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Safety and Effectiveness of Mechanical Thrombectomy for Primary Isolated Distal Vessel Occlusions: a Monocentric Retrospective Comparative Study

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1 **Safety and Effectiveness of Mechanical Thrombectomy for Primary Isolated Distal**
2 **Vessel Occlusions: a Monocentric Retrospective Comparative Study**

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21 **Cover title**

22 Distal vessel occlusions ischemic stroke management.

23 **Key words**

24 Distal occlusion, middle cerebral artery, M2, M3, anterior cerebral artery occlusion, posterior
25 cerebral artery occlusion, acute ischemic stroke, mechanical thrombectomy, reperfusion,
26 outcome.

27 **Tables and figures:** Tables: 2, figures: 1

28 **References:** 24

29 **Word count:** 3999

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42 **Disclaimer**

43 This work represents ongoing research. Hence, it represents the opinions of the authors,
44 and is the product of their professional research. Indeed, it is not meant to represent the
45 opinions of their institutes or its members, nor the official position of any staff members. Any
46 errors are the fault of the authors.

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58 this study or the findings specified in this paper.

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10 outcome.

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22 **Abstract**

23 **Background**

24 Distal vessel occlusions represent about 25-40% of acute ischemic stroke (AIS), either as
25 primary occlusion or secondary occlusion complicating mechanical thrombectomy (MT) for
26 large vessel occlusion.

27 **Objective**

28 Our aim was to evaluate safety and effectiveness of MT associated with the best medical
29 treatment (BMT) in the management of AIS patients with distal vessel occlusion in comparison
30 with the BMT alone.

31 **Methods**

32 Retrospective analysis was conducted on AIS patients treated by MT+BMT for primary distal
33 vessel occlusion between 2015 and 2020, and were compared with a historic cohort managed
34 by BMT alone between 2006 and 2015 selected based on the same inclusion criteria. A
35 secondary analysis was conducted using propensity score matching (PSM) including the
36 following: NIHSS, age and treatment with intravenous thrombolysis (IVT) as covariates.

37 **Results**

38 Of 650 patients screened, 44 patients with distal vessel occlusions treated by MT+BMT were
39 selected and compared with 36 patients who received BMT alone. After PSM, 28 patients in
40 each group were matched without significant difference. Good clinical outcome defined as
41 mRS \leq 2 was achieved by 53.6% of the MT+BMT group and 57% of the BMT group (OR, 0.87;
42 95%CI, 0.3–2.4; P=1.00). The mortality rate was comparable in both groups (7% vs. 10.7% in
43 MT+BMT and BMT patients, respectively; OR=0.64; 95%CI, 0.1-4; P=1.00). Symptomatic
44 intracranial hemorrhage (ICH) was seen in only one patient treated by MT+BMT (3.6%).

45 **Conclusion**

46 Mechanical thrombectomy seems to be comparable with the best medical treatment
47 regarding the effectiveness and safety in the management of patients with distal vessel
48 occlusions.

49 **Abbreviations and acronyms**

50 **DVOs:** Distal vessel occlusions, **AIS:** acute ischemic stroke, **MT:** mechanical thrombectomy, **LVO:**
51 large vessel occlusion, **BMT:** best medical treatment, **IVT:** intravenous thrombolysis, **mTICI:** modified
52 thrombolysis in cerebral infarction scale, **AOL:** Arterial occlusion lesion scale, **mRS:** modified Rankin
53 scale, **ICH:** intracranial hemorrhage, **NIHSS:** National Institutes of Health Stroke Score, **GA:** General
54 anaesthesia.

55 **Introduction**

56 Despite distal vessel occlusions (DVOs) represent about 25% to 40% of acute ischemic
57 stroke (AIS), whether as primary occlusion or complicating mechanical thrombectomy (MT)
58 for large vessel occlusion (LVO), they were underrepresented by the main randomized trials
59 of MT.[1] MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for
60 Acute Ischemic Stroke in the Netherlands) and EXTEND IA (Extending the Time for
61 Thrombolysis in Emergency Neurological Deficits - Intra-Arterial) were the only among the five
62 known randomized trials that included patients with isolated M2 occlusions per protocol, and
63 this subgroup of patients represented about 8% in relation to other occlusion sites.[2, 3]

64
65 The risk-benefit ratio of MT in distal vessel occlusions is still uncertain. On one hand,
66 even if AIS related to a distal occlusion may be considered less severe than a proximal
67 occlusion, the clinical outcome may not be favorable in these patients with significant
68 disability hampering the quality of life. According to the literature, the rate of good clinical
69 outcome at 3 months after a distal intracranial occlusion treated medically ranges from 20%
70 to 77%.[3-5]

71
72 On the other hand, the risks of MT in distal occlusions are well-known. The special
73 characteristics of distal vessels of smaller diameters, increased tortuosity, and longer
74 distances of navigation, along with the iterative advances in endovascular devices necessitate
75 to pay more attention for the management of these types of occlusions.

76
77 The aim of this study was to evaluate effectiveness and the safety of mechanical
78 thrombectomy in the management of AIS patients with distal vessel occlusion in comparison
79 with the best medical treatment alone.

87 **Patients & Methods**

88

89 **Study design**

90

91 A retrospective analysis was primarily conducted on AIS patients who were treated by
92 MT + BMT for primary and isolated distal vessel occlusion at our institution between January
93 2015 and June 2020. These patients were compared with a historic cohort of patients from
94 the same Institution managed by best medical treatment (BMT) alone including intravenous
95 thrombolytic therapy (IVT) between April 2006 and January 2015 and selected based on the
96 same inclusion criteria. The study was approved by the institutional review board that waived
97 the patients' consents. This retrospective study was conducted in accordance with the
98 Declaration of Helsinki.

99

100 **Inclusion criteria**

101

102 Consecutive patients with isolated primary distal vessel occlusion proven by vascular
103 imaging were included except patients with secondary distal vessel occlusion as a
104 complication of MT for LVO who were excluded. Distal vessel occlusion was identified as
105 occlusion of the distal aspect of the M2 segment and M3 segment of the middle cerebral
106 artery, any segment of the anterior cerebral artery, or any segment of the posterior cerebral
107 artery. Occlusion of the distal aspect of the M2 segment was defined as an occlusion above
108 the mid-height of the insula, while M3 occlusion was defined as occlusion at any point from
109 the parietal operculum till emerging from the Sylvian fissure at the lateral surface of the brain
110 according to the Fischer's classification. Proximal M2 occlusions were excluded.[6, 7]

111

112 Clinical severity was assessed using the NIHSS at admission, 24 hours and one week by
113 a vascular neurologist. The modified Rankin Scale (mRS) was evaluated at three-months.

114

115 **Pre-procedure and Post-procedure Imaging Assessments**

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3 116 All the patients underwent a pre-procedure brain magnetic resonance imaging (MRI)
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5 117 including diffusion-weighted imaging (DWI) and 3D Time of Flight (TOF) MR angiography
6
7 118 (MRA). Brain computed tomography (CT) scan was performed if there was contraindication
8
9 119 for MRI, like cardiac pacemakers. An unenhanced brain CT scan and/or MRI was performed
10
11 120 within 24 hours after the endovascular procedure to exclude any haemorrhagic complications.
12

13 121
14 **Procedure and intervention**
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18 124 When eligible, patients received IVT within 4.5 h of stroke symptoms' onset.
19
20 125 Otherwise, an anti-platelets agent was the reference. **Afterward, the individual decision to**
21
22 126 **perform a MT was a multidisciplinary consensus by the neurologist and**
23
24 127 **neurointerventionalist. Arguments to perform MT were a relevant clinical deficit. Moreover,**
25
26 128 **it was upon the operator's discretion to weigh the specific procedural risk against the potential**
27
28 129 **benefit of recanalization; and given the current absence of evidence for MT in such population,**
29
30 130 **the decision was not based on predefined fixed criteria.**
31

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34 132 For MT, all the procedures were systematically performed in a biplane
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36 133 neuroangiography suite using a tri-axial system with a 6F long sheath, an intermediate distal
37
38 134 access catheter (5F or 6F) and a microcatheter. When combined to IVT, endovascular
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40 135 preparation was initiated simultaneously with or soon after IVT administration was started
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42 136 without waiting for evaluation of its initial response (bridging paradigm).
43

44 137
45 138 Mechanical thrombectomy was performed with approved devices, using stent-
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47 139 retrievers with maximal diameter of 3 mm or 3MAX aspiration catheter (Penumbra, Alameda,
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49 140 CA, USA). The choice was left to the attending neuroradiologist's discretion.
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53 142 *Baseline parameters, technical features, and angiographic were noted.*
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146 **Study outcome**

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148 The primary end point was the rate of good clinical outcome defined as mRS \leq 2 at 3-
149 months. Secondary efficacy criteria included the rate of excellent clinical outcome, defined as
150 a 3-month mRS \leq 1 and early neurological improvement, defined as a complete resolution of
151 the neurological deficit or an improvement from baseline in the National Institutes of Health
152 Stroke Scale (NIHSS) by 4 or more points 24 hours after the onset of stroke.[8]

153

154 Moreover, the rate of successful reperfusion, defined as mTICI \geq 2b (Modified
155 Thrombolysis in Cerebral Infarction) at the end of the procedure for the MT + BMT group; and
156 defined as AOL \geq 2 (Arterial Occlusion Lesion scale) on 24 hours MRI and MRA for the BMT
157 group.[9]

158

159 The safety criteria were the rate of symptomatic intracranial hemorrhage (ICH),
160 according to the trial of thrombolytic therapy with intravenous alteplase in acute ischaemic
161 stroke (ECASS II) study criteria [10], asymptomatic ICH, the frequency of distal emboli,
162 procedural arterial dissection and perforation in the MT + BMT group.

163

164 As an additional analysis, we developed a propensity score matched cohort in order to
165 explore the robustness of our analyses. The variables for the propensity score included the
166 following: baseline NIHSS score, age, and treatment with IVT. The patients in the BMT group
167 were matched to those in the MT group using a 1:1 matching technique. We compared
168 primary outcomes and secondary outcomes of the propensity score matched cohort between
169 the MT+BMT and BMT groups. The effects of MT+BMT relative to BMT are displayed as ORs
170 and 95% CIs.

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177 **Statistical Analysis**

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3 178 Data analysis was performed using (IBM Corp. Released 2017. IBM SPSS Statistics for
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5 179 Windows, Version 25.0. Armonk, NY: IBM Corp.) χ^2 or Fisher's exact test was used to compare
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7
8 180 frequencies, when appropriate. Comparison of means was performed using Student-t test or
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10
11 181 Mann-Whitney test, depending on the data distribution. Results were considered statistically
12
13 182 significant when P value <0.05. Propensity score matching was used with a calliper width of
14
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16 183 0.1 based on age, initial NIHSS and treatment with IVT as covariates. The patients in the BMT
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18 184 group were matched to those in the MT+BMT group using a 1:1 matching technique. For
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21 185 outcome variables, unadjusted odds ratios (ORs) were calculated by using univariate logistic
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24 186 regression models, including treatment by MT+BMT as independent variable.

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Results

Among the 650 patients treated by mechanical thrombectomy in our centre during the predetermined period screened (2015-2020), 44 patients with distal vessel occlusions who met the inclusion criteria were treated by MT + BMT and compared with 36 patients who received BMT alone (2006-2015). (**Figure 1** shows the study flow chart)

Table 1 shows baseline characteristics. Compared with patients in the BMT group, those in the MT + BMT group had a higher baseline NIHSS score (median [IQR], 11 [7-21] vs. 6 [3-10], $p < 0.001$) and were older (median [IQR], 78 [64 -85] vs. 70 [57-78], $p < 0.04$); and tended to have higher rates of IVT treatment (63.6 % vs. 41.7 %; $P = 0.07$). There was no difference among the groups for stroke comorbidities.

Regarding MT, stent retrievers (with or without aspiration) was used in 33 cases (75%) and 7 MT procedures (16%) were performed under general anaesthesia.

After the propensity score matching, 28 patients in each group were matched. Baseline characteristics of the two groups after propensity score matching are shown in **Table 1**. No significant difference was noted between the two groups.

Clinical outcomes in the entire cohort

Good clinical outcome (defined as $mRS \leq 2$ at 3-months) was observed in 47.7% and 58.3% ($p = 0.38$) of MT + BMT and BMT patients, respectively; while excellent clinical outcome (defined as $mRS \leq 1$ at 3-months) was achieved by 29.5 % and 38.9% ($p = 0.48$) of MT + BMT and BMT patients, respectively. Early neurological improvement was observed in 45.5 % and 38.9 % ($p = 0.65$) of MT + BMT and BMT patients, respectively.

The overall successful reperfusion rate in the MT group defined as $mTICI \geq 2B$ was 77.3%.

234 Comparing both groups regarding the final recanalization state, the MT + BMT group
235 had significantly higher successful recanalization defined as AOL \geq 2 (90.9% vs. 47.2% in
236 MT+BMT and BMT groups; $p < 0.001$) (**Figure 2** shows an illustrative case)

237
238 For the safety outcome, mortality rate at 90 days occurred in 18.2% and 13.9% ($p = 0.76$)
239 of MT+BMT and BMT patients.

240
241 Symptomatic ICH occurred in two patients (4.5%) in the MT+BMT group with no
242 observed symptomatic ICH in the BMT group ($P = 0.5$). However, asymptomatic ICH occurred
243 in further 4 patients in the MT+BMT group (9%), and one patient in the BMT group (2.8%,
244 $p = 0.37$) (**Table 2**).

245
246 As procedural complications, distal embolization to the same territory occurred in two
247 patients (4.5%). Moreover, vessel perforation occurred during the procedure in two other
248 patients (4.5%); one of them suffered from symptomatic ICH.

249 250 **Clinical outcomes in the propensity score-matched cohort**

251
252 After balancing of both groups by using NIHSS score, age, and treatment with IVT as
253 covariates to develop a propensity score matched model; 3-months good clinical outcome was
254 achieved by 53.6% of the MT+BMT treated patients and by 57% of the BMT group (odds ratio
255 [OR], 0.87; 95% CI, 0.3-2.4; $P = 1.00$). Thirty two percent and 39.3% of patients treated by
256 MT+BMT and BMT, respectively, had achieved excellent clinical outcome at 3-months (odds
257 ratio [OR], 0.73; 95% CI, 0.24-2.2; $P = 0.78$). Early neurological improvement had been achieved
258 by 35.7% and 39.3% in MT+BMT and BMT groups, respectively (odds ratio [OR], 0.86; 95% CI,
259 0.29-2.5; $P = 1.00$).

260
261 For the safety outcome, the mortality rate was comparable in both groups (7% in
262 MT+BMT treated patients vs. 10.7% in patients with BMT; odds ratio [OR], 0.64; 95% CI, 0.1-
263 4; $p = 1.00$). Vessel perforation during the procedure occurred in one patient and led to
264 symptomatic ICH (3.6%). Asymptomatic ICH occurred in 3 patients in the MT+BMT group
265 (10.7%), and one patient in the BMT group (3.6%, $p = 0.61$) (**Table 2**).

266 Discussion

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3 267 The main findings of our study found that both mechanical thrombectomy and best
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5 268 medical treatment could achieve similar rates of good and excellent clinical outcome in distal
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7 269 vessel occlusions despite of the final recanalization rate in the patients treated by MT+BMT
8
9 270 was significantly higher than those in the BMT group. Noting that patients treated by MT+BMT
10
11 271 were the only complicated by symptomatic ICH. The 3-months mortality rate was comparable
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13 272 between both groups.

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16 274 Our results were comparable with those showed by a recent metanalysis by Waqas et
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18 275 al.[11] comparing MT+BMT with BMT only in the management of patients with distal vessel
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20 276 occlusions. This metanalysis had found 77 % successful recanalization of mTICI \geq 2B, 54.7%
21
22 277 good outcome of 3-months mRS \leq 2, 16.5% 3-months mortality rate, and 5.8 % symptomatic
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24 278 ICH. However, this study did not demonstrate a significant difference between both modalities
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26 279 in the management of such patients.

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30 281 Moreover, our results were comparable with a recent large multicenter study by
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32 282 Anadani et al. 2021, studying primary distal vessel occlusions (M3, and anterior and posterior
33
34 283 cerebral arteries) treated by MT.[12] This study showed results of 78 % successful
35
36 284 recanalization of mTICI \geq 2B, 45% good outcome of 3-months mRS \leq 2, 19% 3-months mortality
37
38 285 rate, and 5 % significant and symptomatic ICH.

39 286

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41 287 However, our results were more favorable than those showed by the metanalysis from
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43 288 the HERMES collaborators (mRS score \leq 1 in 27%, and mRS score \leq 2 in 46%). [13] This may be
44
45 289 explained by the differences and non-homogenous cut off point to define distal vessel
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47 290 occlusions; as M2 occlusion was considered to start just after the origin of the anterior
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49 291 temporal artery, bringing no evident landmark between distal M1 segment and proximal M2
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51 292 segment. [13]

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55 294 It is noteworthy that the distal occlusions have not been defined homogenously across
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57 295 all the previous results. Regarding our study, we have defined distal MCA occlusions as
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59 296 occlusions located distally to the insula's mid-height of the M2 segment according to Fischer's

297 classification. [6] On contrary to other studies, considering M2 occlusions starting just by M1
298 bifurcation or the reflecting upward segment [14], we chose the insula's mid-height as a
299 landmark to define distal M2 occlusions, since we think that proximal M2 occlusions are very
300 close to distal M1 occlusions and cannot be considered as distal occlusions.

301
302 Recently, a consensus regarding the precise definition of distal vessel occlusion has
303 been published, which might help to resolve this conflict and better delineating the guidelines
304 to treat such patients. This consensus sheds the light on the importance of evaluating the
305 vessel diameter beside its distal location as both represent a real challenge to navigate
306 through and recanalize safely and efficiently.[1] We did not retain the use of a size threshold
307 to define a distal occlusion in our study, since we believe that measuring the size proximal to
308 an occluded vessel is highly imprecise to evaluate the target artery's size.

309
310 Although the efficacy of MT+BMT in patients with distal vessel occlusion is still unclear,
311 previous retrospective studies and systematic reviews reported encouraging results.[15, 16]
312 Of these, only a few studies compared the efficacy and safety of MT+BMT with those of
313 medical treatment.[14, 17-20] Interestingly, these comparative studies are still having
314 conflicting results. Meyer et al. 2021[21], Miura et al. 2019 [14] and Sarraj et al. 2016 [17] have
315 shown significant higher efficacy of MT+BMT than the medical management. By contrary, Rai
316 et al. 2013 [18], Qureshi et al. 2017 [19] and Nagel et al. 2020 [20] did not find significant
317 difference between both strategies of management.

318
319 Denoting that only our study and Nagel et al.'s study [20] included all distal occlusions
320 sites (M3, anterior and posterior cerebral arteries) in addition to M2 occlusions. However,
321 Nagel et al. 2020 [20] only included patients with minor strokes (NIHSS ≤ 5) despite those distal
322 vessel occlusions frequently cause disabling symptoms if an eloquent area is affected.[1]

323
324 Yet, there is neither consensus on clinical selection criteria nor uniform imaging criteria
325 for MT for DVOs patients. Several studies used an NIHSS threshold of ≥ 6 , as it is currently
326 recommended for LVOs. However, a recent data analysis has shown that more than 30% of
327 DVOs patients have a baseline NIHSS < 6 . Moreover, the variety of clinical symptoms of DVOs,

328 which are dependent on the eloquence of the affected area, also seems to play an important
1
2 329 role in the complexity of decision-making. [22]

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6 331 Furthermore, NIHSS is heavily focused on motor function and thus, unable to capture
7
8 332 the more subtle domain-specific impairment in DVOs stroke-related disability. Therefore,
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10 333 more fine-grained scales or language and cognitive evaluations should be used in DVOs. [23]

11 334
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13 335 More than eighty percent of our patients underwent MT under conscious sedation, as
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15 336 our institute protocol is to initiate MT with conscious sedation with potential conversion to
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17 337 general anaesthesia (GA) if patient presents agitation or excessive motion. However, the
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19 338 higher anatomical variability in distal vessels in relation to proximal vessels and the need for
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21 339 an excellent roadmap to navigate through distally located clots seem to bring GA more
22
23 340 beneficial by complete elimination of the patient's movement. Thus, further trials
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25 341 investigating impact of GA on functional outcome in DVOs are warranted.

26 342
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28 343 From a technical perspective in M2 and M3 occlusions, despite lack of statistical
29
30 344 evidence in our cohort, it was observed that the navigation through the superior division was
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32 345 more challenging with excessive microwire manipulation than the inferior one. A possible
33
34 346 explanation for this is that superior divisions are usually more angulated and tortuous than
35
36 347 the inferior ones. A recent retrospective study compared MT in superior and
37
38 348 inferior division occlusions had found that perforations were non-significantly more frequent
39
40 349 in superior division occlusions compared to inferior division occlusions.[24]

41 350
42
43 351 Distal vessel occlusions are still managed for now subjectively on case-by-case basis,
44
45 352 according to the dispersion of the operator, the degree of vessel tortuosity and the different
46
47 353 institutional protocols. Indeed, distal vessel occlusions management warrant randomised
48
49 354 clinical trials to better precise the selecting criteria of patients who could benefit from
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51 355 MT+BMT in a safe manner, especially those having disabling symptoms despite of the small
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53 356 calibre or the distality of the occluded vessel.

360 **Study limitations**

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4 362 Our study suffers some limitations. First, the monocentric and retrospective fashion of
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6 363 the study. Second, the patient selection for MT+BMT and the devices used for thrombectomy
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8 364 was performed case by case and according to the treating neurologist or
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10 365 neurointerventionalist's choice, **without predefined fixed clinical or radiological criteria;**
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12 366 rendering additional bias to our results. This bias is underlined by the difference of stroke
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14 367 severity between the two cohorts before the propensity score matching. Moreover, the
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16 368 continuous evolution by iterative studies in the eligibility criteria for thrombolysis adds more
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18 369 biases to the study. Finally, the heterogeneity regarding the precise definition of distal vessels
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20 370 between different studies rendering more bias on comparing our results to other trials.
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25 373 **Conclusion**

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28 374 Mechanical thrombectomy and best medical treatment seem to be comparable
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31 375 regarding the effectiveness and safety in the management of patients with distal vessel
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34 376 occlusions. However, further investigations through randomized studies with larger samples
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36 377 are warranted.
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384 **References**

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- 385 1. Saver, J.L., et al., *Thrombectomy for Distal, Medium Vessel Occlusions: A Consensus Statement on Present Knowledge and Promising Directions*. Stroke, 2020. **51**(9): p. 2872-2884.
- 386 2. Berkhemer, O.A., et al., *A randomized trial of intraarterial treatment for acute ischemic stroke*. N Engl J Med, 2015. **372**(1): p. 11-20.
- 387 3. Campbell, B.C., et al., *Endovascular therapy for ischemic stroke with perfusion-imaging selection*. N Engl J Med, 2015. **372**(11): p. 1009-18.
- 388 4. Berkhemer, O.A., W.H. van Zwam, and D.W. Dippel, *Stent-Retriever Thrombectomy for Stroke*. N Engl J Med, 2015. **373**(11): p. 1076.
- 389 5. Ospel, J.M., et al., *Clinical Course of Acute Ischemic Stroke Due to Medium Vessel Occlusion With and Without Intravenous Alteplase Treatment*. Stroke, 2020. **51**(11): p. 3232-3240.
- 390 6. Fischer, E., *Die Lageabweichungen der vorderen Hirnarterie imGefäßbild*. Zentralbl Neurochir, 1938. **3**: p. 300-313.
- 391 7. Shapiro, M., et al., *Neuroanatomy of the middle cerebral artery: implications for thrombectomy*. J Neurointerv Surg, 2020. **12**(8): p. 768-773.
- 392 8. *Tissue plasminogen activator for acute ischemic stroke*. N Engl J Med, 1995. **333**(24): p. 1581-7.
- 393 9. Zaidat, O.O., et al., *Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement*. Stroke, 2013. **44**(9): p. 2650-63.
- 394 10. Hacke, W., et al., *Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke*. N Engl J Med, 2008. **359**(13): p. 1317-29.
- 395 11. Waqas, M., et al., *Mechanical thrombectomy versus intravenous thrombolysis for distal large-vessel occlusion: a systematic review and meta-analysis of observational studies*. Neurosurg Focus, 2021. **51**(1): p. E5.
- 396 12. Anadani, M., et al., *Mechanical Thrombectomy for Distal Occlusions: Efficacy, Functional and Safety Outcomes: Insight from the STAR Collaboration*. World Neurosurg, 2021. **151**: p. e871-e879.
- 397 13. Menon, B.K., et al., *Efficacy of endovascular thrombectomy in patients with M2 segment middle cerebral artery occlusions: meta-analysis of data from the HERMES Collaboration*. J Neurointerv Surg, 2019. **11**(11): p. 1065-1069.
- 398 14. Miura, M., et al., *Endovascular therapy for middle cerebral artery M2 segment occlusion: subanalyses of RESCUE-Japan Registry 2*. J Neurointerv Surg, 2019. **11**(10): p. 964-969.
- 399 15. Wang, J., et al., *Efficacy and safety of mechanical thrombectomy for M2 segment of middle cerebral artery: a systematic review and meta-analysis*. 2020.
- 400 16. Salahuddin, H., et al., *Mechanical Thrombectomy for Middle Cerebral Artery Division Occlusions: A Systematic Review and Meta-Analysis*. Interv Neurol, 2017. **6**(3-4): p. 242-253.
- 401 17. Sarraj, A., et al., *Endovascular Therapy for Acute Ischemic Stroke With Occlusion of the Middle Cerebral Artery M2 Segment*. JAMA Neurol, 2016. **73**(11): p. 1291-1296.
- 402 18. Rai, A.T., et al., *Endovascular therapy yields significantly superior outcomes for large vessel occlusions compared with intravenous thrombolysis: is it time to randomize?* J Neurointerv Surg, 2013. **5**(5): p. 430-4.
- 403 19. Qureshi, A.I., M.A. Saleem, and E. Aytac, *Comparison of Endovascular Treatment with Intravenous Thrombolysis for Isolated M2 Segment of Middle Cerebral Artery Occlusion in Acute Ischemic Stroke*. J Vasc Interv Neurol, 2017. **9**(5): p. 8-14.
- 404 20. Nagel, S., et al., *Distal arterial occlusions in patients with mild strokes - is endovascular therapy superior to thrombolysis alone?* J Stroke Cerebrovasc Dis, 2020. **29**(7): p. 104868.
- 405 21. Meyer, L., et al., *Thrombectomy for secondary distal, medium vessel occlusions of the posterior circulation: seeking complete reperfusion*. J Neurointerv Surg, 2021.
- 406 22. Ospel, J.M. and M. Goyal, *A review of endovascular treatment for medium vessel occlusion stroke*. J Neurointerv Surg, 2021. **13**(7): p. 623-630.

434 23. Marchal, A., et al., *Endovascular Thrombectomy for Distal Medium Vessel Occlusions of the*
1 435 *Middle Cerebral Artery: A Safe and Effective Procedure.* World Neurosurg, 2022.

2 436 24. Seker, F., et al., *Comparison of Superior and Inferior Division Occlusions Treated with*
3 437 *Endovascular Thrombectomy.* Clin Neuroradiol, 2020. **30**(2): p. 339-343.

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454 **Figure captions**

455 **Figure. 1** Study flowchart

456 **Figure. 2** A 89-year-old male presenting a sudden onset of right-sided hemiplegia and aphasia,
457 with initial NIHSS of 18. **(A)** MRI brain diffusion-weighted imaging shows recent infarction in
458 left middle cerebral artery territory (white arrow). **(B)** MRI brain T2 echo gradient sequence
459 shows the occluding clot (black arrow). **(C, D)** Left internal carotid artery (ICA) digital
460 subtraction angiography (DSA) in posterior-anterior (PA) and lateral projections shows left M2
461 segment occlusion (black arrows). **(E, F)** Left ICA DSA in PA and lateral projections shows
462 complete recanalization (mTICI 3) after one passage using a 3x20 mm Trevo XP ProVue
463 stentriever (Stryker Neurovascular, Fremont, CA, USA) in combination with proximal
464 aspiration. NIHSS after 24 hours was 8, NIHSS at discharge was 6 and 3-months mRS was 2.

650 patients with acute ischemic stroke treated by mechanical thrombectomy between 2015 and 2020

663 patients with acute ischemic stroke treated by best medical treatment alone between 2006 and 2015

44 patients met the inclusion criteria for distal vessel occlusion

36 patients met the inclusion criteria for distal vessel occlusion

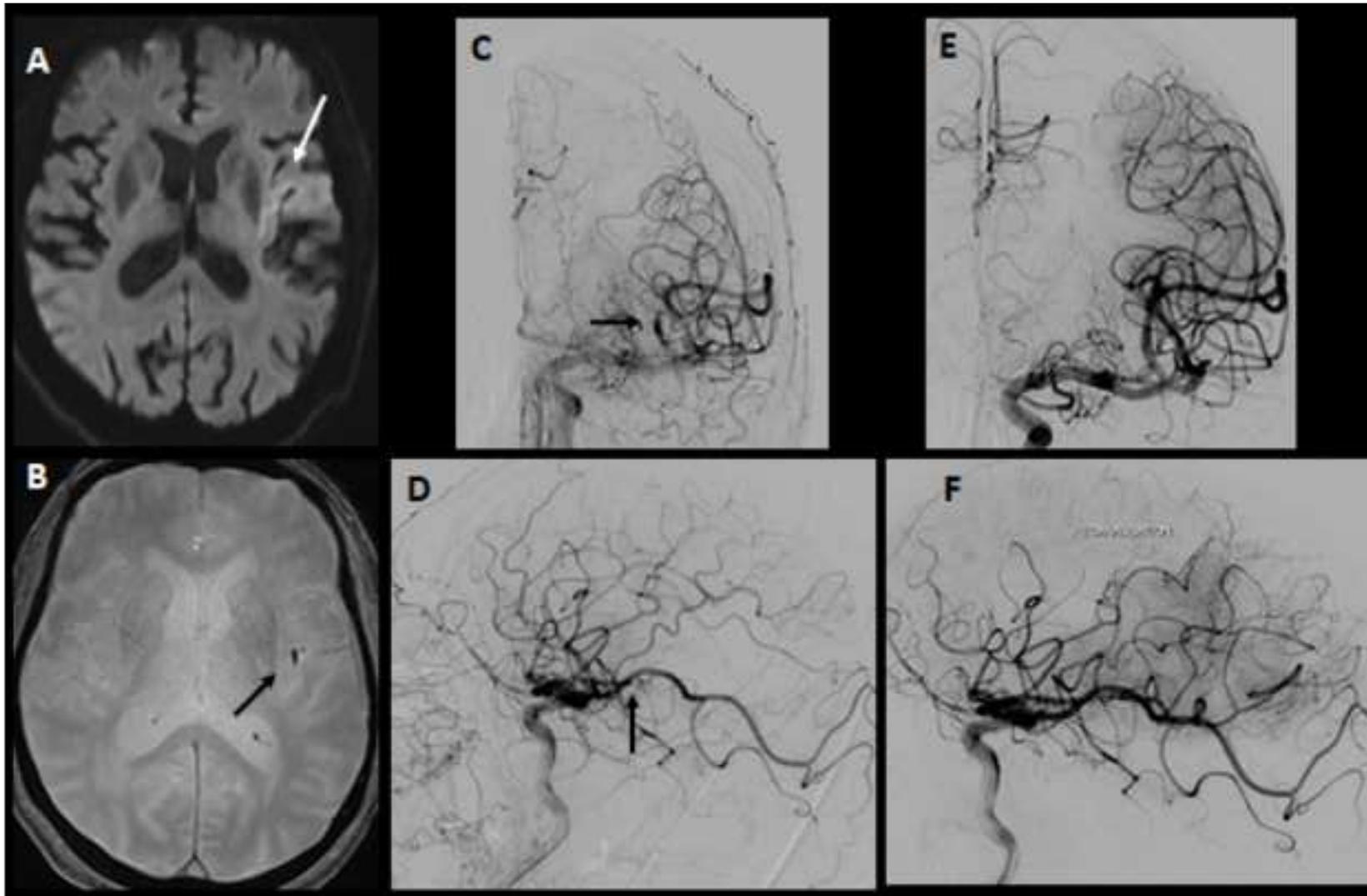
After **propensity score matching** based on initial NIHSS, age, and receiving intravenous thrombolysis

*28 patients included in the **mechanical thrombectomy** group*

*28 patients included in the **best medical treatment** group*

- Good clinical outcome=53.6%
- Excellent clinical outcome= 32%
- Mortality rate=7%
- Symptomatic ICH=3.6%

- Good clinical outcome=57%
- Excellent clinical outcome=39.3%
- Mortality rate=10.7%
- Symptomatic ICH=0%



1 **Table.1 Patients' baseline demographics and procedural parameters**

Parameter	Entire cohort			Propensity score matched cohort		
	MT+BMT Group (n=44)	BMT Group (n=36)	P Value	MT+BMT Group; (n=28)	BMT Group; (n=28)	P Value
Age	78 (64-85)	70 (57-78)	0.04*	74 (61-83)	73 (63-79)	0.61
Initial NIHSS	11 (7-21)	6 (3-10)	<0.001*	10 (5-17)	7 (4-11)	0.28
NIHSS at 24 hours	10 (3-16)	4 (2-8)	0.008*	10 (4-16)	5 (3-9)	0.15
Sex males, N (%)	25/44 (56.8)	24/36 (66.7)	0.49	17/28 (60.7)	18/28 (64.3)	1.00
Vascular risk factors						
HTN N, (%)	21/44 (47.7)	21/36 (58.3)	0.38	13/28 (46.4)	15/28 (53.6)	0.79
DM N, (%)	5/44 (11.4)	9/36 (25)	0.14	4/28 (14.3)	8/28 (28.6)	0.33
AF N, (%)	18/44 (40.9)	8/36 (22.2)	0.1	13/28 (46.4)	7/28 (25)	0.16
IHD N, (%)	15/44 (34)	13/36 (36)	1.00	8/28 (28.6)	11/28 (39.3)	0.57
Smoker N, (%)	14/44 (31.8)	9/36 (25)	0.62	9/28 (32)	7/28 (25)	0.77
Dyslipidemia N, (%)	13/44(29.5)	9/36 (25)	0.8	8/28 (28.6)	8/28 (28.6)	1.00
IVT N, (%)	28/44 (63.6)	15/36 (41.7)	0.07	16/28 (57)	15/28 (53.6)	1.00
Patients under GA N, (%)	7/44 (15.9)	NA	NA	3/28 (10.7)	NA	NA

Time between SO to hospital's door	119 (82-199)	164 (119-233)	0.11	117 (87- 185)	139 (114-196)	0.32
Site of occlusion						
M2 (%)	24/44 (54.5)	7/36 (19.4)		15/28 (53.6)	5/28 (17.9)	
M3 (%)	5/44 (11.4)	9/36 (25)		2/28 (7.1)	7/28 (25)	
P1 (%)	8/44 (18.2)	1/36 (2.8)		6/28 (21.4)	1/28 (3.6)	
P2 (%)	4/44 (9.1)	7/36 (19.4)		4/28 (14.3)	6/28 (21.4)	
P3 (%)	0 (0)	10/36 (27.8)	<0.001*	0/28 (0)	7/28 (25)	<0.001*
A1 (%)	1/44 (2.3)	0/36 (0)		0/28 (0)	0/28 (0)	
A2 (%)	1/44 (2.3)	2/36 (5.6)		0/28 (0)	2/28 (7.1)	
A3 (%)	1/44 (2.3)	0/36 (0)		1/28 (3.6)	0/28 (0)	

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Numbers are median and IQR. MT indicates mechanical thrombectomy, **BMT**; best medical treatment, **IQR**; interquartile range; **NIHSS**; National Institutes of Health Stroke Score, **HTN**; hypertension, **DM**; diabetes mellitus, **AF**; atrial fibrillation, **IHD**; ischemic heart disease, **IVT**; intravenous thrombolysis, **GA**; general anesthesia, **SO**; stroke onset, * indicates $P < 0.05$.

10 **Table 2. Clinical outcomes**

Parameter	Entire cohort			Propensity score matched cohort		
	MT+BMT Group; (n=44)	BMT Group; (n=36)	<i>P</i> Value	MT+BMT Group; (n=28)	BMT Group; (n=28)	<i>P</i> Value
Successful recanalization (AOL ≥ 2) N, (%)	40/44 (90.9)	17/36 (47.2)	<0.001*	24/28 (85.7)	15/28 (53.6)	0.02*
Successful reperfusion (mTICI ≥ 2B) N, (%)	34/44 (77.3)	NA	NA	20/28 (71.1)	NA	NA
ENI N, (%)	20/44 (45.5)	14/36 (38.9)	0.65	10/28 (35.7)	11/28 (39.3)	1.00
mRS 0–2 at 3 months N, (%)	21/44 (47.7)	21/36 (58.3)	0.38	15/28 (53.6)	16/28 (57.1)	1.00
mRS 0–1 at 3 months N, (%)	13/44 (29.5)	14/36 (38.9)	0.48	9/28 (32.1)	11/28 (39.3)	0.78

Mortality at 3 months N, (%)	8/44 (18.2)	5/36 (13.9)	0.76	2/28 (7.1)	3/28 (10.7)	1.00
Symptomatic ICH N, (%)	2/44 (4.5)	0 (0)	0.5	1/28 (3.6)	0 (0)	1.00
Asymptomatic ICH N, (%)	4/44 (9.1)	1/36 (2.8)	0.37	3/28 (10.7)	1/28 (3.6)	0.61

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12 **MT**; mechanical thrombectomy, **BMT**; best medical treatment, **OR**; odds ratio, **95%CI**; confidence
13 interval; **AOL**: Arterial occlusion lesion scale, **mTICI**; modified thrombolysis in cerebral infarction scale,
14 **ENI**; indicates Early neurological improvement, **mRS**; modified Rankin Scale, **ICH**; intracranial hemorrhage,
15 **NA**; not applicable, *When P<0.05.

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