Clinical Neurology and Neurosurgery 123 (2014) 136–141

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Poor outcomes of elderly patients undergoing multimodality intra-arterial therapy for acute ischemic stroke

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ARTICLE INFO

Article history:
Received 12 May 2014
Received in revised form 27 May 2014
Accepted 27 May 2014
Available online 4 June 2014

Keywords:
Stroke
Aged 80 and over
Intra-arterial therapy
Mechanical thrombolysis
Endovascular procedures

ABSTRACT

Objective: The incidence of acute ischemic stroke is highest in the elderly. Information regarding outcomes of elderly patients undergoing different modalities of intra-arterial therapy (IAT) for acute ischemic stroke (AIS) is scarce and conflicting. This study compares the safety, technical efficacy and outcomes of elderly patients (≥80 years) to non-elderly patients (<80 years) who underwent multimodality IAT.

Methods: From a registry of consecutive patients treated with IAT for AIS at our institution over a 3.5-year period, patients with anterior circulation occlusions aged ≥80 years were compared to the patients <80 years.

Results: Between 2008 and 2012, 24 patients ≥80 years (elderly) and 95 patients <80 years (non-elderly) received IAT for anterior circulation occlusions. In the elderly, there were more females (66.7% vs. 28.4%, $p = <0.001$) and atrial fibrillation (58.3% vs. 25.2%, $p = 0.003$). Between the 2 groups, there was no difference in NIHSS score (17.2 vs. 16.3, $p = 0.17$), THRIVE score (4.21 vs. 4.39, $p = 0.633$), recanalization rate (70.1% vs. 85.3%, $p = 0.13$), or severe reperfusion hemorrhages (8.3% vs. 4.2%, $p = 0.425$). There was no significant difference in 3-month mortality (33.3% vs. 16.8%, $p = 0.28$); however, fewer elderly patients reached good 3-month outcome (0% vs. 40.0%, $p = <0.001$). After controlling for baseline factors, only female gender (OR 5.3, 95% CI 1.7–16.7; $p = 0.04$) and higher 3-month mRS (OR 1.6; 95% CI 1.1–2.40; $p = 0.008$) were independently associated with elderly age.

Conclusion: Despite similar safety profiles and recanalization rates, elderly patients had poor functional outcomes after IAT. Intra-arterial therapy in the elderly should be pursued very cautiously only after careful analysis of the risks and benefits for each patient.

1. Introduction

Acute ischemic stroke (AIS) is a strongly age-related disease. Although currently comprising 3.6% of the total U.S. population, patients age 80 and above account for 30% or more of all strokes annually [1,2]. The elderly age group is the fastest growing segment of the population in westernized countries [1,3]. Thus, acute stroke management in the elderly population is of considerable interest.

Intra-arterial therapy (IAT) is an emerging AIS treatment strategy that is being used to compliment IV rt-PA administration to increase target vessel recanalization rates and potentially improve outcomes [4,5]. However, elderly patients are routinely excluded or under-represented in IAT stroke trials [4,6,7]. Therefore, endovascular stroke therapies have not been well studied in the elderly population. In the current study, we compare baseline characteristics, treatment variables, procedural safety and functional outcomes between elderly patients (≥80 years) and non-elderly patients (<80 years) who underwent multimodality intra-arterial treatment of AIS at our institution over a 3.5-year period.

2. Methods

A retrospective review was performed of consecutive patients undergoing endovascular intervention for anterior circulation AIS at our institution over a 43-month period from January 2009 to July

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http://dx.doi.org/10.1016/j.clineuro.2014.05.025
0303-8467/

2012. During the study period, 145 patients received IAT for AIS and 119 met inclusion criteria for this analysis. Twenty-six patients were excluded: posterior circulation occlusion ($n = 18$), time from symptom onset >12 h ($n = 4$), distal branch occlusion ($n = 2$), and no attempt at intracranial recanalization ($n = 2$). The local Institutional Review Board approved this study.

2.1. Patient selection

Inclusion criteria: angiographically confirmed anterior circulation occlusion, National Institute of Health Stroke Scale (NIHSS) score ≥7 or aphasia, time from symptom onset to intervention of ≤12 h (or last time seen well for cases with an unwitnessed ictus), no evidence of hemorrhage or malignant edema on pre-intervention non-contrast CT as defined by the NINDS rt-PA study group protocol [8], large artery occlusion (internal carotid artery, middle cerebral artery M1 or M2 trunks), infarct size smaller than 1/3 the middle cerebral artery (MCA) territory on MRI diffusion weighted imaging (DWI) or CT perfusion cerebral blood volume (CBV) and an ischemic core to perfusion mismatch ratio of greater than 1:1.2 (favorable penumbra pattern) on MR perfusion or CT perfusion scan by qualitative analysis. For this study, core DWI/CBV infarct volumes and perfusion mismatches were not quantitatively measured by radiographic software prior to selection; however, visual qualitative mismatch assessment were used and have been shown to have functional equivalence in the clinical setting [9]. In patients beyond 6 h from symptom onset, the decision to perform IAT was uniformly supported by advanced imaging demonstrating a small infarct (<1/3 the MCA territory) and a favorable diffusion–perfusion mismatch pattern. Finally, patients presenting very early after symptom onset (<3 h) that met all other inclusion criteria, were often taken directly for intervention based on clinical exam and time based parameters at the discretion of the treatment team.

2.2. Data

Patient baseline demographics were collected. Pre-intervention variables recorded include: initial NIHSS score, IV thrombolytic administration, imaging studies performed, and time from symptom onset to the start of IAT. Totaled health risks in vascular events (THRIVE) scores were calculated [10]. Treatment variables included: site of vessel occlusion, length of procedure, thrombolysis method used, IA thrombolytics administered and vessel recanalization score on the thrombolysis in myocardial infarction (TIMI) scale. A TIMI scale score of 2 or 3 was considered vessel recanalization. Safety measures included: procedural vessel rupture, overall reperfusion hemorrhages by the European Cooperative Stroke Study (ECASS) criteria and severe parenchymal hemorrhage type 2 (PH2) ECASS criteria reperfusion hemorrhages on a post-procedure CT within 48 h [11]. Functional outcomes were scored on the Modified Rankin Scale (mRS) and a good outcome was considered mRS 0–2 at 3-months.

2.3. Treatment protocol

Intra-arterial thrombolysis procedures were performed under conscious sedation, unless the patient arrived to the angiography suite previously intubated or experienced respiratory failure during the procedure. Therapies were performed using biplanar flat-panel fluoroscopy (Siemens, Artis zee). The type of procedure performed was at the discretion of the operator, and the types were defined as follows: chemical thrombolysis (rt-PA ± wire maceration), mechanical thrombectomy (MERCI – Concentric Medical, Mountain View, CA; and/or Penumbra – Penumbra, Alameda, CA.; and/or Solitaire – eV3, Irvine, CA); or mechanical + stent/balloon angioplasty (any of the aforementioned devices plus either angioplasty and/or stenting). In mechanical thrombolysis procedures, intra-arterial thrombolytic (2–10 mg rt-PA) was often administered to supplement mechanical thrombectomy. In patients who received pre-procedure IV rt-PA, IA rt-PA dose was limited to less than 5 mg.

2.4. Statistical analysis

Categorical variables were compared by chi-square test or fisher exact test as appropriate. Kolmogorov–Smirnov test was performed to evaluate for normality. Continuous variables were evaluated by independent *T*-test or Mann–Whitney *U*, as appropriate. Statistical significance was set at $p \leq 0.05$. Multivariate binary logistic regression analyses with variable selection method were performed using age (<80 years-old vs. ≥80 years-old) as the dependent variable, and included variables with $p < 0.1$ on univariate analysis.

3. Results

The baseline patient characteristics of the elderly (≥80 years) and non-elderly groups (<80 years) groups were similar with the exception of age, sex, and atrial fibrillation (Table 1). The mean pre-treatment NIHSS score was comparable between groups. There was no difference in THRIVE score between the cohorts (4.21 vs. 4.39, $p = 0.63$). Intravenous rt-PA was administered in a similar proportion of cases (43.4% vs. 59.1%, $p = 0.11$). The type of imaging modality used to select patients for intervention was not different between the groups ($p = 0.13$). The mean time from symptom onset to the start of IAT was equivalent between the groups (6.6 h vs. 6.2 h, $p = 0.264$).

Procedural variables were also similar (Table 1). Successful recanalization (TIMI 2–3) was achieved in 70.1% of the elderly and of the 85.3% non-elderly patients ($p = 0.13$). Mean procedure time, intra-arterial thrombolytic use and intra-procedural vessel ruptures were similar between the groups. The elderly did not have increased post-procedure hemorrhagic complications. Stent retriever devices became available in the final 3 months of the study period and were used as the primary embolectomy device in 9 procedures (1 elderly and 8 non-elderly).

At hospital discharge, 0% of elderly patients had achieved a good functional outcome (mRS 0–2) compared to 15% in the non-elderly group ($p = 0.045$). At 3 months, 0% of the elderly patients had reached a good functional outcome while 40.0% of non-elderly patients had achieved a good functional outcome ($p = <0.001$). However, there was no significant difference in 3-month mortality between the groups (33.3% vs. 16.8% ($p = 0.28$). The distribution of mRS scores at 3-months is summarized in Fig. 1. Six patients in the non-elderly group (6.3%) and 0 patients in the elderly group (0%) were lost to 3-month follow-up.

Due to the complete absence of good outcomes in the elderly group, the ordinal variable mRS (rather than mRS 0–2) was included into the multivariate analysis to avoid statistical artifact. The only factors independently associated with the dependent variable, age ≥80 years, were female gender (OR 5.3, 95% CI 1.7–16.7; $p = 0.04$) and mRS at 3 months (OR 1.6; 95% CI 1.1–2.40; $p = 0.008$) (Table 2).

Sensitivity analysis included univariate and multivariate liner regression for predictors of outcome. Age (unstandardized β 0.31; 95% CI 0.11–0.52; $p = <0.01$), atrial fibrillation (unstandardized β 0.74; 95% CI 0.36–1.44; $p = 0.04$) and TIMI score (unstandardized β −0.48; 95% CI −0.84–0.12; $p = <0.01$) were independently associated with mRS at 3 months (analysis not shown).