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Complete List of Authors:	Villwock, Mark; SUNY Upstate Medical University, Neurosurgery Singla, Amit; SUNY Upstate Medical University, Neurosurgery Padalino, David; SUNY Upstate Medical University, Neurosurgery Deshaies, Eric; SUNY Upstate Medical University, Neurosurgery
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Villwock, Mark R, Singla, Amit and Deshaies, Eric M

Villwock, Mark R

SUNY Upstate Medical University

Neurosurgery

750 East Adams Street

Syracuse

New York

13210

Singla, Amit

SUNY Upstate Medical University

Neurosurgery

750 East Adams Street

Syracuse

New York

13210

United States

Deshaies, Eric M

SUNY Upstate Medical University

Neurosurgery

750 East Adams Street

Syracuse

New York

13210

United States

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ABSTRACT

Objectives: Many physicians debate the efficacy of mechanical thrombectomy for ischemic stroke, but most agree that to establish potential benefit, patient selection must be examined further. People >80 years are a growing population of ischemic stroke patients. The benefit of thrombectomy for them may be greatly reduced due to diminishing neuroplasticity and a larger number of medical co-morbidities. To address this knowledge gap, we examined clinical and economic outcomes after mechanical thrombectomy in the ischemic stroke population from the Nationwide Inpatient Sample. Our hypothesis was that elderly patients (> 80 years) would fare worse at discharge in comparison to their younger counterparts.

Design: Retrospective cohort study.

Setting: A 20-percent stratified sample of U.S. community hospitals within the Nationwide Inpatient Sample.

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

Primary and secondary outcome measures: The primary outcome was the adjusted odds-ratio of mortality. Secondary outcomes included the adjusted odds-ratio for discharge disposition, and the adjusted effect-ratios of hospital charges and length of stay.

Results: Less than 1% of all ischemic stroke cases (9,300) were treated with mechanical thrombectomy. Of these, 18% involved patients > 80 years. The odds of mortality in elderly patients treated with mechanical thrombectomy were more than double that of their younger counterparts (OR:2.107, P<.001) and there was a significant reduction in the odds of being discharged home (OR:0.297, P=.004). Although univariate analysis depicted a significant difference in hospital charges and length of stay, multivariate analysis revealed no significant differences.

Conclusions: The odds of mortality after mechanical thrombectomy in patients > 80 years was twice that of their younger counterparts and few were eligible to be discharged home. Studies to better identify specific subpopulations of patients that would benefit from mechanical thrombectomy are needed urgently.

Strength and limitations of the study

- The strength of the study is the large number of included patients and the ability to study medical practice at large without selection bias.
- Due 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 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 ischemic 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 to clinical outcomes. This is particularly important with the rise of health care 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 centered on the creation of death panels to ration expenses. Although this panel was dismissed as myth, there remains a critical need to analyze the cost of newly-developed stroke interventions in an aging population that may not incur the same benefits as their younger peers due to lack of neuroplasticity and ongoing medical co-morbidities.

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 regards 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 patient outcomes specific to in-hospital mortality, discharge disposition, and economic data (length of stay and hospital charges) after EMT in the elderly ischemic stroke population using the national databases.

METHODS

We analyzed discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (Rockville, MD). This database represents approximately a 20% stratified sample of U.S. 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 through 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 utilizing 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 intra-venous administration of thrombolytics. Additionally, a hospital was classified as "high volume" if its total discharge stroke volume exceeded 147 cases per year.[6] Total hospital charges from 2008 and 2009 were compounded yearly at an inflation rate of 3% to standardize the charges at 2010 levels.

Data were analyzed using SPSS Version 17 (IBM Corporation, Armonk NY, USA). To obtain national estimates, discharge weights were applied. Patient discharge data and hospital demographics were compared between patients >80 yrs of age and patients ≤ 80 yrs of age. Additionally, outcomes were compared in the subset of patients > 80 years between those that received pharmacological thrombolysis only and those that received EMT. Independent samples t-tests, chi-squared tests, and Fisher's exact tests were used to make comparisons as appropriate.

Accounting for hospital and patient level variation in outcome measures (length of stay, total hospital charges, mortality, and discharge disposition), multivariate models were used to compare and make inferences about differences between elderly patients versus younger patients, and elderly patients receiving EMT versus pharmacological thrombolysis alone. This allows comparison while adjusting for confounding variables included in the NIS dataset. The analysis considered the following patient-specific factors: age, gender, race, patient income (<$39,000, $39000 to $47,999, $48,000 to $62,999, and ≥$63,000), payer (Medicare, Medicaid, private insurance, self-pay, or no charge), number of chronic conditions, and severity of illness (APR-DRG severity of illness). The analysis also considered hospital-level factors including: region (Northeast, Midwest, South, West), teaching status, hospital bed-size (small, medium, large), hospital location (rural or urban), ownership of hospital (public, private non-profit, private for profit), and whether the hospital was a "high volume" stroke center. Stepwise regression was performed with variable entry when probability was less than 0.05 and removal when probability exceeded 0.10.

Generalized linear models were used to analyze the outcome measures. A model using Gamma as the distribution and Log as the link function was used to calculate the estimated marginal means of the continuous variables including the total hospital charges and length of stay. The effect ratio was expressed as the quotient of the estimated marginal mean for patients > 80 yrs of age over the estimated marginal mean for patients ≤ 80 yrs of age; and the estimated marginal mean for patients > 80 years receiving EMT over the estimated marginal mean for patients > 80 years receiving only pharmacological thrombolysis. The binary outcomes, mortality and discharge home, were analyzed in binary logistic regression. Odds ratios and their 95% confidence intervals were reported. Bonferroni correction for multiple tests resulted in a probability value <.0125 (.05/4) being considered statistically significant.

RESULTS

Nationally, there were 1,674,200 acute ischemic stroke cases during the years 2008 through 2010, 9,300 (< 1%) of which received EMT. The overall rate of mortality for all acute ischemic stroke cases was 7.9%. This rate increased to 23.8% when considering only patients receiving intervention with EMT. Patients greater than 80 yrs of age receiving EMT had a mortality rate of 33.7%, significantly exceeding the rate for patients 80 yrs of age and younger that was found to be 21.6% (P < .001) (Table 1). In comparison to younger patients, the patient over 80 was more likely to be a white female on Medicare and to have received pharmacological thrombolysis (Table 1).

Multivariate analysis was performed to examine the outcome variables while controlling for confounding factors (Table 2). The odds for mortality in patients older than 80 treated with EMT were more than double in comparison to younger patients (OR 2.107, 95% CI: 1.549-2.866, P<.001). Elderly patients also had a significant reduction in the odds of being discharged home in comparison to their younger counterparts (OR 0.297, 95% CI: 0.131-0.673, P=.004). Although univariate analysis depicted a significant difference in hospital charges and length of stay based on age, the multivariate analysis revealed no significant differences (Table 2).

Lastly, the effect of pharmacological thrombolysis was examined in patients > 80 years of age. In comparison to the relatively small number of similarly aged patients treated with EMT (n = 1686), a drastic increase in the number of patients treated with thrombolysis was observed (n = 16493). Patients treated with thrombolysis alone had significantly reduced mortality in comparison to those treated with EMT, 15.2% versus 33.7%, respectively (P < .001). These patients also had a significantly greater rate of being discharged home, 9.0% versus 2.1% (P < .001). Multivariate models documented the odds of mortality following EMT to significantly increase by 84% in comparison to only thrombolysis; and hospital charges for cases involving EMT increased by 73% in comparison to cases with only thrombolysis (Table 3).

DISCUSSION

The paucity of data on EMT in the elderly impedes the ability of physicians and patients to make informed 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 US. The higher mortality and decreased functional outcome in patients aged over 80 years is in agreement with other database analyses involving AIS patients. For example, the Specialized Program of Translational Research in Acute Stroke (SPOTRIAS) examined patients ≥ 80 years of age that received intravenous rt-PA and/or inra-arterial therapy.[7] The database contained more than 1100 patients aged 80 years and greater. It documented a higher risk of in-hospital mortality for the elder stroke patient (OR: 2.13), but no difference in mortality rates between intervention modalities. Similary, 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 AIS patients aged > 80 years, and documented higher mortality and worse functional outcomes.[8,9] Specifically, the SITS-MOST registry documented an increase in mortality by 18% for patients > 80 years, and a 22% reduction in independence.[9]

The current study documented a significant increase in mortality for patients >80 years of age receiving EMT in comparison to their same age counterparts receiving only pharmacological thrombolysis. This is in contrast to the findings of Willey et al. which concluded that intra-arterial therapy does not raise the risk of in-hospital mortality among those aged > 80 years compared to treatment with intravenous thrombolysis alone.[7] Our study suggests an elevated risk of mortality in patients of this age group receiving EMT.

Two possible reasons for this notable increase in mortality include: (1) older patients may respond poorly after prolonged general anesthesia commonly used for EMT, which other researchers have cited to influence mortality,[10,11] and (2) different disease states in each population. Patients receiving EMT likely had a higher NIHSS from a more proximal large vessel occlusive lesion refractory to medical management and pharmacological thrombolysis. Of those not in the refractory group, it can be presumed that the individual may have 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.

Due 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 NIHSS score.[12–14] 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 study outcomes do not include any specific neurological or functional assessment, as these are not recorded in the NIS. The fact that a patient was discharged home 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 AIS patients older than 80 years resulted in significantly increased mortality and reduced functional independence 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 over 80 years of age that would benefit from EMT may improve outcomes and reduce the gap currently observed in age stratifications. Ongoing endeavors to develop new revascularization devices may also improve AIS outcomes after EMT.

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Contributorship Statement: EMD and MV: study concept and design. MRV: acquisition of the data. MRV, AS, DJP, and EMD: analysis and interpretation of the data. MRV and EMD: drafting of the manuscript. AS and DJP: critical revision of the manuscript for important intellectual content. EMD: guarantor.

Competing Interests: MRV: none. AS: none. DJP: none. EMD is a physician consultant for MicroVention, Covidien Neurovascular, Integra LifeSciences Corporation, and McKesson Health Solutions.

Ethics approval: This study used the Nationwide Inpatient Sample, a de-identified patient database. Therefore, this study did not require IRB review in accordance with the Code of Federal Regulations, 45 CFR 46.

Data sharing statement: Data were generated from the Nationwide Inpatient Sample, a publicly-available database. There is no additional data available

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TABLES

Table 1. Patient- and hospital-level characteristics of the population receiving mechanical thrombectomy for acute ischemic stroke

	≤ 80 yrs (n = 7614 cases)	> 80 yrs (n = 1686 cases)	*P*
Age	61.4 (14.0)	85.2 (4.0)	<.001
Gender, female	46.9%	66.7%	<.001
Race, white	60.2%	67.6%	.013
Median income level			
<$39,000	26.7%	23.5%	
$39,000 to $47,999	24.8%	25.6%	.607
$48,000 to $62,999	23.6%	23.5%	
≥$63,000	24.9%	27.4%	
Payer, Medicare	44.9%	90.5%	<.001
Number of chronic conditions	7.1 (2.7)	7.7 (2.7)	.001
Number of procedures	6.9 (3.2)	6.4 (2.7)	.012
APR-DRG severity of illness			
Mild	0%	0%	
Moderate	1.5%	0.6%	.418
Major	53.5%	53.9%	
Extreme	45.0%	45.5%	
Thrombolysis (intravenous or intra-arterial)	55.5%	63.1%	.013
Length of stay, days	10.5 (10.2)	9.4 (7.8)	.033
Total charges, $	169,763 (125,050)	156,361 (103,574)	.040
Discharged home	12.7%	2.1%	<.001
Mortality	21.6%	33.7%	<.001
Hospital owner			
Government, non-federal	22.6%	18.8%	
Private, non-profit	69.2%	74.6%	.150
Private, investor-own	8.2%	6.6%	
Teaching hospital	84.2%	80.6%	.122

Continuous variables expressed as: mean (SD).

Table 2. The effect of mechanical thrombectomy on patients > 80 years versus their younger counterparts with regards to mortality, discharge disposition, hospital charges, and length of stay after accounting for patient and hospital confounding factors.

	Effect Ratio	95% CI	*P*
Mortality*	2.107	1.549 – 2.866	<.001
Discharged home*	0.297	0.131 – 0.673	.004
Hospital charges†	0.948	0.879 – 1.022	.164
Length of stay ‡	0.948	0.845 – 1.063	.360

* OR: odds for patient > 80 yrs/odds for patient ≤ 80 yrs.
† Mean charge ($) for patient > 80 yrs/mean charge for patient ≤ 80 yrs.
‡ Mean length (in days) for patient > 80 yrs/mean length for patient ≤ 80 yrs.

Table 3. The effect of mechanical thrombectomy compared to only thrombolysis in patients > 80 years with regards to mortality, discharge disposition, hospital charges, and length of stay after accounting for patient and hospital confounding factors.

	Effect Ratio	95% CI	*P*
Mortality*	1.842	1.382 – 2.455	<.001
Discharged home*	0.394	0.179 – 0.866	.020
Hospital charges†	1.733	1.603 – 1.876	<.001
Length of stay ‡	1.115	1.022 – 1.215	.014

* OR: odds for patient receiving mechanical thrombectomy/odds for patient receiving only thrombolysis.
† Mean charge ($) for patient receiving mechanical thrombectomy/mean charge for patient receiving only thrombolysis.
‡ Mean length (in days) for patient receiving mechanical thrombectomy/mean length for patient receiving only thrombolysis.

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

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

Mark R. Villwock MS[1], Amit Singla MD[1], David J. Padalino MD[1], Eric M. Deshaies, MD[1*]

[1]SUNY Upstate Medical University, Department of Neurosurgery, Syracuse, New York, USA

*CORRESPONDING AUTHOR:

Eric M. Deshaies, MD

Director, SUNY Upstate Neurovascular Institute

Director of Cerebrovascular, Endovascular, and Skull Base Neurosurgery

Director, Neurosurgery Critical Care

Associate Professor of Neurosurgery, Neuroscience and Physiology

SUNY Upstate Medical University, Syracuse NY 13210 USA

Phone: 1-315-464-5502

Fax: 1-315-464-6373

DeshaieE@upstate.edu

Key words: endovascular therapy; stroke; thrombolysis; mechanical thrombectomy.

Word count: 1,774.

ABSTRACT

Objectives: Many physicians debate the efficacy of mechanical thrombectomy for ischemic stroke, but most agree that to establish potential benefit, patient selection must be examined further. People >80 years are a growing population of ischemic stroke patients. The benefit of thrombectomy for them may be greatly reduced due to diminishing neuroplasticity and a larger number of medical co-morbidities. To address this knowledge gap, we examined clinical and economic outcomes after mechanical thrombectomy in the ischemic 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-percent stratified sample of U.S. community hospitals within the Nationwide Inpatient Sample.

Participants: All patients from 2008-2010 with a primary diagnosis of ischemic 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 ischemic stroke cases (9,300) 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 (OR:1.993, P<.001). The elderly experienced no significant difference in hospital charges (P=.105) and length of stay (P=.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 EMT may improve outcomes and reduce the gap currently observed in age stratifications.

Strength and limitations of the study

- The strength of the study is the large number of included patients and the ability to study medical practice at large without selection bias.
- Due 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 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 ischemic 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 to clinical outcomes. This is particularly important with the rise of health care 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 centered on the creation of death panels to ration expenses. Although this panel was dismissed as myth, there remains a critical need to analyze the cost of newly-developed stroke interventions in an aging population that may not incur the same benefits as their younger peers due to lack of neuroplasticity and ongoing medical co-morbidities.

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 regards 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 ischemic 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 to 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 analyzed discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (Rockville, MD). This database represents approximately a 20% stratified sample of U.S. 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 through 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 utilizing 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 intra-venous administration of thrombolytics. Additionally, a hospital was classified as "high volume" if its total discharge stroke volume exceeded 147 cases per year.[6] Total hospital charges from 2008 and 2009 were compounded yearly at an inflation rate of 3% to standardize the charges at 2010 levels. The length of hospital stay and associated hospital charges were only calculated for patients who did not die during their hospital course. This was done to eliminate the artificial shortening of these variables in cases involving a withdrawal of care. The comorbidity burden of each patient was expressed as the sum of the Elixhauser comorbidity measures.[7,8]

Data were analyzed using SPSS Version 17 (IBM Corporation, Armonk NY, USA). To obtain national estimates, discharge weights were applied. Univariate comparisons were performed using Mann-Whitney U-tests and Chi-squared tests, as appropriate.

Binary logistic regression was used to analyze the primary objective, inpatient mortality. The analysis considered the following factors known to affect stroke outcome: elderly age (>80 yrs), thrombolysis administration, presentation to a "high-volume" stroke center, gender, and All Patient Refined Diagnosis Related Group Severity of Illness (APR-DRG SOI). Backward stepwise regression was performed with variable entry when probability was less than 0.05 and removal when probability exceeded 0.10. Odds ratios and their 95% confidence intervals were reported.

Generalized linear models with the use of generalized estimated equations were used to analyze the economic measures. To meet the distributional requirements of a generalized linear model, we used the logarithm of length of hospital stay and the logarithm of total inflation-adjusted charges as targeted outcomes in analyses. The exponential parameter estimates were reported along with their 95% confidence intervals. A probability value of .01 was considered statistically significant in order to nominally control for Type I error.

RESULTS

Nationally, there were 1,674,200 acute ischemic stroke cases during the years 2008 through 2010, 9,300 (< 1%) of which received EMT. Overall inpatient mortality for acute ischemic stroke was 7.9%. This rate increased to 23.8% when considering only patients receiving intervention with EMT. Patients greater than 80 yrs 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 < .001) (Table 1). In comparison to younger patients, the patient over 80 was more likely to be a white female 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 centers were discharged home (0/70). This is opposed to 10.8% of patients admitted to high-volume stroke centers (P=.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 to their younger counterpart (OR 1.993, 95% CI: 1.763-2.254, P<.001). The factors noted to significantly (P<.01) reduce mortality were presentation to a high-volume stroke center (OR=0.378), thrombolysis administration (OR=0.873), female gender (0.855), and decreased severity of illness (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 severity of illness (Figure 1).

DISCUSSION

The paucity of data on EMT in the elderly impedes the ability of physicians and patients to make informed 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 US. 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 that 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 elder stroke patient (OR: 2.13), but no difference in mortality rates between intervention modalities. Similary, 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 AIS patients aged > 80 years, and documented higher mortality and worse functional outcomes.[10,11] Specifically, the SITS-MOST registry 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 AIS patients and noted the male sex to be a predictor of early mortality. Yet, Niewada et al.[13] reported the results of 17,370 AIS patients and documented that females had higher 14-day and 6-month mortality; while Adams et al.[14] collected data on 1,281 AIS patients and found no relationship between outcome and gender. Further research is warranted to investigate any gender-effects with regard to AIS patients, 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. Although 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 anonymized database used in this study.

Due 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 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 AIS patients 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 endeavors to develop new revascularization devices may also improve AIS outcomes after EMT.

Conflicts-of-interest/Disclosures: MRV: none. AS: none. DJP: none. EMD is a physician consultant for MicroVention, Covidien Neurovascular, Integra LifeSciences Corporation, and McKesson Health Solutions.

Contributor statement: EMD and MV: study concept and design. MRV: acquisition of the data. MRV, AS, DJP, and EMD: analysis and interpretation of the data. MRV and EMD: drafting of the manuscript. AS and DJP: critical revision of the manuscript for important intellectual content. EMD: guarantor.

Funding: None

Ethics approval: This study used the Nationwide Inpatient Sample, a de-identified patient database. Therefore, this study did not require IRB review in accordance with the Code of Federal Regulations, 45 CFR 46.

Data sharing statement: Data were generated from the Nationwide Inpatient Sample, a publicly-available database. There is no additional data available.

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

	≤ 80 yrs (n = 7614 cases)	> 80 yrs (n = 1686 cases)	*P*
Age	63 (53-73)	84 (82-87)	
Gender, female	46.9%	66.7%	<.001
Race, white	60.2%	67.6%	.013
Median income level			
<$39,000	26.7%	23.5%	.607
$39,000 to $47,999	24.8%	25.6%	
$48,000 to $62,999	23.6%	23.5%	
≥$63,000	24.9%	27.4%	
Payer, Medicare	44.9%	90.5%	<.001
Elixhauser comorbidity score			
≤ 2	37.2%	30.6%	<.001
3	21.7%	26.5%	
≥ 4	41.1%	42.9%	
APR-DRG severity of illness			
Mild	0%	0%	.418
Moderate	1.5%	0.6%	
Major	53.5%	53.9%	
Extreme	45.0%	45.5%	
Thrombolysis (intravenous or intra-arterial)	55.5%	63.1%	.013
Length of stay, days	9 (5-14)	9 (6-13.6)	.711
Total charges, $	137,692 (95,139-207,687)	137,756 (87,582-198,103)	.021
Discharged home	12.7%	2.1%	<.001
Inpatient mortality	21.6%	33.7%	<.001
Hospital owner			
Government, non-federal	22.6%	18.8%	.150
Private, non-profit	69.2%	74.6%	
Private, investor-own	8.2%	6.6%	
Teaching hospital	84.2%	80.6%	.122

Continuous variables expressed as: median (25^{th} percentile – 75^{th} percentile).

Figure Legend:

Figure 1. Multivariate analysis of inpatient mortality and economic measures. Inpatient mortality expressed as the odds ratio along with the 95% confidence interval derived from binary logistic regression. Length of stay and charges are both expressed using the exponential parameter estimate along with the 95% confidence interval derived from generalized estimating equations. P-values are adjacent to the 95% confidence intervals. 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.

Acute ischemic stroke outcomes following ~~Outcomes after m~~mechanical thrombectomy in the elderly versus their younger counterpart~~in acute ischemic stroke patients over 80 years of age~~: a retrospective cohort study

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Mark R. Villwock MS[1], Amit Singla MD[1], David J. Padalino MD[1], Eric M. Deshaies, MD[1*]

[1]SUNY Upstate Medical University, Department of Neurosurgery, Syracuse, New York, USA

*CORRESPONDING AUTHOR:

Eric M. Deshaies, MD

Director, SUNY Upstate Neurovascular Institute

Director of Cerebrovascular, Endovascular, and Skull Base Neurosurgery

Director, Neurosurgery Critical Care

Associate Professor of Neurosurgery, Neuroscience and Physiology

SUNY Upstate Medical University, Syracuse NY 13210 USA

Phone: 1-315-464-5502

Fax: 1-315-464-6373

DeshaieE@upstate.edu

Key words: endovascular therapy; stroke; thrombolysis; mechanical thrombectomy.

Word count: 1,774~~858~~.

ABSTRACT

Objectives: Many physicians debate the efficacy of mechanical thrombectomy for ischemic stroke, but most agree that to establish potential benefit, patient selection must be examined further. People >80 years are a growing population of ischemic stroke patients. The benefit of thrombectomy for them may be greatly reduced due to diminishing neuroplasticity and a larger number of medical co-morbidities. To address this knowledge gap, we examined clinical and economic outcomes after mechanical thrombectomy in the ischemic 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~~Our hypothesis was that elderly patients (> 80 years) would fare worse at discharge in comparison to their younger counterparts~~.

Design: Retrospective cohort study.

Setting: A 20-percent stratified sample of U.S. community hospitals within the Nationwide Inpatient Sample.

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

Primary and secondary outcome measures: The primary outcome was~~ the adjusted odds-ratio of~~ inpatient mortality. Secondary outcomes included ~~the adjusted odds-ratio for discharge disposition, and the adjusted effect-ratios of ~~hospital charges and length of stay.

Results: Less than 1% of all ischemic stroke cases (9,300) 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~~more than double~~ that of their younger counterparts (OR:1.993~~2.107~~, P<.001)~~ and there was~~

a significant reduction in the odds of being discharged home (OR:0.297, P=.004). Although univariate analysis depicted aThe elderly experienced no significant difference in hospital charges (P=.105) and length of stay (P=.498), multivariate analysis revealed no significant differences.

Conclusions: The odds of inpatient mortality after mechanical thrombectomy in patients over> 80 years of age wereas twice that of their younger counterparts and few were eligible to be discharged home. 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.Studies to better identify specific subpopulations of patients that would benefit from mechanical thrombectomy are needed urgently.

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Strength and limitations of the study

- The strength of the study is the large number of included patients and the ability to study medical practice at large without selection bias.
- Due 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 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 ischemic 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 to clinical outcomes. This is particularly important with the rise of health care 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 centered on the creation of death panels to ration expenses. Although this panel was dismissed as myth, there remains a critical need to analyze the cost of newly-developed stroke interventions in an aging population that may not incur the same benefits as their younger peers due to lack of neuroplasticity and ongoing medical co-morbidities.

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 regards 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 patient outcomes specific to in-hospital mortality, discharge disposition, and economic data (length of stay and hospital charges) after EMT in the elderly ischemic stroke population treated with EMT in using the a national databases. 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. The primary outcome was inpatient mortality. Secondary outcomes included hospital charges and length of stay.

METHODS

We analyzed discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (Rockville, MD). This database represents approximately a 20% stratified sample of U.S. 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 through 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 utilizing 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 intra-venous administration of thrombolytics. Additionally, a hospital was classified as "high volume" if its total discharge stroke volume exceeded 147 cases per year.[6] Total hospital charges from 2008 and 2009 were compounded yearly at an inflation rate of 3% to standardize the charges at 2010 levels. The length of hospital stay and associated hospital charges were only calculated for patients who did not die during their hospital course. This was done to eliminate the artificial shortening of these variables in cases involving a withdrawal of care. The comorbidity burden of each patient was expressed as the sum of the Elixhauser comorbidity measures.[7,8]

Data were analyzed using SPSS Version 17 (IBM Corporation, Armonk NY, USA). To obtain national estimates, discharge weights were applied. Univariate comparisons Patient discharge data and hospital demographics were compared between patients >80 yrs of age and patients ≤ 80 yrs of agewere performed using . Additionally, outcomes were compared in the subset of patients > 80 years between those that received pharmacological thrombolysis only and those that received EMT. Mann-Whitney U-tests and CIndependent samples t-tests, chi-squared tests, and Fisher's exact tests, were used to make comparisons as appropriate.

Binary logistic regression Accounting for hospital and patient level variation in outcome measures (length of stay, total hospital charges, mortality, and discharge disposition), multivariate models wasere used to analyze the primary objective, inpatient mortalitycompare and make inferences about differences between elderly patients versus younger patients, and elderly patients receiving EMT versus pharmacological thrombolysis alone. This allows

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comparison while adjusting for confounding variables included in the NIS dataset.. The analysis considered the following patient-specific factors known to affect stroke outcome: elderly age (>80 yrs), thrombolysis administration, presentation to a "high-volume" stroke center, gender, and All Patient Refined Diagnosis Related Group Severity of Illness (APR-DRG SOI). age, gender, race, patient income (<$39,000, $39000 to $47,999, $48,000 to $62,999, and ≥$63,000), payer (Medicare, Medicaid, private insurance, self-pay, or no charge), number of chronic conditions, and severity of illness (APR-DRG severity of illness). The analysis also considered hospital-level factors including: region (Northeast, Midwest, South, West), teaching status, hospital bed-size (small, medium, large), hospital location (rural or urban), ownership of hospital (public, private non-profit, private for profit), and whether the hospital was a "high volume" stroke center. Backward sStepwise regression was performed with variable entry when probability was less than 0.05 and removal when probability exceeded 0.10. Odds ratios and their 95% confidence intervals were reported.

Generalized linear models with the use of generalized -estimated equations linear models were used to analyze the economic outcome mmeasures. To meet the distributional requirements of a generalized linear model, we used the logarithm of length of hospital stay and the logarithm of total inflation-adjusted charges as targeted outcomes in analyses. A model using Gamma as the distribution and Log as the link function was used to calculate the estimated marginal means of the continuous variables including the total hospital charges and length of stay. The exponential parameter estimates were reported along with their 95% confidence intervals. effect ratio was expressed as the quotient of the estimated marginal mean for patients > 80 yrs of age over the estimated marginal mean for patients ≤ 80 yrs of age; and the estimated marginal mean for patients > 80 years receiving EMT over the estimated marginal mean for patients > 80 years receiving only pharmacological thrombolysis. The binary outcomes, mortality and discharge home, were analyzed in binary logistic regression. Odds ratios and their 95% confidence intervals were reported. A probability value of .01 wasBonferroni correction for multiple tests resulted in a probability value <.0125 (.05/4) being considered statistically significant in order to nominally control for Type I error.

RESULTS

Nationally, there were 1,674,200 acute ischemic stroke cases during the years 2008 through 2010, 9,300 (< 1%) of which received EMT. The oOverall rate of inpatient mortality for all acute ischemic stroke cases was 7.9%. This rate increased to 23.8% when considering only patients receiving intervention with EMT. Patients greater than 80 yrs of age receiving EMT had an inpatient mortality rate of 33.7%, significantly exceeding the rate for their younger counterpart patients 80 yrs of age and younger that was found to be 21.6% (P < .001) (Table 1). In comparison to younger patients, the patient over 80 was more likely to be a white female on Medicare, and to have received pharmacological thrombolysis, and to not be discharged home (Table 1). Interestingly,

no patients, young or elderly, treated at low-volume stroke centers were discharged home (0/70). This is opposed to 10.8% of patients admitted to high-volume stroke centers (P=.004).

Multivariate analysis was performed to examine the primary and secondary outcome measures variables while controlling for confounding factors (Figure 1Table 2). The odds for inpatient

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mortality in the elderly patients older than 80 treated with EMT were approximately more than double in comparison to their younger counterpartpatients (OR 1.9932.107, 95% CI: 1.763549-2.866254, P<.001). The factors noted to significantly (P<.01) reduce mortality were presentation to a high-volume stroke center (OR=0.378), thrombolysis administration (OR=0.873), female gender (0.855), and decreased severity of illness (Figure 1). Elderly patients also had a significant reduction in the odds of being discharged home in comparison to their younger counterparts (OR 0.297, 95% CI: 0.131-0.673, P=.004). Although univariate analysis depicted aThere was no significant difference in hospital charges and length of stay for the elderly (Figure 1). The economic measures were most influenced by severity of illness (Figure 1). based on age, the multivariate analysis revealed no significant differences (Table 2).

Lastly, the effect of pharmacological thrombolysis was examined in patients > 80 years of age. In comparison to the relatively small number of similarly aged patients treated with EMT (n = 1686), a drastic increase in the number of patients treated with thrombolysis was observed (n = 16493). Patients treated with thrombolysis alone had significantly reduced mortality in comparison to those treated with EMT, 15.2% versus 33.7%, respectively (P < .001). These patients also had a significantly greater rate of being discharged home, 9.0% versus 2.1% (P < .001). Multivariate models documented the odds of mortality following EMT to significantly increase by 84% in comparison to only thrombolysis; and hospital charges for cases involving EMT increased by 73% in comparison to cases with only thrombolysis (Table 3).

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DISCUSSION

The paucity of data on EMT in the elderly impedes the ability of physicians and patients to make informed 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 US. The higher mortality and decreased functional outcome in patients aged over 80 years is in agreement with the overall worse prognosis seen in the natural history of this age group. other database analyses involving AIS patients. For example, the Specialized Program of Translational Research in Acute Stroke (SPOTRIAS) examined patients ≥ 80 years of age that received intravenous rt-PA and/or intra-arterial therapy.[9][7] The database contained more than 1100 patients aged 80 years and greater. It documented a higher risk of in-hospital mortality for the elder stroke patient (OR: 2.13), but no difference in mortality rates between intervention modalities. Similary, 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 AIS patients aged > 80 years, and documented higher mortality and worse functional outcomes.[10,11][8,9] Specifically, the SITS-MOST registry documented an increase in mortality by 18% for patients > 80 years, and a 22% reduction in independence.[11][9]

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

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The role of gender in stroke outcomes is not clearly defined. In agreement with our study, Saposnik et al.[12] reported on 12,262 AIS patients and noted the male sex to be a predictor of early mortality. Yet, Niewada et al.[13] reported the results of 17,370 AIS patients and documented that females had higher 14-day and 6-month mortality; while Adams et al.[14] collected data on 1,281 AIS patients and found no relationship between outcome and gender. Further research is warranted to investigate any gender-effects with regard to AIS patients, and specifically those undergoing EMT.

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thrombolysis. This is in contrast to the findings of Willey et al. which concluded that intra-arterial therapy does not raise the risk of in-hospital mortality among those aged > 80 years compared to treatment with intravenous thrombolysis alone.[7] Our study suggests an elevated risk of mortality in patients of this age group receiving EMT.

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Two possible reasons for this notable increase in mortality include: (1) older patients may respond poorly after prolonged general anesthesia commonly used for EMT, which other researchers have cited to influence mortality,[10,11] and (2) different disease states in each population. Patients receiving EMT likely had a higher NIHSS from a more proximal large vessel occlusive lesion refractory to medical management and pharmacological thrombolysis. Of those not in the refractory group, it can be presumed that the individual may have 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.

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Due 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 NIHSS score.[20–22][12–14] 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 study outcomes do not include any specific neurological or functional assessment, as these are not recorded in the NIS. DThe fact that a patient was discharged to home was not considered as a primary objective as this variable may be influenced

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CONCLUSION

EMT for AIS patients older than 80 years of age resulted in significantly increased inpatient mortality ~~and reduced functional independence~~ 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 ~~over 80 years of age~~ that would benefit from EMT may improve outcomes and reduce the gap currently observed in age stratifications. Ongoing endeavors to develop new revascularization devices may also improve AIS outcomes after EMT.

Conflicts-of-interest/Disclosures: MRV: none. AS: none. DJP: none. EMD is a physician consultant for MicroVention, Covidien Neurovascular, Integra LifeSciences Corporation, and McKesson Health Solutions.

Contributor statement: EMD and MV: study concept and design. MRV: acquisition of the data. MRV, AS, DJP, and EMD: analysis and interpretation of the data. MRV and EMD: drafting of the manuscript. AS and DJP: critical revision of the manuscript for important intellectual content. EMD: guarantor.

Funding: None

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~~TABLES~~

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

	≤ 80 yrs (n = 7614 cases)	> 80 yrs (n = 1686 cases)	*P*
Age	63 (53-73)~~61.4 (14.0)~~	84 (82-87)~~85.2 (4.0)~~	~~<~~.001
Gender, female	46.9%	66.7%	<.001
Race, white	60.2%	67.6%	.013
Median income level			
<$39,000	26.7%	23.5%	
$39,000 to $47,999	24.8%	25.6%	.607
$48,000 to $62,999	23.6%	23.5%	
≥$63,000	24.9%	27.4%	
Payer, Medicare	44.9%	90.5%	<.001
~~Number of chronic conditions~~	~~7.1 (2.7)~~	~~7.7 (2.7)~~	~~.001~~
~~Number of procedures~~	~~6.9 (3.2)~~	~~6.4 (2.7)~~	~~.012~~
Elixhauser comorbidity score			
≤~~<=~~ 2	37.2%	30.6%	
3	21.7%	26.5%	<.001
≥ ~~>=~~4	41.1%	42.9%	
APR-DRG severity of illness			
Mild	0%	0%	
Moderate	1.5%	0.6%	.418
Major	53.5%	53.9%	
Extreme	45.0%	45.5%	
Thrombolysis (intravenous or intra-arterial)	55.5%	63.1%	.013
Length of stay, days	9 (5-14)~~10.5 (10.2)~~	9 (6-13.6)~~9.4 (7.8)~~	.711~~.033~~
Total charges, $	137,692 (95,139-207,687)~~169,763 (125,050)~~	137,756 (87,582-198,103)~~156,361 (103,574)~~	.021~~.040~~
Discharged home	12.7%	2.1%	<.001
Inpatient m~~M~~ortality	21.6%	33.7%	<.001
Hospital owner			
Government, non-federal	22.6%	18.8%	
Private, non-profit	69.2%	74.6%	.150
Private, investor-own	8.2%	6.6%	
Teaching hospital	84.2%	80.6%	.122

Continuous variables expressed as: median~~mean~~ (25th percentile – 75th percentile~~SD~~).

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Table 2. The effect of mechanical thrombectomy on patients > 80 years versus their younger counterparts with regards to mortality, discharge disposition, hospital charges, and length of stay after accounting for patient and hospital confounding factors.

	Effect Ratio	95% CI	*P*
Mortality*	2.107	1.549 – 2.866	<.001
Discharged home*	0.297	0.131 – 0.673	.004
Hospital charges†	0.948	0.879 – 1.022	.164
Length of stay ‡	0.948	0.845 – 1.063	.360

Figure Legend:

Figure 1. Multivariate analysis of inpatient mortality and economic measures. Inpatient mortality expressed as the odds ratio * OR: odds for patient > 80 yrs/odds for patient ≤ 80 yrsalong with the 95% confidence interval derived from binary logistic regression. Length of stay and charges are both expressed using the exponential parameter estimate along with the 95% confidence interval derived from generalized estimating equations. P-values are adjacent to the 95% confidence intervals. 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..

† Mean charge ($) for patient > 80 yrs/mean charge for patient ≤ 80 yrs.

‡ Mean length (in days) for patient > 80 yrs/mean length for patient ≤ 80 yrs.

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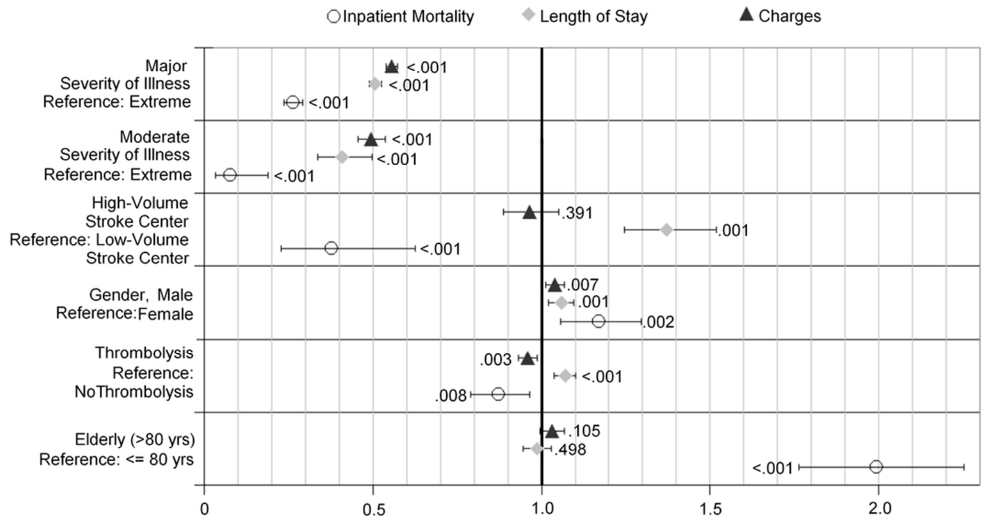
Table 3. The effect of mechanical thrombectomy compared to only thrombolysis in patients > 80 years with regards to mortality, discharge disposition, hospital charges, and length of stay after accounting for patient and hospital confounding factors.

	Effect Ratio	95% CI	*P*
Mortality*	1.842	1.382 – 2.455	<.001
Discharged home*	0.394	0.179 – 0.866	.020
Hospital charges†	1.733	1.603 – 1.876	<.001
Length of stay ‡	1.115	1.022 – 1.215	.014

* OR: odds for patient receiving mechanical thrombectomy/odds for patient receiving only thrombolysis.

† Mean charge ($) for patient receiving mechanical thrombectomy/mean charge for patient receiving only thrombolysis.

‡ Mean length (in days) for patient receiving mechanical thrombectomy/mean length for patient receiving only thrombolysis.



Multivariate analysis of inpatient mortality and economic measures. Inpatient mortality expressed as the odds ratio along with the 95% confidence interval derived from binary logistic regression. Length of stay and charges are both expressed using the exponential parameter estimate along with the 95% confidence interval derived from generalized estimating equations. P-values are adjacent to the 95% confidence intervals. 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.
92x52mm (300 x 300 DPI)

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

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Complete List of Authors:	Villwock, Mark; SUNY Upstate Medical University, Neurosurgery Singla, Amit; SUNY Upstate Medical University, Neurosurgery Padalino, David; SUNY Upstate Medical University, Neurosurgery Deshaies, Eric; SUNY Upstate Medical University, Neurosurgery

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

Mark R. Villwock MS[1], Amit Singla MD[1], David J. Padalino MD[1], Eric M. Deshaies, MD[1*]

[1]SUNY Upstate Medical University, Department of Neurosurgery, Syracuse, New York, USA

*CORRESPONDING AUTHOR:

Eric M. Deshaies, MD

Director, SUNY Upstate Neurovascular Institute

Director of Cerebrovascular, Endovascular, and Skull Base Neurosurgery

Director, Neurosurgery Critical Care

Associate Professor of Neurosurgery, Neuroscience and Physiology

SUNY Upstate Medical University, Syracuse NY 13210 USA

Phone: 1-315-464-5502

Fax: 1-315-464-6373

DeshaieE@upstate.edu

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ABSTRACT

Objectives: Many physicians debate the efficacy of mechanical thrombectomy for ischemic stroke, but most agree that to establish potential benefit, patient selection must be examined further. People >80 years are a growing population of ischemic stroke patients 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 co-morbidities. To address this knowledge gap, we examined clinical and economic outcomes after mechanical thrombectomy in the ischemic 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-percent stratified sample of U.S. community hospitals within the Nationwide Inpatient Sample.

Participants: All patients from 2008-2010 with a primary diagnosis of ischemic 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 ischemic stroke cases (9,300) 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 (OR:1.993, P<.001). The elderly experienced no significant difference in hospital charges (P=.105) and length of stay (P=.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 EMT may improve outcomes and reduce the gap currently observed in age stratifications.

Strength and limitations of the study

- The strength of the study is the large number of included patients and the ability to study medical practice at large without selection bias.
- Due 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 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 ischemic 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 to clinical outcomes. This is particularly important with the rise of health care 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 centered on the creation of death panels to ration expenses. Although this panel was dismissed as myth, there remains a critical need to analyze the cost of newly-developed stroke interventions in an aging population that may not incur the same benefits as their younger peers due to lack of neuroplasticity and ongoing medical co-morbidities.

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 regards 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 ischemic 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 to 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 analyzed discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (Rockville, MD). This database represents approximately a 20% stratified sample of U.S. 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 through 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 utilizing 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 intra-venous administration of thrombolytics. Additionally, a hospital was classified as “high volume” if its total discharge stroke volume exceeded 147 cases per year.[6] Total hospital charges from 2008 and 2009 were compounded yearly at an inflation rate of 3% to standardize 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 done 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 analyzed using SPSS Version 17 (IBM Corporation, Armonk NY, USA). To obtain national estimates, discharge weights were applied. Univariate comparisons were performed using Mann-Whitney U-tests and Chi-squared tests, as appropriate.

Binary logistic regression was used to analyze the primary objective, inpatient mortality. The analysis considered the following factors known to affect stroke outcome: elderly age (>80 yrs), thrombolysis administration, presentation to a "high-volume" stroke center, gender, and All Patient Refined Diagnosis Related Group Severity of Illness (APR-DRG SOI). Backward stepwise regression was performed with variable entry when probability was less than 0.05 and removal when probability exceeded 0.10. Odds ratios and their 95% confidence intervals were reported.

Generalized linear models with a gamma distribution and log link function were used to analyze the economic measures. The exponential parameter estimates were reported along with their 95% confidence intervals. 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 .01 was considered statistically significant in order to nominally control for Type I error.

RESULTS

Nationally, there were 1,674,200 acute ischemic stroke cases during the years 2008 through 2010, 9,300 (< 1%) of which received EMT. Overall inpatient mortality for acute ischemic stroke was 7.9%. This rate increased to 23.8% when considering only patients receiving intervention with EMT. Patients greater than 80 yrs 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 < .001) (Table 1). In comparison to younger patients, the patient over 80 was more likely to be a white female 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 centers were discharged home (0/70). This is opposed to 10.8% of patients admitted to high-volume stroke centers (P=.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 to their younger counterpart (OR 1.993, 95% CI: 1.763-2.254, P<.001). The factors noted to significantly (P<.01) reduce mortality were presentation to a high-volume stroke center (OR=0.378), thrombolysis administration (OR=0.873), female gender (0.855), and decreased severity of illness (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 severity of illness (Figure 1).

DISCUSSION

The paucity of data on EMT in the elderly impedes the ability of physicians and patients to make informed 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 US. 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 that 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 elder stroke patient (OR: 2.13), but no difference in mortality rates between intervention modalities. Similary, 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 AIS patients aged > 80 years, and documented higher mortality and worse functional outcomes.[10,11] Specifically, the SITS-MOST registry 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 AIS patients and noted the male sex to be a predictor of early mortality. Yet, Niewada et al.[13] reported the results of 17,370 AIS patients and documented that females had higher 14-day and 6-month mortality; while Adams et al.[14] collected data on 1,281 AIS patients and found no relationship between outcome and gender. Further research is warranted to investigate any gender-effects with regard to AIS patients, 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 utilization 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 anonymized database used in this study.

Due 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 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 AIS patients 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 endeavors to develop new revascularization devices may also improve AIS outcomes after EMT.

Contributor statement: EMD and MV: study concept and design. MRV: acquisition of the data. MRV, AS, DJP, and EMD: analysis and interpretation of the data. MRV and EMD: drafting of the manuscript. AS and DJP: critical revision of the manuscript for important intellectual content. EMD: guarantor.

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Ethics approval: This study used the Nationwide Inpatient Sample, a de-identified patient database. Therefore, this study did not require IRB review in accordance with the Code of Federal Regulations, 45 CFR 46.

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Data sharing statement: Data were generated from the Nationwide Inpatient Sample, a publicly-available database. There is no additional data available.

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

	≤ 80 yrs (n = 7614 cases)	> 80 yrs (n = 1686 cases)	*P*
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Continuous variables expressed as: median (25^{th} percentile – 75^{th} percentile).

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Figure 1. Multivariate analysis of inpatient mortality and economic measures for survivors. Inpatient mortality expressed as the odds ratio along with the 95% confidence interval derived from binary logistic regression. Length of stay and charges are both expressed using the exponential parameter estimate along with the 95% confidence interval derived from generalized estimating equations. P-values are adjacent to the 95% confidence intervals. 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.

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

Mark R. Villwock MS[1], Amit Singla MD[1], David J. Padalino MD[1], Eric M. Deshaies, MD[1*]

[1]SUNY Upstate Medical University, Department of Neurosurgery, Syracuse, New York, USA

*CORRESPONDING AUTHOR:

Eric M. Deshaies, MD

Director, SUNY Upstate Neurovascular Institute

Director of Cerebrovascular, Endovascular, and Skull Base Neurosurgery

Director, Neurosurgery Critical Care

Associate Professor of Neurosurgery, Neuroscience and Physiology

SUNY Upstate Medical University, Syracuse NY 13210 USA

Phone: 1-315-464-5502

Fax: 1-315-464-6373

DeshaieE@upstate.edu

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ABSTRACT

Objectives: Many physicians debate the efficacy of mechanical thrombectomy for ischemic stroke, but most agree that to establish potential benefit, patient selection must be examined further. People >80 years are a growing population of ischemic stroke patients 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 co-morbidities. To address this knowledge gap, we examined clinical and economic outcomes after mechanical thrombectomy in the ischemic 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-percent stratified sample of U.S. community hospitals within the Nationwide Inpatient Sample.

Participants: All patients from 2008-2010 with a primary diagnosis of ischemic 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 ischemic stroke cases (9,300) 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 (OR:1.993, P<.001). The elderly experienced no significant difference in hospital charges (P=.105) and length of stay (P=.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 EMT may improve outcomes and reduce the gap currently observed in age stratifications.

Strength and limitations of the study

- The strength of the study is the large number of included patients and the ability to study medical practice at large without selection bias.
- Due 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 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 ischemic 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 to clinical outcomes. This is particularly important with the rise of health care 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 centered on the creation of death panels to ration expenses. Although this panel was dismissed as myth, there remains a critical need to analyze the cost of newly-developed stroke interventions in an aging population that may not incur the same benefits as their younger peers due to lack of neuroplasticity and ongoing medical co-morbidities.

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 regards 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 ischemic 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 to 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 analyzed discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (Rockville, MD). This database represents approximately a 20% stratified sample of U.S. 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 through 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 utilizing 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 intra-venous administration of thrombolytics. Additionally, a hospital was classified as "high volume" if its total discharge stroke volume exceeded 147 cases per year.[6] Total hospital charges from 2008 and 2009 were compounded yearly at an inflation rate of 3% to standardize the charges at 2010 levels. The length of hospital stay and associated hospital charges were ~~only~~ calculated for all patients (including in-hospital deaths) and additionally for surviving patients ~~who did not die during their hospital course~~. The second analysis ~~is~~ was done to examine the economic measures without ~~eliminate~~ the artificial shortening of these variables that may occur in cases of comfort rather than curative care ~~in cases involving a withdrawal of~~

care. The comorbidity burden of each patient was expressed as the sum of the Elixhauser comorbidity measures.[7,8]

Data were analyzed using SPSS Version 17 (IBM Corporation, Armonk NY, USA). To obtain national estimates, discharge weights were applied. Univariate comparisons were performed using Mann-Whitney U-tests and Chi-squared tests, as appropriate.

Binary logistic regression was used to analyze the primary objective, inpatient mortality. The analysis considered the following factors known to affect stroke outcome: elderly age (>80 yrs), thrombolysis administration, presentation to a "high-volume" stroke center, gender, and All Patient Refined Diagnosis Related Group Severity of Illness (APR-DRG SOI). Backward stepwise regression was performed with variable entry when probability was less than 0.05 and removal when probability exceeded 0.10. Odds ratios and their 95% confidence intervals were reported.

Generalized linear models with ta gamma distribution and log link function he use of generalized estimated equations were used to analyze the economic measures. To meet the distributional requirements of a generalized linear model, we used the logarithm of length of hospital stay and the logarithm of total inflation-adjusted charges as targeted outcomes in analyses. The exponential parameter estimates were reported along with their 95% confidence intervals. 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 .01 was considered statistically significant in order to nominally control for Type I error.

RESULTS

Nationally, there were 1,674,200 acute ischemic stroke cases during the years 2008 through 2010, 9,300 (< 1%) of which received EMT. Overall inpatient mortality for acute ischemic stroke was 7.9%. This rate increased to 23.8% when considering only patients receiving intervention with EMT. Patients greater than 80 yrs 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 < .001) (Table 1). In comparison to younger patients, the patient over 80 was more likely to be a white female 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 centers were discharged home (0/70). This is opposed to 10.8% of patients admitted to high-volume stroke centers (P=.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 to their younger counterpart (OR 1.993, 95% CI: 1.763-2.254, P<.001). The factors noted to significantly (P<.01) reduce mortality were presentation to a high-volume stroke center (OR=0.378), thrombolysis administration (OR=0.873), female gender (0.855), and decreased severity of illness (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 severity of illness (Figure 1).

DISCUSSION

The paucity of data on EMT in the elderly impedes the ability of physicians and patients to make informed 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 US. 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 that 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 elder stroke patient (OR: 2.13), but no difference in mortality rates between intervention modalities. Similary, 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 AIS patients aged > 80 years, and documented higher mortality and worse functional outcomes.[10,11] Specifically, the SITS-MOST registry 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 AIS patients and noted the male sex to be a predictor of early mortality. Yet, Niewada et al.[13] reported the results of 17,370 AIS patients and documented that females had higher 14-day and 6-month mortality; while Adams et al.[14] collected data on 1,281 AIS patients and found no relationship between outcome and gender. Further research is warranted to investigate any gender-effects with regard to AIS patients, 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 utilization of comfort rather than curative measures in the elderly population as evident by their increased rate of in-hospital mortality. Additionally, ~~lthough~~ 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 anonymized database used in this study.

Due 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 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 AIS patients 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 endeavors to develop new revascularization devices may also improve AIS outcomes after EMT.

Conflicts-of-interest/Disclosures: MRV: none. AS: none. DJP: none. EMD is a physician consultant for MicroVention, Covidien Neurovascular, Integra LifeSciences Corporation, and McKesson Health Solutions.

Contributor statement: EMD and MV: study concept and design. MRV: acquisition of the data. MRV, AS, DJP, and EMD: analysis and interpretation of the data. MRV and EMD: drafting of the manuscript. AS and DJP: critical revision of the manuscript for important intellectual content. EMD: guarantor.

Funding: None

Ethics approval: This study used the Nationwide Inpatient Sample, a de-identified patient database. Therefore, this study did not require IRB review in accordance with the Code of Federal Regulations, 45 CFR 46.

Data sharing statement: Data were generated from the Nationwide Inpatient Sample, a publicly-available database. There is no additional data available.

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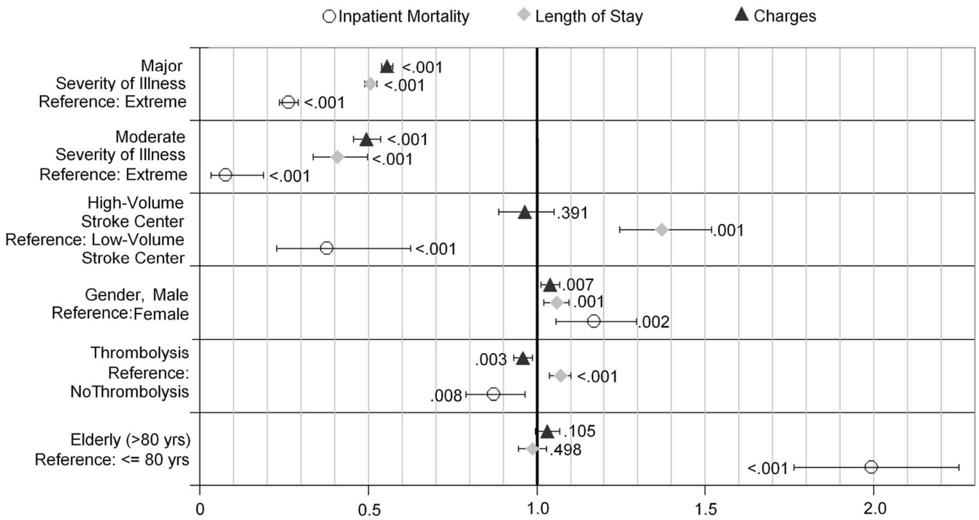

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