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Cost-Utility Analysis of Mechanical Thrombectomy Using Stent Retrievers in Acute Ischemic Stroke

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Background and Purpose—Recently, 5 randomized controlled trials demonstrated the benefit of endovascular therapy compared with intravenous tissue-type plasminogen activator in acute stroke. Economic evidence evaluating stent retrievers is limited. We compared the cost-effectiveness of intravenous tissue-type plasminogen activator alone versus mechanical thrombectomy and intravenous tissue-type plasminogen activator as a bridging therapy in eligible patients in the UK National Health Service.

Methods—A model-based cost-utility analysis was performed using a lifetime horizon. A Markov model was constructed and populated with probabilities, outcomes, and cost data from published sources, including 1-way and probabilistic sensitivity analysis.

Results—Mechanical thrombectomy was more expensive than intravenous tissue-type plasminogen activator, but it improved quality-adjusted life expectancy. The incremental cost per (quality-adjusted life year) gained of mechanical thrombectomy over a 20 year period was $11 651 (£7061). The probabilistic sensitivity analysis demonstrated that thrombectomy had a 100% probability of being cost-effective at the minimum willingness to pay for a quality-adjusted life year commonly used in United Kingdom.

Conclusions—Although the upfront costs of thrombectomy are high, the potential quality-adjusted life year gains mean this intervention is cost-effective. This is an important factor for consideration in deciding whether to commission this intervention. **(*Stroke*. 2015;46:2591-2598. DOI: 10.1161/STROKEAHA.115.009396.)**

Key Words: cost-effectiveness ■ stents ■ stroke ■ thrombectomy ■ tissue-type plasminogen activator

Ischemic stroke is the third highest cause of death in the United Kingdom and a leading cause of disability.[1] The overall incidence is postulated to increase over the next 5 years by the WHO.[2] The economic burden of stroke is estimated at £9 billion per year in the United Kingdom ($38 billion in the United States) and is estimated to rise.[3,4] Intravenous tissue-type plasminogen activator (IV-tPA) for cerebral arterial occlusion is the proven therapy for acute ischemic stroke.[5,6] However, new strategies are increasingly involving adjunctive endovascular techniques, especially when fibrinolysis is contraindicated or has failed.

Recently, 5 randomised controlled trials (Endovascular Treatment for Acute Ischemic Stroke in the Netherlands [MR CLEAN], Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke (ESCAPE), Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial (EXTEND-IA), Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME) Trial, and Endovascular Revascularization With Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 Hours (REVASCAT)) demonstrated superior benefit of adjunctive mechanical thrombectomy versus IV-tPA alone when there is a major vessel occlusion.[7–11] This has been propagated by a new generation of thrombectomy devices, stent retrievers, which demonstrate a higher arterial recanalization rate and a better clinical outcome.[12–14] More importantly, this is in patients with proximal large vessel occlusions who are known through the natural history of the disease to have a poor outcome.[15]

Stent retrievers have consistently shown significantly better angiographic, safety, and clinical outcome data than the Merci Retriever.[16–21] Stent retrievers also seem to produce higher complete recanalization rates than Penumbra, although no head-to-head trial has been performed.[22] A meta-analysis demonstrated that early vessel recanalization, using a range of methods, is

Received March 28, 2015; final revision received June 16, 2015; accepted June 19, 2015.

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The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health, or Boehringer Ingelheim Ltd.

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The online-only Data Supplement is available with this article at http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.115.009396/-/DC1.

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associated with a 4- to 5-fold increase in the odds of good final clinical outcome, with a similar decrease in odds of death.[12]

Benefit of treatments is usually measured according to functional outcome at 3 months. Implementation of new treatments also depends on cost and affordability, for which a health economic study is usually needed. Stroke itself is an expensive disease in terms of its societal, personal, and financial impact. The rationalization concerning the clinical value and effectiveness of thrombectomy is guided by information regarding the benefits, risks, and costs associated. It has been suggested that although the upfront costs of thrombectomy are high, the potential reduction in morbidity can result in savings downstream both in the hospital and in the community setting, resulting in a significant reduction in the overall economic burden from stroke.

Decisions to implement new technologies in the UK National Health Service are increasingly being made taking into account economic considerations, such as cost-effectiveness and budget impact. Previous economic evaluations of thrombectomy have been undertaken in the United States and are based on single arm studies of a range of mechanical devices, now superseded in a rapidly developing field.[22–25] Therefore, the purpose of this study was to model the cost-effectiveness of mechanical thrombectomy in the hyperacute management of stroke in the United Kingdom, based on a meta-analysis of the data recently published using the 5 randomized control trials, which have used predominantly stent retrievers.

Methods

This was a model-based cost-utility analysis, with outcomes measured in terms of quality adjusted life years (QALYs),[26] which are the recommended outcomes for economic evaluation in the United Kingdom.[27] The number of deaths averted is also reported as an additional outcome measure.

Model Structure

A short-run decision analytic model (Figure 1A) was created to analyze data on costs and clinical outcomes within 3 months from stroke and subsequently was used to distribute a theoretical cohort of patients into 1 of 3 possible health states (see Outcomes). A long-run Markov state-transition model was then used to estimate the expected costs and outcomes over a life-time horizon of 20 years, using cycles of 3 months (Figure 1B). The analysis was undertaken from the perspective of the UK National Health Service and Personal Social Services. Costs were calculated in 2013–2014 UK pounds and are presented in US$ using an exchange rate of £1=US$1.65.[28] Where appropriate, costs were converted to 2013–2014 prices using National Health Service Pay and Prices Indices.[29] Outcomes are measured in terms of deaths averted and quality adjusted life years (QALYs) gained. In the long-run model, all costs and outcomes after the first year are discounted at an annual rate of 3.5%.[27]

Management Strategies

Two treatment options were considered, IV-tPA alone versus mechanical thrombectomy and IV-tPA used as a bridging therapy. Only data from the recently published randomized controlled trials using predominantly stent retrievers were used (see Table I in the online-only Data Supplement). For both strategies, outcomes were based on modified Rankin Scale (mRS) scores measured at 90 days after stroke, which were assumed to be affected by recanalization rates and symptomatic hemorrhage rates. We assumed that all other aspects of inpatient care, including imaging and laboratory studies, would be otherwise comparable and consistent with published clinical guidelines.[30]

Costs

The cost of IV-tPA was estimated to be $2953 (£1214). This includes the cost of the medication (assuming an average patient weight of 76 kg)[31,32] and the cost of staff time for the administration[29,33] (Table 1). Staff costs were estimated using the data on the average cost per hour.[29]

The cost of the mechanical thrombectomy was estimated to be $13 803 (£8365), including the cost of the stent, the materials, and the surgery.[29,36,37] The cost of the procedure was calculated using a microcosting approach, multiplying the average time of an intervention for the hourly cost for each grade of personnel[29] (see Table II in the online-only Data Supplement).

The costs for the acute management of patients in the first 3 months after stroke and the following ongoing annual costs were taken from a published report.[33] Acute and ongoing costs differ according to the level of disability, measured by mRS score. Acute costs include the length of stay in the Hyper Acute Stroke Unit, in the Acute High Dependence Unit, and in the rehabilitation ward, as well as the supported discharge cost and community care costs.

The cost of a recurrent stroke has been assessed internally assuming the cost is the same in each intervention arm. Because it is not possible to predict the type and severity of a recurrent stroke and

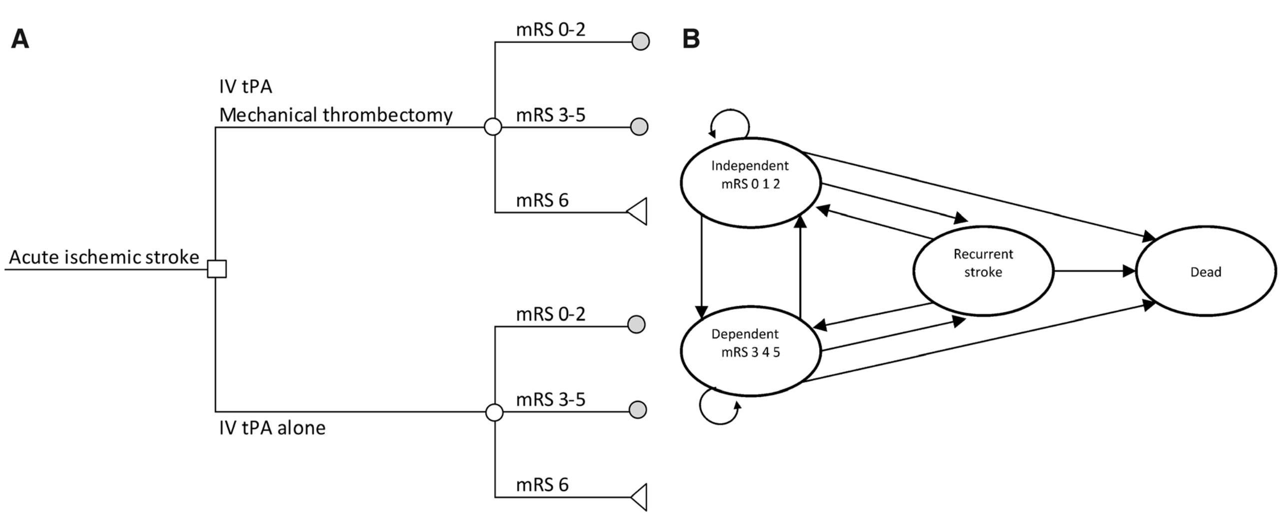

Figure 1. Decision model. **A**, Short-run analytic model. **B**, Long-run Markov model structure. IV-tPA indicates intravenous tissue-type plasminogen activator; and mRS, modified Rankin Scale.

Table 1. Model Parameters and Range of Values for Sensitivity Analysis: Utilities Scores, Costs, Probabilities, and Transition Probabilities

	Base-Case Value	Univariate Sensitivity Analysis	Distribution	Range	Alpha-Beta	Source
Probabilities						
mRS 0-1-2 after IV-tPA and thrombectomy	0.46		Dirichlet	0–1	291-342	Multiple sources
mRS 3-4-5 after IV-tPA and thrombectomy	0.39		Dirichlet	0–1	247-386	Multiple sources
mRS 6 after IV-tPA and thrombectomy	0.15		Dirichlet	0–1	95-538	Multiple sources
mRS 0-1-2 after IV-tPA alone	0.26		Dirichlet	0–1	169-481	Multiple sources
mRS 3-4-5 after IV-tPA alone	0.55		Dirichlet	0–1	358-293	Multiple sources
mRS 6 after IV-tPA alone	0.19		Dirichlet	0–1	124-527	Multiple sources
If IV-tPA alone						
mRS 0-1-2 after recurrent stroke	0.26		Dirichlet	0–1	260-740	Short-run model
mRS 3-4-5 after recurrent stroke	0.55		Dirichlet	0–1	550-450	Short-run model
mRS 6-death after recurrent stroke	0.19		Dirichlet	0–1	190-810	Short-run model
If mechanical thrombectomy						
mRS 0-1-2 after recurrent stroke	0.46		Dirichlet	0–1	460-540	Short-run model
mRS 3-4-5 after recurrent stroke	0.39		Dirichlet	0–1	390-610	Short-run model
mRS 6-death after recurrent stroke	0.15		Dirichlet	0–1	150-850	Short-run model
Transition probabilities						
Movement from up to end of year 1 to 3 months						
Independent mRS 0-1-2						
Independent mRS 0-1-2	0.955		Dirichlet	0–1	1337-63	Ref. 33
Dependent mRS 3-4-5	0.024		Dirichlet	0–1	34-1366	Ref. 33
Recurrent stroke	0.013		Dirichlet	0–1	18-1382	Ref. 33
Dead mRS 6	0.008		Dirichlet	0–1	11-1389	Ref. 33
Dependent mRS 3-4-5						
Dependent mRS 3-4-5	0.919		Dirichlet	0–1	1287-113	Ref. 33
Independent mRS 0-1-2	0.029		Dirichlet	0–1	41-1359	Ref. 33
Recurrent stroke	0.013		Dirichlet	0–1	18-1382	Ref. 33
Dead mRS 6	0.039		Dirichlet	0–1	55-1345	Ref. 33
Movement from after year 1 to 3 months						
Independent mRS 0-1-2						
Independent mRS 0-1-2	0.979		Dirichlet	0–1	1371-28	Ref. 33
Dependent mRS 3-4-5	0.000		Dirichlet	0–1	17-1382	Ref. 33
Recurrent stroke	0.013		Dirichlet	0–1	11-1388	Ref. 33
Dead mRS 6	0.008		Dirichlet	0–1	11-1388	Ref. 33
Dependent mRS 3-4-5						
Dependent mRS 3-4-5	0.948		Dirichlet	0–1	1327-72	Ref. 33
Independent mRS 0-1-2	0.000		Dirichlet	0–1	17-1382	Ref. 33
Recurrent stroke	0.013		Dirichlet	0–1	54-1345	Ref. 33
Dead mRS 6	0.039		Dirichlet	0–1	55-1345	Ref. 33
Recurrent stroke						
Independent mRS 0-1-2 after IV-tPA alone	0.834		Dirichlet	0–1	834-165	Ref. 33, 34
Dependent mRS 3-4-5 after IV-tPA alone	0.137		Dirichlet	0–1	136-863	Ref. 33, 34
Dead mRS 6 after IV-tPA alone	0.029		Dirichlet	0–1	28-971	Ref. 33, 34
Independent mRS 0-1-2 after IV-tPA and thrombectomy	0.867		Dirichlet	0–1	867-132	Ref. 33, 34
Dependent mRS 3-4-5 after IV-tPA and thrombectomy	0.104		Dirichlet	0–1	103-896	Ref. 33, 34
Dead mRS 6 after IV-tPA and thrombectomy	0.029		Dirichlet	0–1	28-971	Ref. 33, 34

(*Continued*)

Table 1. Continued

	Base-Case Value	Univariate Sensitivity Analysis	Distribution	Range	Alpha-Beta	Source
Utilities						
Independent mRS 0-1-2	0.74	0.7–0.77	Beta	0–1	684-3021	Ref. 35
Dependent mRS 3-4-5	0.38	0.29–0.47	Beta	0–1	60-590	Ref. 35
Recurrent stroke	0.34	0.32–0.36	Beta	0–1	540-5685	Ref. 34
Dead mRS 6	0			0		
Costs						
Cost of alteplase IV-tPA	$2953.59		Gamma			Ref. 29, 31–33
Cost of thrombectomy	$13 803.04	$9677–$17 943	Gamma			Ref. 29, 31, 36, 37
Acute costs first 3 months						
3 months acute costs independent mRS 0-1-2	$11 309.46		Gamma			Ref. 29, 33, 36, 37
3 months acute costs dependent mRS 3-4-5	$24 201.35		Gamma			Ref. 29, 33, 36,37
Cost of acute event fatal stroke mRS 6	$15 547.44		Gamma			Ref. 29, 33, 36, 37
Cost of recurrent stroke	$589.20		Gamma			Internal model
Ongoing costs every 3 months						
Independent mRS 0-1-2	$771.88		Gamma			Ref. 29, 33, 36, 37
Dependent mRS 3-4-5	$2074.62		Gamma			Ref. 29, 33, 36, 37

IV-tPA indicates intravenous tissue-type plasminogen activator; and mRS, modified Rankin Scale.

therefore the correspondent treatment, the cost to treat a recurrent stroke is calculated as the mean expected cost to treat an average stroke that may not need thrombolysis or thrombectomy.

Outcomes

Patients were categorized into 1 of 3 health outcome states based on their predicted mRS scores: independent (mRS score ≤2), dependent (mRS score 3–5), or dead (mRS=6).[38] We assumed the patient remained in the same health state for the first 3 months. After the initial allocation of patients into mRS categories, a Markov model distributed a theoretical cohort of 1000 patients into the 3 states over time and includes the additional health status of a patient having a recurrent stroke. The cohort of patients receiving the intervention treatment has been estimated using the national UK data from the stroke audit.[39] According to the audit, 19 638 patients had a stroke between January and March 2014. Only 11.5% were given IV-tPA. We assume that patients eligible for thrombectomy are around 80% of those with a major occlusion (National Institute of Health Stroke Scale (NIHSS) score >16), which means 1800 patients.

QALYs combine length of life and quality of life, the latter being measured by utility scores. A utility score of 1 represents full health and a score of 0 of death. We used the utility scores from Dorman et al,[35] the Sandercock et al[40] systematic review, and the ScHARR report[33] for the independent and dependent states because these are the most updated and reliable values available that take into account the EuroQol elicitation method (Table 1). We used the utility scores from Morris et al[34] for recurrent strokes (Table 1). Other sources were used[23,33] for the sensitivity analysis.

Probabilities

The probability of being independent, dependent, or dead in each treatment arm were calculated using the data provided from the 5 randomized controlled trials.[7–11] We applied the transition probabilities in Table 1,[23] transformed for cycles of 3 months. In the base-case, the transition probability of moving from an independent state to recurrent stroke was assumed to be the same as moving from a dependent state to recurrent stroke, but this was varied in sensitivity analysis. Those who were in the dependent state at 12 months were assumed to be unable to move to the independent state thereafter. Those in the independent state at 12 months were assumed to remain in that state unless they survived another stroke, in which case they could either die or move into a dependent state or remain independent.[32,40,41]

Measuring Cost-Effectiveness

Total QALYs and costs were calculated by multiplying the number of patients in each state by the calculated utilities and costs for that state.

Cost-effectiveness was measured in terms of the incremental cost per QALY gained and the Net Monetary Benefits (NMB) of thrombectomy plus IV-tPA compared with IV-tPA alone. The NMB was calculated as the mean QALYs per patient accruing to that treatment multiplied by the decision-maker's maximum willingness to pay for a QALY (also referred to as the cost-effectiveness threshold) minus the mean cost per patient for the treatment. In the United Kingdom, the lower and upper limit of the maximum willingness to pay for a QALY are $33 000 (£20 000) and $49 500 (£30 000), respectively.[27]

Sensitivity Analysis

One-way sensitivity analysis was undertaken, varying the probabilities, utilities, and costs, one at a time within the ranges listed in Table 1.

A probabilistic sensitivity analysis was also undertaken to determine the impact of the uncertainty surrounding the model input parameters (see Table III in the online-only Data Supplement).[27] In Table 1, we describe the distribution assigned to each parameter value.[42] A random value from the corresponding distribution was selected. This generated an estimate of the mean cost and mean QALY and the NMB associated with each treatment. This was repeated 10 000 times, and the results for each simulation were noted. The proportion of times either treatment (thrombectomy or IV-tPA) had the highest NMB was calculated for a range of values of the willingness to pay for a QALY. The results are summarized using cost-effectiveness acceptability curves in Figure 2. The mean cost, QALYs, and NMB for each treatment were calculated from the 10 000 simulations; these are probabililistic results (Figure 3; online-only Data Supplement).

Results

Using base-case values, mechanical thrombectomy after an IV-tPA to treat acute large-vessel ischemic stroke was associated with incremental costs of $12 262 (£7431) per patient and a gain

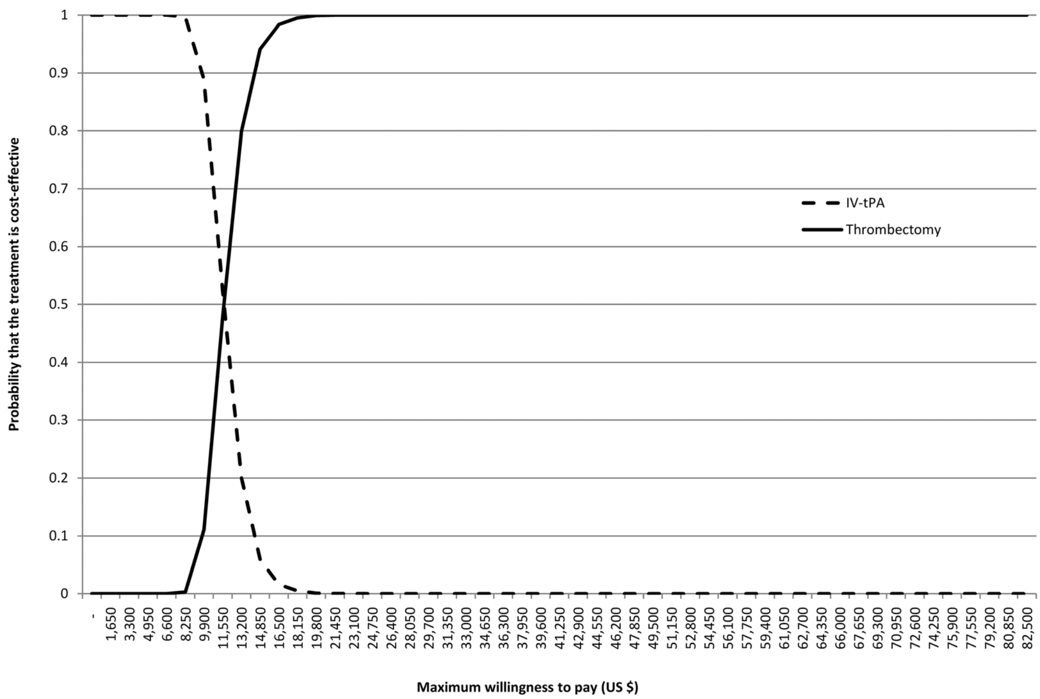

Figure 2. Cost-effectiveness acceptability curves showing the probability that each option is cost-effective at different values of the willingness to pay for a quality-adjusted life years (QALY). In the United Kingdom, the lower and upper limit of the maximum willingness to pay for a QALY are $33 000 (£20 000) and $49 500 (£30 000) respectively.

of 1.05 QALYs per patient over 20 years (Table 2). The additional costs were because of the cost of the device and the cost of the procedure. QALYs are higher for mechanical thrombectomy because it saves more lives, and those patients who survive are more likely to have a better health outcomes and be independent (mRS 0,1,2). Assuming a cohort of 1000 patients, the number of deaths over 20 years was 787 in patients treated with IV-tPA alone and 716 in patients treated with thrombectomy. Therefore, the mechanic thrombectomy averted 71 deaths over 20 years.

The incremental cost-effectiveness ratio of mechanical thrombectomy compared with IV-tPA was $11 651(£7061) per QALY gained. The NMB of thrombectomy plus IV-tPA was higher than the NMB of IV-tPA alone at both the lower and upper limits of the maximum willingness to pay for a QALY, indicating that this option was preferred on cost-effectiveness ground. As expected, the probabilistic results were similar (see Table III in the online-only Data Supplement).

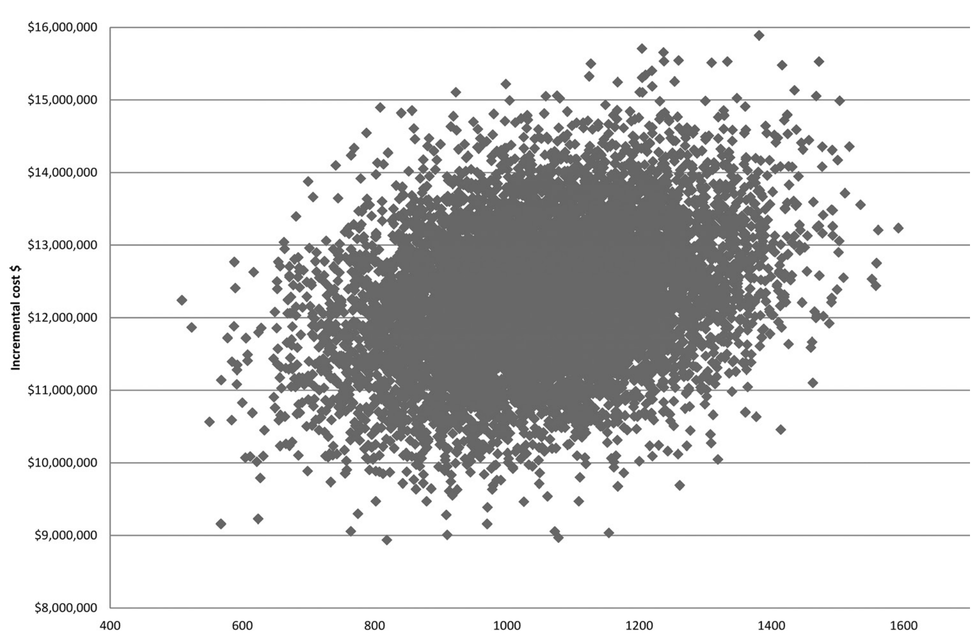

Figure 3. Monte Carlo simulations of incremental cost per quality-adjusted life years (QALY) gained of the mechanical thrombectomy on a cohort of 1000 patients.

Table 2. Base-Case Results: Expected Values per 1000 Patients

	IV-tPA	Mechanical Thrombectomy	Difference
Costs	$52 494 730	$64 757 281	$12 262 551
Deaths	787	716	−71
QALYs	3790	4842	1052
ICER			$11 651
Net monetary benefit			
Lower	$72 563 794	$95 031 346	
Upper	$135 093 056	$174 925 660	

Costs are based on 2013–2014 prices. The point estimates are calculated using base-case values of the model parameters (deterministic results). The Net Monetary Benefit is calculated at the lower and upper limits of the willingness to pay for a QALY, which in the UK are $33 000 (£20 000) and $49 500 (£30 000), respectively. ICER indicates Incremental cost-effectiveness ratio; IV-tPA, intravenous tissue-type plasminogen activator; and QALY, quality-adjusted life years.

The results of the 1-way sensitivity analysis showed that increasing the cost of thrombectomy by 139% from $13 803 (£8365) to US $33 000 (£20 000) will make the new intervention borderline cost-effective for the lower value of the maximum willingness to pay for QALY. If the utility for the independent patients (mRS 0-1-2) were decreased from 0.74 to 0.34, then the intervention is borderline cost-effective. The results were not sensitive to changing the values of any of the other parameters included in the univariate sensitivity analysis.

The cost-effectiveness acceptability curves for the 2 interventions show that mechanical thrombectomy had 100% probability of being cost-effective at the lower and upper values of the maximum willingness to pay for QALY commonly used in United Kingdom (Figure 2).

Discussion

Our principle finding is that the interventional treatment arm consisting of IV-tPA followed by mechanical thrombectomy for acute large-vessel ischemic stroke saves 1 life for every 14 thrombectomies performed, reduces disability, and is cost-effective when compared with IV-tPA alone.

Although the cost of thrombectomy is higher than that of IV-tPA initially, it leads to savings downstream in the stroke care pathway because of better outcomes. Between January and March 2014, 19 638 new cases of stroke were registered in the United Kingdom[39]; 87.3% were ischemic strokes and 11.5% had thrombolysis. 15% of ischemic strokes registered an acute large vessel stroke with an NIHSS score >16; therefore, thrombectomy could potentially be performed in 20% of patients who had thrombolysis. This means that in 1 year, around 1800 patients could have had a thrombectomy, for an incremental cost (budgetary impact) of $22 million (£13.4 million).

The recent Oxford Vascular study reports that each additional point in the NIHSS score can increase total costs over 5 years by 15%.[43] Therefore, modest improved outcomes are often cost-effective from a societal perspective. These benefits need to be weighed against the procedural risks and the increased risk of symptomatic intracerebral hemorrhages. Although initially symptomatic hemorrhage appeared to be higher among those undergoing thrombectomy, subsequent studies have shown similar rates for IV-tPA and thrombectomy versus tPA alone as evident in Tables III in the online-only Data Supplement. In fact, in the studies included in this article, the average hemorrhage rates were similar (4.6% for thrombectomy versus 3.8% for IV-tPA).

Earlier this year, the first randomized controlled studies, MR CLEAN, ESCAPE, EXTEND IA, SWIFT-PRIME, and REVASCAT, demonstrate significant benefit with thrombectomy, which was contributed by the higher recanalization rate.[7–11] Studies to date have shown a correlation between recanalization and clinical outcome.[12,44] It is likely that the development and evolution of mechanical thrombectomy in time will lead to better recanalization rates. We expect the cost of thrombectomy to decrease over time because of decreasing costs of the intervention and discounts in the device used secondary to market competition. This will improve the cost-effectiveness of the new intervention.

There is no other cost-effectiveness study for thrombectomy performed in the United Kingdom. However, similar studies have been done in the United States based on single arm studies, which also demonstrated cost-effectiveness of $16 001 per QALY gained,[23] $12 120 per QALY gained,[25] and $9386 per QALY gained.[24] Patil et al focussed on patients whom could receive treatment within 8 hours but were not eligible for IV-tPA. Nguyen-Huynh et al studied patients beyond 3 hours and who were then offered mechanical thrombectomy or antiplatelet therapy and supportive care.[24] However, Kim et al looked at a similar question to ours, that is, the use of IV-tPA as a bridging therapy to mechanical thrombectomy versus IV-tPA alone.[23] However, their data were based on the Multi-MERCI study using the Merci retrieval systems (Concentric, s-Hertogenbosch, Netherlands), as well as some use of intra-arterial thrombolysis and angioplasty. As mentioned earlier, stent retrievers have been shown to be significantly better than the Merci retrieval system.[16–21] The advantage of this study is that we have used data from randomized controlled trials predominantly using stent retriever devices. Despite several differences among cost-effectiveness studies, all have concluded that mechanical thrombectomy is cost-effective compared with medical therapy.

The analysis has several limitations. In the absence of data, we have assumed the probability of a recurrent stroke is the same irrespective of the level of disability after initial stroke, when we might expect the probability of recurrent stroke to be higher among the more disabled. The results of our sensitivity analysis showed that our conclusions were not sensitive to this assumption.

The analysis was undertaken from the perspective of the UK National Health Service. A wider perspective, such as a societal one, would also include impacts on the rest of society, including patients, families, and business. Given that stroke is the leading cause of disability in United Kingdom,[1] it is likely that the cost savings attributable to mechanical thrombectomy would be greater than demonstrated if costs from other viewpoints were included.

Summary

We have demonstrated in this first cost-effectiveness study that the use of predominantly stent retrievers in mechanical thrombectomy after IV-tPA is cost-effective in the United Kingdom, based on current data. However, we hope that this study will supplement the recently published randomized controlled trials together with evidence demonstrating an increasing prevalence of stroke among young adults[45,46] to assist healthcare commissioners regarding purchasing and investing in this new aspect of acute stroke services.

Acknowledgments

All authors have made substantial contributions to this study. J. Ganesalingam, E. Pizzo, S. Morris, D. Ames, and K. Lobotesis were responsible for the conception and design of the study. J. Ganesalingam, E. Pizzo, T. Sunderland, S. Morris, and K. Lobotesis were responsible for the acquisition of data. J. Ganesalingam, E. Pizzo, T. Sunderland, S. Morris, and K. Lobotesis were responsible for the analysis and interpretation of data. J. Ganesalingam, E. Pizzo, T. Sunderland, D. Ames, S. Morris, and K. Lobotesis were responsible for drafting the article or revising it critically for important intellectual content.

Sources of Funding

The research was supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care North Thames at Barts Health National Health Service (NHS) Trust.

Disclosures

T. Sunderland is a permanent employee of Boehringer Ingleheim. The other authors report no conflicts.

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