Thrombectomy and Thrombolysis of Isolated Posterior Cerebral Artery Occlusion

Cognitive, Visual, and Disability Outcomes

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Background and Purpose—We investigated efficacy and safety of acute revascularization with intravenous thrombolysis (IVT) and endovascular treatment (EVT) in ischemic stroke from isolated posterior cerebral artery occlusion, by assessing recanalization, disability, visual, cognitive outcomes, and hemorrhagic complications.

Methods—For this retrospective single-center cohort study, we selected all consecutive patients with stroke with isolated posterior cerebral artery occlusion from the Acute Stroke Registry and Analysis of Lausanne registry between January 2003 and July 2018, and compared (1) IVT with conservative treatment (CTr) and (2) EVT to best medical therapy (BMT, ie, CTr or IVT) in terms of 3-month disability and visual field defect, and cognitive domains impaired after stroke. Unadjusted analysis, multivariable logistic regression, and propensity score matched analyses were performed.

Results—Among 106 patients with isolated posterior cerebral artery occlusion, 21 received EVT (13 bridging), 34 IVT alone, and 51 CTr. Median age was 76 years, 47% were female and median National Institutes of Health Stroke Scale score was 7. Complete 24-hour recanalization was more frequent with IVT than CTr (51% versus 9%; OR [95% CI]=10.62 [2.13–52.92]) and with EVT compared with BMT (68% versus 34%; OR [95% CI]=4.11 [1.35–12.53]). Higher proportions of good disability, visual and cognitive outcomes were observed in IVT versus CTr, $_{adj}$ORs (95% CI)=1.65 (0.60−4.52), 2.01 (0.58−7.01), 2.94 (0.35−24.4), respectively, and in EVT versus BMT, $_{adj}$ORs (95% CI)=1.44 (0.51−4.10), 4.28 (1.00−18.29), 4.37 (0.72−26.53), respectively. Hemorrhagic complications and mortality did not increase with IVT or EVT.

Conclusions—We show increased odds of recanalization following IVT and even higher after EVT. We observed a trend for a positive effect on disability, visual, and cognitive outcomes with IVT over CTr and with EVT over BMT. **(*Stroke*. 2020;51:254-261. DOI: 10.1161/STROKEAHA.119.026907.)**

Key Words: conservative treatment ■ female ■ posterior cerebral artery ■ stroke ■ visual fields

Ischemic strokes in the posterior cerebral artery (PCA) territory have a clinical presentation distinct from carotid territory strokes, with peculiar neurological and cognitive deficits.[1] Often considered as less disabling, PCA strokes may lead to neuropsychological deficits and visual symptoms significantly affecting a patient's functional independence and quality of life.[1,2] While the general clinical and radiological features of PCA strokes have been well described,[1,3] little is known about the response to acute revascularization therapies in stroke from isolated PCA occlusion (IPCAO). According to current evidence, these patients should receive intravenous thrombolysis (IVT) within 4.5 hours from symptom onset (or in presence of mismatch between MRI diffusion weighted imaging [DWI] and fluid attenuated inversion recovery [FLAIR] on magnetic resonance imaging for patients with unknown stroke onset).[4,5] However, these recommendations come from clinical trials performed on broad-spectrum stroke populations, where information about acute vascular occlusion was largely missing and PCA strokes were likely underrepresented or in some cases excluded.[6] Regarding endovascular treatment (EVT), there is no randomized data on PCA occlusion as none of the pivotal trials included these patients. While it would be straightforward to assume that a rapid recanalization leads to better outcome also in this context, there are currently no specific studies on the impact of acute revascularization therapies for PCA occlusion.

In this retrospective study, we aimed to assess patients with acute ischemic stroke (AIS) from IPCAO treated with EVT (direct or bridging after IVT), IVT alone, or conservative treatment (CTr) inspecting the rate of arterial recanalization, early neurological improvement, disability and visual field

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defect at 3 months, and subacute poststroke cognitive impairment. Furthermore, we evaluated hemorrhagic complications and 3-month mortality as measures of safety.

Methods

Data Availability Statement

Any data not published within the article is available. Anonymized data can be shared by request from any qualified investigator.

Patient Selection

The study used the Acute STroke Registry and Analysis of Lausanne (ASTRAL) that collects all AIS admitted to the stroke unit and intensive care unit of the Lausanne University Hospital, presenting within 24 hours of stroke onset or last proof of good health.[7] From all consecutive patients entered in ASTRAL between January 1, 2003 and July 1, 2018, we selected cases with good quality vascular imaging performed within 24 hours of stroke onset (or last proof of good health). We retained cases showing unilateral and isolated complete PCA occlusion in P1 segment (in nonfetal PCA), posterior communicating artery (in fetal PCA), or P2 segment potentially accessible for endovascular treatment. We considered PCA occlusion as isolated in absence of basilar artery occlusion, stenosis of the top of the basilar artery and acute occlusion of other intracranial arteries (middle and anterior cerebral arteries or cerebellar arteries). Tandem lesions with extracranial vertebral artery stenosis or occlusion were not an exclusion criterion from the study. We adopted these criteria to identify a stroke population as homogeneous as possible, minimizing confounding factors, primarily brain stem involvement. In addition, to have comparable treatment groups, we excluded patients with distal PCA occlusion not accessible to EVT (see below) and PCA subocclusion. The presence of acute radiological, asymptomatic ischemic lesions in other territories was not an exclusion criterion.

Data Collection

ASTRAL includes a large set of prespecified demographic, clinical, radiological and biological variables. Neuroimaging data consists mainly of acute noncontrast CT, cervico-cerebral CT angiography and CT perfusion following a prespecified protocol.[7] Follow-up imaging with brain CT or magnetic resonance imaging at ≈24 hours is routinely performed in all patients receiving acute recanalization treatment and in the remaining patients when clinically indicated. In patients with initial arterial occlusion, recanalization is routinely reassessed at 24 hours using CT-angiography, MR-angiography, or transcranial Doppler imaging. Collection and definition of neuroradiological variables in ASTRAL registry as well as patients' treatment are further detailed in the online-only Data Supplement.

Outcome Assessment

Radiological efficacy outcome was recanalization status (complete recanalization versus partial or absent recanalization; as defined in the online-only Data Supplement) on 24-hour follow-up imaging. Short-term clinical outcomes were difference between baseline National Institutes of Health Stroke Scale (NIHSS) and NIHSS at 24 hours and 7 days (Δ-NIHSS).

We determined 3-month disability outcome using modified Rankin Scale (mRS) at the routine clinical examination in the outpatient clinic (or by a structured telephonic interview), nonblinded to acute treatment.[8] We considered as favorable disability outcome 3-month mRS score ≤1 for patients without prestroke disability (ie, prestroke mRS score=0), while for patients with prestroke disability we defined favorable outcome as a maximum of one point increase in the 3-month mRS as compared with the prestroke mRS (which can be resumed as difference between 3 month and prestroke mRS, ie, Δ-mRS score, ≤1). Only 2 patients missed the 3-month mRS assessment and were kept in the study as subacute cognitive evaluation was available but were excluded from the disability outcome analysis.

In patients with clinical evidence of visual field defects at stroke onset, we assessed visual outcome using the confrontation test at the routine clinical examination in the stroke outpatient clinic, 3 months after stroke onset. Good visual outcome was considered as complete visual field normalization (versus quadrantopsia or complete hemianopsia).

In ASTRAL-registered patients, certified neuropsychologists routinely evaluate cognition in the subacute hospital phase. We considered the cognitive outcome favorable if 2 or less cognitive domains were impaired among language, praxia, visual gnosia, unilateral spatial neglect, long-term memory, executive functions, attention.[9] Details of neuropsychological evaluations, cognitive domains assessed, and respective test usually performed are provided in the online-only Data Supplement.

Safety outcomes were death within 90 days and the occurrence of symptomatic intracranial hemorrhage (SICH) on follow-up imaging defined according to ECASS (European Cooperative Acute Stroke Study) II criteria. For patients undergoing endovascular treatment, an additional safety outcome was the rate and type of complications occurring during the endovascular procedure.

Statistical Analysis

The first analysis sought to measure impact of IVT in patients with IPCAO by comparing IVT-treated patients with those receiving CTr (ie, no IVT or EVT).

The second analysis assessed the effect of EVT. As a substantial proportion of the patients treated by thrombectomy (8/21) arrived in a late time window (>4.5 hours from symptom onset) and underwent direct EVT, we compared patients treated with EVT to patients receiving the best medical therapy (BMT, ie, IVT or CTr).

For both analyses, we compared baseline clinical and radiological features as well as outcome measures of the 2 treatment groups using Fisher exact test for categorical data and Mann-Whitney *U* tests for numeric variables. For each outcome variable, we calculated unadjusted and adjusted ORs, the latter obtained from multivariable logistic regression models, including as independent variables the type of treatment together with variables independently associated with outcome (selected, using a stepwise backward elimination procedure, from those showing association with outcome in the univariate analysis at the $P<0.2$ level).

In addition, for both analyses, we used a 1:1 propensity score weighting method to match the treatment groups (in analysis 1: IVT versus CTr; analysis 2: EVT versus BMT). This has been validated also for small sample sizes,[10] which is the case in our study. Two propensity score models were fitted by logistic regression to assign a probability to each patient of belonging to each of the treatment groups. Covariates considered were age, baseline NIHSS, prestroke disability, site of arterial occlusion [P1 versus P2], and presence of visual field deficits at stroke onset for both analysis 1 and 2. For the latter, IVT was also entered as covariate. Outcome measures (mRS, visual field and cognitive deficits) were then compared in matched cohorts to obtain propensity score–adjusted ORs.

We performed statistical analysis with R statistical software, version 3.3.2. $P<0.05$ were considered significant. As this was an exploratory analysis, no correction for multiple analyses was necessary.

This observational study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

The ethics commission for research on humans of the Canton of Vaud approved collection, analysis and publication of data from ASTRAL (no specific patients' consent was required for this study).

Results

During the observation period, 4888 consecutive patients with AIS were entered into the ASTRAL registry. After applying the inclusion and exclusion criteria of the study (Figure I in the online-only Data Supplement), we kept 106 patients with isolated proximal PCA occlusion in the final study population. The median age was 76 years (IQR, 67.0–82.5 years) and 47% were

females (n=50). Fifty-one patients (48%) received conservative treatment, 34 (32%) had IVT, and 21 (20%) underwent EVT (13 bridging therapy and 8 direct EVT). A description of the overall population and treatment groups, including treatment delays, is given in Table 1 and Table I in the online-only Data Supplement. The reasons for withholding IVT in the conservative treatment group and in patients undergoing direct endovascular treatment are listed in Table II in the online-only Data Supplement.

Endovascular treatment was performed with stent retrievers in 15 patients and with Direct Aspiration First Pass Technique in 4. In 1 patient, the endovascular procedure consisted of intraarterial administration of urokinase without mechanical treatment and in the remaining patient no device was used due to an early procedural complication (PCA perforation). Details of endovascular procedures are listed in Table III in the online-only Data Supplement.

We assessed recanalization at 24 hours in 74/106 (70%) patients, with complete recanalization observed in 32/74 (43%). Forty-five out of 104 patients (43.3%) had good functional outcome (3-month Δ-mRS score ≤1). A visual field defect was present at baseline in 83/106 patients (78%) that resolved at follow-up in 25/83 (30%). We acquired neuropsychological evaluation between 1 and 10 days (median 4 days) after stroke onset in 68/106 (64%) patients (60 right-handed), including 34 EVT, 22 IVT, and 12 CTr patients. Fifteen (22%) had a favorable neuropsychological outcome.

Regarding safety outcomes, SICH was observed in 2/82 (1.6%; 24 patients, all in the CTr group, had no follow-up imaging at 24 hours) and 3-month mortality rate was 16%, n=17 (in-hospital mortality was 6.6%, n=7).

IVT Versus Conservative Treatment

Age, vascular risk factors, prestroke disability, clinical presentation, stroke cause, and site of vascular occlusion (P1 versus P2) were similar in the 2 groups (IVT versus CTr, see Table 1 and Table I in the online-only Data Supplement). Despite identical baseline NIHSS in the 2 groups, the IVT group had a lower proportion of patients with minor clinical deficits (defined as NIHSS ≤3). The IVT group displayed also a more frequent involvement of both deep and superficial PCA territories, a lower rate of stroke with unknown/wake-up onset, and a shorter delay from symptom onset to hospital arrival. Complete intracranial recanalization at 24 hours was significantly more frequent in patients treated with IVT (51% versus 9%, OR [95% CI]=10.62 [2.13–52.92], simulation analysis on missing data reported in Figure II in the online-only Data Supplement).

Patients treated with IVT had significantly greater NIHSS improvement at 24 hours, while the NIHSS difference at 7 days was similar in the 2 groups (Tables 2 and 3). The proportion of good functional outcome at 3 months was similar in the 2 groups (41.2% versus 40%), while we observed a

Table 1. Main Baseline Features of: the All Cohort; Conservative Treatment and IVT Groups; Best Medical Therapy and Endovascular Treatment Groups

	Total (n=106)	IVT (n=34)	Conservative Treatment (n=51)	*P* Value	Endovascular Treatment (n=21)	Best Medical Therapy (n=85)	*P* Value
Age	75.9 (67–82.5)	78.7 (69.5–85.8)	76.5 (67.2–81.1)	0.133	71 (64–78.2)	76.6 (68.3–83.8)	0.077
Female sex	50 (47.2%)	17 (50%)	20 (39.2%)	0.448	13 (61.9%)	37 (43.5%)	0.205
Baseline NIHSS	7 (4–11)	7 (4.9–12.1)	7 (3–12)	0.556	7 (5–8.3)	7 (4–12)	0.525
Minor neurological deficit (NIHSS, 0–3)	21 (19.8%)	4 (11.8%)	14 (27.4%)	0.342	3 (14.3%)	18 (21.2%)	0.052
Basline visual field defect	83 (78.3%)	29 (85.3%)	37 (72.5%)	0.264	17 (81%)	66 (77.7%)	0.973
Stroke topography				0.011			0.597
Deep (thalamus)	4 (3.8%)	0 (0%)	4 (7.8%)		0 (0%)	4 (4.7%)	
Superficial	19 (17.9%)	2 (5.9%)	13 (25.5%)		4 (19.1%)	15 (17.6%)	
Mixed (deep and superficial)	83 (78.3%)	32 (94.1%)	34 (66.7%)		17 (81%)	66 (77.7%)	
Occlusion site				0.808			0.357
P1	34 (32.1%; n=3 fetal)	9 (26.5%; n=2 fetal)	16 (31.4%; n=1 fetal)		9 (42.9%; n=0 fetal)	25 (29.4%; n=3 fetal)	
P2	72 (67.9%; n=4 fetal)	25 (73.5%; n=1 fetal)	35 (68.6%; n=2 fetal)		12 (47.1%; n=1 fetal)	60 (70.6%; n=3 fetal)	
Treatment delay							
Onset-to-door (min)	141.5 (75.9–366.1)	92.5 (68.8–129.7)	241 (83.7–734.5)	0.001	258 (97–318)	134 (70.7–427.7)	0.250
Door-to-IVT (min)	40 (26.3–56)	41 (32–60.3)	…	…	26 (21.3–46.7)*	41 (32–60.3)	0.097
Onset-to-IVT (min)	145 (107.5–200.8)	135 (106.7–175)	…	…	145 (113.3–255.3)	135 (106.7–175)	0.302
Onset-to-groin puncture (min)	…	…	…	…	290 (198–384)	…	…

For numerical variables are displayed median and interquartile range. *P* value of Fisher exact test for categorical data and Mann-Whitney *U* tests for numeric variables. Complete cohort description is provided in Table I in the online-only Data Supplement. IVT indicates intravenous thrombolysis; and NIHSS, National Institutes of Health Stroke Scale.

*Calculated for 13 patients receiving bridging therapy.

Table 2. Outcome Differences Between Conservative Treatment and IVT Groups

	Total (n=85)	IVT (n=34)	Conservative Treatment (n=51)	Unadjusted OR* (95% CI)
Intracranial recanalization at 24 h	19/55 (34.5%)	17/33 (51.5%)†	2/22 (9.1%)†	10.62 (2.13–52.92)¶
24-h Δ-NIHSS	−1 (−3 to 0)	−3 (−4 to −1)	0 (−2.1 to 0)	−1.94 (−3.37 to −0.52)¶
7-d Δ-NIHSS	−2 (−4.3 to −1)	−3 (−4.3 to −1)	−2 (−4.6 to −1)	+0.17 (−2.38 to +2.71)
3-mo Δ-mRS score, 0–1	34/84 (40.5%)	14/34 (41.2%)	20/50 (40%)	1.05 (0.43–2.55)
3-mo visual field normalization	17/67 (25.4%)	10/29 (34.5%)‡	7/38 (18.4%)‡	2.33 (0.76–7.16)
≤2 cognitive domains impaired	9/56 (16.1%)	5/22 (22.7%)§	4/34 (11.8%)§	2.21 (0.52–9.34)
SICH	1/61 (1.6%)	1/34 (2.9%)	0/27 (0%)	…‖
3-mo mortality	13/85 (15.3%)	6/34 (17.6%)	7/51 (13.7%)	1.35 (0.41–4.42)

Numerical variables are displayed median and interquartile range. CTr indicates conservative treatment; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; and SICH, symptomatic intracranial hemorrhage.

*For 24 h and 7 d, Δ-NIHSS are displayed the β coefficients obtained from linear regression model.

†Control imaging at 24 h not performed in 1 and 29 patients in IVT and CTr groups, respectively.

‡No visual field defect at baseline in 5 and 13 patients in IVT and CTr groups, respectively.

§Cognitive evaluation not available in 12 and 17 patients in IVT and CTr groups, respectively.

‖Not calculated because zero events in the conservative treatment group.

¶Significant result.

nonsignificant absolute 16% difference in visual field normalization at 3 months in favor of IVT over CTr (34.5% versus 18.4%, respectively), as well as a trend toward better cognitive outcome with IVT (Tables 2 and 3). In both adjusted and propensity score analyses, we observed a trend for better functional, visual and cognitive outcome in patients treated with IVT (Figure 1, upper). Variables used for adjustment in each logistic regression model are listed in Figure 1 legend. The frequency of SICH and 3-month mortality did not statistically differ between the 2 groups.

Endovascular Treatment (±IVT) Versus Best Medical Therapy

Patients undergoing endovascular treatment were nonsignificantly younger (median age 71 versus 76 years), had similar baseline features and a nonsignificant higher proportion of P1 occlusions compared with the BMT group (for details, see Table 1 and Table I in the online-only Data Supplement). Complete recanalization at 24 hours was achieved in 68% of patients undergoing EVT (34.5% in BMT group, OR [95% CI]=4.11 [1.35–12.53]). A trend for more pronounced NIHSS improvement at 24 hours and 7 days was observed in EVT patients (Tables 2 and 3). We observed a 15% absolute difference in the proportion of good outcome at 3 months in favor of the EVT group (55% versus 40.5%, EVT versus BMT, respectively), a 25% absolute difference in visual field normalization at 3 months (50% versus 25.4%, EVT versus BMT, respectively), and a significantly better cognitive outcome with EVT (50% versus 16.1%, EVT versus BMT, respectively); these differences reached statistical significance only for cognitive outcome (Tables 2 and 3). Multivariable and propensity score analyses confirmed the tendency of better outcomes with EVT but only visual outcome was

Table 3. Outcome Differences Between Best Medical Therapy and Endovascular Treatment

	Total (n=106)	Endovascular Treatment (n=21)	Best Medical Therapy (n=85)	Unadjusted OR* (95% CI)
Intracranial recanalization at 24 h	32/74 (43.2%)	13/19 (68.4%)†	19/55 (34.5%)†§	4.11 (1.35–12.53)¶
24-h Δ-NIHSS	−1 (−4 to 0)	−2.5 (−5 to −0.4)	−1 (−3 to 0)	−0.66 (−2.4 to +1.08)
7-d Δ-NIHSS	−3 (−5 to −1)	−3.5 (−6 to −1.4)	−2 (−4.3 to −1)	−0.15 (−3.1 to +2.79)
3-mo Δ-mRS, 0–1	45/104 (43.3%)	11/20 (55%)	34/84 (40.5%)	1.80 (0.67–4.80)
3-mo visual field normalization	25/83 (30.1%)	8/16 (50%)‡	17/67 (25.4%) ‡	2.94 (0.96–9.05)
≤2 cognitive domains impaired	15/68 (22.1%)	6/12 (50%)§	9/56 (16.1%) §	5.22 (1.37–19.9)¶
SICH	2/82 (2.4%)	1/21 (4.8%)	1/61 (1.6%)	3.00 (0.18–50.21)
3-mo mortality	17/106 (16%)	4/21 (19.1%)	13/85 (15.3%)	1.30 (0.38–4.50)

Numerical variables are displayed median and interquartile range. BMT indicates best medical therapy; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; and SICH, symptomatic intracranial hemorrhage.

*For 24 h and 7 d, Δ-NIHSS are displayed the β coefficients obtained from linear regression model.

†Control imaging at 24 h not performed in 2 and 30 patients in EVT and BMT groups, respectively.

‡No visual field defect at baseline in 5 and 18 patients in EVT and BMT groups, respectively.

§Cognitive evaluation not available in 9 and 29 patients in EVT and BMT groups, respectively.

¶Significant result.

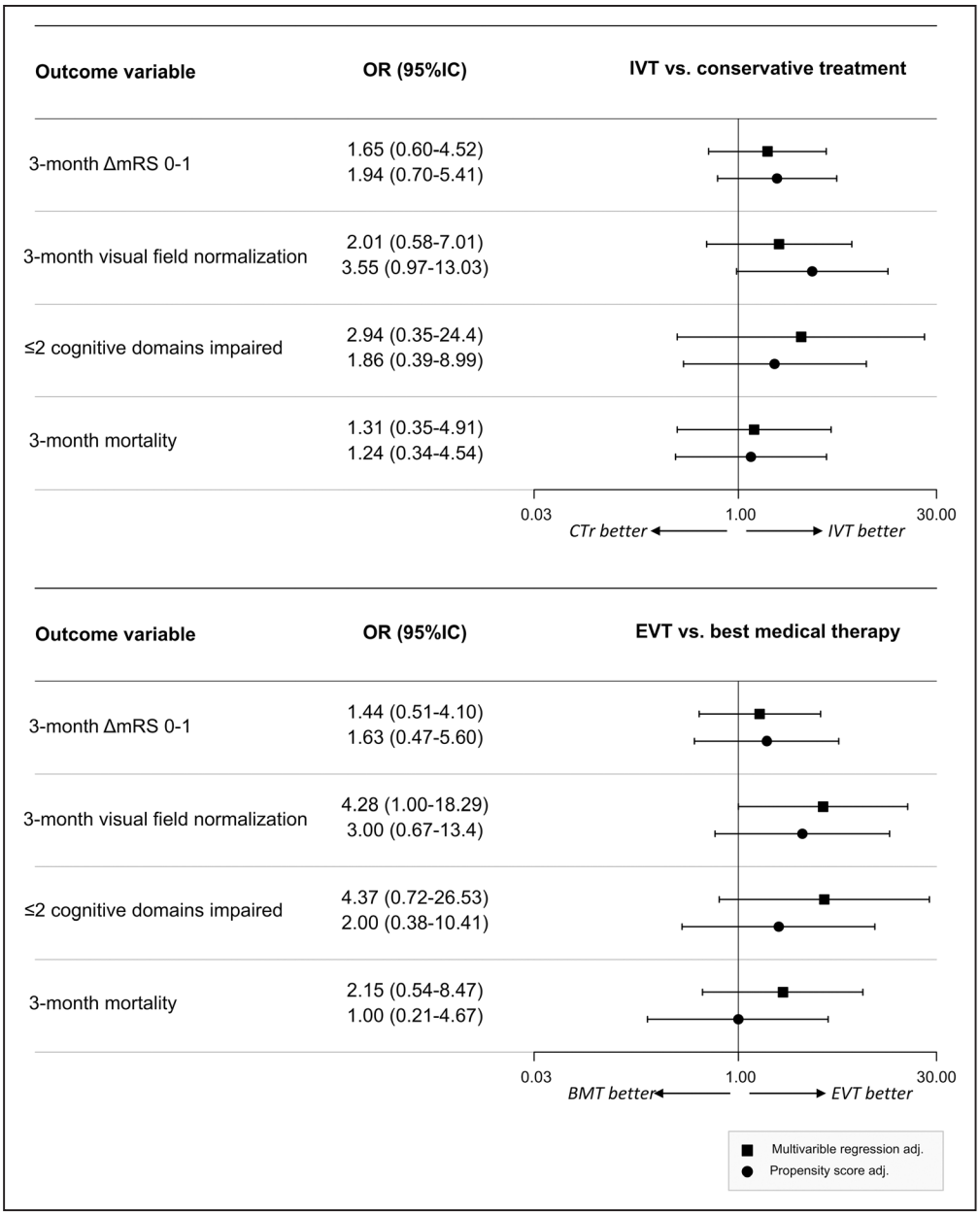

Figure 1. Odds ratios (ORs) and 95% CIs resulting from multivariable logistic regression analysis (squares) and propensity score matched analysis (circles) on the treatment effect of intravenous thrombolysis (IVT) vs conservative treatment (CTr) (upper) and endovascular treatment (EVT) vs best medical therapy (BMT; lower) on functional, visual, cognitive outcomes and mortality. Upper: ORs of multivariable analysis (squares) are adjusted for: age, baseline National Institutes of Health Stroke Scale (NIHSS), prestroke cognitive deficit (cognitive outcome); baseline NIHSS, stroke topography, chronic ischemic lesion (visual outcome); age, baseline NIHSS, stroke topography (modified Rankin Scale [mRS]); age, baseline NIHSS (mortality). Lower: ORs of multivariable analysis (squares) are adjusted for the same variables as in upper panel, plus IVT; visual field analysis also adjusted for onset-to-door time.

borderline significant in multivariable analysis (Figure 1, lower). The frequency of SICH and 3-month mortality were similar in the 2 groups.

Additional Neuropsychological Results

Sixteen patients had cognitive impairment before stroke onset (mild in 9, moderate-to-severe in 7), without significant differences between the treatment groups (Table I in the online-only Data Supplement). Overall, of the 7 cognitive domains tested at subacute examination, the median number of domains impaired was 4. Attention, executive functions, and anterograde memory were the most frequently harmed. In both CTr and IVT, the median number of cognitive domains impaired was 4 (IQR, 3–5; P=0.311, Mann-Whitney U test) while 2.5 (IQR, 1.4–4) in the EVT group (versus BMT; P=0.045, Mann-Whitney U test). For each cognitive domain tested, patients treated with EVT had a lower frequency of abnormal performance than those treated with IVT that in turn performed better compared with the CTr group (Figure 1). Differences between the 3 groups were significant (χ^2 for trend test) for praxies (P=0.002), anterograde memory (P=0.017), and executive functions (P=0.032), while a nonsignificant trend was observed for language and, to a lesser extent, for unilateral spatial neglect and attention. Cognitive rehabilitation was

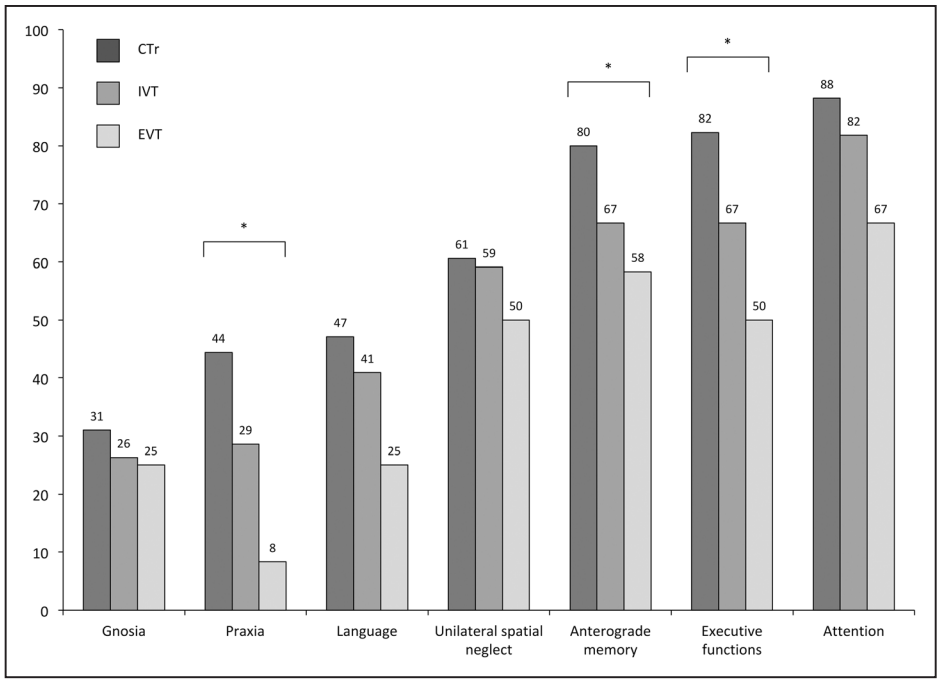

Figure 2. Frequency of impairment (*y*-axis) in each cognitive domain tested (*x*-axis) in patients treated by conservative treatment (CTr), intravenous thrombolysis (IVT), and endovascular treatment (EVT; gray bars). *Significant differences on χ^2 test for trend.

necessary in 24/34 (70.6%), 14/22 (63.6%), and 4/12 (33.3%) patients receiving CTr, IVT, and EVT, respectively (*P*=0.034).

Discussion

In this retrospective exploratory analysis of 106 patients with AIS with IPCAO, we found improved recanalization and tendency toward better outcome supporting the efficacy of IVT over conservative treatment. In addition, we showed potential efficacy of EVT over BMT (defined as IVT or CTr), with trends for better prognosis in terms of cognitive, visual field, and global disability outcomes.

The clinical trials demonstrating IVT efficacy mainly focused on anterior circulation strokes. Two retrospective analyses, despite lack of information regarding baseline intracranial vessel status and recanalization, indicated similar treatment response to IVT and long-term outcome in anterior compared with posterior circulation or to PCA territory strokes.[11,12] Our results seem to support these findings, as we observed a recanalization rate of 50%, similar to the overall recanalization rate after IVT,[13] and a trend for better outcome in patients treated with IVT compared with conservative treatment. As recanalization was not assessed in 29/51 patients in the CTr group, it is possible that we overestimated the effect of IVT on recanalization, but it is unlikely that assessing recanalization in all CTr patients would have led to a nonsignificant result: this would require a recanalization rate >45% in the 29 patients with missing data (Figure II in the online-only Data Supplement), which seems unlikely given our observed rate of 9% and the overall rate of spontaneous recanalization in AIS around 25%.[13] Considering the magnitude of treatment effect, the point estimate of the odds ratio for good outcome (mRS score, 0–1) was 1.94 in our propensity score–matched cohort and 1.65 in the multivariable analysis, compared with 1.75 (if treated <3 hours) or 1.26 (if treated between 3.0 and 4.5 hours) in the meta-analysis of randomized IVT trials.[14] This suggests a benefit of IV r-tPA in IPCAO similar to that observed in the general stroke population. Our observed rate of SICH after IVT (2.9%) was similar to that observed in general stroke population of 5%.[15]

To date, only case reports or case series exist about safety and efficacy of EVT for IPCAO.[16,17] One case series, from the prethrombectomy era, compared intraarterial versus intravenous thrombolysis (9 patients per group) and showed favorable outcome in the majority of patients after both intraarterial and intravenous thrombolysis, without major complications. Despite technical progress that now allows mechanical thrombectomy for medium size arteries like the PCA,[18] little data regarding outcome after PCA mechanical thrombectomy exists.[19–21] Our data show a 15% absolute difference in the proportion of patients achieving good functional outcome at 3 months comparing thrombectomy to BMT. This difference did not quite reach statistical significance in unadjusted or adjusted analyses, not surprisingly given the small number of included patients. However, this treatment effect was consistent with other exploratory analyses assessing cognitive and visual outcomes (the first being significant only in unadjusted analysis, the second only in adjusted analysis), where the difference in favor of EVT was much larger. It is likely that the peculiar clinical features of PCA stroke represent a challenge for outcome assessment, as the mRS may not completely capture the impact of this kind of handicap in everyday life.[2]

Mortality and SICH were not statistically different in the EVT group compared with BMT. They had similar ranges to those observed in clinical trials on proximal occlusion (SICH, 4.4%; mortality, 15.3% in HERMES meta-analysis)[22] and in case series on distal artery occlusion (SICH, not reported; parenchymal hematoma, 7%; mortality, 20%).[21] Also, our procedural complication rate of 14% (n=3/21, one arterial

perforation, one embolization in a different artery, one arterial dissection) was similar to the average rate of 15% observed in thrombectomy clinical trials.[23] Of note, only the one vessel perforation had a repercussion on the clinical outcome: the frequency of this complication (4.8%) was in the upper range limit of that observed in clinical trials (range, 0.9%–4.9%).[23]

The overall 3-month mortality in our cohort was considerably higher (16%) than in previous studies of PCA strokes, which reported rates below 10%.[11,17,24–27] It is likely that our selection of only patients with proximal occlusive PCA strokes was responsible for this higher mortality rate. This is also supported by our unpublished data from ASTRAL showing mortality of 9.1% (n=33/363) in PCA strokes without PCAO, and of 5.2% (n=11/210) if the stroke is limited to the PCA territory. This implies that while PCA strokes may still be regarded as a stroke type with overall good prognosis, this may not be true in the presence of a PCA occlusion. Indeed, at 3 months, more than half of our patients had a ≥1 point increase in their prestroke mRS or were dead, 70% had a persistent visual field deficit, and almost 80% had a significant impairment in >2 cognitive domains.

The 2 cognitive domains most frequently impaired in our patients were attention and executive functions. This result is consistent with previous studies on general stroke population and might reflect the wide distribution of these functions through the cerebral cortex and in thalamus.[28,29] Memory dysfunction after stroke is typically related to lesions in the mesiotemporal and anterothalamic structures, both supplied by the posterior cerebral artery.[30]

The limitations of our study include its retrospective, observational, noncontrolled, nonrandomized design as well as the relatively small number of patients in each group that limited our ability to detect significant outcome differences. In addition, some baseline imbalances existed between the 3 treatment groups that could only partially be overcome by the multivariable and propensity-adjusted analyses. It is possible that this affected the point estimate of the ORs for various beneficial outcomes in favor of the more extensively treated groups. This prompts a careful interpretation of our results. A further potential source of bias is that outcome data were obtained from routine clinical practice; therefore, outcome assessment was nonblinded to treatment. Recanalization was not assessed in all patients, especially in the CTr group, which might have led to overestimation of the treatment effect of IVT on recanalization, as already discussed. As short-term outcome, we used NIHSS variation from baseline to 24 hours and 7 days: we acknowledge that for posterior circulation strokes NIHSS might not fully capture the extent of the neurological deficit. However, no alternative widely accepted scale exists for this purpose, and, despite its limitation, we decided to use it as a measure of short-term outcome, which can provide information on treatment response complementary to 3-month outcome measures. Regarding 3-month outcomes, mRS was not available in 2 patients, and 23/106 (21%) patients were not included in the analysis on visual outcome because they had no visual field defect at baseline. The clinical rather than computerized assessment of visual field defect might underestimate the extent of the visual field amputation and is also a limitation of the study. The absence of subacute neuropsychological evaluation in 1/3 of our patients demands caution in the interpretation of our results on cognitive outcome, as well as the absence of long-term cognitive testing. Finally, because of the very limited number of event, our study was not sufficiently powered to detect any statistically significant difference in SICH between the treatment groups.

Strengths of our study are the consecutive nature of the collected data over a long period with prespecified and standardized data collection using up-to-date scales, definitions and neurovascular imaging methods. In addition, we included a typical comprehensive stroke center population that includes subjects from both a primary and tertiary referral population. Furthermore, our detailed selection criteria based on intracranial vessel status identified a homogenous stroke population and we included analysis of visual and cognitive outcome measures, specific to this type of stroke. Finally, the majority of patients analyzed in the EVT group (95%) were treated with modern thrombectomy devices.

To the best our knowledge, our study represents to date the largest study and the best available evidence for revascularization therapies in isolated PCA occlusion. We show increased odds of recanalization following IVT and even higher after EVT, with trend for a positive effect on clinical outcomes and without significant increase in mortality. While the little number of hemorrhagic events does not allow definite conclusion, the rate of SICH observed in our patients did not exceed that reported after IVT and EVT in large studies on the overall stroke population. However, given the potential procedural complications, in particular, in smaller caliber vessels, mechanical thrombectomy for IPCAO should be performed by experienced neurointerventional operators, in high-volume stroke centers. These promising results need to be further investigated in larger prospective controlled studies.

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