1.24, p=0.47, I^2=70%, Table 2). However, there was a tendency towards achieving excellent functional outcome (mRS≤1) in the LA group (compared to GA) (3 studies; OR=1.44, 95%CI 1.00-2.08, p=0.05, I^2=70%, Table 2) but not when LA was compared to CS (3 studies; OR=1.40, 95%CI 0.87-2.25, p=0.16, I^2=84%, Table 2).

Procedural Outcomes

The door to groin puncture time was statistically significantly shorter in the LA group (compared to GA) (3 studies; MD = -14.36 mins, 95%CI -20.91 to -7.81, p<0.0001, I^2=64%, Table 2). However, there was no statistical difference in the groin puncture to reperfusion time (5 studies; MD= -1.66 mins, 95%CI -8.83 to 5.50, p=0.65, I^2=83%, Table 2), successful reperfusion (TICI ≥2b) (6 studies; OR=0.90, 95%CI 0.54 to 1.49, p=0.69, I^2=88%, Table 2), first pass effect (2 studies; OR=1.15, 95%CI 0.63 to 2.12, p=0.65, I^2=76%, Table 2), or frequency of procedure-related complications (4 studies; OR=1.20, 95%CI 0.55 to 2.62, p=0.65, I^2=69%, Table 2).

Similarly, there was no statistical difference between LA and CS in achieving successful reperfusion (TICI ≥2b) (5 studies; OR=0.92, 95%CI 0.56-1.50, p=0.73, I^2=86%, Table 2) or in the frequency of procedure-related complications (3 studies; OR=1.17, 95%CI 0.74-1.83, p=0.5, I^2=0%, Table 2). Only 1 study reported the first pass effect and door to groin puncture time for LA vs CS which precluded pooled analysis. However, the groin puncture to reperfusion time was significantly shorter in the LA group compared to CS (3 studies; MD= -7.31 mins, 95%CI –11.44 to -3.19, p=0.0005, I^2=0%, Table 2).

Analyses on adjusted data

Adjustments for unbalanced variables included at least the age, sex, baseline NIHSS score, and onset to door time, whilst some studies also included the ASPECTS, co-morbidities, collaterals, IV-tPA, and blood pressure (baseline systolic or mean arterial pressure). After extracting data adjusted for potential confounders, there remained no statistically significant difference between the anaesthesia type and good functional outcome (mRS≤2) at 90 days (GA vs LA; 5 studies; OR=0.98, 95%CI 0.70-1.37, p=0.89, I^2=57%) and (CS vs LA; 2 studies; OR=0.76, 95%CI 0.17-3.45, p=0.72, I^2=96%) (Supplementary figure 3). There was a tendency towards increased odds of mortality for GA at 3 months (GA vs LA; 5 studies; OR=1.24, 95%CI 1.00-1.54, p=0.05, I^2=0%) but not for CS (CS vs LA; 2 studies; OR=1.16, 95%CI 0.41-3.27, p=0.78, I^2=91%) (Supplementary figure 4).

Sub-group analysis: GA vs non-GA

In a subgroup analysis of GA vs non-GA (composite of CS and LA), GA was associated with higher odds of mortality (5 studies; OR=1.18, 95%CI 1.02-1.36, p=0.02, I^2=8%) but no statistical difference was demonstrated for good functional outcome (mRS≤2) at 90 days (6 studies; OR=0.87, 95%CI 0.63-1.22, p=0.42, I^2=79%) and sICH (6 studies; OR=0.90, 95%CI 0.69-1.18, p=0.45, I^2=0%).

Sub-group analysis: anterior circulation

Analysing anterior circulation strokes, we found no statistical difference in the odds of achieving 90-day good functional outcome (mRS≤2) and mortality respectively between the LA vs GA groups (4 studies; OR=1.24, 95%CI 0.62-2.47, p=0.54, I^2=87%) and (3 studies; OR = 0.93, 95%CI 0.74-1.17, p=0.55, I^2=0%). There were also no differences in the LA vs

CS comparison (3 studies; OR = 1.20, 95%CI 0.53-2.70, p=0.66, I^2=91%) and (2 studies; OR = 0.98, 95%CI 0.51-1.90, p=0.96, I^2=85%).

Risk of bias

All studies had an overall moderate risk of bias (Supplementary Figure 5). Visual inspection of funnel plots did not reveal asymmetry in studies that reported the primary outcome (mRs≤2) at 90 days (Supplementary Figure 6) and there was no evidence of publication bias (Egger's test; LA vs GA, p=0.99 and LA vs CS, p=0.56).

DISCUSSION

In this systematic review and meta-analysis the use of LA without sedation for EVT in AIS was shown to yield similar rates of good functional outcome (mRS≤2 at 90 days) compared to CS and GA. No statistical differences were found in mortality, successful re-canalisation (TICI ≥2b), sICH, procedural times or complications in the unadjusted analysis. There was a tendency towards achieving excellent functional outcome (mRS≤1) in the LA group versus GA comparison. There was also a tendency towards higher odds of 90-day mortality in GA versus LA using extracted data adjusted for confounders.

The findings in our study are difficult to directly compare with recent meta-analyses that assessed GA versus a merged non-GA (LA and CS) group and did not include any of the studies in the present analysis. Gravel et al[2] found non-GA to be associated with better 90-day functional outcomes and mortality in their unadjusted analysis. Interestingly, Goyal et al[3] reported no difference between anaesthesia type (GA vs non-GA) for 90-day good functional outcomes when excluding studies published before the stent-retriever era. Furthermore, the difference in their unadjusted analysis did not retain significance when imbalances in baseline NIHSS scores were factored by way of meta-regression. The studies in our analysis also predominantly included patients who received modern stent retriever/aspiration treatment and it is plausible that any potential 'real world' effect-size of anaesthetic choice has attenuated with increasing levels of experience of anaesthesiologists in the setting of EVT for AIS.

One of the rationales for using LA without sedation is to avoid iatrogenic hypotension from intravenous or inhaled sedative agents. Samuels et al[25] recently reported patients treated under CS had a lower average procedural BP and more BP drops compared to patients treated under LA. Whilst there is evidence that blood pressure (BP) drops are associated with poor functional outcome due to collateral failure[26,27]; the neurotoxic or neuroprotective effects of hypnotic agents and optimal intra- and peri-procedural BP targets during the acute ischaemia-reperfusion injury are incompletely understood[28]. Of note, in the present analysis, only one of the included studies reported intra-procedural BP measurements and found no statistical differences in their selected haemodynamic parameters[18].

The purported disadvantages of using LA alone are lack of airway protection, patient movement and patient discomfort. These factors may require conversion to either CS or GA with resultant delays in procedural times and a theoretical detrimental effect on outcomes. Our analysis showed a conversion rate of LA to GA (17.5%), comparable to those reported for CS to GA in the previous randomized trials (15.6% in the anesthesia during stroke (ANSTROKE) trial[6] and 14.2% in the sedation versus intubation for endovascular stroke treatment (SIESTA) trial[5]. Conversion rates from CS to GA (8.8%) were however lower in our analysis. Despite this, Flottmann et al[19] found similar rates of functional independence when the 9.8% of patients in their cohort that required emergency conversion were compared to the primary anaesthesia groups. On the other hand, LA allows for real-time monitoring of the patient's neurological status which may guide intra-procedural treatment decisions. Cost and length of stay in hospital or intensive care were not assessed as outcome variables but these are also potential resource factors favouring a LA first strategy[29]. Radiation exposure was also not assessed however a recent study reported no difference between GA and CS comparisons[30].

Unsurprisingly, due to the logistics of anaesthetic induction and intubation, we found significantly shorter door-to-groin puncture times in the LA group compared to the GA group, which was also shown to favour LA versus CS in the single study reporting on this metric[18]. No statistical difference was identified in groin puncture-to-reperfusion times in the LA vs GA comparison (±SD, minutes) 52.5±31.8 and 56.0±34.5 respectively. This is in contrast to the previous meta-analysis by Goyal et al[3] that found statistically significant longer groin puncture to reperfusion times in the non-GA cohort compared to GA (81.3±32.3 and 75.7±25.8 respectively). This may be explained by the overall marked reduction in the procedural times between the studies which in turn may reflect continued improvement of modern-day EVT techniques and increasing levels of operator experience. In addition to these factors, refinement in selection of patients likely to remain compliant during EVT performed under LA without sedation may also explain why no differences were revealed in successful reperfusion (TICI≥2b) or procedural complications.

Our analysis included several limitations. Firstly, due to the observational design of all included studies, confounding by indication may have influenced the results. Patient related factors could have influenced the decision whether or not to perform EVT under LA,CS or GA. Secondly, there were differences in between-group baseline characteristics, including baseline NIHSS. Whilst these differences were small, we also performed a meta-analysis of extracted adjusted data which revealed similar outcomes. Thirdly, four of the included studies[14,16,18,19] provided data on a per-protocol analysis basis, whilst the rest provided data on the basis of an intention-to-treat analysis, which may have confounded the final outcomes. Fourthly, a disproportionate number of posterior circulation strokes were included in the GA group which tend to have worse clinical outcomes. However, no statistically significant difference remained following sub-group analysis for anterior circulation stroke only.

Conclusion:

To our knowledge, this is the first meta-analysis assessing LA as a distinct comparator versus

CS and GA for EVT in AIS. LA without sedation was not significantly superior to CS or GA in improving functional outcome or mortality. However, as the majority of the data is drawn from registries, the quality of included studies impairs interpretation; the inclusion of a LA only arm in future multi-centre randomised trials remains a gold-standard for assessing an effect size between anaesthetic modalities. Nonetheless, these findings reflect ‘real world’ practice and conducting a well-designed sufficiently powered trial with generalisability may prove challenging. In the interim, we advise a patient-tailored and expertise-dependent approach to optimal anaesthetic management.

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Author, Year of Study	Country	Study recruitment period	Study Design	Comparator	Sample size, n	Risk of bias
Benvegnu, 2020[15]	France	2018	Prospective multi centre ETIS registry	LA vs CS	LA = 272 CS = 636	M
Cappellari, 2020[14]	Italy	2011 to 2017	Prospective multi centre IRETAS registry	LA vs CS vs GA	LA = 1131 CS = 1285 GA = 2013	M
Flottmann, 2020[19]	Germany	2015 to 2018	Retrospective single centre	LA vs CS vs GA	LA = 794 CS = 76 GA = 59	M
Goldhoorn, 2020[16]	Netherlands	2014 to 2016	Prospective multi centre MR CLEAN registry	LA vs CS vs GA	LA = 821 CS = 174 GA = 381	M
Marion, 2020[18]	USA	2014 to 2018	Single centre retrospective	LA vs CS	LA = 111 CS = 47	M
Pop, 2020[17]	France	2018 to 2018	Prospective multi centre observational registry	LA vs GA	LA = 219 GA = 142	M
Wu, 2019[20]	China	2013 to 2017	Prospective single centre observational registry	LA vs GA	LA = 112 GA = 75	M
Wu, 2020[21]	China	2012 to 2018	Prospective single centre observational registry	LA vs GA	LA = 71 GA = 112	M

LA = local anaesthesia, CS = conscious sedation, GA = general anaesthesia, ETIS = endovascular treatment in ischaemic stroke, IRETAS = Italian registry of endovascular treatment in acute stroke, MR CLEAN = multicentre randomized clinical trial of endovascular treatment for acute ischaemic stroke in the Netherlands, M = moderate

Table 1: Characteristics of included studies

	GA	CS	GA+CS	LA	LA vs GA					LA vs CS					LA vs (GA+CS)				
	n/N (%) or mean± SD/N	n/N (%) or mean± SD/N	n/N (%) or mean± SD/N	n/N (%) or mean± SD/N	number of studies	OR, or MD	95% CI	P-value	I^2 (%)	number of studies	OR, or MD	95% CI	P-value	I^2 (%)	number of studies	OR, MD	95% CI	P-value	I^2 (%)
Clinical outcomes																			
(mRS≤2) at 90 days	1077/2651 (40.6)	929/2074 (44.8)	2006/4725 (42.5)	1217/2733 (44.5)	6	1.22	0.84-1.76	0.30	82	8	1.01	0.73-1.39	0.98	80	8	1.05	0.77-1.42	0.77	83
(mRS≤1) at 90 days	682/2345 (29.1)	614/1958 (31.4)	1296/4304 (30.1)	697/2252 (31)	3	1.44	1.00-2.08	0.05*	70	3	1.40	0.87-2.25	0.16	84	4	1.31	0.91-1.90	0.15	82
sICH	86/2428 (3.5)	84/2033 (4.1)	170/4461 (3.8)	146/2740 (5.3)	6	1.18	0.88-1.58	0.26	0	5	1.18	0.85-1.64	0.33	5	8	1.17	0.92-1.48	0.20	0
Death	588/2597 (22.6)	411/2005 (20.5)	999/4602 (21.7)	536/2647 (20.2)	5	0.83	0.64-1.07	0.15	51	4	0.88	0.62-1.24	0.47	70	6	0.92	0.72-1.18	0.50	61
Procedural outcomes																			
Successful reperfusion (TICI ≥2b)	2063/2764 (74.6)	1615/2151 (75.1)	3678/4915 (74.8)	1963/2788 (70.4)	6	0.90	0.54-1.49	0.69	88	5	0.92	0.56-1.50	0.73	86	8	0.76	0.50-1.15	0.20	87
First pass effect	621/1258 (49.4)	481/905 (53.1)	1102/2163 (50.9)	564/977 (57.7)	2	1.15	0.63-2.12	0.65	76	1	NA	NA	NA	NA	2	1.12	0.66-1.91	0.67	70
Procedure related complications	57/388 (14.7)	54/669 (8.1)	111/1057 (10.5)	109/844 (12.9)	4	1.20	0.55-2.62	0.65	69	3	1.17	0.74-1.83	0.50	0	6	1.18	0.76-1.81	0.46	39
Door to groin puncture time (mins)	70.8±37.1/329	81.3±49.7/47	72.2±39/376	53.4±36.8/513	3	-14.36	-20.91 to -7.81	<0.001*	64	1	NA	NA	NA	NA	4	-15.06	-20.35 to -9.77	<0.001*	46
Groin puncture to reperfusion time (mins)	56±34.5/769	54.8±33.5/297	55.6±34.2/1066	52.5±31.8/1428	5	-1.66	-8.83 to 5.50	0.65	83	3	-7.31	-11.44 to -3.19	<0.001*	0	6	-2.23	-7.28 to 2.61	0.36	70
Onset to groin puncture (mins)	255.4±128.9/2451	234.4±91.9/2006	245.9±114.2/4457	222.9±157.5/2285	4	-24.03	-66.50 to 18.44	0.27	95	3	-13.62	-52.39 to 25.15	0.49	96	4	-15.18	-47.41 to 17.05	0.36	95

LA = local anaesthesia, CS = conscious sedation, GA = general anaesthesia, n = number of events, N = number of patients, SD = standard deviation, OR = odds ratio, CI = confidence interval, MD = mean difference, mRS = modified Rankin scale, sICH = symptomatic intracranial haemorrhage, TICI = thrombolysis in cerebral infarction, NA= not available. * = statistically significant

Table 2: Meta-analysis of outcomes according to anaesthesia types.

FIGURES

Figure 1: Forest plot demonstrating the odds of a good functional outcome (mRS≤2) at 90 days comparing local anaesthesia (LA) and general anaesthesia (GA).

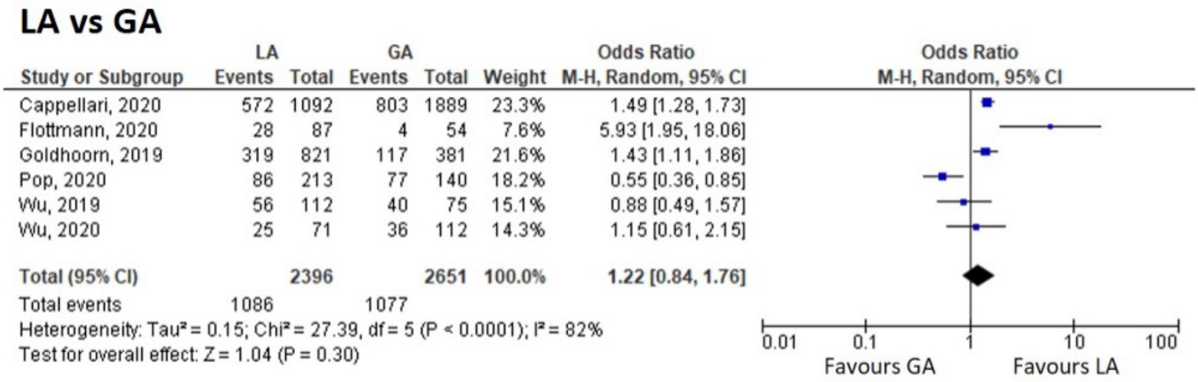
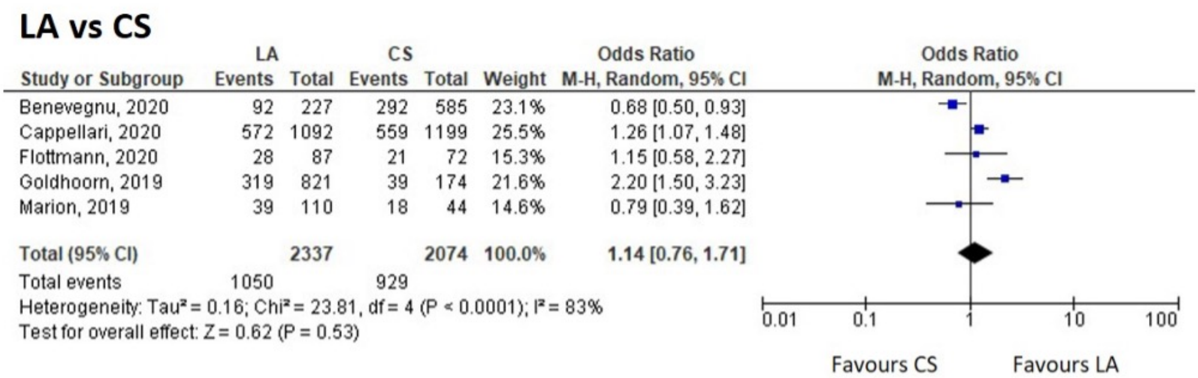
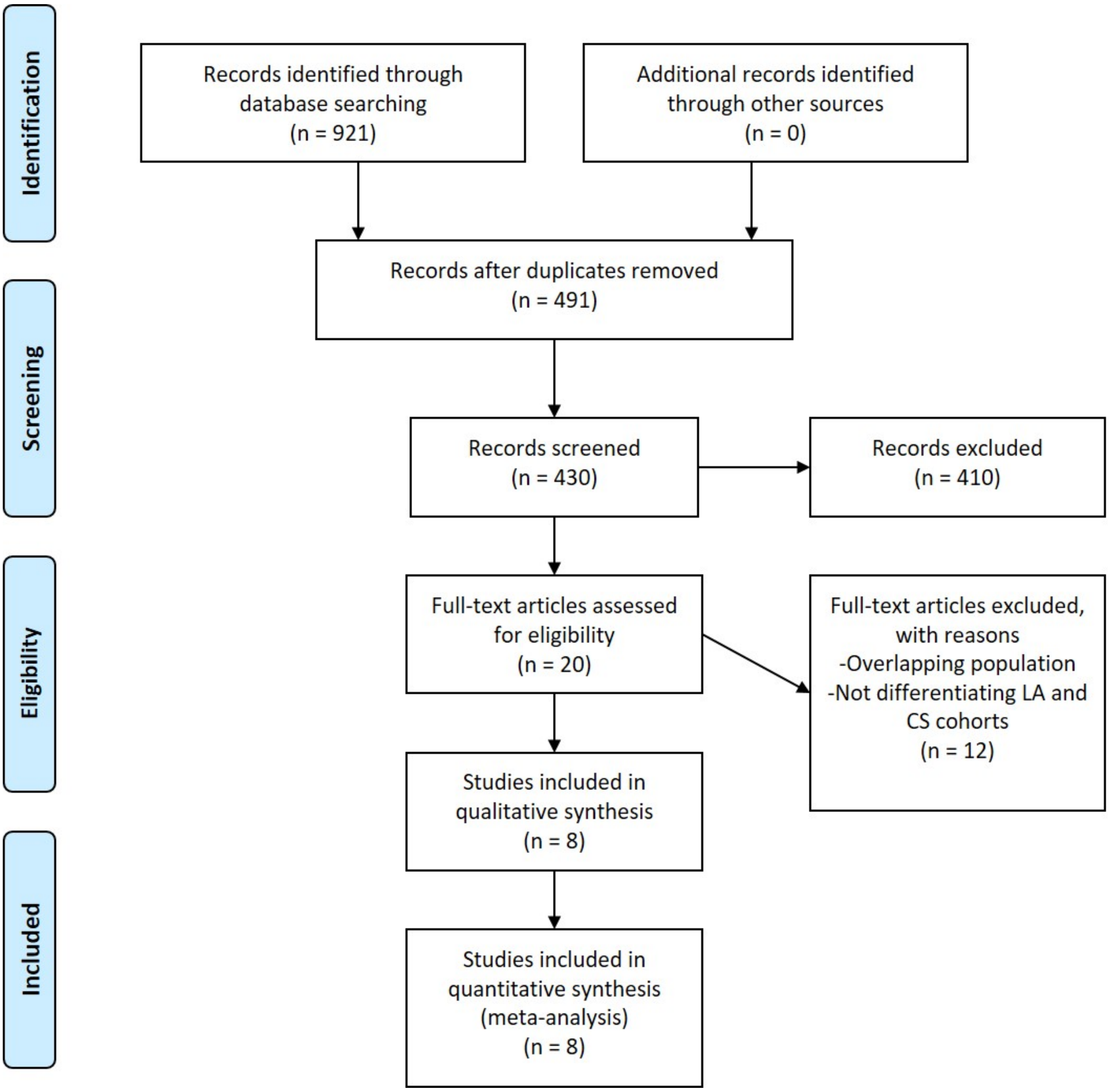


Figure 2: Forest plot demonstrating the odds of a good functional outcome (mRS≤2) at 90 days comparing local anaesthesia (LA) and conscious sedation (CS).



SUPPLEMENTARY DATA



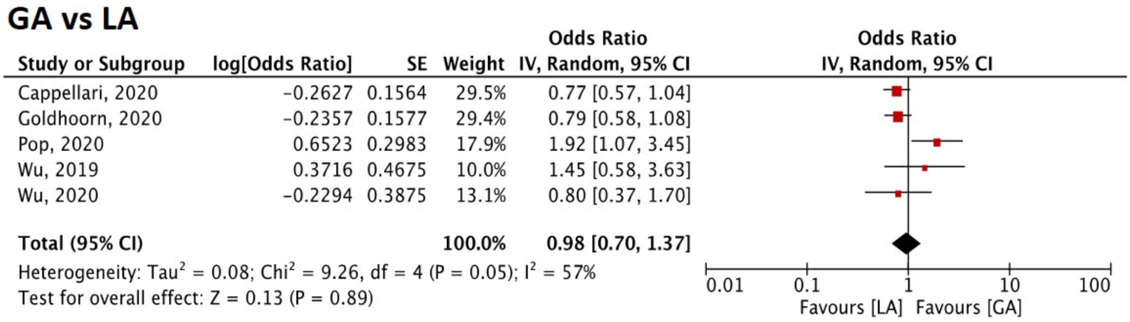
LA = local anaesthesia, CS = conscious sedation

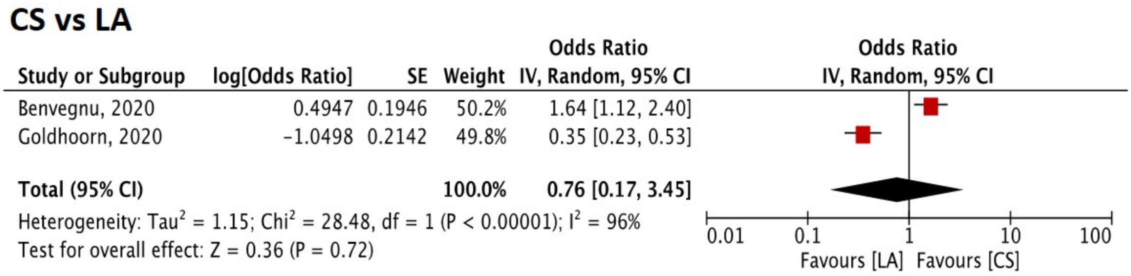
Supplementary Figure 1: PRISMA Flow chart of study selection.

Feature	GA, n/N (%) or mean±SD/N	CS, n/N (%) or mean±SD/N	GA+CS, n/N (%) or mean±SD/N	LA, n/N (%) or mean±SD/N
Socio-demographics				
Sample size	2782	2218	5000	2797
Gender (Male)	1549/2782 (55.7)	1063/2217 (47.9)	2611/4999 (52.2)	1420/2796 (50.8)
Age (years)	69.2±15.1/2782	71.7±14.2/2218	70.3±14.8/5000	70.9±14.0/2797
Baseline characteristics				
Baseline NIHSS	18.0±6.6/2601	16.6±6.1/2186	17.4±6.4/4787	15.9±6.7/2792
Baseline mRS (≤1)	1710/2157 (79.3)	1168/1360 (85.9)	2878/3517 (81.8)	1668/2134 (78.2)
ASPECTS	9.0±1.8/1757	8.7±1.8/1855	8.8±1.8/3612	8.8±1.6/1827
Good collaterals	623/1259 (49.5)	366/694 (52.7)	989/1953 (50.6)	496/1255 (39.5)
IV-thrombolysis	1380/2778 (49.7)	1203/2212 (54.4)	2583/4990 (51.8)	1680/2795 (60.1)
Anaesthesia conversion	N/A	58/661 (8.8)	N/A	97/553 (17.5)
Co-morbidities				
HTN	1526/2420 (63.1)	1265/198 (63.6)	2791/4409 (63.3)	1642/2707 (60.7)
DM	451/2420 (18.6)	363/1986 (18.3)	814/4406 (18.5)	485/2707 (17.9)
Hyperlipidaemia	693/2420 (28.6)	552/1983 (27.8)	1245/4403 (28.3)	776/2707 (28.7)
AF	581/2278 (25.5)	443/1366 (32.4)	1023/3644 (28.1)	690/2251 (30.7)
Prior Stroke	175/2107 (8.3)	85/1290 (6.6)	260/3397 (7.7)	223/2086 (10.7)
Smoking	563/2420 (23.3)	410/1959 (20.9)	973/4379 (22.2)	632/2707 (23.3)
Coronary artery disease	144/1651 (8.7)	243/1735 (14.0)	387/3386 (11.4)	190/1390 (13.7)
Heart failure	125/1651 (7.6)	82/1069 (7.7)	207/2720 (7.6)	60/1042 (5.8)
Medications				
Antiplatelet	531/2013 (26.4)	644/1901 (33.9)	1175/3914 (30.0)	487/1367 (35.6)
Anticoagulation	179/2013 (8.9)	134/1285 (10.4)	313/3298 (9.5)	125/1131 (11.1)
Statin	296/2013 (14.7)	174/1285 (13.5)	470/3298 (14.3)	188/1131 (16.6)
Clot Localisation				
Left-hemispheric stroke	343/598 (57.4)	109/221 (49.3)	452/819 (55.2)	641/1257 (51.0)
ICA	587/2645 (22.2)	472/2216 (21.3)	1059/4861 (21.8)	543/3121 (17.4)
M1	1055/2645 (39.9)	1069/2216 (48.2)	2124/4861 (43.7)	1439/3121 (46.1)
M2	239/2570 (9.3)	294/2216 (13.3)	533/4786 (11.1)	343/3009 (11.4)
Tandem occlusion	290/2189 (13.2)	253/1995 (12.7)	543/4184 (13.0)	229/1679 (13.6)
Vertebrobasilar	553/2100 (26.3)	98/1330 (7.4)	651/3430 (19.0)	142/1310 (10.8)
First-line EVT technique				
SR	969/1951 (49.7)	690/1781 (38.7)	1659/3732 (44.5)	1131/2324 (48.7)
CA	553/1599 (34.6)	504/1625 (31.0)	1057/3224 (32.8)	693/1618 (42.8)
Combined (SR & CA)	293/1487 (19.7)	523/1625 (32.2)	816/3112 (26.2)	331/1547 (21.4)

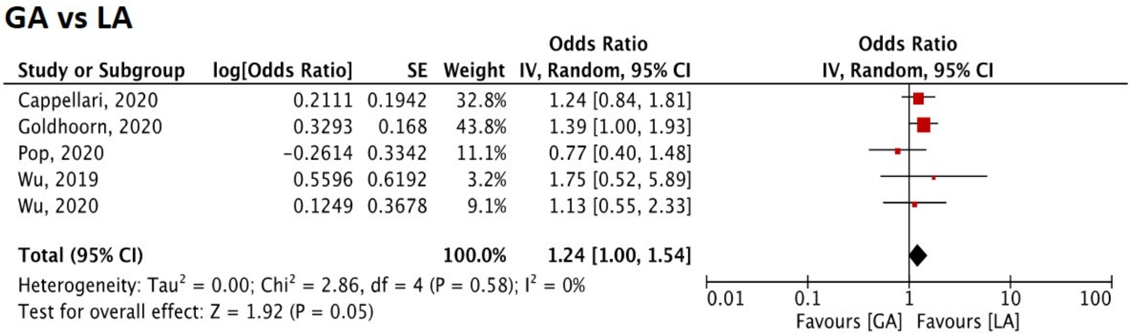
LA = local anaesthesia, CS = conscious sedation, GA = general anaesthesia, EVT = endovascular technique, NIHSS = National Institutes of Health Stroke Scale, mRS = modified Rankin Scale, IV-tPA = intravenous tissue plasminogen activator, ASPECTS = Alberta stroke program early CT score, HTN = hypertension, DM = diabetes mellitus, AF = atrial fibrillation, SR = stentretriever, CA = contact aspiration,

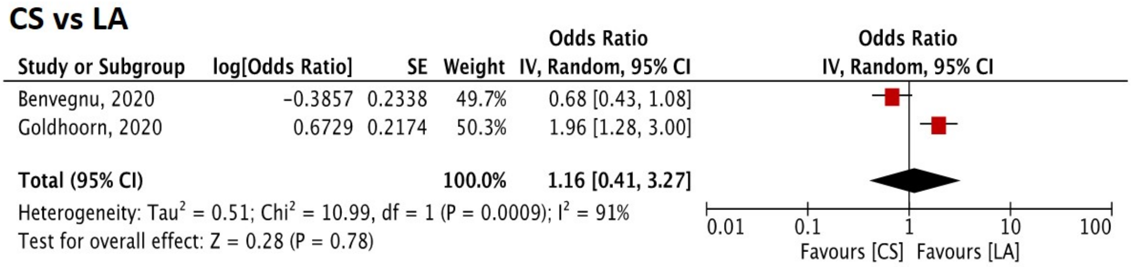
Supplementary Figure 2: Population characteristics according to the anaesthetic regime.



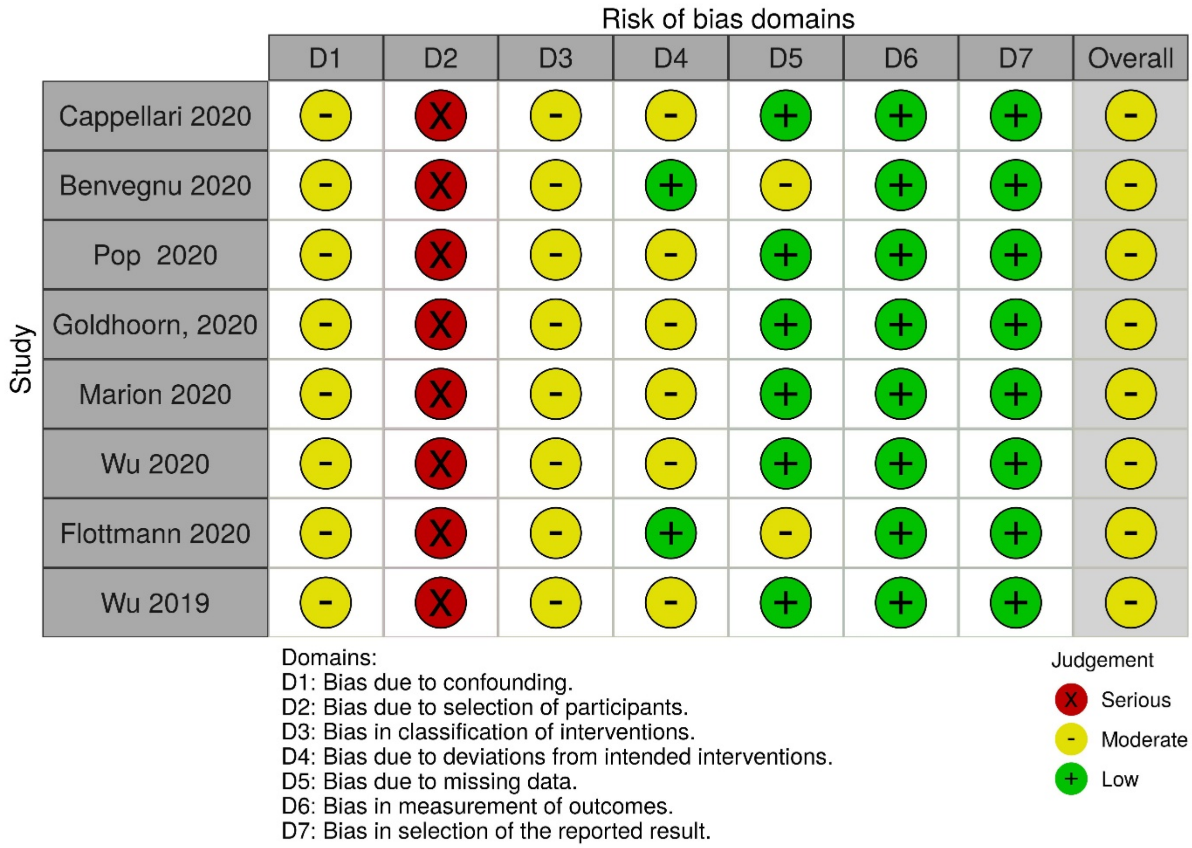


Supplementary Figure 3: Forest plot demonstrating the odds of a good functional outcome (mRs≤2) at 90 days between local anaesthesia (LA) and general anaesthesia (GA) or conscious sedation (CS) using data adjusted for confounders.

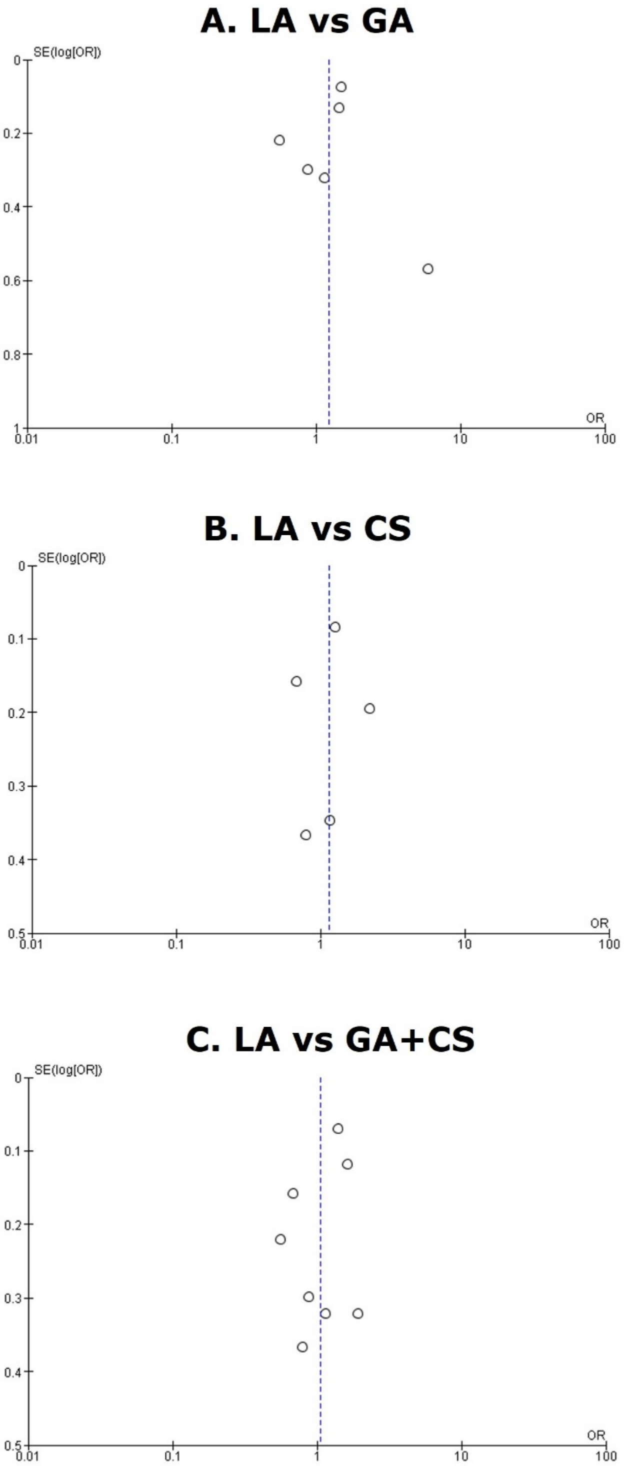




Supplementary Figure 4: Forest plot demonstrating the odds of death at 90 days between local anaesthesia (LA) and general anaesthesia (GA) or conscious sedation (CS) using data adjusted for confounders.



Supplementary Figure 5: Risk of bias assessment based on the ROBINS-I tool for non-randomised studies.



Supplementary Figure 6: Funnel plot for publication bias for good functional outcome (mRs≤2) at 90 days between local anaesthesia (LA) and general anaesthesia (GA) or conscious sedation (CS).