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ABSTRACT

Purpose: Stroke is a disease of the elderly, however it can affect the younger patients. We present a retrospective review of our series of young patients (55 years old and younger), treated at our institution from 2007 to 2012, to assess the safety, efficacy and patient outcome of multimodal endovascular treatment in this patient population.

Methods: A total of 42 patients underwent multimodal endovascular revascularization for acute ischemic events. Recanalization rates were assessed using the Thrombolysis in Myocardial Infarction (TIMI)and clinical outcomes were assessed using the Modified Rankin Scale (mRS) obtained at discharge and follow-up visits. Patient demographics, medical co-morbidities, treatment complications and mortality data were collected and analyzed.

Results: Of 42 patients, an improvement in Thrombolysis in Myocardial Infarction score (TIMI score) was noted in 38 patients (90.47%). The average modified Rankin Scale score on discharge was 3.2 with 25 patients (60%) having a favorable score of 0-3. All 21 patients (100%) with available clinical follow-up had a favorable mRS score (mean follow-up of 10.4 months). Symptomatic intracranial hemorrhage occurred in four patients (9.5%); none required surgery. Three fatalities resulted from intraoperative vessel rupture (7.14%).

Conclusion: We observed good recanalization rates and favorable clinical outcomes after endovascular stroke intervention in young patients. Also, there was a low morbidity and mortality rate overall. Therefore multimodal endovascular recanalization of acute ischemic stroke is an effective treatment in younger patients, which justifies aggressive management of those patients.

Keywords: *Acute stroke in younger patients (55 years old and younger); Multimodal endovascular treatment; TIMI; mRS*

INTRODUCTION

Stroke is one of the most important causes of long-term disability; it is also the third leading cause of death in the USA. One in every 18 deaths in the United States is due to stroke. Approximately 800,000 strokes occur in the United States each year, leading to an estimated cost of 74 billion dollars in 2010. The severity and prognosis of patients with acute arterial occlusions is extremely poor. Studies have shown that 16-55% of patients will die from complications related to the infarction, 40-69% will be left with a profound deficit, and only 2-12% will make a reasonable recovery.[9] During the initial years stroke management was mainly focused on prevention, supportive care and rehabilitation. But over the past few decades there has been a breakthrough in the medical management of stroke especially with the use of intravenous tissue plasminogen activator (iv r-TPA) approved by the FDA in 1996[1]. However results from trials utilizing these techniques have still not been encouraging.[2,3] Among the most recent modalities of stroke management, endovascular management achieved amazing growth and development since late 1990's.[1] There have been several small case reports of endovascular stent-assisted thrombolysis as a treatment option for patients with carotid occlusions and near occlusions.[4-8] Today angioplasty and stenting are increasingly performed alongside mechanical and chemical thrombolysis to maximize recanalization and improve flow restoration, with favorable results.[21-23]

Younger adults, from 18 to 45 years of age constitute 10-14% of all the ischemic strokes.[10-17] As compared to the older individuals, these younger adults have a greater variety of etiological factors that further varies from one geographical area to another.[14,17-19] So far, there have been only a few studies published on ischemic stroke in young adults [11-14] and even these were carried out a few decades ago. However the recent development in diagnostic tests for stroke especially the neuroimaging along with the novel effective therapeutic approaches including the endovascular management and establishment of tertiary stroke centers have made significant changes in the statistics documented so far for the acute ischemic stroke in young patients, which needs to be updated.[20] We retrospectively studied the safety, efficacy and patient outcome of multimodal endovascular treatment for acute stroke in younger patients (age 55 years old and younger) treated at our institution.

METHODS

The institutional review board approval was obtained. A retrospective review of the charts of patients 55 years old and younger treated at our institution from 2007 to 2012 was done. A total of 42 patients met the inclusion criteria. On admission all patients were assessed by the NIH Stroke Scale (NIHSS). Prior to endovascular intervention, a non-contrast head CT was performed as a pre-operative baseline and to exclude intracranial hemorrhage or completed infarctions. In addition, CT angiography and CT perfusion studies were obtained emergently. The decision to

proceed with endovascular thrombolysis was based on clinical and radio-graphic analysis of pre-operative data. In summary, a minimum NIHSS score of 6, absence of intracranial hemorrhage or completed infarctions on the initial non contrast CT, CT perfusion (CTP) with abnormal mean transient time and cerebral blood flow but preservation of cerebral blood volume, and a detectable arterial occlusion on CT angiography were the inclusion criteria for patients to be candidates intervention. All arterial occlusions were confirmed by subsequent digital subtraction angiography. CTP is a rapidly emerging diagnostic imaging tool that is useful in acute stroke diagnosis. Standardization of this technology can be very helpful in making clinical decision based on quantitative data[24] although several reports have raised concerns with its safety, reproducibility and accuracy.[25-27]

Patient demographics, admission and discharge neurological examinations, medical co-morbidities, treatment complications and mortality data were collected and analyzed. Medical co-morbidities included smoking, hypertension, diabetes, hyperlipidemia and atrial fibrillation. The neurological assessment on admission was done on the basis of the NIHSS score. The time from the onset of the symptoms until groin puncture was recorded and analyzed. Treatment complications included intraoperative vessel perforation, dissection, reocclusion of target vessel or new vessel, as well as post intervention intracranial hemorrhage. Recanalization rates were assessed using the Thrombolysis in Myocardial Infarction (TIMI). Clinical outcomes were assessed using the Modified Rankin Scale (mRS) obtained at discharge and follow-up visits. We used the inpatient hospital records, imaging studies, operative reports and outpatient office records for the analysis.

ENDOVASCULAR TREATMENT

All endovascular procedures were performed under general endotracheal anesthesia. Digital subtraction angiography was obtained focusing on the occluded vessel. A triaxial system was used in most cases. If there was a tandem lesion, extracranial carotid occlusion associated with an intracranial lesion, the carotid occlusion was addressed first with balloon angioplasty and stenting. Once the carotid artery was opened, angiography was performed to assess the intracerebral circulation. Intracranial mechanical thrombectomy was performed with the merci device, Penumbra or solitaire. Patients who were in the 6 hours window got in addition intra-arterial injection of Tpa at the site of occlusion. Postoperatively, all patients were transferred to the neurointensive care unit and a non-contrast head CT was routinely performed 24 hours later.

RESULTS

There were 22 female and 20 male patients. The mean age was 44.43 years (range 20-55 years). Seventeen (40.48%) patients had hypertension, fourteen (33.33%) had hypercholesterolemia, seven (16.66%) had diabetes mellitus, six (14.28%) had atrial fibrillation and fourteen (33.33%) had a significant history of smoking. Mean National Institutes of Health Stroke Scale score at admission was 13.05. The middle cerebral artery was occluded in 24(55.81%) patients, the ICA in 9 (21.42%) patients, the basilar artery in ten (23.25%) patients and the anterior cerebral artery (ACA) in 1 (2.32%). Twenty (47.62%) patients received intravenous tissue plasminogen activator prior to admission. The average time from symptom onset to endovascular intervention was 6 hours. In 22 patients (52.38%), more than one endovascular treatment modality was employed. Thirty-four (80.95%) underwent mechanical thrombolysis either with Penumbra, Merci System or solitaire. The penumbra device was used in 16 patients, the Merci device in 15, solitaire in 1 patient and both devices in 2. Two (4.76%) patients underwent stent placement, thirteen (30.95%) underwent balloon angioplasty and twelve (28.57%) underwent both angioplasty and stent placement. Twenty-one (50%) required adjunctive intra-arterial thrombolytics. At baseline, 39 (92.86%) patients had a TIMI score of 0 (mean TIMI score at baseline was 0.12). An improvement in Thrombolysis in Myocardial Infarction score (TIMI score) was noted in 38 patients (90.47%). In a total of 42 patients, post-recanalization TIMI scores were 0 in two (4.76%) patients, 1 in five (11.9%) patients, 2 in seven (16.66%) patients and 3 in 28(66.66%) patients (mean TIMI score post-recanalization being 2.45). A total of four patients (9.5%) showed some degree of intracranial hemorrhage on post-operative imaging; all four were confluent hematomas (PH-1 and PH-2, by the ECASS (European Cooperative Acute Stroke Study) classification); all four were symptomatic but none required surgery. Three fatalities resulted from intraoperative vessel rupture (7.14%). The average modified Rankin Scale score on discharge was 3.2 with 25 patients (60%) having favorable score of 0-3. The data of mRS score at follow up visits were available for 21 patients for which the average score was 1.67 with all of the 21 patients (100%) having favorable score of 0-3 at follow-up, the mean duration of follow-up visit being 10.4 months.

DISCUSSION

Stroke, the third leading cause of death in USA, has generally been regarded as the disease of elderly. The incidence of stroke doubles every 10 years after the age of 50. Considering the increase in elderly population in developed countries with the improved healthcare, it is estimated that the prevalence of stroke would increase by 24.9% over next 20 years.[29] Ironically, the overall stroke incidence rates have been reported to decline in the 21st century. As per the Framingham heart study there was a decrease in age-adjusted stroke incidence per 1,000 person-years from 1950 to 2004 of 7.6 to 5.3 in men and 6.2 to 5.1 in women.[30] However, with a fall in the overall incidence of stroke, it has been documented that the incidence of stroke in younger adults is increasing. Among the adults of 14-44 yrs of age, Ischemic stroke admissions in the US Nationwide Inpatient Sample increased annually from 1995 to 2008. [31, 32] In one of the studies Kissela et al.[33] came up with the conclusion that the proportion of total first-ever stroke accounted for by those ages 20–54 years increased from 12.9% in 1993–1994 to 18.6% in 2005. Also, in this age group, incident stroke increased from 26 per 100,000 in 1993–1994 to 48 in 2005 among white patients, and 83 in 1993–1994 to 128 in 2005 among black patients.[32] In any case, if the incidence of stroke rises in younger ages, with increasing life span, stroke-related disability would increase even more causing a significant health care burden ahead.[32]

In our study we found that out of 42 patients, seventeen (40.48%) patients had arterial hypertension, fourteen (33.33%) had hypercholesterolemia, seven (16.66%) had diabetes mellitus, six (14.28%) had atrial fibrillation and fourteen (33.33%) had a significant history of smoking. In one of the studies von Sarnowski B et al.[34] concluded that among 4467 patients

(median age, 47 years; interquartile range, [40-51] the most frequent well-documented and modifiable risk factors were smoking (55.5%), physical inactivity (48.2%), arterial hypertension (46.6%), dyslipidemia (34.9%), and obesity (22.3%). Modifiable less well-documented or potentially modifiable risk factors like high-risk alcohol consumption (33.0%) and short sleep duration (20.6%) were more frequent in men, and migraine (26.5%) was more frequent in women. Despite a vast difference in the total number of patients, the rates were comparable. In another study Yao XY et al.[35] compared the rates of these risk factors in the younger and the elderly patients and concluded that younger age group had a higher incidence of smoking and drinking while hypertension and atrial fibrillation were found to be higher in the elderly. There was an interesting case documented by Ogawa et al.[42] which raised the possibility of Crohn's disease of being an important risk factor for stroke most probably due to dehydration and other complex mechanisms.

Total perioperative morbity was 16.67% which was again less than the 27.5% in the study of elderly patients at our center.[36] Seven patients showed intraoperative ruptures or postoperative hemorrhage out of which 4 patients had symptomatic hematoma. There were three fatalities from the intraoperative rupture (procedure related mortality being 7.14%) and these were identified as extravasation of contrast intraoperatively. The mean mRS at follow-up was 1.67. This was also less than the 3.9 in the elderly study at our center.[36] Similar comparison rates between the younger and the elderly patient cohorts were found in other studies. Chandra et al. [37] documented dismal clinical outcomes in elderly patients (>80) yrs with average mRS score 4-6 as compared to the younger patients despite of similar rates of TIMI reperfusion of 2-3. A recent review of the SITS-ISTR registry revealed that patients aged older than 80 had significantly higher mortality than younger patients after IV tPA treatment, despite a similar symptomatic intracranial hemorrhage rate.[38] A meta-analysis of 2244 patients that included 477 patients aged 80 years or older also yielded similar findings.[37,39] The higher mortality in the elderly may result from higher incidences of medical comorbidities and post-stroke complications.[37-41]

In previous series of stroke patients, time from ictus to endovascular intervention ranged from a mean of 4.3 to 6.25 h.[43,44] Our study had an average time to intervention of 6 hrs. As a tertiary referral center, most patients at our center are evaluated at an outside institution and then transferred on clinical suspicion of stroke. The use of CTP criteria (which allowed the extension of the therapeutic window) to select patients for endovascular intervention also explains the long interval from stroke onset in our study. Fourteen patients in our study underwent stent placement either alone or with balloon angioplasty. Primary use of self-expanding stents have gained popularity and found to enhance early revascularization.[45-47] Recanalization is found to be an appropriate biomarker of therapeutic activity in early phase trials of thrombolytic treatment with a strong correlation with improved functional outcomes and reduced mortality in acute ischemic stroke.[48] Angioplasty has been shown to have lower stroke rate after 1 year than medical therapy alone.[49] In one another study it was found that addition of retrievable stents to the multimodal endovascular approach for acute ischemic stroke treatment significantly reduces time to recanalization and further increases the recanalization rate.[50] Moreover, Xavier et all showed that delayed recanalization beyond 8 hours is a viable option with the help of stent assisted intracranial recanalization in a selective group of patients presenting with acute ischemic stroke.[51] Recent use of enterprise, wingspan and solitaire stents have been shown to achieve high rates of technical success with acceptable periprocedural morbidities.[28,52-54]

In acute ischemic stroke, patient's outcome mainly depends on restoring the blood flow to the cerebral penumbra and impedes the progression of parenchymal infarct. Penumbra is the local ischemic tissue of brain where the function is decreased but the neurons are still viable if the blood flow is restored. The penumbra may have small or large area minutes to hours after the onset of symptoms.[55,56] The success of revascularization techniques for acute ischemic stroke depends on a strict patient selection process before initiating any medical or surgical processes, including but not limited to age, comorbidities, anatomical and pathophysiological (irreversible damaged brain volume, penumbra volume, and cerebral vasculature), and ethical (benefit versus risk and consent considerations) factors.[55] Traditionally the success of the stroke treatment has been related to the time-criteria for patient selection, however recent studies lay more importance on physiologic neuroimaging such as CT perfusion. Turk et al.[57] demonstrated similar rates of good functional outcome and intracranial hemorrhage in patients with ischemic stroke when endovascular treatment was performed based on CT perfusion selection rather than time-guided selection. An initial evaluation with CT scan is a must to exclude the presence of completed infarct or intracranial hemorrhage, which would otherwise increase the rate of hemorrhagic conversion after the endovascular treatment.[58] In the Penumbra Pivotal Stroke Trial, Goyal et al. found that a baseline CT scan by ASPECTS score >7 (Alberta Stroke Program Early CT Scale) had a 50% chance of a favorable clinical outcome with early recanalization (p=0.0001). In addition, ASPECTS scores of less than 4 did not show clinical improvement regardless of endovascular recanalization. (1,59). Similarly it is also important to evaluate the patient with angiography before the commencement of endovascular procedure, to determine the ischemic etiology. All procedures at our institution are carried out under general endotracheal anesthesia. Although general anesthesia contributes to safety and increased efficacy by motion elimination,[1,60] there has been some studies claiming that local anesthesia and conscious sedation leads to better neurological outcome as well as morbidity and mortality than general anesthesia by decreasing time delay and cerebral ischemia from hypoperfusion.[61,62]

Our study was limited by its retrospective nature and small number of patients, but again stroke being widely prevalent in elderly, it is difficult to find younger patients fulfilling all the clinical and radiographic criteria. It is necessary to carry out larger prospective randomized control trials to further study the risk factors for acute ischemic stroke in young patients and investigate the efficacy and clinical outcome of multimodal endovascular interventions in them. So far, few studies exist in the literature.

CONCLUSION

We observed excellent recanalization rates and clinical outcomes respectively in terms of improvement in TIMI scores from admission to discharge and mRS scores at discharge

and follow-up visits. Also there was a low morbidity and mortality rate overall. This leads us to the conclusion that multimodal endovascular recanalization of acute ischemic stroke is a very effective treatment in patients 55 years of age or younger.

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