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Sex Differences in Outcome After Endovascular Stroke Therapy for Acute Ischemic Stroke

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Abstract

Background and Purpose: We determine the effect of sex on outcome after endovascular stroke therapy (EST) in acute ischemic stroke (AIS), including lifelong disability outcomes.

Methods: We analyzed patients treated with the Solitaire stent retriever in the combined SWIFT, STAR, and SWIFT-PRIME cohorts. Ordinal and logistic regression were used to examine known factors influencing outcome after EST and study the effect of sex on the association between these factors and outcomes, including age and time to reperfusion. Years of optimal life after thrombectomy were defined as disability adjusted life-year (DALYs) and calculated by projecting disability through adjusted post-stroke life expectancy (LE) by sex.

Results: Among 389 patients treated with EST, 55% were females, and median NIHSS was 17 [IQR 8–28]. There were no differences between females vs. males in presenting deficit severity (NIHSS 17 vs. 17, p=0.21), occlusion location (69% vs. 64% M1, p=0.62), presenting infarct extent (ASPECTS 8 vs. 8, p=0.24), rate of substantial reperfusion (TICI 2b/3, 87% vs. 83%, p=0.37), onset to reperfusion time (294 vs. 302 mins, p=0.46). Despite older ages (69 vs. 64, p<0.001) and higher rate of atrial fibrillation (45% vs. 30%, p=0.002) for females compared to males, adjusted rates of functional independence at 90 days were similar (odds ratio, 1.0; 95% CI,

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0.6–1.6). After adjusting for age at presentation and stroke severity, females had more years of optimal life (DALYs) following EST, 10.6 vs. 8.5 years (p<0.001).

Conclusions: Despite greater age and higher rate of atrial fibrillation, females experienced comparable functional outcomes and greater years of optimal life after intervention compared to males.

Keywords

Acute Stroke; Endovascular Procedures; Sex Differences

Introduction

Acute ischemic stroke (AIS) appears to affect females differently than males.[1] For stroke treatments, intravenous and intra-arterial thrombolysis may have differing recanalization effectiveness by sex.[2–8] In addition, a number of studies have suggested worse outcomes from AIS for females compared to males[1,9–11], including worse functional outcomes for females despite adjustment for age, pre-stroke mRS, and stroke severity.[12,13] However, other studies have suggested that these differences may be secondary to differing presentations in females compared to males, including later age of onset, differences in stroke etiology, and greater pre-stroke disability.[14–16]

In recent years, endovascular stroke thrombectomy (EST) has demonstrated dramatic improvements in outcomes for eligible patients with large vessel occlusion (LVO) AIS. The rates of substantial reperfusion and effect on 90-day disability are far greater than those observed in the thrombolysis-only era, and as such the influence of sex on these outcomes may be different. A post hoc analysis of the MR CLEAN Trial suggested greater 90-day mortality and more adverse events after EST in females compared to males, though other series including a large meta-analysis have shown no differences.[17–19] However, because of differences in age of onset and post-stroke mortality between the sexes, 90-day outcomes may be insufficient to characterize the differences in EST outcome on post-stroke disability, as they do not account for post-stroke lifetime disability, which could be substantially different between males and females.[15]

In this study, we aimed to perform a comprehensive evaluation of the effect of sex on outcome after EST in AIS. To do so, we studied the differential effect of factors known to influence outcomes after EST in females versus males, including age, onset to reperfusion time (OTR), collateral grade and final infarct volume. We then determined disability-adjusted life years (DALYs), integrating disability and mortality after disease to quantify the disease burden and treatment benefits, to provide a thorough study of the effect of sex on outcomes in EST.[20,21]

Materials and Methods

Study design and participants

The authors declare that all supporting data are available within the article and its online supplementary files.

We performed a pooled, post-hoc, exploratory analysis of the Solitaire FR With the Intention for Thrombectomy (SWIFT), Solitaire FR Thrombectomy for Acute Revascularization (STAR), and Solitaire FR with the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME) clinical trials. Patients were included if they were treated with EST with the Solitaire FR stent-retriever within the inclusion criteria for these studies. Details of these trials have been published previously and are briefly summarized here. SWIFT was a multicenter, randomized, prospective, parallel-group trial with blinded primary endpoint ascertainment.[22] The STAR trial was an international, prospective, multicenter, single-arm study.[23] SWIFT-PRIME was a multicenter, randomized, prospective, dual-arm study with blinded primary and secondary endpoint assessment.[24] Briefly, for all three studies, patients were eligible if they had AIS with moderate to severe neurological deficits, harbored angiographically confirmed occlusions of proximal cerebral arteries, and were treatable by thrombectomy within 8 hours of stroke symptom onset (6 hours for SWIFT-PRIME). Key inclusion criteria included age (22–85 years in SWIFT, 18–85 in STAR, 18–80 in SWIFT-PRIME) and National Institutes of Health Stroke Scale (NIHSS) score 8–30. While SWIFT and STAR required ineligibility for or failure to respond to intravenous tissue plasminogen activator (IV-tPA) with documented occlusion of an anterior intracranial artery, SWIFT-PRIME required that all enrolled patients have received IV-tPA within 4.5 hours of symptom onset (within 3 hours in the U.S.). Key exclusion criteria included uncontrolled hypertension, serious sensitivity to radiographic contrast agents, and CT or MRI evidence of intracranial hemorrhage or major ischemic infarction (acute ischemic change in more than a third of the middle cerebral artery territory or more than 100 mL of tissue in other territories). The studies were approved by the appropriate national regulatory bodies and by the ethics committee at each center. All patients or their legally authorized representatives provided signed, informed consent.

Procedures

In the SWIFT trial, once enrolled, patients were treated with the Solitaire stent-retriever device (roll-in phase) or randomized to treatment with the Solitaire stent-retriever device or the Merci device (randomized phase). All patients in the STAR study were treated with the Solitaire device. In SWIFT-PRIME, patients were randomized to either receiving treatment with the Solitaire stent-retriever device (with tPA) or medical therapy alone. In this analysis, we included only patients treated with the Solitaire device for anterior circulation occlusions (internal carotid artery (ICA) or middle cerebral artery (MCA)). Successful reperfusion in SWIFT was defined as TIMI 2 or 3 flow in all treatable vessels.[22] Successful reperfusion in STAR and SWIFT-PRIME was defined as TICI 2b or 3.[23,24] For the purpose of this analysis and to be consistent with the other two studies, angiograms in the SWIFT study were re-scored on the TICI scale. All imaging data were adjudicated by blinded independent core labs. Thus, successful reperfusion throughout this study has been defined as TICI 2b or 3. Onset to reperfusion time (OTR) was defined as the time from when the patient was last known to be well until the visualization of successful reperfusion as defined above in all treatable vessels. Global disability at 3 months was assessed with the 7 level modified Rankin Scale in all three studies. Intracranial hemorrhage was graded by as hemorrhagic infarct (Type 1 or 2) or parenchymal hematoma (Type 1 or 2).[25] Angiographic collateral

scales were graded by the SIR/ASITN grading scale, which assigns five possible scores ranging from no collateral flow to complete and rapid flow to the ischemic territory.

Disability Adjusted Life Year Calculations

The primary outcome of this study was differences in DALYs for females versus males after EST. DALY outcomes were defined as "DALYs gained" to represent life expectancy adjusted for disability, and as such, an increase in DALYs indicates an improved outcome. "DALYs gained" was calculated for each patient in the study individually by estimating post-stroke life expectancy and adjusting that life expectancy by disability weightings related to their 90-day mRS outcomes. Post-stroke life expectancy was determined by two methods.

In the first method, males and females were with differing post stroke mortality rates. Age-specific life expectancy given observed 90-day post-stroke disability outcomes were determined from two European studies, as described previously.[26] Full healthy life expectancy (age-specific life expectancy without stroke) was derived from the 2004 US life table for sex and race.[27] Disability weightings for the ordinal mRS were obtained using the person trade-off procedure developed by the World Health Organization Global Burden of Disease Project ranging from 0 (normal) to 1 (dead) and utilized to develop mRS specific mortality hazard ratios as previously described.[28] As such, we modeled "DALYs gained (years of optimal life)= Full healthy life expectancy – (life expectancy of normal age of stroke X mRS-specific DW)" for males. For DALYs in females, mortality rates for females relative to males after stroke adjusted for age, stroke severity, atrial fibrillation and pre-stroke disability were obtained from a population-based study of nearly 17,000 participants across 4 continents and 27 years. In this study, females were found to have lower post-stroke mortality after these adjustments compared to males.[15] As such, for post-stroke life expectancy in females, the lower mortality rate (a fixed multiplier of 0.76) was combined with a model of males by dividing "life expectancy of normal age of stroke X mRS-specific DW" with the lower rate. Then in sensitivity analysis, post-stroke life expectancy for males and females were kept the same, excluding the lower mortality for females.

Disability adjusted life years were then summed up after adjustment for age and stroke severity, pre-stroke mRS, atrial fibrillation, smoking status, and use of IV-tPA. Results are presented in both unadjusted results (not accounting for age of onset, stroke severity, pre-stroke mRS, atrial fibrillation, smoking status, use of IV-tPA, and post-stroke mortality differences) as well as adjusted results, which do account for these differences.

Statistical analysis

Key statistical analyses, including the primary endpoint analysis, were validated by an independent external statistician. For unadjusted (e.g., baseline) metrics, analyses of continuous variables were calculated by t-test (when mean is reported) or Wilcoxon test (when median is reported). Analyses of discrete variables were conducted using Fisher's exact test.

For analysis of DALY values, polynomial regression was employed, adjusted for age and NIHSS at baseline. Model fit was tested using quadratic and interaction terms for the various

predictors incorporated into generalized linear models and significant higher-order terms were included in modeling; these included quadratic terms for age and interaction terms for age by NIHSS and age by sex. P-values were derived via ANCOVA, using Type III errors.

In comparisons of 90-day neurological outcomes, good neurological outcome was defined as mRS 0–2 and adjusted for age, baseline NIHSS, atrial fibrillation, and pre-morbid mRS using multivariate logistic regression. We then examined the differential effect of age and OTR on EST outcomes in females versus males using multivariate logistic regression, with a dichotomous endpoint (mRS 0–2). These analyses were adjusted for baseline NIHSS[29–34], target occlusion location[19,35,36], ASPECTS[37], baseline serum glucose[31,38], pre-stroke mRS[29,32,33,38], atrial fibrillation[29–34,38–42], smoking status[29,32,33,38], atrial fibrillation[29–34,38–42], use of IV-tPA[30,31,34,42], year of age by sex (AGE X SEX interaction term)[15] and age[29–34,38–42]. Of note, in the logistic regression examining the differential effect of age on EST outcomes in females versus males, all the above co-variates were included except age and AGE X SEX interaction term. In addition, adjusted ordinal logistic regression was used to model the effect of OTR on 90-day outcomes across the 7-level entire distribution of mRS and adjusted for same variables. In the multivariate analyses on the differential effect of age and OTR on EST outcomes in females versus males, only patients with TICI 2b/3 reperfusion were included, for consistency with prior studies.[43]

All p-values are two-sided, with values less than 0.05 defined as statistically significant. SAS version 9.3 (SAS Institute, Cary, NC, USA) and R version 3.2 (R Foundation for Statistical Computing, Vienna, Austria) were used for statistical analysis.

Results

Among the 542 patients enrolled in the SWIFT, STAR, and SWIFT-PRIME studies, 98 patients were excluded because they did not receive EST (SWIFT-PRIME), and 55 were excluded because they received EST with an older generation device (SWIFT). Thus, 389 (72%) met inclusion criteria for this study. The cohort consisted of 98 patients from SWIFT PRIME, 202 patients from STAR and 89 patients from SWIFT. Among this cohort, 214 (55%) were females and 175 (45%) were males. Average age was 67 ± 13, NIHSS was 17 ± 5, presentation ASPECTS was 8 ± 2, and nearly equal number of patients suffered infarcts of the left hemisphere (48%) compared to the right hemisphere.

As shown in Table 1, there were notable differences in presentation characteristics between females and males. Compared to males, in our cohort females were approximately 5 years older (69 vs. 64 years, $p<0.001$) Females were less likely to have a history of smoking (11% vs. 28%, p=0.000). In addition, rates of atrial fibrillation and coronary disease/myocardial infarction differed, with females more likely to be diagnosed with atrial fibrillation (45% vs. 30%, p=0.002) and less likely to be diagnosed with coronary disease (4% vs. 9%, p=0.03). Importantly, pre-morbid mRS (32% vs. 20%, mRS>0, p=0.06), rates of diabetes (16% vs. 18%, p=0.79), hyperlipidemia (36% vs. 41%, p=0.35) and prior stroke (17% vs. 14%, p=0.58), and hypertension (69% vs. 60%, p=0.09) were similar. Rates of IV thrombolysis were similar between the two groups. Also noteworthy were the very comparable time

intervals for females and males, in terms of time from onset to ER presentation (166 vs. 165 mins, p=0.96), as well as time from ER presentation to groin puncture (89 vs. 93 mins, p=0.39) and onset to reperfusion time (294 vs. 302 mins, p=0.46).

Treatment and outcomes characteristics for females and males can be found in Table 2. Rates of successful reperfusion (TICI 2b/3) were nearly identical (87% vs. 83%, p=0.37). Other procedural characteristics including number of Solitaire device passes as well as procedural time (puncture to reperfusion time) were comparable. Radiographic outcomes, however, differed in that more females suffered from hemorrhagic infarction Type 1 (10% vs. 5%, p=0.04) while more males suffered from hemorrhagic infarction Type 2 (2% vs. 9%, p=0.003). Despite females presenting at an older age and with higher rates of atrial fibrillation, there were no statistical differences in clinical outcomes at 90 days (mRS 0–2) by sex after adjustment for age, atrial fibrillation, pre-morbid mRS, and baseline NIHSS using logistic regression (odds ratio, 1.01; 95% CI, 0.64–1.59).

We then further examined factors known as effect modifiers of clinical outcomes in EST, to compare the relationship by sex. As shown in Figure 1a, OTR had a clear effect on outcome, with the likelihood of good neurological outcome diminishing with increased OTR. However, the relationship between OTR and outcome was not different between females and males. In ordinal analysis across the 7-level mRS, the likelihood of shift in mRS at 90 days was 1.2% for females and 1% for males per 5-minute delay in reperfusion (p=0.27 for difference between females and males). We then examined the effect of infarct size on clinical outcomes for females versus males. As shown in Supplemental Table I, in trichotomized analysis of ASPECTS from 24 hour CT scan, the likelihoods of good neurological outcome were similar across all three levels. As such, the likelihood of good neurological outcome did not differ in females compared to males by final infarct size.

Next, we examined the effect of age on outcome. As shown in Figure 1b, in logistic regression adjusted for baseline NIHSS, target occlusion location, ASPECTS, baseline serum glucose, pre-stroke mRS, atrial fibrillation, smoking status, and IV-tPA use, the likelihood of a good neurological outcome diminished with increased age. However, there was no statistically significant difference in the likelihood of good neurological outcome with advancing age for females versus males. The degree and quality of angiographic collaterals were similar between males and females. As shown in Supplemental Table II, the rates of excellent collaterals (grade 3–4) were nearly identical between the two sexes. Looking at only the subset of patients with TICI 2b/3 reperfusion, collateral grade did not lead to better outcomes in one sex compared to the other.

We then calculated the effect of sex on DALY after EST with successful reperfusion. Because prior studies have demonstrated that differences in stroke outcomes for females compared to males may be a function of age of onset, stroke severity, pre-stroke function, and presence of atrial fibrillation, these features were included in our model. As shown in Supplemental Table III, in unadjusted analysis, full life expectancy for males was greater than for females by approximately 1 year. After adjusting for age of onset of stroke, stroke severity (which was similar between the two sexes), pre-stroke mRS, atrial fibrillation, smoking status, and use of IV-tPA, as shown in Table 3 females experienced better post-

stroke disability outcomes. Specifically, females were observed to have an 8.9 DALY benefit relative to males, which decreased by 0.1 per year of age at the time of stroke. The mean advantage to females over the entire cohort was 1.8 DALY, after averaging over all ages but still controlling for presentation NIHSS. These findings were similar in our sensitivity analysis, in which an alternative method was used to calculate post-stroke life expectancy. As shown in Supplementary Tables IV and V, females in this analysis enjoyed a 11.2 DALY benefit relative to males, with a decrease of 0.13 per year of age at the time of stroke, for a mean advantage to females of 2.2 DALY for the cohort.

Discussion

In this study of almost 400 patients treated with EST, females with large vessel occlusion were older than males, with higher rates of atrial fibrillation. Despite these differences, 90 day clinical outcomes were similar between the sexes after adjustment for age, stroke severity, atrial fibrillation, and pre-stroke mRS. Age at onset, OTR, ASPECTS, and collateral grade did not have differential effects on outcome after EST in females compared to males. Using published population-level data on post-stroke mortality, we found a benefit of approximately two disability adjusted life years after EST in females compared to males across the cohort.

Our finding of greater rates of atrial fibrillation and older age are consistent with sex demographic data reported in a number of studies.[14–16] Multiple prior studies have evaluated the differential outcomes for females compared to males after AIS. These results have covered the full range of possibilities, with many suggesting worse outcomes, others neutral and some improved outcomes.[2–8,15] In this study, we sought to assess the effect of sex on outcome in the modern-day era of AIS with EST, as this treatment is associated with a dramatic effect size on patient outcome in appropriately selected patients. As such, prior reports on the influence of sex on stroke outcomes may not apply to patients who receive this treatment.

Studies of the effect of intravenous thrombolysis have shown similar outcomes between females and males at 90 days, while in the Pro-Urokinase for Acute Cerebral Thromboembolism-2 (PROACT-2) study, intra-arterial thrombolysis resulted in improved outcomes for females relative to males.[7,8] Conversely, in the Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands (MR CLEAN), EST demonstrated improved 90-day clinical outcomes in males but not females relative to medical management alone.[22] This finding, however, was not replicated in a large meta-analysis of multiple EST trials.[19]

In addition, because some of the variability in the reported differences in outcomes for females compared to males with AIS may be secondary to differences in presentation characteristics, we sought to perform a comprehensive analysis of the effect of sex on the association between clinical outcome and factors affecting outcome in EST. The influence of advancing age, greater OTR, and collateral grade have all been well described in LVO stroke treated with EST.[35,36,43,44] In our study, we found that these features continued to

remain important outcomes predictors; however, there was no effect of sex on the effect of these predictors on outcome.

As has been shown previously, life expectancy and post-stroke life expectancy differ between females and males.[15] As such, 90-day disability outcomes will not accurately represent treatment impact for comparisons by sex. To this end, we determined the effect of EST on optimal life years, by calculating DALYs. This metric, which is widely used in epidemiological studies, provides a continuous metric to measure years of healthy life lost due to disability and years of life lost due to premature mortality. It has been used previously in AIS treatment studies to demonstrate that treatment with IV tPA within 3 hours resulted in 4.4 additional years of optimal life.[26] Here, because of the previously described association of age, stroke severity, pre-morbid mRS, and presence of atrial fibrillation with sex, we adjusted our analysis for these factors and found a relative advantage to females compared to males in optimal life years gained after EST, which diminished with increasing age of onset as shown in Figure 2. Based on our findings, females treated with EST in our cohort enjoyed a DALY advantage over males up to the age of late 80s.

Our study has limitations. The analyses in this work were derived from data from three clinical trials with strict selection criteria. As such, these findings should not be generalized to all EST procedures, if performed without the same rigid criteria as may be frequently done in clinical practice (i.e. treating patients with advanced age, minor stroke, greater pre-morbid disability, and/or less stringent imaging selection criteria). In addition, this analysis combined multiple trials with different inclusion/exclusion criteria. In sensitivity analysis, the largest effect was seen in the STAR trial (Supplemental Figure I), which was also the study that contributed the most patients to the cohort. In addition, our DALY calculation made use of population-level data on post-stroke mortality in females versus males. It is possible that this mortality rate may change over time, or other studies will find differing rates. For this reason, we performed an additional, sensitivity analysis with a different methodology, in which we found very similar results.

In this comprehensive assessment of the impact of sex on outcome in EST, we found that sex did not differentially influence the relationship between outcome after EST and OTR, age, ASPECTS, and collateral grade. Despite presentations at an older age, a lower rate of post-stroke mortality rate coupled with equivalent adjusted 90-day post-stroke disability outcomes resulted in females benefitting from 2 years of greater optimal life compared to males after EST.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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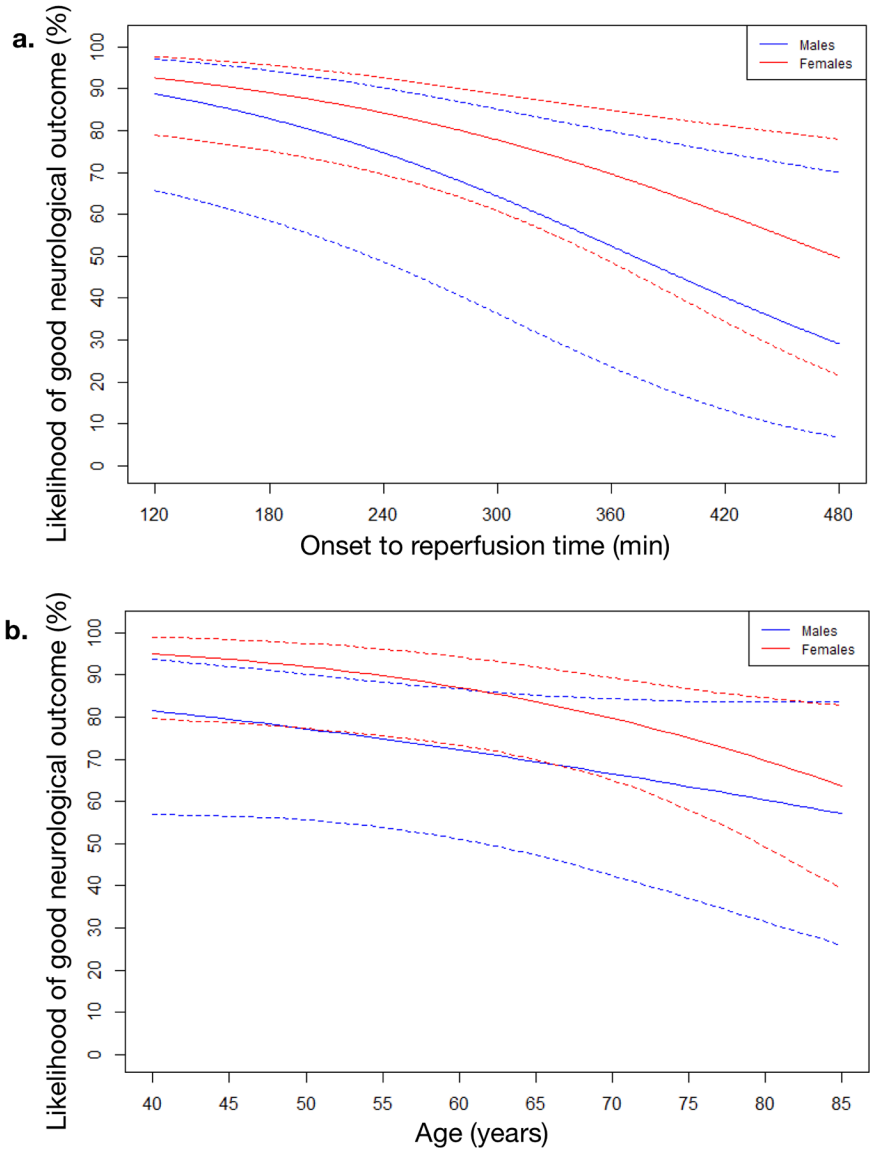

Figure 1. Effect of Onset to Reperfusion (OTR) Time and Age on Outcomes after Endovascular Stroke Therapy (EST) in Females and Males.

Adjusted logistic regressions demonstrating the likelihood of good neurological outcome at 90 days (mRS 0–2 at 90 days) relative to OTR **(a)** and age **(b)** by sex. Solid line represents point estimates and dashed lines represent 95% confidence intervals.

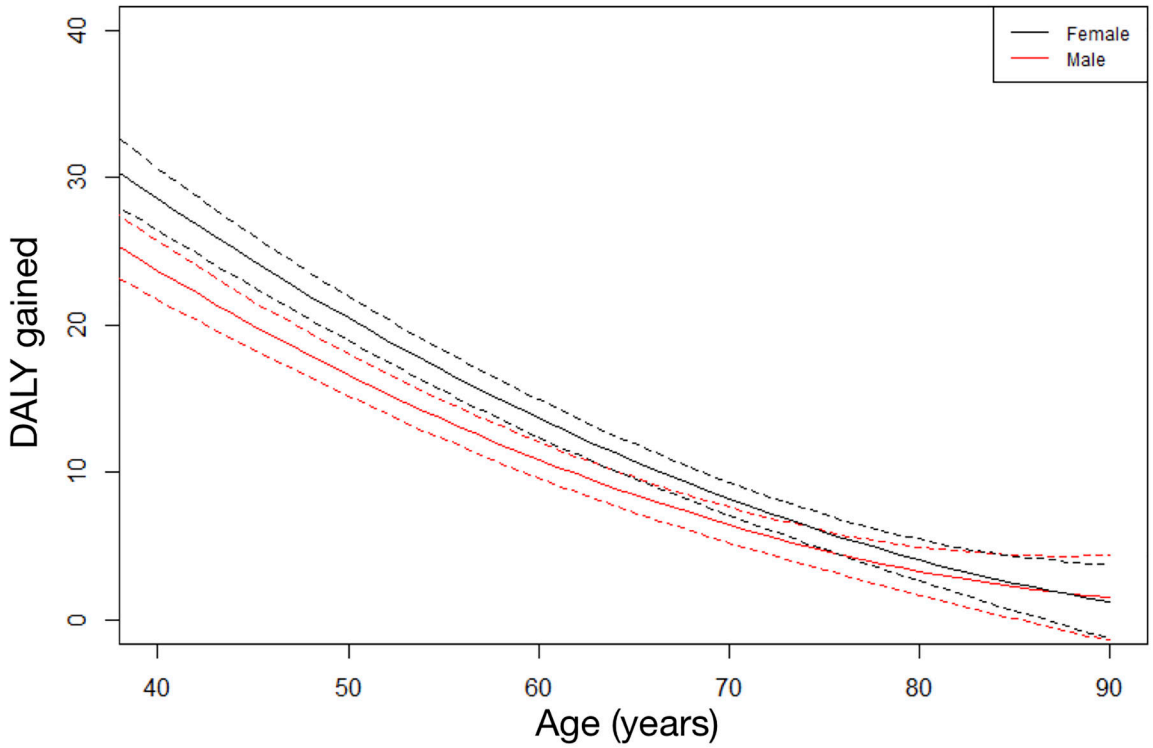

Figure 2. Effect of Age on Adjusted Disability Adjusted Life Years (DALY) outcomes in Females and Males.

Predicted DALY outcomes adjusted for age and stroke severity after EST in females and males by age. Solid line represents point estimates and dashed lines represent 95% confidence intervals.

Table 1.

Patient demographics by sex

Characteristic	Males (n=175)	Females (n=214)	p-value
Age (year)	64 ± 12	69 ± 13	<0.001
NIHSS at baseline	17 ± 5	17 ± 5	0.21
Left side infarct	75 (44%)	107/210 (51%)	0.22
Medical history			
Atrial fibrillation	53 (30%)	97 (45%)	0.002
Hypertension	105 (60%)	147 (69%)	0.09
CAD/myocardial disease	16 (9%)	8 (4%)	0.03
Diabetes mellitus	31 (18%)	35 (16%)	0.79
Hyperlipidemia	72 (41%)	78 (36%)	0.35
Peripheral artery disease	7 (4%)	6 (3%)	0.58
Smoking	49/173 (28%)	23 (11%)	0.000
Prior stroke/TIA	25 (14%)	36 (17%)	0.58
Prestroke mRS			
0	127/158 (80%)	129/187 (69%)	0.06
1	19/158 (12%)	37/187 (20%)	0.06
2	8/158 (5%)	18/187 (10%)	0.06
3	4/158 (3%)	2/187 (1%)	0.06
4	0/158 (0%)	1/187 (1%)	0.06
Occlusion location			
ICA	33/166 (20%)	38/207 (18%)	0.62
M1	106/166 (64%)	143/207 (69%)	0.62
M2	26/166 (16%)	24/207 (12%)	0.62
M3	1/166 (1%)	2/207 (1%)	0.62
ASPECTS at baseline	8 ± 2	8 ± 2	0.24
IV-alteplase	117 (67%)	141 (66%)	0.91
Baseline glucose	125 ± 49	131± 57	0.30
Time intervals (min)			
Onset to ER	165 ± 104	166 ± 101	0.96
ER to groin	93 ± 50	89 ± 49	0.39
Onset to groin	254 ± 97	256 ± 90	0.87
Onset to reperfusion	302 ± 95	294 ± 94	0.46

*Data are reported as Mean ± SD or n/N (%)

†Abbreviations: NIHSS, national institutes of health stroke scale; CAD, coronary artery disease; TIA, transient ischemic attack; ICA, internal carotid artery; M, middle cerebral artery; ASPECT, Alberta stroke program early CT scan score; IV, intravenous; ER, emergency room.

‡NOTE: instances in which data were missing or incompletely captured are represented with the appropriate denominator as above.

Table 2.

Procedural characteristics and outcomes

Characteristic	Males (n=175)	Females (n=214)	p-value
TICI 2b/3	145 (83%)	186 (87%)	0.37
Passes	2 ± 1	2 ± 1	0.17
Puncture to reperfusion (min)	48 ± 34	44 ± 26	0.23
Intracranial hemorrhage			
Any ICH	43 (25%)	41 (19%)	0.22
HI-1	8 (5%)	22 (10%)	0.04
HI-2	15 (9%)	4 (2%)	0.003
PH-1	9 (5%)	6 (3%)	0.29
PH-2	2 (1%)	4 (2%)	0.70
Functional independence (mRS 0–2)	98 (56%)	114 (53%)	0.54
Mortality at 90 days	17 (10%)	21 (10%)	1.000
Modified Rankin scale			
mRS 0	29 (16%)	34 (16%)	0.61
mRS 1	40 (23%)	54 (25%)	0.61
mRS 2	29 (17%)	26 (12%)	0.61
mRS 3	21 (12%)	38 (18%)	0.61
mRS 4	29 (16%)	37 (17%)	0.61
mRS 5	7 (4%)	7 (3%)	0.61
mRS 6	20 (12%)	18 (9%)	0.61

*Data are reported as Mean ± SD or N (%)

†Abbreviations: TICI, thrombolysis in cerebral infarction; ICH, intracranial hemorrhage; HI[25], hemorrhagic infarction; PH[25], parenchymal hemorrhage; mRS, modified Rankin scale

Table 3.

Disability-adjusted life year outcomes

Parameter	Change in DALY per unit of parameter	StandardError	p-value
Age (linear, per year of age)	−1.5	0.2	<.0001
Age (quadratic, per year of squared age)	0.007	0.001	<.0001
NIHSS at baseline (linear, per point)	−1.2	0.3	0.0004
Age by NIHSS interaction (quadratic, per year x point)	0.01	0.005	0.0107
Pre-stroke mRS (per point)	−1.4	0.4	0.0007
Atrial fibrillation (yes vs no)	0.5	0.6	0.4200
Smoking status (yes vs no)	0.7	0.8	0.3495
IV-tPA administered (yes vs no)	0.05	0.6	0.9288
Female sex (versus male)	8.9	3.1	0.0038
Per year of age, female sex (versus male)	−0.1	0.05	0.0253

*Abbreviation: NIHSS, national institutes of health stroke scale; mRS, modified Rankin Scale; IV-tPA, intravenous tissue plasminogen activator