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Acute ischaemic stroke outcomes following mechanical thrombectomy in the elderly versus their younger counterpart: a retrospective cohort study

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ABSTRACT

Objectives: Many physicians debate the efficacy of mechanical thrombectomy for ischaemic stroke, but most agree that to establish potential benefit, patient selection must be examined further. People >80 years are a growing population of patients with ischaemic stroke but are largely excluded from clinical trials. The benefit of thrombectomy for them may be greatly reduced due to diminishing neuroplasticity and a larger number of medical comorbidities. To address this knowledge gap, we examined clinical and economic outcomes after mechanical thrombectomy in the ischaemic stroke population from the Nationwide Inpatient Sample. Our null hypotheses were that elderly patients (>80 years) would have a similar rate of inpatient mortality in comparison to their younger counterparts and incur a similar economic expense.

Design: Retrospective cohort study.

Setting: A 20% stratified sample of US community hospitals within the Nationwide Inpatient Sample.

Participants: All patients from 2008 to 2010 with a primary diagnosis of ischaemic stroke that received mechanical thrombectomy were included.

Primary and secondary outcome measures: The primary outcome was inpatient mortality. Secondary outcomes included hospital charges and length of stay.

Results: Less than 1% of all ischaemic stroke cases (9300) were treated with mechanical thrombectomy. Of these, 18% involved patients over 80 years of age. The odds of inpatient mortality in elderly patients treated with mechanical thrombectomy were approximately twice that of their younger counterparts (OR1.993, p < 0.001). The elderly experienced no significant difference in hospital charges (p=0.105) and length of stay (p=0.498).

Conclusions: The odds of inpatient mortality after mechanical thrombectomy in patients over 80 years of age were twice that of their younger counterparts. This is consistent with the overall worse prognosis seen in the natural history of this age group. Studies to better identify patients that would benefit from endovascular mechanical thrombectomy may improve outcomes and reduce the gap currently observed in age stratifications.

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Strength and limitations of this study

- The large number of included patients and the ability to study medical practice at large without selection bias.
- Owing to limitations in the database we could not control for disease specifics in each population such as location/size of occlusion, collateral reperfusion, blood glucose level and admission National Institutes of Health Stroke Scale (NIHSS) score.
- The time period of the study predated the arrival of stent-retriever devices, which may prove to be safer and more efficacious than previous generation devices.

INTRODUCTION

Controversy over the utility of endovascular mechanical thrombectomy (EMT) for acute ischaemic stroke (AIS) has arisen since the Interventional Management of Stroke III trial (IMS III) was stopped in 2012 because of statistical futility.[1] Two additional trials, MR-RESCUE and SYNTHESIS Expansion, similarly failed to show any significant benefit with EMT for AIS.[1–3] Although individuals may disagree on the conclusions and debate the limitations of these trials, most agree that better selection criteria need to be established in order to identify potential subpopulations of patients who may benefit from EMT for AIS. Additionally, the cost-effectiveness of this intervention must be assessed and weighed in comparison with clinical outcomes. This is particularly important with the rise of healthcare costs in the USA, which at its current pace is expected to reach one-fifth of the gross domestic product by 2018.[4] Early debates of the Affordable Care Act centred on the creation of death panels to ration expenses. Although this panel was dismissed as myth, there remains a critical need to analyse the cost of newly developed stroke interventions in an ageing

population that may not incur the same benefits as their younger peers due to lack of neuroplasticity and ongoing medical comorbidities.

The elderly population is expected to grow dramatically over the coming decades, specifically with the percentage of persons over 80 years of age doubling by 2050.[5] Given the growing percentage of elderly and their growing life expectancy, discussions regarding procedural risk versus clinical benefit will expand in importance, particularly with regard to costly interventions like EMT. The paucity of data on EMT, specifically in the elderly population, limits the physician's ability to adequately counsel patients and their families regarding any potential benefit from this emergent intervention.

To address this knowledge gap, we examined the elderly ischaemic stroke population treated with EMT in a national database. Our null hypotheses were that elderly patients (>80 years) would have a similar rate of inpatient mortality in comparison with their younger counterparts and incur a similar economic expense. The primary outcome was inpatient mortality. Secondary outcomes included hospital charges and length of stay.

METHODS

We analysed discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (Rockville, Maryland, USA). This database represents approximately a 20% stratified sample of US community hospitals. Detailed information on the design of the NIS is available at http://www.hcup-us.ahrq.gov. We examined the prevalence of EMT for AIS using data published from NIS for 2008–2010.

Patients with AIS were identified in the NIS using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes (433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91 and 437.1). Intervention utilising EMT was identified using the ICD-9-CM procedure code 39.74, and pharmacological thrombolysis was documented with procedure code 99.10. Of note, there is no distinction in the ICD-9-CM code between intra-arterial and intravenous administration of thrombolytics. Additionally, a hospital was classified as 'high volume' if its total discharge stroke volume exceeded 147 cases/year.[6] Total hospital charges from 2008 to 2009 were compounded yearly at an inflation rate of 3% to standardise the charges at 2010 levels. The length of hospital stay and associated hospital charges were calculated for all patients (including in-hospital deaths) and additionally for surviving patients. The second analysis was conducted to examine the economic measures without the artificial shortening of these variables that may occur in cases of comfort rather than curative care. The comorbidity burden of each patient was expressed as the sum of the Elixhauser comorbidity measures.[7] [8]

Data were analysed using SPSS V.17 (IBM Corporation, Armonk, New York, USA). To obtain national estimates, discharge weights were applied. Univariate comparisons were performed using Mann-Whitney U tests and χ^2 tests, as appropriate.

Binary logistic regression was used to analyse the primary objective, inpatient mortality. The analysis considered the following factors known to affect stroke outcome: elderly age (>80 years), thrombolysis administration, presentation to a 'high-volume' stroke centre, gender and All Patient Refined–Diagnosis Related Group (APR–DRG) severity of illness (SOI). Backward stepwise regression was performed with variable entry when probability was less than 0.05 and removal when probability exceeded 0.10. ORs and their 95% CIs were reported.

Generalised linear models with a γ-distribution and log link function were used to analyse the economic measures. The exponential parameter estimates were reported along with their 95% CIs. The exponential parameter estimates are equivalent to the ratio of the estimated marginal means with the denominator being the reference category. A probability value of 0.01 was considered statistically significant in order to nominally control for type I error.

RESULTS

Nationally, there were 1 674 200 AIS cases during the years 2008–2010, 9300 (<1%) of which received EMT. Overall inpatient mortality for AIS was 7.9%. This rate increased to 23.8% when considering only patients receiving intervention with EMT. Patients greater than 80 years of age receiving EMT had an inpatient mortality rate of 33.7%, significantly exceeding the rate for their younger counterpart that was found to be 21.6% (p<0.001; table 1). In comparison with younger patients, the patient over 80 was more likely to be a Caucasian woman on Medicare, to have received pharmacological thrombolysis and to not be discharged home (table 1). Interestingly, no patients, young or elderly, treated at low-volume stroke centres were discharged home (0/70). This is opposed to 10.8% of patients admitted to high-volume stroke centres (p=0.004).

Multivariate analysis was performed to examine the primary and secondary outcome measures (figure 1). The odds for inpatient mortality in the elderly treated with EMT were approximately double in comparison with their younger counterpart (OR 1.993, 95% CI 1.763 to 2.254, p<0.001). The factors noted to significantly (p<.01) reduce mortality were presentation to a high-volume stroke centre (OR=0.378), thrombolysis administration (OR=0.873), female gender (0.855) and decreased SOI (figure 1). There was no significant difference in hospital charges and length of stay for the elderly (figure 1). The economic measures were most influenced by SOI (figure 1).

DISCUSSION

The paucity of data on EMT in the elderly impedes the ability of physicians and patients to make informed

Table 1 Patient-level and hospital-level characteristics of the population receiving mechanical thrombectomy for acute ischaemic stroke compared between the elderly and their younger counterpart

	≤80 years (n=7614 cases)	>80 years (n=1686 cases)	p Value
Age	63 (53–73)	84 (82–87)	
Gender, female	46.9%	66.7%	<0.001
Race, Caucasian	60.2%	67.6%	0.013
Median income level			
<US$39 000	26.7%	23.5%	0.607
US$39 000–$47 999	24.8%	25.6%	
US$48 000–$62 999	23.6%	23.5%	
≥US$63 000	24.9%	27.4%	
Payer, Medicare	44.9%	90.5%	<0.001
Elixhauser comorbidity score			
≤2	37.2%	30.6%	<0.001
3	21.7%	26.5%	
≥4	41.1%	42.9%	
APR-DRG severity of illness			
Mild	0%	0%	0.418
Moderate	1.5%	0.6%	
Major	53.5%	53.9%	
Extreme	45%	45.5%	
Thrombolysis (intravenous or intra-arterial)	55.5%	63.1%	0.013
Length of stay, days (survivors)	9 (5–14)	9 (6–13.6)	0.711
Length of stay, days (all patients)	8 (4–13)	8 (4–12)	0.004
Total charges, US$ (survivors)	137 692 (95 139–207 687)	137 756 (87 582–198 103)	0.021
Total charges, US$ (all patients)	132 828 (90 661–205 835)	126 238 (86 230–188 294)	<0.001
Discharged home	12.7%	2.1%	<0.001
Inpatient mortality	21.6%	33.7%	<0.001
Hospital owner			
Government, non-federal	22.6%	18.8%	0.150
Private, non-profit	69.2%	74.6%	
Private, investor-owned	8.2%	6.6%	
Teaching hospital	84.2%	80.6%	0.122

Continuous variables expressed as median (25th centile–75th centile).
APR-DRG, All Patient Refined–Diagnosis Related Group.

decisions. As this segment of the population is forecasted to dramatically increase, additional information on the risk versus benefit of intervention will facilitate physician–patient discussions.

This study quantifies clinical and economic outcomes following EMT for AIS in patients older than 80 years of age across the USA. The higher mortality in patients aged over 80 years is in agreement with the overall worse prognosis seen in the natural history of this age group. For example, the Specialized Program of Translational Research in Acute Stroke (SPOTRIAS) examined patients ≥80 years of age who received intravenous rt-PA and/or intra-arterial therapy.[9] The database contained more than 1100 patients aged 80 years and greater. It documented a higher risk of in-hospital mortality for the elderly patient with stroke (OR 2.13), but no difference in mortality rates between intervention modalities. Similarly, data from the European BIOMED Study of Stroke Care Group and the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) registry reported outcomes from patients with AIS aged >80 years, and documented higher mortality and worse functional

outcomes.[10 11] Specifically, the SITS-MOST documented an increase in mortality by 18% for patients >80 years and a 22% reduction in independence.[11]

It is reassuring to note that the population of elderly patients in the present study exhibited similar mortality in comparison to the above-mentioned thrombolysis trials. Patients in the current study were all treated with EMT, likely for one of two reasons: (1) failure of intravenous rt-PA to clear a proximal large vessel occlusive lesion or (2) the individual arrived to the hospital after a prolonged time lapse from symptom onset, thereby leaving EMT as the last line of therapy within the accepted time windows. Both of these indications represent a group of exceptionally disease burdened patients.

The role of gender in stroke outcomes is not clearly defined. In agreement with our study, Saposnik et al[12] reported on 12 262 patients with AIS and noted the male sex to be a predictor of early mortality. Yet, Niewada et al[13] reported the results of 17 370 patients with AIS and documented that women had higher 14-day and 6-month mortality; while Adams et al[14] collected data on 1281 patients with AIS and found no
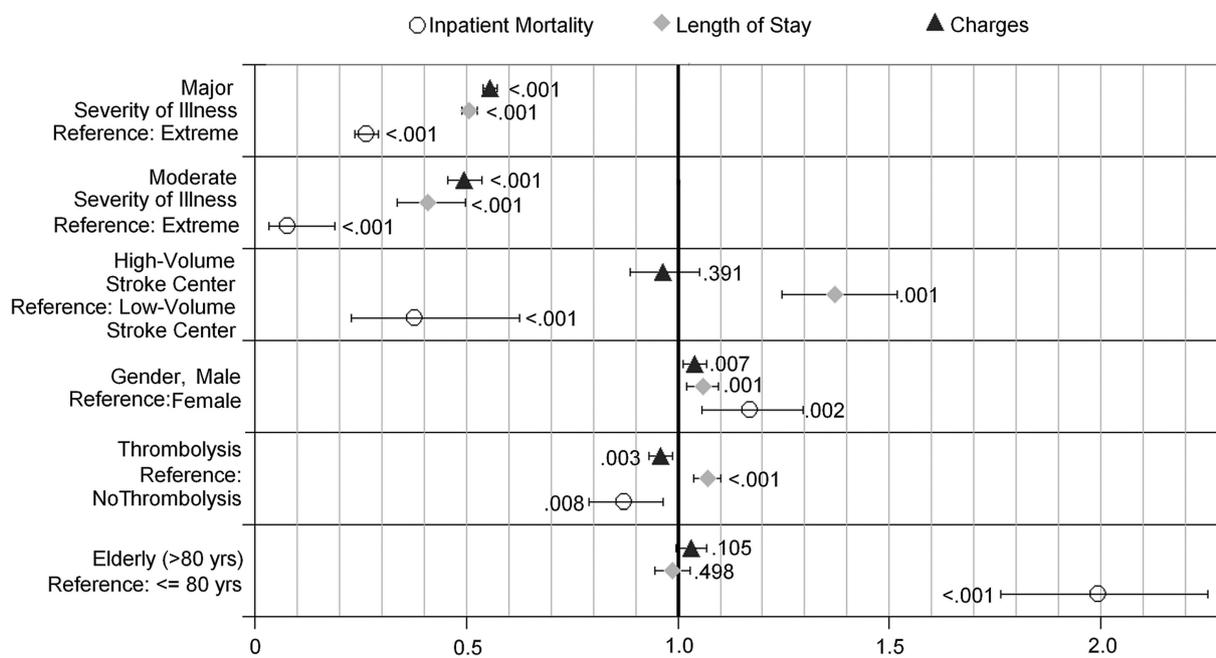
Figure 1 Multivariate analysis of inpatient mortality and economic measures for survivors. Inpatient mortality expressed as the OR along with the 95% CI derived from binary logistic regression. Length of stay and charges are both expressed using the exponential parameter estimate along with the 95% CI derived from generalised estimating equations. p Values are adjacent to the 95% CIs. Points to the right of 1.0 reflect an increase in the odds/effect ratio relative to the indicated reference category. Points to the left of 1.0 reflect a decrease in the odds/effect ratio relative to the indicated reference category.

relationship between outcome and gender. Further research is warranted to investigate any gender effects with regard to patients with AIS, and specifically those undergoing EMT.

We anticipated increased expenses for the elderly with regard to their overall inpatient admission due to the larger number of chronic conditions, higher morbidity burden and diminished efficiency of rehabilitation.[15 16] It was surprising to note no significant differences in the economic measures based on age for survivors. If deaths were included, the length of stay and hospital charges were reduced in the elderly population. We believe largely due to increased utilisation of comfort rather than curative measures in the elderly population as evident by their increased rate of in-hospital mortality. Additionally, we must point out that our analysis does not reflect the true societal cost.[17–19] Long-term rehabilitation and care should be considered in future studies, but these measures were beyond the scope of the anonymised database used in this study.

Owing to limitations in the NIS we could not further investigate disease specifics in each population such as location/size of occlusion, collateral reperfusion, blood glucose level and admission National Institutes of Health Stroke Scale (NIHSS) score.[20–22] These variables are known to affect stroke outcome and the distribution within each population is unknown. While this is a limitation of the analysis, it is common to any large database study, and the benefits of large database examination include the ability to study medical practice at large without selection bias. An additional limitation is that

the primary and secondary objectives do not include any specific neurological or functional assessment, as these are not recorded in the NIS. Discharge to home was not considered as a primary objective as this variable may be influenced by the payor status and social factors, rather than a true assessment of independence and self-care. Lastly, the data collected for NIS predates the arrival of stent-retriever devices, which may prove to be safer and more efficacious than previous generation devices.

CONCLUSION

EMT for patients with AIS older than 80 years of age resulted in significantly increased inpatient mortality in comparison to their younger counterparts. This is consistent with the overall worse prognosis seen in the natural history of this age group. Studies to better identify patients that would benefit from EMT may improve outcomes and reduce the gap currently observed in age stratifications. Ongoing endeavours to develop new revascularisation devices may also improve AIS outcomes after EMT.

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