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Original Article

Transfer of stroke patients impairs eligibility for endovascular stroke treatment

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A B S T R A C T

Background. – Many patients who are potentially eligible for endovascular stroke treatment (EST) receive intravenous rtPA in the closest stroke unit before being transferred to tertiary centres for EST. It has been shown that clinical outcome of transferred and EST-treated patients is comparable to that of patients with direct access to EST. We analysed clinical outcome of patients, who were transferred and eventually not treated due to clinical and/or radiological deterioration.
Methods. – We retrospectively analysed our prospectively maintained stroke registry for patients who were transferred for stroke therapy.
Results. – Four hundred twenty-two of 1208 patients (35.1%), who were admitted for acute reperfusion stroke therapy between 03/10 and 01/15 were eligible for EST. Ninety-one (7.5%) of these patients were admitted specifically for EST from remote hospitals. Favorable clinical outcome rates after 90 days (mRS $\leq$ 2) were comparable between 63 transferred and 295 directly-admitted patients, who received EST ($P = 0.699$). However, transferred patients, who were eligible for EST on initial admission, were less likely to receive EST after transfer ($P < 0.001$): twenty-two of 91 patients (24.2%), who were transferred for EST, became ineligible during transfer due to infarct demarcation. Procedural times of treated and untreated transferred patients were comparable ($P \geq 0.508$). There was a trend towards worse clinical outcome in untreated patients, without reaching statistical significance (OR, 0.269; 95% CI, 0.55–1.324; $P = 0.119$).
Conclusions. – EST should be provided directly whenever possible as one in four transferred stroke patients becomes ineligible for EST during transfer. If direct transfer is not possible, indication for EST should be re-assessed after transfer.

Introduction

Endovascular stroke treatment (EST) has recently become a standard treatment option for acute ischemic stroke due to large-vessel-occlusion (LVO) [1–7]. Even though EST has become very common, full EST coverage has not yet been established in many regions. This is why patients who are eligible for EST often receive systemic thrombolysis in the closest hospital first, before being transferred to another hospital for EST [8–10]. Several authors have demonstrated that clinical outcome of transferred patients who actually receive EST is comparable to that of patients with direct access to EST [8,9,11]. As clinical outcome is time-dependent, delays in onset-to-puncture times diminish odds for good clinical outcome and hamper the initiation of EST altogether [12–14]. Mokin et al. reported that one-third of transferred patients became ineligible for EST due to ASPECTS deterioration during transfer [15]. Prabhakaran et al. showed that interhospital transfer delays are a major factor for patients to become ineligible for EST [10]. While clinical outcome of treated patients appears to be favorable, little attention has been given to patients who were transferred and eventually not treated due to clinical or radiological deterioration. This is why we analyzed clinical outcome of transferred patients with special emphasis on patients who became ineligible for EST during transfer.

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Material and methods

Patients

We retrospectively analyzed our stroke registry for patients who were admitted for acute stroke therapy. Between March 2010 and January 2015, 1208 patients were admitted for acute reperfusion therapy of acute ischemic stroke. One hundred sixty-four (13.6%) of these patients had been transferred from remote hospitals and 1044 patients were admitted directly to our hospital. An ambulance was used for the transportation in all cases.

Clinical, procedural, and radiological data

After receiving permission from our local ethics board (RWTH Aachen university), we evaluated the patients' demographical data, clinical presentation (NIHSS, national institute for health stroke scale) and disability (mRS, modified Rankin scale) upon admission, cerebrovascular risk factors, stroke etiology (adapted from trial of ORG 10172 in acute stroke treatment, TOAST), and disability at follow-up (mRS after 90 days) [16]. All radiological data were re-evaluated by a second neuroradiologist, who was blinded to clinical data. We included radiological and procedural data of initial and postinterventional/follow-up imaging with site of LVO, type of intra-arterial (IA) treatment (including bridging therapy), and reperfusion result (thrombectomy in cerebral infarction [TICI]) [17]. We assessed the following procedural times: onset-to-door, door-to-image, image-to-puncture, puncture-to-revascularization, external image-to-door; and external image-to-internal image. Primary outcome measures were procedural times and clinical outcome (morbidity defined as mRS ≤ 2 and mortality after 90 days).

Treatment decision-making

Our stroke network structures ensured that all "transferred" AIS patients were sent from primary stroke centres with neurovascular expertise (stroke unit and administration of systemic thrombolysis). In our hospital, patients were considered eligible for EST when there was clinical stroke due to large-vessel-occlusion accessible for EST and absence of large infarction or hemorrhage, regardless of time of onset. A neurological stroke team and a neuroradiological interventional team ensured full-time stroke treatment. After the rescue coordination centre informed the neurologist in charge about a possible stroke, the neurologist informed the neuroradiologist on call. If a clinical examination confirmed the stroke, the anesthesiologist was also informed. The patient was transferred to the CT suite, where an unenhanced CT, CT angiography and CT perfusion were performed [18]. Systemic thrombolysis was administered if symptoms occurred within a time window of 4.5 hours, there was no hemorrhage, and CT indicated the absence of large infarction (Alberta stroke program early CT score, ASPECTS ≥ 6, or area of suspected ischemia ≤ one third of the affected territory). Assessment of infarction size was not based on a strict ASPECTS interpretation, as its binary nature implies low scores when there are small but multiple infarctions. Results of CT perfusion were taken into account for decision-making whenever there was a mismatch between clinical symptoms and infarction (e.g. motor deficits without infarction of the motor cortex or pyramidal tract), or whenever time of onset was unknown or beyond 4.5 hours after symptom onset. EST was initiated in these cases if there was mismatch between cerebral blood volume and cerebral blood flow that indicated clinically relevant salvageable brain tissue. LVO was defined as occlusion of large cerebral arteries accessible for EST. These are the internal carotid artery (ICA), the M1 and M2 segments of the middle cerebral artery (MCA), the A1 and A2 segments of the anterior cerebral artery (ACA) as well as the vertebral artery (VA), the basilar artery (BA), and P1 and P2 segments of the posterior cerebral artery (PCA). In the remote hospitals, eligibility for EST was mainly based on absence of large infarction on cranial CT imaging, a hyperdense artery sign, and severe clinical symptoms indicating LVO. Vascular imaging for the proof of LVO was performed inconsistently (see Results).

An interventionalist and an experienced neurologist decided about the indication for EST on a case-to-case basis, with decision-making being also built on clinical and social criteria. The patient and/or the patient's relatives are involved in the decision process whenever possible. If the decision to perform EST was made, the patient was transferred to the angiography suite. All endovascular procedures were performed using general anesthesia. Standard endovascular treatment with and without stent retrievers was performed as reported previously [6].

Statistical analysis

Pearson's χ^2 tests and Fisher's exact tests were used, when applicable. Student's t tests and Mann-Whitney U tests were applied after testing for normal data distribution with a Shapiro Wilk test. P values ≤ 0.05 were defined as significant. All statistical analyses were performed with SPSS 23 software (IBM, Armonk, New York).

Results

Fig. 1 provides an overview of all admitted patients. Five of 164 transferred patients were in-house strokes in the remote hospitals and were excluded from our analysis. Sixty-five of the remaining 159 patients were transferred for acute reperfusion therapy of any kind. The remaining 94 transferred patients were specifically admitted for EST after initial evaluation in a remote hospital (Fig. 1). Three of the 94 patients had stroke mimics and were excluded from further analysis. The decision to transfer the remaining 91 patients specifically for EST was based on radiological and clinical data in the remote hospitals. External cerebral imaging was available for our analysis in 52 patients who were specifically admitted for EST. Vascular imaging was available in 9 of these 52 patients. The sending hospitals of the 91 patients were located at a distance of < 10 km (4 patients), 10–25 km (71 patients), and > 25 km (16 patients). Four of 328 primarily admitted patients, who were eligible for EST, declined this treatment option and were excluded from our analyses.

Online Table 1 issues an overview of clinical, radiologic, and procedural data of all patients, who were eligible for endovascular stroke treatment. Transferred patients were significantly younger (P < 0.001) and had a significantly higher NIHSS score and larger infarctions on admission (P ≤ 0.003) (Online Table 1). While onset-to-door and onset-to-revascularization intervals were significantly longer (P < 0.001), in-house procedures were either comparable or significantly faster when patients were transferred for EST (Online Table 1).

EST was initiated in 295 of 324 (91.0%) primarily admitted patients and in 63 of 91 (69.2%) transferred patients, respectively (P < 0.001). In primarily admitted patients, improvement of clinical symptoms or mild clinical symptoms in the first place were the reasons not to initiate EST in 10 of 29 untreated patients, while more severe clinical symptoms and no expectable benefit from EST were the reasons not to initiate EST in the remaining 19 untreated patients. In transferred patients, EST was not initiated in 6 of 28 patients because of complete recovery or considerable improvement of clinical symptoms during transport. EST was not initiated in the remaining 22 patients because there was (near) complete infarction of the affected territory on imaging in our hospital. All 8

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