**SUPPLEMENTAL MATERIAL FOR:**

**Mechanical thrombectomy**

**in patients with acute ischemic stroke and ASPECTS ≤6:**

**A Meta-Analysis**

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**Supplemental Table 1.** Search syntax

|  |  |  |
| --- | --- | --- |
| **PubMed search accessed on 1 June 2019**  **(10 studies)** | **Embase search accessed on 1 June 2019**  **(63 studies)** | **Scopus search accessed on 1 June 2019**  **(406 studies)** |
| **First Search Syntax**  (((((((thrombectomy) AND (intermediate OR unfavorable ASPECTS) AND stroke)) OR ((revascularization) AND (intermediate OR unfavorable ASPECTS) AND stroke)) OR ((endovascular treatment) AND low ASPECTS AND stroke)) OR ((endovascular treatment) AND low ASPECTS)) OR ((thrombectomy) AND low ASPECTS)) AND ((revascularization) AND low ASPECTS AND stroke)  **Second Search Syntax**  ((((((Borderline) AND ASPECTS) AND (stroke OR occlusion))) OR (((Borderline) AND ASPECTS) AND (acute ischemic stroke OR occlusion))) OR ((Low DWI-ASPECTS) AND (thrombectomy OR endovascular))) AND ((thrombectomy) AND large stroke AND ASPECTS) | (thrombectomy AND low AND aspects OR  (('thrombectomy':ab,ti OR  'endovascular':ab,ti) AND ('low':ab,ti OR  'intermediate':ab,ti) AND 'aspects':ab,ti  AND 'stroke':ab,ti)) AND ('article'/it OR  'review'/it) OR ('thrombectomy':ti AND  'large infarct':ti) | (thrombectomy AND aspects AND ≤ 5 ) OR ( thrombectomy AND aspects AND ≤ 6 ) OR (thrombectomy AND low AND aspects AND stroke ) AND (LIMIT-TO ( LANGUAGE , "English" ) ) AND ( LIMIT-TO ( DOCTYPE , "ar" ) ) AND ( LIMIT-TO ( SUBJAREA , "MEDI" ) OR LIMIT-TO (SUBJAREA , "NEUR" ) ) |

**Supplemental Table 2.** Summary of studies included in meta-analysis

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study Name** | **Design** | **Definition of Low-ASPECTS** | **N of Cases (EVT treatment)** | **N of Controls (Medical treatment)** | **Type of EVT** | **Imaging modality** | **Median Initial NIHSS (cases vs controls)** | **m RS0-2 3 months**  **(CASES)** | **m RS0-2 3 months**  **(CONTROLS)** | **sICH (CASES)** | **sICH (CONTROLS)** | **TICI 2b-3 EVT group** |
| **Mourand I 201815** | R | ≤5 | 60 | 48 | SR | MRI DWI | 20/22 | 18/60 | 1/48 | 3/60 | 3/48 | 45/60 |
| **Desilles JP 201720** | PRe | ≤6 | 206 | NA | SR or AS | MRI DWI | 19/NA | 65/206 | NA | 119/206 | NA | 145/218 |
| **Manceau PF 201826** | R | ≤5 | 82 | NA | SR or AS | MRI DWI | 18/NA | 29/82 | NA | 32/80 | NA | 41/82 |
| **Ohta T 201816** | R | ≤6 | 15 | 23 | SR | MRI DWI | 18/NA | 4/15 | 0/23 | 0/15 | 7/23 | NA |
| **Bracard S 201614** | PRa | ≤4 | 22 | 35 | SR or AS | MRI DWI | NA | 8/22 | 9/35 | NA | NA | NA |
| **Hungerford JP 201621** | R | ≤6 | 31 | NA | AS | CT perfusion | NA | 13/31 | NA | 5/31 | NA | 5/31 |
| **Kim SK 201623** | R | 4-6 | 51 | NA | SR | MRI DWI | 15/NA | 20/51 | NA | 2/51 | NA | 43/51 |
| **Spiotta AM 201428** | R | 3-6 | 26 | NA | SR | CT perfusion | NA | 10/26 | NA | 8/26 | NA | NA |
| **Logan C 201825** | R | ≤6 | 35 | NA | SR | CT | 18/NA | 13/35 | NA | 3/35 | NA | 26/35 |
| **Wasser K 201617** | R | ≤5 | 42 | 59 | SR | CT | 16/16 | 0/41 | 0/59 | 29/41 | 50/59 | NA |
| **Li W 201724** | PRe | 5 and 6 | 41 | NA | SR | CT | NA/NA | 7/41 | NA | 8/41 | NA | 35/41 |
| **Song K 201927** | R | ≤5 | 19 | NA | SR | MRI DWI | 16/NA | 10/19 | NA | 2/19 | NA | 19/19 |
| **Danière F 201419** | PRe | ≤5 | 26 | NA | SR | MRI DWI | NA/NA | 8/26 | NA | NA | NA | 21/26 |
| **Inoue M 201422** | PRe | ≤5 | 75 | NA | SR | MRI DWI | 18/NA | 34/75 | NA | 15/75 | NA | NA |
| **Yoo AJ 201618** | PRa | ≤4 | 11 | 19 | SR + IAT | CT | 19/21 | 1/11 | 0/19 | 1/11 | 1/19 | NA |
| **Kaesmacher J 201931** | PRe | ≤5 | 237 | NA | SR | MRI-DWI and CT | 19/NA | 58/237 | NA | 17/237 | NA | 165/236 |
| **Panni P 201932** | PRe | ≤5 | 216 | NA | SR + AS | MRI DWI | 20/NA | 55/216 | NZ | 10/216 | NA | 149/216 |

R=retrospective study; PRe=prospective registry; PRa= prospective randomized study Pts=patients; SR= stent retriever; AS= aspiration; EVT= endovascular treatment; m RS= modified Ranking Scale; s ICH= symptomatic intracranial hemorrhage; NIHSS = National Institute of Health Stroke Score; TICI= thrombolysis in cerebral infarction; IAT= intraarterial thrombolysis

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study Name** | **Selection** | | | | | | | | **Comparability** | | | | **Exposure** | | | | | **Total** |
| **1)** | | **2)** | | **3)** | | **4)** | | **a)** | | **b)** | | **1)** | | **2)** | | **3)** |
| **RETROSPECTIVE DESIGN (score 0 to 9; “high-quality”=studies with 6 or more stars)** | | | | | | | | | | | | | | | | | | |
| **Mourand I 2018** | \* | | | \* | |  | \* | | \* | | \* | | \* | | \* | | \* | 8 |
| **Manceau PF 2018** | \* | | | \* | |  |  | |  | |  | | \* | |  | |  | 3 |
| **Ohta T 2018** | \* | | | \* | |  | \* | | \* | | \* | | \* | | \* | | \* | 8 |
| **Hungerford JP 2016** | \* | | | \* | |  |  | |  | |  | | \* | |  | |  | 3 |
| **Kim SK 2016** | \* | | | \* | |  |  | |  | | \* | | \* | |  | |  | 4 |
| **Spiotta AM 2014** | \* | | | \* | |  |  | |  | |  | | \* | |  | |  | 3 |
| **Logan C 2018** | \* | | | \* | |  |  | |  | |  | | \* | |  | |  | 3 |
| **Wasser K 2016** | \* | | | \* | |  | \* | | \* | | \* | | \* | | \* | | \* | 8 |
| **Song K 2019** | \* | | | \* | |  |  | |  | |  | | \* | |  | |  | 3 |
| **Study Name** | **Selection** | | | | | | | | **Comparability** | | | | **Outcome** | | | | | **Total** |
| **1)** | | | **2)** | | **3)** | **4)** | | a) | | b) | | **1)** | **2)** | | **3)** | |
| **PROSPECTIVE DESIGN/COHORT (score 0 to 9; “high-quality”=studies with 6 or more stars)** | | | | | | | | | | | | | | | | | | |
| **Desilles JP 2017** | | \* | |  | | \* | | \* | |  | \* | \* | | \* | | | \* | 7 |
| **Bracard S 2016** | | \* | | \* | | \* | | \* | | \* |  | \* | | \* | | | \* | 8 |
| **Li W 2017** | | \* | |  | | \* | | \* | |  | \* | \* | | \* | | | \* | 7 |
| **Deniere F 2014** | | \* | |  | | \* | | \* | |  |  | \* | | \* | | | \* | 6 |
| **Inoue M 2014** | | \* | |  | | \* | | \* | |  | \* | \* | | \* | | | \* | 7 |
| **Yoo AJ 2016** | | \* | | \* | | \* | | \* | | \* |  | \* | | \* | | | \* | 8 |
| **Kaesmacher J 2019** | | \* | |  | | \* | | \* | |  | \* | \* | | \* | | | \* | 7 |
| **Panni P 2019** | | \* | |  | | \* | | \* | |  | \* | \* | | \* | | | \* | 7 |

**Supplemental Table 3.** Quality measure of included studies by the Newcastle-Ottawa quality assessment scale

Each star (\*) indicates one point of the scale

**Note=** a) Comparability (point A) was tested comparing the final m RS 0-2 among patients with acute large vessel occlusion treated endovascularly vs patients with acute large vessel occlusion undergoing medical management

b) Comparability (point B) was tested comparing the secondary outcomes (m RS 0-2 among subgroups of ASPECTS and subgroups of age, morality, symptomatic intracranial hemorrhage) among the thrombectomy group vs the control group.

**Supplemental Table 4.** Characteristics of patients with acute ischemic stroke and low ASPECTS treated by mechanical thrombectomy and medical therapy.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variables** | ***EVT group (95% CI)*** | ***N of Studies EVT group*** | ***Medical treatment group***  ***(95% CI)*** | ***N of Studies Medical Treatment group*** | ***p-value*** |
| **Overall N of Patients** | 1194 | 17 | 184 | 5 |  |
| **Male** | 611/1140= 53.6%  (50-56) | 12 | 69/130= 53%  (44-61) | 3 | 0.9 |
| **Mean age** | 68.7 (43-91) | 10 | 75 (50-94) | 3 | 0.1 |
| **Hypertension** | 531/1044= 50.8%  (48-53) | 10 | 73/130=56%  (47.5-64) | 3 | 0.2 |
| **Dyslipidemia** | 223/788= 28.3%  (25-31) | 10 | 26/130=20%  (14-27.7) | 3 | **0.04** |
| **Diabetes** | 255/882= 28.9%  (14.6-21) | 11 | 25/130= 19%  (13-27) | 3 | **0.02** |
| **Median Initial NIHSS** | 18 (9-28) | 11 | 19 (5-40) | 3 | 0.4 |
| **Intravenous thrombolysis** | 620/1091= 56.8%  (53-59.7) | 11 | 68/142= 47.8%  (40-56) | 3 | **0.04** |
| **Location of Occlusion**  **M1**  **M2**  **Carotid Bifurcation**  **Tandem** | 563/990= 56,8% (53-59)  44/990= 4.4% (3.3-5.9)  271/990= 27% (24-30)  140/990= 14% (12-16) | 9 | 80/130= 61.5% (53-69)  4/130= 3% (0.9-8.9)  25/130= 19% (13-27)  21/130= 16% (11-23.5) | 3 | 0.3  0.4  0.09  0.5 |
| **Mean symptoms onset to groin puncture time (minutes)** | 271.6 (164-320) | 8 | NA | NA | NA |
| **Mean symptoms onset to recanalization time (minutes)** | 286 (153-370) | 6 | NA | NA | NA |
| **Mean symptoms onset to admission time (minutes)** | 115 (10-380) | 4 | 130 (37-642) | 3 | 0.7 |

EVT= endovascular treatment; N=number; NIHSS= National Institute of Health Stroke Score

**Supplemental Figure 1 (A, B, C).** Random-effect meta-analysis of the proportion of patients with mRS 0-2 at 3-months follow-up after MT: the funnel plot followed by Egger’s linear regression test excludes publication bias (A). Meta-regression showed an insignificant variation of the effect size (B) over the investigated years. The sensitivity analysis showed that no individual study significantly influenced the proportion of good functional outcome at 3-months follow-up after MT (C).



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