Mechanical Recanalization after Transfer from a Distant Primary Stroke Center: Effectiveness and Future Directions

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Introduction: Little is known about the effectiveness of endovascular treatment (EVT) in patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO) admitted to a primary stroke center (PSC). The aim of this study was to assess EVT effectiveness after transfer from a PSC to a distant (156 km apart; 1.5 hour by car) comprehensive stroke center (CSC), and to discuss perspectives to improve access to EVT, if indicated. *Patients and Method:* Analysis of the data collected in a 6-year prospective registry of patients admitted to a PSC for AIS due to LVO and selected for transfer to a distant CSC for EVT. The rate of transfer, futile transfer, EVT, reperfusion (thrombolysis in cerebral infarction score ≥2b-3), and relevant time measures were determined. *Results:* Among the 529 patients eligible, 278 (52.6%) were transferred and 153 received EVT (55% of transferred patients) followed by reperfusion in 115 (overall reperfusion rate: 21.7%). Median times (interquartile range) were: *90* minutes *(76-110)* for PSC-door-in to PSC-door-out, *88* minutes *(65-104)* for PSC-door-out to CSC-door-in, *262* minutes *(239-316)* for PSC-imaging to reperfusion, and *393* minutes *(332-454)* for symptom onset to reperfusion. At 3 months, rates of favorable outcome (modified Rankin Scale 0-2) were not significantly different between patients eligible for EVT (42.4%), transferred patients (49.1%) and patients who underwent EVT (34.1%). *Discussion and Conclusions:* Our

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Ethical approval: Ethical approval for this study was waived by the institutional ethics committee of the Perpignan and Montpellier hospitals. This study was completed in accordance with the Helsinki Declaration as revised in 2013.

Disclosures: None.

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study suggests that transfer to a distant CSC is associated with reduced access to early EVT. These results argue in favor of on-site EVT at high volume PSCs that are distant from the CSC.

Key Words: Thrombectomy—stroke unit—stroke management—reperfusion—ischemic strokes

Introduction

Numerous prospective randomized trials have consistently confirmed that if performed within 6 hours of symptom onset, endovascular treatment (EVT)[1-6] is beneficial in patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO) and a favorable imaging profile. In 2018, this time window was extended to 24 hours[7] for selected patients, after the positive results of the Dawn and Defuse 3 trials.[8,9] These clinical trials showed that rescue thrombectomy after transfer from a primary stroke center (PSC) to a comprehensive stroke center (CSC) is a valid option.[1-6,8,9] However, EVT clinical benefit decreases with any reperfusion delay.[1-6,10] Therefore, it is important to identify criteria (patient load and achievable time metrics) that might promote rapid EVT, particularly for patients who are far away from a CSC with on-site interventional neuroradiology service. We used a 6-year database to assess the effectiveness of early EVT at a CSC after transfer from a distant (156 km apart; 1.5 hour by car) high-volume PSC. We then discussed the perspective for speeding up access to EVT in the case of important inter-hospital distances.

Methods

Geographical Considerations and Transfer of Selected Patients

Perpignan General Hospital (Perpignan-GH) provides secondary care in a semi-rural area with approximatively 450,000 inhabitants in the southernmost department of France (Pyrénées-Orientales). The PSC of this hospital was created in 2000. The stroke-unit team includes 12 senior neurologists on duty 24/7 who can deliver intravenous thrombolysis (IVT) within 4.5 hour from symptom onset. Perpignan-GH is 156 km away from the closest regional CSC in Montpellier that has a state-of-the-art interventional neuroradiology service (Fig 1). Since 2010, based on a close and structured collaboration between Montpellier CSC and Perpignan-GH, patients with AIS and intracranial LVO are transferred from Perpignan-GH to Montpellier for EVT if they meet the following predefined criteria: (1) time from AIS symptom onset less than 4.5 hours or, if unknown, no visible brain infarction on T2-FLAIR sequences of the initial MRI; (2) clinically significant neurological deficit, as indicated by a score more than or equal to 8 in the National Institutes of Health Stroke Scale (NIHSS); and (3) imaging-based evidence of proximal occlusion of the M1 or M1-M2 segment of the middle cerebral artery (MCA) with or without concomitant occlusion of the internal carotid artery, or basilar artery (BA) occlusion. In the case of occlusion of the BA, M2 segment of MCA, P1 segment of the posterior cerebral artery or A1 segment of the anterior cerebral artery (ACA), patient transfer is discussed on a case-by-case basis. Patients with a large ischemic core on diffusion-weighted MRI images (DWI), as indicated by an Alberta Stroke Program Early Computed Tomography Score (DWI-ASPECTs) less than 5, are excluded from transfer.

After agreement between the CSC and PSC stroke neurologists, patients are transferred as quickly as possible by the Perpignan-GH medical emergency mobile unit using air transport, if available, or by road. On arrival at the CSC, MRI is repeated in the case of clinical worsening or improvement during transfer (NIHSS score increase or decrease of more than 4 points compared with the initial score), or of transfer time longer than 90 minutes. Patients do not undergo EVT when the new MRI data suggest low likelihood of clinical improvement, according to the imaging criteria described in previous clinical trials[2,4] (DWI-ASPECT score <5 and poor collateral circulation distal to the occlusion). Daytime was from 8 am to 18:30 pm.

Study Design

From the 1st of January 2012 to the 31st of December 2017, the clinical data of all patients with AIS admitted to the Perpignan-GH PSC within 4.5 hours from symptom onset were extracted from a prospectively maintained database and included in this comprehensive observational study. In 2010 (when the transfer protocol was initiated), patients admitted to the PSC after 4.5 hours were judged ineligible for transfer because of the anticipated transport delay that would have precluded EVT implementation within 6 hours from symptom onset. During the 6-year period, some changes were introduced in the protocol: (1) after the positive results of randomized clinical trials[1-5] in 2015, patients with NIHSS less than 8 or with DWI-ASPECT score less than 5 are now selected for EVT on a case-by-case basis. Moreover, patients with occlusion of the M2 segment of the MCA are now systematically transferred; (2) after February 2015, a quality improvement program to reduce door-to-needle time and door-in-door-out time was implemented at the PSC for AIS management[11,12]; (3) after January 2016, imaging data are systematically transmitted to the CSC using a regional

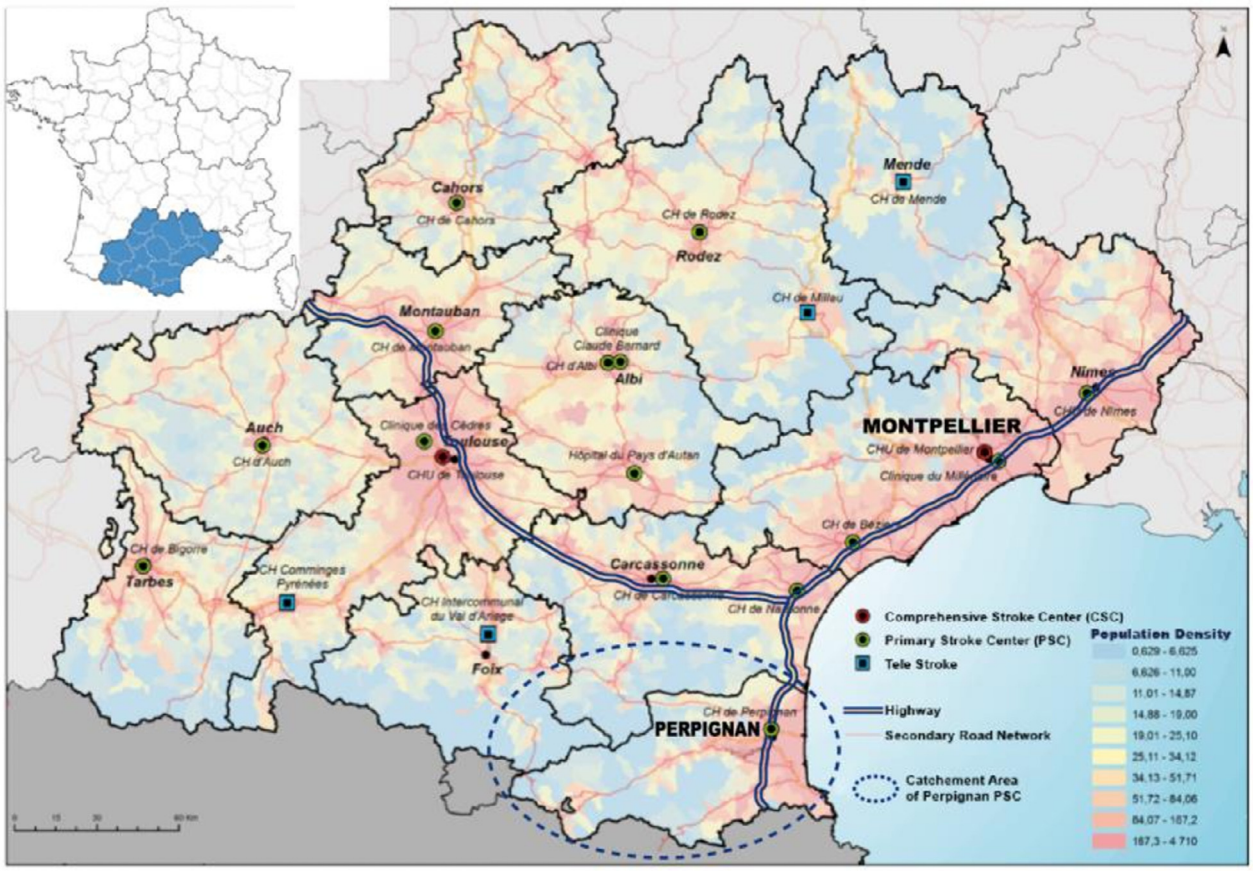

Figure 1. *Map of the regional stroke network. Perpignan: primary stroke center (PSC); Montpellier: comprehensive stroke center (CSC). The PSC catchment area is highlighted by the dotted-line circle.*

digital image transfer program; (4) after March 2016, patients with IVT contra-indications are directly admitted to the CSC (mothership model), and from May 2017 also patients with wake-up stroke; (5) following the publication of the meta-analysis by Saver et al in 2016,[10] patients may be transferred for EVT with delays longer than 6 hours on a case-by-case basis, based on criteria of good clinical outcome, by using MRI and/or CT perfusion imaging (large DWI/perfusion-weighted imaging mismatch and good collateral circulation distal to the occlusion). The Dawn and Defuse 3 trials,[8,9] which define a new standard of care in the AHA/ASA guidelines,[7] are subsequent to our study.

Data were prospectively collected in a specific Stroke database under the supervision of dedicated clinical research assistants and only anonymized information was used for this analysis. The institutional ethics committee of the Perpignan and Montpellier hospitals approved this study.

Statistical Analysis

Continuous variables were presented using medians, interquartile ranges (IQR), means and standard deviations, and categorical variables as percentages. Groups were compared using the Student's *t* or the Wilcoxon Mann Whitney U tests for quantitative variables, as appropriate, and the Fisher's exact and X_2 tests for qualitative variables. The significance threshold was set at 5%. Statistical analyses were performed with the on-line free-access "biostaTGV" program (http://marne.u707.jussieu.fr/biostatgv/).

Results

Cohort Characteristics

During the study period, 529 patients with AIS due to proximal LVO according to the initial MRI results were considered potentially eligible for EVT (flow chart in Fig 2; see Table 1 for their characteristics and details on the occlusion location). Their mean age was 73 years (standard deviation 14), 52.8% were men, and their median baseline NIHSS score was 16 (IQR: 8-21).

Among these 529 eligible patients (43 with contraindication for IVT and 446 who received IVT), 278 were transferred to the CSC for EVT alone (n = 67) or for EVT after IVT (n = 211) (transfer rate = 52.6%, see Table 1 and Fig 2). Overall, the average annualized number of candidates for EVT and of transferred patients was 88/year and 46/year, which corresponded to 20/ and 10 of 100,000 inhabitants/year, respectively.

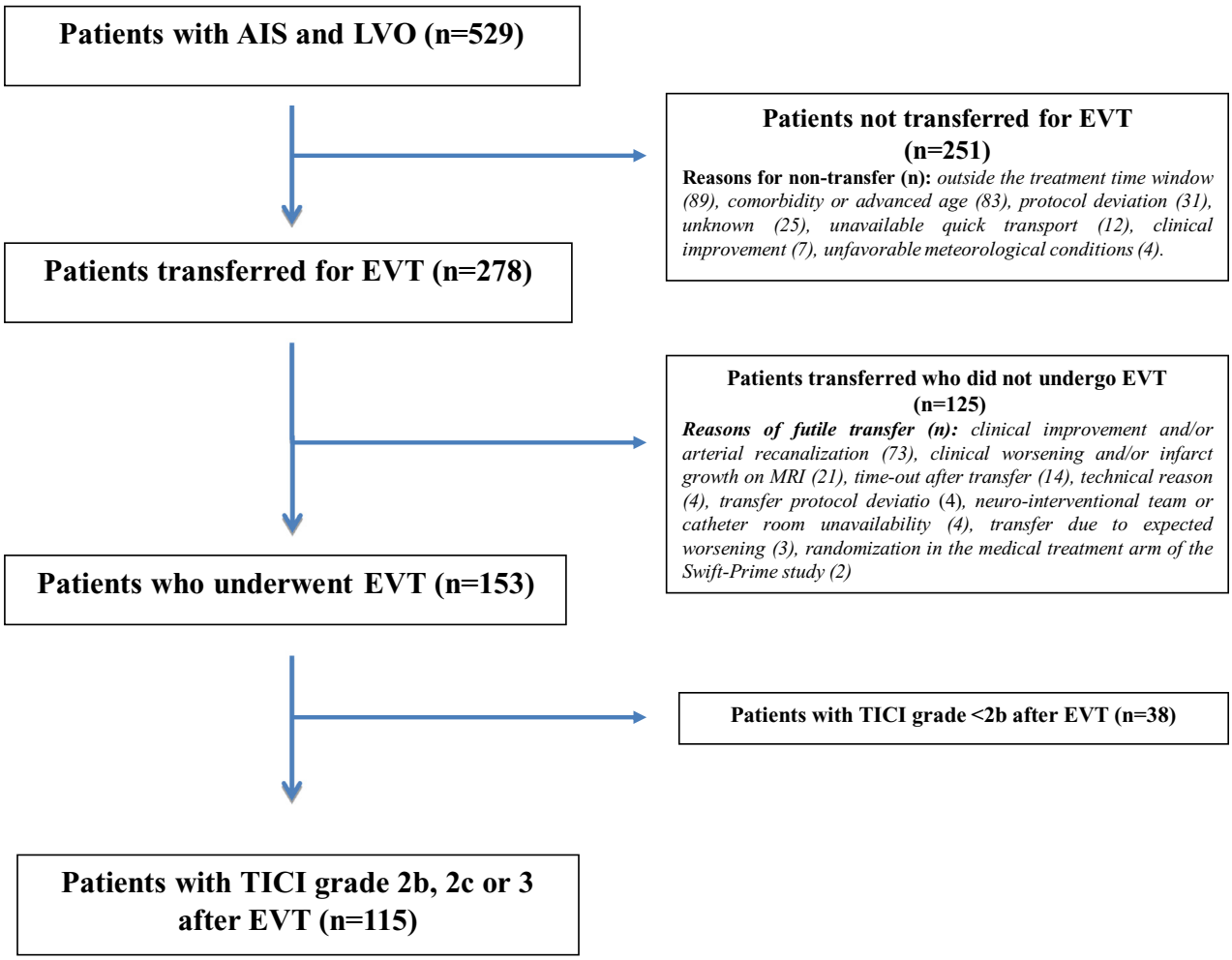

Figure 2. *Study flowchart describing the selection of patients with acute ischemic stroke and large artery occlusion for transfer from a primary stroke center to a comprehensive stroke center for mechanical thrombectomy. Abbreviations: AIS, acute ischemic stroke; EVT, mechanical thrombectomy; LVO, large vessel occlusion; TICI, thrombolysis in cerebral Infarction.*

The rate of transfer without EVT (futile transfers) was 45% (n = 135/278), mainly because of clinical and imaging improvement on arrival at the CSC (58.4%, see Table 1 for all the other reasons). Overall, 153 patients underwent EVT (28.9% of the 529 eligible patients) among whom 115 had a thrombolysis in cerebral infarction score greater than or equal to 2b-3. This corresponds to a reperfusion rate of 75.2% for the patients who underwent EVT, and to an overall reperfusion rate of 21.7% for all eligible patients.

Main Time Parameters

Patients received IVT within 3 hours (median "symptom onset to IVT start" time: 145 minute, (IQR: 115-180)) and EVT was generally performed after 6 hours from symptom onset (median "symptom onset to reperfusion" time: 393 minute, IQR: 332-454; for details see Table 1). The rate of EVT reperfusion after 6 hours was 62.9%. The median daytime (n = 168) and night-time (n = 110) "PSC door-out to CSC door-in" times were similar (85 versus 88 minutes, $P = .25$). Air transport was used in 65% of cases with shorter transfer time compared with road transport [76 minute (IQ 60-95) versus 100 minute (92-110)], although this difference was not significant ($P = .5$).

Outcome

During the 6-year study period, 1 major adverse event occurred during transfer (respiratory insufficiency requiring mechanical ventilation). At 3 months, the rates of favorable outcome (modified Rankin Scale 0-2) were 42.4% (patients eligible for EVT), 49.1% (transferred patients) and 34.1% (transferred patients who underwent EVT; difference not significant). Mortality was not significantly different between patients who underwent EVT and patients who were eligible but nontransferred ($P = .46$; Fig 3).

Table 1. *Clinical characteristics and main time measures*

	Patients with AIS and LVO (n=529)	*Patients transferred for EVT (n=278)*	*Patients who underwent EVT (n=153)*	*Patients with TICI grade 2b or 3 after EVT (n=115)*
***Age**, mean (SD)*	*73 (14)*	*69 (14)*	*70 (13)*	*70 (14)*
***Male**, n (%)*	*279 (52.8%)*	*162 (58.3%)*	*84 (54.9%)*	*62 (53.9%)*
***NIH-SS**, median (IQR)*	*16 (8-21)*	*17 (10-21)*	*18 (12-21)*	*18 (11-22)*
***DWI-ASPECTS**, median (IQR)*	*7 (6-8)*	*7 (6-8)*	*7 (6-8)*	*7 (6-8)*
***Occlusion location**, n (%)*				
IC ICA and carotid terminus	*52 (9.8%)*			
IC ICA and M1 segment of MCA	*69 (13%)*			
M1 segment of MCA	*248 (46.9%)*			
M2 segment of MCA	*75 (14.2%)*			
BA	*52 (9.8%)*			
P1 segment of PCA	*20 (3.8%)*			
Other or multiple LVO	*13 (2.5%)*			
***Causes of non-transfer**, n (%)*				
Outside the treatment time window[¶]	*89 (35.4%)*			
Comorbidity or advanced age	*83 (33%)*			
Protocol deviation	*31 (12.4%)*			
Unknown	*25 (10%)*			
Unavailable quick transport[¶]	*12 (4.8%)*			
Clinical improvement	*7 (2.8%)*			
Meteorological conditions[¶]	*4 (1.6%)*			
***Causes of futile transfer**, n (% of all futile transfer)*		***125/278***		
Clinical improvement and/or arterial recanalization		*73 (58.4%)*		
Clinical worsening and/or infarct growth on MRI[¶]		*21 (16.8%)*		
Time-out after transfer[¶]		*14 (11.2%)*		
Technical reason		*4 (3.2%)*		
Transfer protocol deviation[†]		*4 (3.2%)*		
Neuro-interventional team or catheter room unavailability[¶]		*4 (3.2%)*		
Transfer due to expected worsening		*3 (2.4%)*		
Randomization in the medical treatment arm of the Swift-Prime study		*2 (1.6%)*		
***Median Time** in minutes (IQR)*				
Symptom onset to IVT start (n=430) [‡]	*145 (115-180)*			
Door to needle (n=443)	*61 (45-87)*			
Door in to door out at the PSC (n=269)[§]		*90 (76-110)*		
Symptom onset to CSC door (n=199) [‡]		*275 (239-319)*		
Imaging at PSC to reperfusion (n=115)		*262 (239-316)*		
PSC door out to CSC door in (n=223)		*88 (65-104)*		
Symptom onset to EVT puncture (n=111) [‡]			*317 (278-373)*	
IVT start to EVT puncture (n=92)		*186 (158-214)*		
CSC door to EVT puncture (n=125)		*64 (33-82)*		
Symptom onset to reperfusion (n=105) [‡]		*393 (332-454)*		

Discussion

Recent clinical trials have consistently shown the clinical benefits of EVT for selected patients with AIS and proximal artery occlusion,[1-6,8,9] and indicated that the transfer of patients from a PSC to a CSC for rescue thrombectomy is a valid option. However, to our knowledge, only very few studies included all patients eligible for EVT in the analysis, and not just a selection.[13] In this observational study, we analyzed quantitative (patient volume, transfer ratio, EVT ratio, reperfusion ratio) and qualitative variables (safety analysis, exclusion criteria of potential candidates for EVT, time to reperfusion, follow-up of eligible patients) in a comprehensive, real-life, monocentric cohort. The main quantitative result of our study is the very low overall reperfusion rate by EVT for patients with LVO admitted to a distant PSC. Indeed, although the reperfusion rate in patients who underwent EVT was 75.2%, only 21.7% of all potential EVT candidates (n = 529) were recanalized by EVT. This confirms and expands the interim results (at 3 years) we previously reported.[13] It is uncertain whether the transfer protocol criteria that were used to identify the 529 patients eligible for transfer/EVT during the 6-year study period match

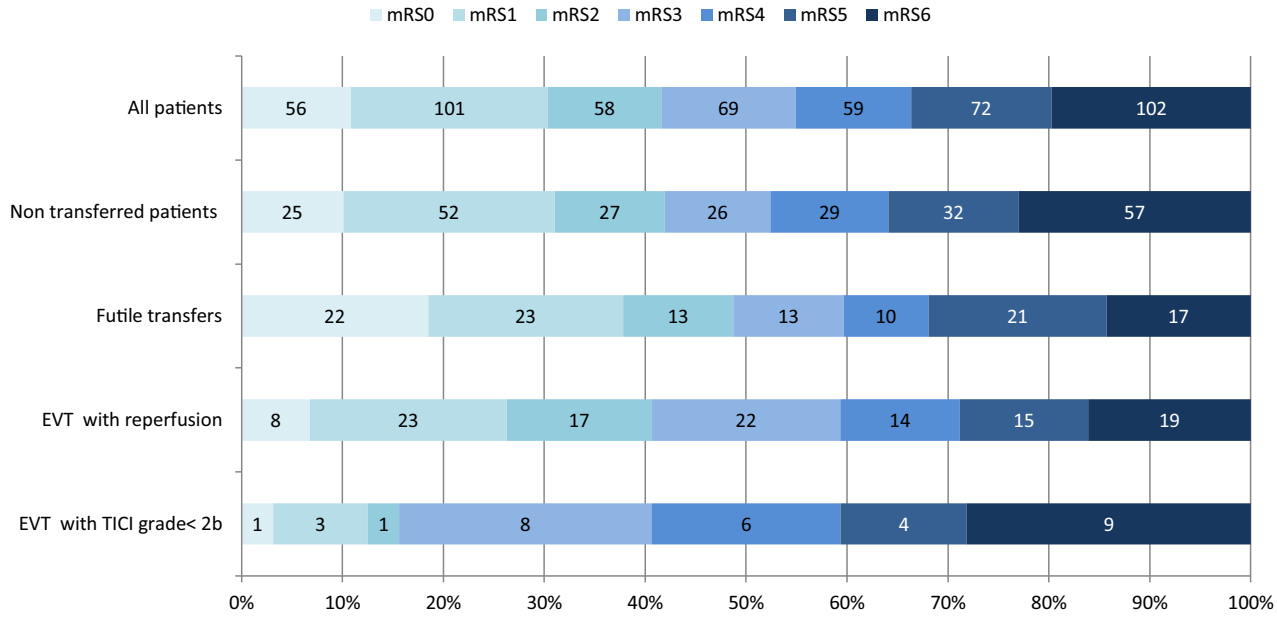

Figure 3. *Clinical outcome of the different groups of patients at the 3-month follow-up visit. The rate of good outcome (mRS 0-2) was not significantly different among patients who underwent EVT with reperfusion, patients who were not transferred (P = .85), and patients with futile transfer (P = .22).* Abbreviations: AIS, acute ischemic stroke; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; TICI, thrombolysis in cerebral Infarction.

the current criteria for EVT. First, the protocol was amended several times during the study period following the publication of new trials and guidelines.[7-10] Second, our cohort included patients with important comorbidities or advanced age. These features are associated with uncertain benefit from EVT, although recent studies show a positive trend.[14] Third, some patients were not included in the initial cohort because of the restrictive criteria of the regional transfer protocol concerning the delay (<6 hours for EVT), stroke severity (NIHSS >8 and DWI-ASPECT >5), and LVO location (M2 segment of MCA not systematically included) that were defined before the publication of the results of several randomized clinical trials.[1-6] Since then, new studies argued for the extension of criteria, such as age,[14] large infarct volume,[15-17] LVO location,[17] and delays.[8-10] Nevertheless, our results suggest that in settings comparable to ours, the absence of on-site interventional neuroradiology facilities may preclude EVT accessibility to the majority of patients due to the long transportation times. For instance, in the less than 4.5-hour window, we retrospectively identified a group of 144 patients (27.2% of all eligible patients) who could have been treated by EVT if on-site interventional neuroradiology facilities had been available. Among them, 105 patients (19.8% of all eligible patients) were not transferred because of inappropriate time window, unavailable transfer, or meteorological conditions. For the other 39 patients (7.4% of all eligible patients), the transfer was defined futile due to the extremely long transport time, neurological worsening during transfer, or unavailability of the interventional neuroradiology team or room upon arrival at the CSC (Table 1). We thus estimate that in the absence of EVT facilities in our secondary care center, more than 25% of patients had an obvious loss of chance due to time-related or random factors. This is in accordance with previous studies that suggested a 1%-2.5% decrease in the chance of performing intra-arterial therapy for every minute lost during transfer.[18,19]

The main qualitative result is the extreme delay from symptom onset to reperfusion that correlates with the low overall reperfusion rate. Patients treated beyond the 6 hour time-window were mostly selected on the basis of penumbral imaging patterns (indicating an infarction core volume <50 ml that reflects the adequacy of collateral blood flow), and/or of a diffusion- and perfusion-weighted mismatch used to identify low progressor profiles. In fact, this group of patients treated beyond 6 hours represents the majority (62.9%) of all patients that finally underwent EVT. Therefore, the slow progressor profile was the most important treatment determinant in patients transferred from the PSC to the CSC. As EVT clinical benefit is higher with short reperfusion delay,[1-6,10,18-22] alternative options to reduce symptom-onset-to-reperfusion time are necessary, especially in distant PSCs. Direct admission to the CSC could avoid loss of time linked to the primary management at the PSC, and reduce the time to EVT. However, Perpignan-GH is the closest point to the Montpellier CSC (Fig 1), and virtually all villages and

towns in its catchment area are further away from Montpellier. This means that direct transfer to the CSC without stopping at the PSC (mothership model) would result in a time loss of approximately 2 hours for patients with indication for IVT. Consequently, patients must be first admitted to Perpignan-GH PSC, and then transferred to the CSC if eligible for EVT. Moreover, the improvement of the transfer workflow had a limited impact (<1 hour gain of time), and led mainly to a reduction of the door-in-to-door-out times at PSC.[23] Thus, despite new facilities and networks, a short reperfusion time is very unusual in large catchment areas that are far away from the CSC. Consequently, the benefits of centralizing endovascular AIS therapy in larger CSCs within stroke networks must be weighed against the risks related to longer transport times. Decision-making on the optimal distribution of interventional neuroradiology facilities should take into account both transport times and the need to maintain adequate care access. Therefore, we think that in areas that are far away from a CSC, the conversion of high-volume PSCs into CSCs would be sensible and effective in terms of public health.

Our study has several limitations. First, not all potential candidates for EVT were included in our analysis, especially patients admitted to the PSC after more than 4.5 hours from symptom onset. Thus, our cohort only represents a selected group of all the patients who could have been eligible for EVT. Second, the MRI protocol did not systematically evaluate the existence and quality of collateral arteries that could be an important protective factor for salvageable tissue, and thus of the clinical outcome after EVT, even for patients with low ASPECT score. Third, despite the regional transfer protocol, our series was very heterogeneous. The transfer of patients with occlusion of the M2 segment of the MCA, P1 segment of the posterior cerebral artery, A1 segment of the ACA or BA was discussed on a case-by-case basis, and eligibility for EVT was based on the clinical judgement of the on-call neuroradiologist. Fourth, indications for EVT, particularly the time delay criterion, varied during the study period. Fifth, our results reflect a setting with a specific stroke network organization that is strongly influenced by local and geographical considerations. This limits their generalization. Nevertheless, our experience may help to rationalize and develop stroke networks in similar areas to improve EVT accessibility for eligible patients in regions with a large distance between PSC and CSC.

Conclusions

Our transfer protocol to a distant CSC with an anticipated transport time of 1.5 hour offers effective mechanical recanalization only to a minority of patients with a slow progressor profile. Therefore, long transfer delays and high volume are the main reasons to convert a PSC with a large population catchment area in a CSC that can deliver both thrombolysis and endovascular therapy.

Author Contribution

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Alain Bonafe: conception and design of the work, analysis, interpretation of data, drafting, writing and final approval.

Conflicts of Interest

All authors declare no conflict of interest.

References

1. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11-20.
2. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 2015;372:1009-1018.
3. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019-1030.
4. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 2015;372:2285-2295.
5. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 2015;372:2296-2306.
6. Bracard S, Ducrocq X, Mas JL, et al. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. Lancet Neurol 2016;15:1138-1147.
7. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2018;49:e46-e99.
8. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med 2018;378:11-21.
9. Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. N Engl J Med 2018.
10. Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. JAMA 2016;316:1279-1288.
11. Sablot D, Gaillard N, Colas C, et al. Results of a one-year quality improvement process to reduce door-to-needle time for acute ischemic stroke with MRI screening. Rev Neurol 2017;173:47-54.
12. Sablot D, Ion I, Khlifa K, et al. Target door-to-needle time for tissue plasminogen activator treatment with magnetic resonance imaging screening can be reduced to 45 min. Cerebrovasc Dis 2018;45:245-251.
13. Sablot D, Gaillard N, Smadja P, et al. Thrombectomy accessibility after transfer from a primary stroke center: analysis of a three-year prospective registry. Int J Stroke 2017;12:519-523.
14. Campbell BC, Hill MD, Rubiera M, et al. Safety and efficacy of solitaire stent thrombectomy: individual patient data meta-analysis of randomized trials. Stroke 2016;47:798-806.
15. Gilgen M, Klimek D, Liesirova K, et al. Younger stroke patients with large pretreatment diffusion-weighted imaging lesions may benefit from endovascular treatment. Stroke 2015;46:2510-2516.
16. Danière F, Lobotesis K, Machi P, et al. Patient selection for stroke endovascular therapy−DWI-ASPECTS thresholds should vary among age groups: insights from the RECOST study. AJNR Am J Neuroradiol 2015;36:32-39.
17. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723-1731.
18. Prabhakaran S, Ward E, John S, et al. Transfer delay is a major factor limiting the use of intra-arterial treatment in acute ischemic stroke. Stroke 2011;42:1626-1630.
19. Regenhardt RW, Mecca AP, Flavin SA, et al. Delays in the air or ground transfer of patients for endovascular thrombectomy. Stroke 2018;49:1419-1425.
20. Mazighi M, Chaudhry SA, Ribo M, et al. Impact of onset-to-reperfusion time on stroke mortality: a collaborative pooled analysis. Circulation 2013;127:1980-1985.
21. Mazighi M, Meseguer E, Labreuche SJM, et al. Dramatic recovery in acute ischemic stroke is associated with arterial recanalization grade and speed; Stroke 2012;43:2998-3002.
22. Khatri P, Abruzzo T, Yeatts SD, et al. Good clinical outcome after ischemic stroke with successful revascularization is time-dependent. Neurology 2009;73:1066-1072.
23. Sablot D, Farouil G, Laverdure A, et al. Shortening time to reperfusion after transfer from a primary to a comprehensive stroke center. NEURCLINPRACT/2018/034603, Published July 12, 2019. https://doi.org/10.1212/CPJ.0000000000000675.