A Regional Network Organization for Thrombectomy for Acute Ischemic Stroke in the Anterior Circulation; Timing, Safety, and Effectiveness

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Background: Mechanical thrombectomy (MT) in association with intravenous thrombolysis is recommended for treatment of acute ischemic stroke (AIS), with large vessel occlusion (LVO) in the anterior circulation. Because MT is only available in comprehensive stroke centers (CSC), the challenge of stroke organization is to ensure equitable access to the fastest endovascular suite. Our aim was to evaluate the feasibility, efficacy, and safety of MT in patients initially managed in 1 CSC (mothership), compared with patients first managed in primary stroke center (PSC), and then transferred to the CSC for MT (drip-and-ship). *Methods:* We retrospectively analyzed 179 consecutive patients (93 in the mothership group and 86 in the drip-and-ship group), with AIS secondary to LVO in the anterior cerebral circulation and a clinical-radiological mismatch (NIHSS $\geq$ 8 and DWI-ASPECT score $\geq$5), up to 6 hours after symptoms onset. We evaluated 3-month functional modified Rankin scale (mRS), periprocedural time management, mortality, and symptomatic intracranial haemorrhage (sICH). *Results:* Despite significant longer process time in the drip-and-ship group, mRS $\leq$ 2 at 3 months (39.8% versus 44.1%, $P = .562$), Thrombolysis in cerebral infarction 2b-3 (85% versus 78%, $P = .256$), and sICH (7.0% versus 9.7%, $P = .515$) were similar in both group regardless of baseline clinical or radiological characteristics. After multivariate logistic regression, the predictive factors for favorable outcome were age (odds ratio [OR] $_{\text{-5years}}$= 1.32, $P <$ .001), initial NIHSS (OR $_{\text{-5points}}$ = 1.59, $P = .010$), absence of diabetes (OR = 3.35, $P = .075$), and the delay magnetic resonance imagining-puncture (OR $_{\text{-30min}}$ = 1.16, $P = .048$). *Conclusions:* Our study showed encouraging results from a regional protocol of MT comparing patients transferred from PSC or brought directly in CSC.

Key Words: Acute ischemic stroke—endovascular treatment—thrombolysis—srip-and-ship—outcome.

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Until December 2014, intravenous thrombolysis (IVT) was the unique recommended recanalization therapy for patients with acute ischemic stroke (AIS).[1,2] However, IVT use has been limited by numerous contraindications,[3,4] and it provides incomplete benefit in patients with large vessel occlusion (LVO).[5,6] Seven randomized clinical trials (RCTs) demonstrated the superiority of the bridging therapy (IVT followed by mechanical thrombectomy [MT]), compared with IVT alone, in patients with AIS and intracranial LVO in the anterior circulation.[7-12] The current challenge is to identify eligible patients for MT, to improve their access for recanalization therapies and to start reperfusion therapies as soon as possible. Because, MT is only available in comprehensive stroke centers (CSC), collaborative stroke center networks with interhospital transfers of eligible patients are necessary.

In our region, a standardized prospective assessment was initiated between the CSC with a stroke unit (SU) and the interventional neuroradiology (INR) department, and 3 primary stroke centers (PSC) with referral SU to streamline and ascertain a coalescent decision-making process in patients with AIS secondary to LVO.[13]

The aim of this observational study was to evaluate the feasibility and safety of MT and to compare the neurologic outcome in stroke patients with a LVO in the anterior circulation admitted directly to the CSC (mothership patients) versus those referred from 3 PSC (drip-and-ship [DS] patients).

Materials and Methods

Population and Initial Stroke Center Management

Between September 2010 and December 2012, we retrospectively analyzed consecutive patients treated with MT, first admitted to 4 SU located in Languedoc-Roussillon, a region in the south of France (more than 2,700,000 inhabitants with an area of 27,376 km^2). Patients with suspicion of AIS were admitted to the nearest SU in relation to the patient origin. National Institutes of Health Stroke Scale (NIHSS) was assessed on admission by a stroke neurologist. All patients underwent acute multimodal 1.5T magnetic resonance imagining (MRI) with a standardized imaging protocol performed, including T2 gradient echo, Diffusion weighted images (DWI), B1000 and Apparent diffusion coefficient (ADC), map, FLAIR, and an intracranial magnetic resonance angiography, Alberta Stroke Program Early CT Score (ASPECTS), was used to evaluate the extension of the ischemic lesion on ADC mapping. IVT was administrated in patients presenting within 4.5 hours of symptoms onset following current guidelines.[2] Among patients with unknown time of stroke onset, we used the DWI−FLAIR mismatch to treat the patients with IVT.[14,15]

In 2009, a regional protocol proposed MT to eligible patients presenting with AIS and LVO in the anterior circulation in association with IVT as a bridging therapy or alone in case of contraindication for IVT. Our selection criteria for MT were: (1) Age ≥18 years; (2) AIS in the anterior circulation, confirmed by cerebral MRI, related to a LVO (internal carotid artery, M1 or proximal M2 middle cerebral artery); (3) presence of a clinico-radiological mismatch, defined by NIHSS ≥ 8 and a small lesion volume, defined with a DWI-ASPECT score ≥5; (4) enrollment up to 6 hours after stroke symptoms onset; (5) prestroke mRS score ≤1. The following data were systematically recorded: demographic, arterial risk factor, characteristic of IS, and treatment with IVT.

CSC Management for MT

For patients from PSC, the CSC was contacted by the neurologist of PSC, while IVT was administered. Cerebral imaging was delivered to the CSC, using an electronic transmission system, and were analyzed between neurologist and neuroradiologist before coalescent-decision to transfer or not the patient for MT. During transportation to the CSC, with IVT ongoing, the patient was monitored by the emergency team. If the time lapse between initial MRI in the PSC and patient arrival to the CSC was within 90 minutes, the patient was reassessed in front of the angiosuite door by the stroke neurologist and the neuroradiologist. In case of significant NIHSS worsening or improvement (NIHSS ± 4 points), patients underwent another imaging in order to screen for brain haemorrhagic transformation or vessel recanalization. If the time lapse was beyond 90 minutes, MRI was repeated to confirm a remaining clinical/radiological mismatch and to avoid futile recanalization. Among mothership patients, candidates for MT were directly transferred to the angiosuite after MRI and IVT was performed on the angiographic table, if indicated. Consent for treatment was obtained from patients or their family members before MT.

MT was performed via a femoral artery approach under general anesthesia. An 8F or 9F Merci balloon-guide catheter (Concentric Medical) was inserted through a sheath. A 0.21-inch internal diameter microcatheter (Prowler Select Plus; Cordis or Vasco 21; Balt) was navigated distal to the occlusion over a 0.014-inch steerable guidewire, which was then exchanged with the thrombectomy device. During the retrieval, the balloon-guide catheter was inflated to interrupt anterograde flow. Manual aspiration with a 50-mL syringe was performed through the hemostatic valve during the retrieval, to reverse the flow and to aspirate clot debris possibly lost in the guide catheter lumen. The number of attempts to retrieve the thrombus was limited to 5 passes by occluded vessel. Successful recanalization was defined as thrombolysis in cerebralinfarction 3-2b.

Safety and Clinical Outcome

Follow-up cerebral computed tomography scan or MRI was performed 24 hours after the procedure in order to assess the extent of infarction and/or hemorrhagic complications. For safety outcome, we reported symptomatic cerebral haemorrhage (sICH), embolic complications in a new territory, clinically relevant procedural complications, and mortality at 3 months. For neurological outcome, the modified Rankin scale (mRS) at 90 days were assessed by a stroke neurologist. Favorable outcome was defined by a mRS less than or equal to 2.

Delays from stroke onset-to-initial MRI, stroke onset-to-needle, stroke onset-to-groin puncture, initial MRI-to-groin puncture, admission-to-CSC-to-groin puncture, needle-to-groin puncture, and stroke onset-to-recanalization were calculated for all patients.

Statistical Analysis

Patients' characteristics were presented using median and interquartile range ($IQR_{25\text{-}75}$) for continuous variables and frequencies and proportions for categorical variables. Groups (mothership patients versus DS patients and 3 months mRS ≤ 2 versus. >2) were compared using Wilcoxon Mann-Whitney test for continuous variables and Chi-square or Fisher test for categorical ones.

To determine the relative importance of the covariables on the favorable evolution (3 months mRS ≤ 2 versus. >2), a multivariate logistic regression was performed. All relevant variables significantly associated with good outcome in the univariate analysis, were entered in the model. A stepwise selection was used with an alpha-to-enter and alpha-to-exit set at 0.20 and 0.10, respectively. Odds-ratio (OR) and their 95% confidence intervals were reported. The group variable was tested in the model. Statistical analysis was performed using SAS v.9 statistical software (SAS Institute, Cary, NC).

Results

Baseline Patient Characteristics

During the study period, 179 consecutive patients (93 mothership patients and 86 DS patients) with AIS and LVO in the anterior circulation, were included. There was no significant difference between groups with regards to baseline clinical and imaging characteristics (Table 1).

Recanalisation Treatments

IVT rate was significantly higher in DSpatients (81.4% versus 51.6%; $P < .001$). Near 92% (164 out of 179 patients) were treated with the Solitaire FR device (Medtronic, Irvine, CA). Thrombectomy was not performed in 6 patients because of: arterial recanalization in 2 outpatients, 2 failed carotid catheterization, 1 arterial perforation, and the death of 1 patient at the time of induction of anaesthesia. A good recanalization rate (thrombolysis in cerebral infarction 2b or 3) appears similar in both groups (84.9% for DSpatients versus 78.3% for mothership patients; $P = .256$), with a median number of passes of 2 ($IQR_{25\text{-}75} = 1\text{-}3$) (Table 2).

Workfow Timing

Median process times were significantly longer for the DS patients group compared to the mothership patients group: stroke-onset-to-puncture, 315 minutes ($IQR_{25\text{-}75} = 280\text{-}360$) versus 215 ($IQR_{25\text{-}75} = 174\text{-}283$; $P < .001$), needle-to-puncture, 149 minutes ($IQR_{25\text{-}75} = 123\text{-}184.5$) versus 31 minutes ($IQR_{25\text{-}75} = 15\text{-}66\text{-}92$; $P < .001$), onset-to-recanalization, 363 minutes ($IQR_{25\text{-}75} = 331\text{-}440$) versus 306 ($IQR_{25\text{-}75} = 243\text{-}343$; $P < .001$), baseline MRI-to-recanalization, 244 minutes ($IQR_{25\text{-}75} = 211\text{-}313$) versus 131 ($IQR_{25\text{-}75} = 105\text{-}179$; $P < .001$). There was no significant difference between groups for median stroke onset-MRI times or stroke onset-to-IVT times (Table 3).

Clinical Outcome

Three patients were lost to follow-up. Favorable clinical outcome at 3 months was not statistically significantly different between the 2 groups. Shift on the mRS at 3 months in our different populations are summarized in Figure 1. sICH was found in 8.4% of the overall population without significant differences between both subgroups. Mortality rates were significantly higher in the mothership patients (24 [25.8%] versus 7 [8.1%] in DS patients; $P = .002$) (Table 2). Twelve (6.7%) clinically relevant procedural complications were observed: vasospasm (n = 1), ICA dissection (n = 1), arterial perforation (n = 2), embolic infarct in a new territory (n = 5), and 3 stent-failure.

Predictive Factors for Clinical Outcome

For the favorable outcome analysis (3 months mRS ≤ 2), the following factors were tested: age, vascular risk factors, NIHSS, ASPECT score, delays, etiology, IVT, recruitment site, and interaction between the last 2 variables. After multivariate analysis, the predictive factors for favorable outcome were age ($OR_{-5years} = 1.32$ [95% CI = 1.15-1.50], $P < .001$), the initial NIHSS ($OR_{-5points} = 1.59$ [95% CI = 1.12-2.26], $P = .010$), absence of diabetes (OR = 3.35 [95% CI = 0.89-12.66], $P = .075$), and the delay MRI-to-puncture ($OR_{-30min} = 1.16$, [95 CI = 1.00-1.34], $P = .048$) (Table 4).

Discussion

Our study provides the following findings: first, patients with AIS and LVO in the anterior circulation and clinical-radiological mismatch treated by MT had a similar recanalization and favorable clinical outcome at 3 months rates with acceptable safety, whether first admitted to CSC or PSC. Second, DS bridging therapy, despite the longer delay due to the transfer, was safe without higher rates of sICH or mortality and did not impact clinical outcome negatively.

Table 1. *Baseline characteristics*

	Population n = 179		Drip-and-ship patients n = 86 (48%)		Mothership patients n = 93 (52%)		*P* values
Male, n (%)	94	(52.5)	39	(45.3)	55	(59.1)	.065
Age, median (IQR_{25-75})	69	(55-77)	66.5	(54.0-76.0)	70	(60.0-77.0)	.080
Recruitment, n (%)							
CSC			-		93	(100)	
PSC1			34	(39.5)	-		
PSC2			27	(31.4)	-		
PSC3			25	(29.1)	-		
Comorbidities, n (%)							
Hypertension	100	(55.9)	43	(50.0)	57	(61.3)	.129
Smoking	47	(26.3)	25	(29.1)	22	(23.7)	.411
Dyslipidemia	63	(35.2)	31	(36.0)	32	(34.4)	.819
Diabetes	20	(11.2)	11	(12.8)	9	(9.7)	.509
Previous stroke	13	(7.3)	8	(9.3)	5	(5.4)	.312
NIHSS, *median* (IQR_{25-75})	18	(15-20)	17.5	(14-20)	18	(15-21)	.323
MRI characteristics							
MCA territory, n (%)							.771
Deep	88	(49.2)	40	(46.5)	48	(51.6)	
Superficial	15	(8.4)	8	(9.3)	7	(7.5)	
Total	76	(42.5)	38	(44.2)	38	(40.9)	
ASPECT score, median *(*IQR_{25-75}*)*	7	(6-8)	7	(6-8)	7	(5-8)	.628
Arterial occlusion, n (%)							.564
MCA (M1, M1-M2)	108	(60.3)	50	(58.1)	58	(62.4)	
ICA	71	(39.7)	36	(41.9)	35	(37.6)	
Etiology, n (%)							.004
Cardioembolic	81	(45.3)	32	(37.2)	49	(52.7)	
Atherothrombotic	29	(16.2)	10	(11.6)	19	(20.4)	
Dissection	13	(7.3)	6	(7.0)	7	(7.5)	
Undetermined	56	(31.3)	38	(44.2)	18	(19.4)	

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; CSC, comprehensive stroke center; ICA, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; NIHSS National Institute of Health Stroke Scale; PSC, primary stroke centers.

Current debate is the mothership and DS paradigms, and the potential superiority of one of them. Indeed, inter-hospital transfer to endovascular-capable centers in DS would result in treatment delays for MT and worse clinical outcomes compared with direct presentation. On the other hand, mothership would increase the risk that many eligible patients will be denied early, effective IVT. Data on the DS versus mothership paradigms is limited, and moreover, RCT is lacking. Recently, 4 studies published on the effect of the DS paradigm on patients undergoing bridging therapy, produced conflicting results.[16-19] Three studies[16,17,19] concluded that drip and ship thrombectomy concept can be effectively organized in a metropolitan stroke network. The Korean study[18] found that the DS paradigm might cause an increase in the onset-to-groin puncture time with higher risk of unfavorable outcomes and sICH.

In our study, inclusion of patients with no upper age limit and with wake-up-stroke resulted in a population which is representative for stroke patients with LVO, and which does not differ in important aspects to inclusion criteria of patients in recent RCTs[7-12] regarding median baseline NIHSS (18 versus 16-17 in RCTs) or ASPECTS (7 versus 7-9 in RCTs). Our overall results are comparable to the Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials (HERMES).[20] meta-analysis in terms of favorable outcome (42% versus 46% for HERMES), successful recanalization rate (81.5% versus 71% for HERMES) and mortality rate (17.3% versus 15.3% for HERMES). In contrast the overall sICH rate of 8.4% is higher (4.4% for HERMES).

We postulate that the use of the clinical-diffusion mismatch[21] in our study has contributed to our good results by providing careful selection of patients and, therefore avoiding futile and dangerous recanalization as well as the new neurological assessment at CSC's admission and in selected cases, a new cerebral imaging. In all positive recent RCT, patients were selected with the presence of salvageable tissue, defined either with the clinical-diffusion mismatch,[9] the mismatch between infarct volume and hypoperfusion[8-11] or the presence of good collateral circulation.[10]

Table 2. *Treatment and outcomes*

	Population n = 179		Drip-and-ship patients n = 86 (48%)		Mothership patients n = 93 (52%)		*P* values
Treatment							
IVT, n (%)	118	(66)	70	(81.4)	48	(51.6)	< .001
Contraindications, n (%)	61	(34)	16	(18.6)	45	(48.4)	
Anticoagulants	12	(19.6)	2	(12.5)	10	(22.2)	
Radiological severity	4	(6.5)	2	(12.5)	2	(4.4)	
Clinical severity	4	(6.5)	2	(12.5)	2	(4.4)	
Delay	29	(47.5)	7	(43.7)	22	(48.8)	
Others neurological CI	4	(6.5)	2	(12.5)	2	(4.4)	
General CI	8	(13.1)	1	(6.2)	7	(15.5)	
Thrombectomy, n (%)	173	(96.7)	83	(96.5)	90	(96.8)	1
Outcome							
mRs ≤ 2, n (%)	74	(42.0)	33	(39.8)	41	(44.1)	.562
TICI 2b-3, n (%)	145	(81.5)	73	(84.9)	72	(78.3)	.256
Death, n (%)	31	(17.3)	7	(8.1)	24	(25.8)	.002
Malignant infarct	8	(25.8)	3	(42.8)	5	(20.8)	
sICH	7	(22.5)	2	(28.5)	5	(20.8)	
Vascular	3	(9.6)	0		3	(12.5)	
General	10	(32.2)	1	(14.2)	9	(37.5)	
unknown	3	(9.6)	1	(14.2)	2	(80.3)	
sICH, n (%)	15	(8.4)	6	(7.0)	9	(9.7)	.515

Abbreviations: CI, contraindication; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; sICH, symptomatic Intracranial hemorrhage; TICI, thrombolysis in cerebral ischemia.

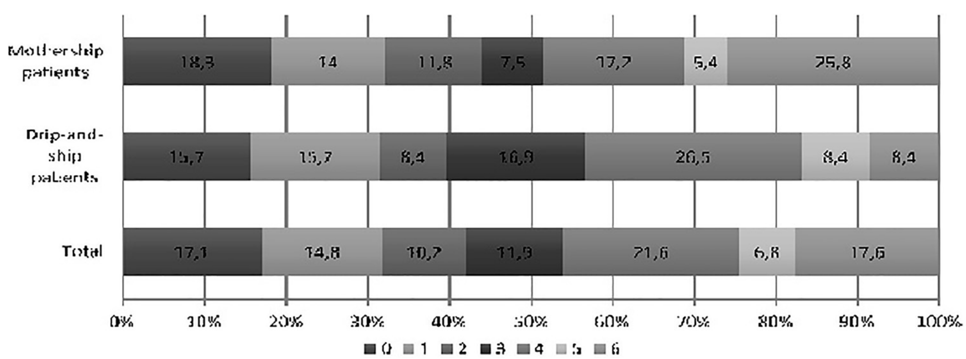

Figure 1. *modified Rankin scale (mRS) at 90 days in the thrombectomy and in the control groups. Scores on the mRS range from 0 to 6, with 0 indicating no symptoms: (1) no clinically significant disability; (2) slight disability; (3) moderate disability; (4) moderately severe disability; (5) severe disability; and (6) death. There was no significant difference between the mothership patients and drip-and-ship patients groups in the distribution of scores especially for the favorable score defined by an mRS ≤ 2 in analysis* (P = .562) *except for the mortality rate (mRS 6)* (P = .002).

IVT, Mortality Rate, and Delay

In our study, IVT rate was significantly lower in mothership patients compared to DS patients (51.6% versus 81.4%, $P < .001$). It was not a consequence of a difference of stroke severity, but rather due to the therapeutic window of IVT. Indeed, DS patients had to arrive in CSC within 6 hours to be treated with MT, so they were mainly selected in the PSC before 4.5 hours taking into account the delay of transfer, which matched with the therapeutic window of tPA. By contrast, in the CSC, patients admitted between 4.5 hours and 6 hours could be treated with standalone MT.

The mortality rate was 17% in our overall population, comparable to RCTs,[7-12] but significantly lower in DS group. As it is not attributable to the initial severity of stroke, it could be related to a more careful selection of transferred patients in PSC. DS patients were younger (even if it was not significant) and most importantly, had more chance to have IVT. It is interesting to note that the main cause of death in mothership patients were extra-neurological reasons (cardiogenic, haemorrhagic, or septic shock. . .). Of course, it could be due to the small number of patients included with a lack of statistical relevance.

In our study, predictors of bad outcome were age, diabetes, initial NIHSS, and the time from stroke onset to

Table 3. *Timing*

	Population n = 179		Drip-and-ship patients n = 86		Mothership patients n = 93		*P* values
Distance from CSC (miles),							
Time to transfert by ambulance (mn)							
PSC1			34.8	(50)			
PSC2			97.5	(165)			
PSC3			45.4	(55)			
Delay (mn)							
Median ($IQR_{25\text{-}75}$)							
Onset-MRI (n = 148)	124	(92-163)	115	(92-162)	131	(93-175)	.133
Onset-IVT (n = 103)	155	(130-200)	152	(130-195)	165	(135-205)	.480
Onset-puncture (n = 134)	283	(216-335)	315	(280-360)	215	(174-283)	<.001
Needle-puncture (n = 99)	122	(53-160)	149	(123-185)	31	(15-66)	<.001
MRI-puncture (n = 163)	122	(67-193)	193	(164-225)	69	(55-97)	<.001
Onset-Recanalization (n = 122)	335	(290-410)	363	(331-440)	306	(243-343)	<.001
MRI-Recanalization (n = 149)	193	(127-250)	244	(211-313)	131	(105-173)	<.001

Abbreviations: CSC, comprehensive stroke center; PSC, primary stroke centers.

MT. Age, diabetes, and initial NIHSS are well known predictive factors of outcome[1,22,23] and time-dependent effect of reperfusion has been well addressed, showing that the faster the patient's occluded artery is recanalized, the better the outcome.[1] Saver et al found in a pooled meta-analysis that benefit of thrombectomy therapy becomes nonsignificant when onset-to-puncture time is longer than 438 minutes.[24] In our study,the overall median stroke-onset-to-puncture time was 238 minutes.

The delay from symptom onset to recanalization due to interhospital transfer could result in worse clinical outcomes and higher rates of sICH. It was not the case in our study, even if the onset to MT time was, as expected, significantly longer in DS patients due to the time of transfer. Nevertheless, both groups were comparable, in terms of initial clinical and imaging stroke severity, or delay from stroke onset to tPA. And, despite a difference in time to reperfusion, there was no significant difference for good clinical outcome between in and DS patients. Of course, it could be due to the relatively low number of patients, but the most important point is that out-patients were reevaluated after arrival in CSC to verify that they were still good candidates.

The Necessary Re-Organization of AIS Management

During the past 20 years, AIS management has evolved dramatically, with development of SU, imaging, new effective, and recommended therapy. In response, stroke

Table 4. *Predictive factors of favorable outcome*

	Univariate analysis					Multivariate analysis			
	mRS ≤ 2 n = 74 (42%)		mRS > 2 n = 102 (58%)		P_{raw}	Units	OR (95% CI)		P_{adj}
Median age ($IQR_{25\text{-}75}$)	62	(49-71)	73.5	(63-78)	<.001	- 5 years	1.32	(1.15-1.51)	<0.01
Comorbidities, n (%)									
Hypertension	32	(43.2)	67	(65.7)	0.003				NS
Diabetes	4	(5.4)	16	(15.7)	0.034	No vs. Yes	3.35	(0.89-12.66)	.075
NIHSS	16	(13-20)	19	(16-21)	0.001	- 5 points	1.59	(1.12-2.26)	.010
Etiology, n (%)									
Cardioembolic	28	(37.8)	53	(52.0)	0.064				NS
Others	46	(62.2)	49	(48.0)					
Atherothrombotic	*13*	*(17.6)*	*16*	*(15.7)*					
Dissection	*8*	*(10.8)*	*5*	*(4.9)*					
Undetermined	*25*	*(33.8)*	*28*	*(27.5)*					
Median time to ($IQR_{25\text{-}75}$).									
Imaging – puncture	131.0	(91.5-203.0)	168.0	(112.0-242.0)	0.008	-30 mn	1.56	(1.00-1.34)	.048

Abbreviations: CI, confidence interval; IQR, interquartile range; mRS, modified Rankin scale; NIHSS, National Institute of Health Stroke Scale; OR, odds ratio.

system care should ensure equitable access to the fastest endovascular treatment suite.

Most of previous studies published on the effect of the DS paradigm on patients undergoing bridging therapy concern centers in metropolitan areas, thus the findings may not be relevant to more rural areas. Moreover, our regional networking system does not match completely to the DS versus the mothership paradigm. First, hospitals in our region are not geographically closer together, so there is long transfer time between PSC and CSC. Second, it does not seem conceivable that every community develops a CSC with INR. In France, only one third of SU are CSC with on-site INR. Third, patients who are eligible for alteplase, as well as MT, should always first receive alteplase, as soon as possible within 4.5 hours of symptoms onset, as it is not proven that primary MT is safe and effective. As suggested by Holodinsky,[25] the mothership model is superior to DS model when transport times between PSC and CSC are short (10-30 minutes) and the DS model becomes a superior option when the patient is close to the PSC and the time between the PSC and CSC is 45 mm or longer. It means that patients, who live far away from CSC, as in our region, may be outside the 4.5 hours alteplase time window by the time they reach a CSC. IVT has to be administred as soon as possible at the nearest center, because increased process times would result in worse clinical outcome.

From our point of view, the main factors to be considered are: (1) prehospital stroke factors impacting decision have to be considered and correspond to major initial triaging processes: age, stroke severity, comorbidities, and premorbid functional status; (2) protocols have to minimize the time medical and paramedics spend in PSC emergency department; (3) activation of the endovascular team in parallel with initiation of alteplase; (4) standardized imaging used in all stroke centers, with evaluation of core (with the ASPECT score), mismatch (with collateral and/or perfusion assessment) and occlusion site; (5) electronic transmission system in real time; (6) determining the best transportation option including geographic location of the PSC and CSC, ambulance response time and availability, and traffic.

Our experience with this regional protocol since 2009 facilitated the development of MT in our region after 2015.

Strenghts-Limitations

Our study has several strengths. All SU in our region had similar practice, and all MT were done by the same neuroradiologists team. All IVT was done by a stroke neurologist in a SU. At CSC admission, all patients were reexamined by a neurologist and, if necessary, imaging was repeated to confirm the inclusion criteria. All initial imaging was analyzed by the neurologist and neuroradiologist at the CSC to a coalescent decision to transfer or not the patient. Only 1.7% of patients did not have a 3-month mRS assessment.

Our study had several limitations. It was a retrospective analysis of our databank and the number of patients was quite small. The main limitation is that only patients treated by MT were included and we did not study DS patients not transferred, because an estimated delay for MT out of therapeutic window or those excluded after arrival to the CSC on the basis of a large ischemic core or absence of mismatch. We also cannot rule out the possibility that many of these futile transfers might have benefited from MT, if they were treated earlier. Nevertheless, our study was not designed to address the question of the loss of chance for untreated patients.

Conclusions

Our study suggests that our regional protocol for MT, organized with 1 CSC with INR and PSCs, according to rapidly and effectively treat highly selected patients, is feasible, safe, and efficient. The key point is a good patient's selection based on the clinico-radiological mismatch concept, and checking that patients remain good candidates over time. This approach could be translated to similar areas centered by only 1 INR.

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