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### Article

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## ORIGINAL RESEARCH

# INfluence of Revascularization Attempts on Clinical Outcomes of Mechanical Thrombectomy Patients and its Economic BURDEN

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**BACKGROUND:** Emerging evidence suggests that clinical and economic benefits of treatment with mechanical thrombectomy vary by level of reperfusion achieved, and the number of passes required to achieve revascularization. This study aimed to investigate the **IN**fluence of revascularization **A**tempts on **C**linical outcomes of mechanical **T**hrombectomy and the economic **BURDEN** (**INF**act **BURDEN**) in Ireland using single center real-world data from the Irish National Thrombectomy Service database.

**METHODS:** Primary clinical outcomes were reperfusion (modified thrombolysis in cerebral infarction 2b-3 or <2b) and functional outcome (90-day modified Rankin Scale  $\leq 2$  or modified Rankin Scale  $> 2$ ) among patients treated with 1–3 passes compared with  $\geq 4$  passes. Multivariable generalized linear models examined the association between number of passes with outcomes, with adjustment for covariates that may affect outcomes (eg, age, pre-procedure modified Rankin Scale, National Institutes of Health Stroke Scale, Alberta Stroke Program Early CT Score, occlusion site, time from symptom onset to groin puncture). A 90-day decision-tree and Markov model with a 5-year time horizon evaluated the cost-effectiveness of mechanical thrombectomy from the Irish public healthcare payer perspective.

**RESULTS:** Eight hundred twenty three patients met the inclusion criteria. Compared with patients in the  $\geq 4$  passes group, patients in the 1–3 passes group achieved a significantly higher rate of successful reperfusion (94% versus 78%, odds ratio [OR], 4.7;  $P < 0.001$ ) and a higher rate of functional independence (49% versus 33%, OR, 2.0;  $P < 0.001$ ). Patients in the 1–3 passes group had a shorter time from onset to reperfusion, lower incidence of procedural complications, including distal emboli into non-involved territory and intra-procedure rupture, as well as lower 90-day mortality. The cost-effectiveness analysis demonstrated that patients successfully revascularized in 1–3 passes had 0.19 additional QALYs and lower costs (€3328; \$3800) such that 1–3 passes was dominant compared with  $\geq 4$  passes over a 5-year time horizon.

**CONCLUSION:** This study illustrates that the number of passes has a significant effect on both clinical outcomes and health care costs.

**Key Words:** cost ■ first pass ■ stroke ■ thrombectomy

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**S**troke is a major cause of disability and the second leading cause of mortality worldwide, affecting 16 million people each year.<sup>1</sup> In Europe, stroke is the primary cause of long-term disability<sup>2</sup> and up to 33% of stroke survivors lose their independence.<sup>3</sup> With a rising incidence in developing countries, stroke imposes a substantial socioeconomic burden on both patients and health care systems.<sup>4</sup> The overall annual cost of stroke is estimated to be €60 billion in the European Union and over \$100 billion in the United States (US), the bulk of which is attributed to acute ischemic stroke.<sup>5,6</sup>

Rapid and complete reperfusion of ischemic brain tissue is required to achieve optimal clinical and functional outcomes for patients with acute ischemic stroke.<sup>7</sup> Although intravenous thrombolysis has traditionally been used to restore cerebral blood flow, it has several contraindications and is not as effective in restoring perfusion when a large artery is occluded.<sup>8</sup> Mechanical thrombectomy (MT) is the guideline-recommended standard of care for patients with acute ischemic stroke caused by large vessel occlusion.<sup>9,10</sup> In patients with large vessel occlusion, MT is associated with better functional outcomes and has been shown to be cost-effective compared with intravenous thrombolysis alone within many health care systems in Europe.<sup>8,11–14</sup>

Among patients treated with MT, the clinical and economic benefits of treatment vary by the level of reperfusion achieved.<sup>15,16</sup> A growing body of evidence suggests an association between increasing number of passes and reduction in the likelihood of good outcomes.<sup>17–24</sup> Although multiple passes are often required to achieve complete reperfusion, the number of passes impacts survival and functional independence.<sup>18,19,23</sup> Specifically, the likelihood of successful recanalization is reduced with each subsequent pass<sup>17,19,24</sup> and the number of passes needed to achieve revascularization is reported to be a significant modifier for favorable outcome.<sup>18,23</sup>

There is limited published research on the number of passes and the associated economic impact. In 2 published studies that included patients treated with MT, the economic benefit of achieving complete reperfusion on the first pass was demonstrated.<sup>15,16</sup> Among patients achieving complete reperfusion, reduced health care resource use and lower costs were observed among those who were treated with a single pass.<sup>16</sup>

The aim of this study was to investigate the INFLUence of the revascularization Attempts on Clinical outcomes of MT patients and its associated economic burden in Ireland, using data from the Irish National Thrombectomy Service database.

## Nonstandard Abbreviations and Acronyms

<b>HIQA</b>	Health Information and Quality Authority
<b>mRS</b>	modified Rankin Scale
<b>MT</b>	mechanical thrombectomy
<b>mTICI</b>	modified thrombolysis in cerebral infarction
<b>QALY</b>	quality-adjusted life year

## CLINICAL PERSPECTIVE

- In a large single-center cohort in Ireland, treatment of acute ischemic stroke with mechanical thrombectomy in 1–3 device passes was associated with higher rates of successful reperfusion and functional independence, shorter time from onset to first reperfusion, lower rate of embolization into a new territory, reduced incidence of hemorrhage, and lower mortality compared with 4 or more passes.
- The number of thrombectomy passes has a significant effect on both clinical outcomes as well as short and long-term health care costs, with each failed revascularization attempt increasing the economic burden to health care payers and providers.
- Successful revascularization within 3 device passes is a relevant goal in the treatment of patients with acute ischemic stroke and research to elucidate the factors and methods that increase the probability of achieving successful revascularization in the fewest number of attempts is needed.

## METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request. This study includes a retrospective analysis of real-world evidence which informs an economic model.

## Study Design and Patient Population

This was a single-center, retrospective, observational, comparative analysis of consecutive acute ischemic stroke patients suffering from large vessel occlusion,

treated with MT procedures, captured in the National Thrombectomy Service database.<sup>25</sup> Data on all thrombectomy cases were prospectively maintained in a database in Beaumont Hospital (Dublin, Ireland) under the remit of ongoing service audit of the National Thrombectomy Service and it is registered with Beaumont Hospital Institutional Quality and Standards Department.

Patients were included in the analysis if they were treated with MT procedures for large vessel occlusion in the anterior circulation within 24 hours of symptom onset, had an Alberta Stroke Program Early CT Score of  $\geq 6$ , and good ( $>50\%$ ) collateral circulation on computed tomography angiogram or with penumbra on perfusion as per the DAWN<sup>26</sup>/DEFUSE<sup>27</sup> trials. Patients with isolated extracranial internal carotid artery occlusions were excluded. Thrombectomy technique varied by physician, clot location, and features.

## Outcomes

The primary clinical outcomes were post-procedure reperfusion assessed with the modified thrombolysis in cerebral infarction (mTICI) score post-procedure (categorized as mTICI 2b-3 or mTICI  $<2b$ ) and 90-day functional outcome (modified Rankin Scale [mRS] score) (categorized as mRS  $\leq 2$  or mRS  $>2$ ). Time from onset to first reperfusion was also assessed. Safety outcomes included hemorrhage on follow-up imaging, distal embolus into a non-involved territory, intra-procedural rupture, and all-cause mortality at 90 days.

All study outcomes were compared between groups based on the number of MT passes. In the primary analysis, patients were grouped into those who were treated with 1–3 passes, and those with  $\geq 4$  passes. A sensitivity analysis aligned with the primary analysis was conducted in which patients who did not achieve mTICI 2b-3 were excluded to avoid any potential bias introduced by inclusion of patients who did not achieve complete/near-complete reperfusion. In the secondary analysis, patients who achieved mTICI 2c-3 were grouped into those treated with 1 pass and those treated with  $\geq 2$  passes.

## Statistical Analysis

The associations between mTICI and mRS categories between 1–3 versus  $\geq 4$  passes were considered as co-primary end points for this study. A sample size of 800 with a ratio of 3:1 for patients treated with 1–3 versus  $\geq 4$  passes was estimated to provide 90% power for the co-primary end points at an alpha level of 0.025 with Bonferroni correction for multiple comparisons. All other comparisons and statistical tests were considered exploratory.

All study variables were analyzed descriptively. Counts and proportions were produced for categorical variables although means, medians, and SDs were calculated for continuous variables. Multivariable generalized linear models were constructed to examine the association between the number of passes with outcomes (mTICI and mRS score categories, and time from onset to first reperfusion) although adjusting for the covariates that may affect these outcomes. Covariates were determined based on clinical knowledge a priori, and included age, sex, intravenous thrombolysis, National Institutes of Health Stroke Scale at presentation, mRS pre-procedure, Alberta Stroke Program Early CT Score pre-procedure, CT angiography occlusion site, time from onset to groin puncture, and collateral circulation score. Safety outcomes were summarized descriptively. All analyses were conducted using R Studio version 3.6.0. Statistical significance was set at  $P < 0.025$  (2-sided) for the co-primary end points. When 90-day mRS was missing, values at 30 days were carried forward.  $P$ -values for all other end points are considered exploratory.

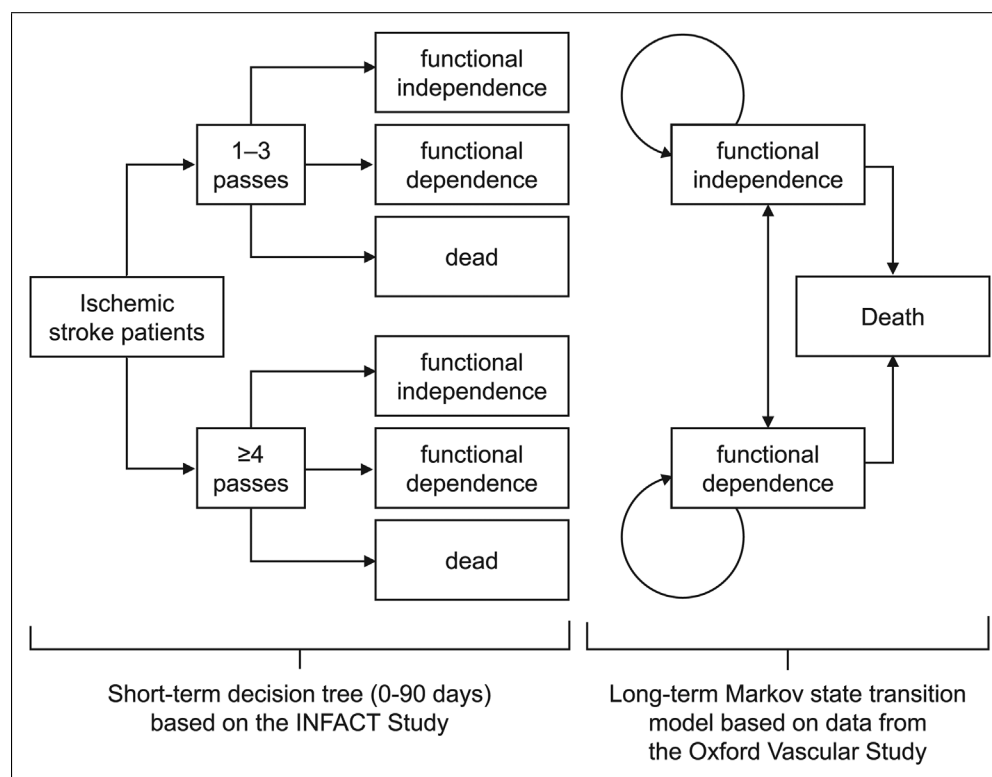
Study reporting adheres to STROBE guidelines for observational studies.

## Economic Analysis

A cost-effectiveness analysis of MT among patients treated with 1–3 passes compared with  $\geq 4$  passes were conducted based on the influence of the revascularization attempts on clinical outcomes of mechanical thrombectomy analysis and population described above. The analysis was conducted from the hospital (first 90 days) and public health care payer (up to 5 years) perspectives, with all costs discounted annually at 5%.<sup>28</sup> Health benefits were measured in quality-adjusted life years (QALYs) gained over a 5-year time horizon. The incremental cost per QALY gained was calculated.

## Model Structure

A decision tree for the acute care phase (0–90 days post-stroke) and a Markov time-heterogenous cohort model for the long-term care phase (91 days to 5 years) was constructed in R Studio version 4.0.0 (Figure 1). Within the model, patients with acute ischemic stroke were treated with MT with either 1–3 or  $\geq 4$  passes. In the acute phase, patients could be alive and functionally independent (mRS 0–2), functionally dependent (mRS 3–5), or dead (mRS 6) at 90-days post-stroke. After 90 days, a Markov model with monthly cycles was used with health states for functionally independent (mRS 0–2), functionally dependent (mRS 3–5), or dead (mRS 6).



**Figure 1. Model structure.**

## Model Inputs

All input values for the model are described in the Supplementary Tables S1 and S2. Probability of mortality and functional outcome (mRS) at 90 days was informed by the influence of the revascularization attempts on clinical outcomes of mechanical thrombectomy patients and its associated economic burden study as described above. Monthly time-dependent transition probabilities for the long-term phase were informed by the Ontario health technology assessment of MT in acute ischemic stroke, which leveraged the OXVASC (Oxford Vascular) study (this methodology aligns with that for the health technology assessment of MT from the Ireland Health Information and Quality Authority [HIQA]).<sup>4,29–31</sup> All costs were obtained from the assessment of MT from the Ireland HIQA<sup>30</sup> and reported in 2020 Euros (inflated where required using the monthly Harmonised Consumer Price Index [Health], as per guidelines for the economic evaluation of health technologies in Ireland)<sup>28,32,33</sup> and USD equivalents. Costs were calculated by health state (functionally independent versus functionally dependent). Acute care costs capture health care resource use and costs related to the MT procedure (staff, devices, angiography suite), length of stay, complications, and complexity of care. Long-term costs capture inpatient and outpatient rehabilitation, medication, outpatient visits, and rehos-

pitalizations for recurrent stroke. Health utilities were obtained from the health technology assessment of MT from the Ireland HIQA<sup>30</sup> which pooled utility values from multiple studies. All inputs and assumptions as well as the model structure were validated by clinicians (J.A., D.H., A.H., P.B., S.P., A.O., M.C., J.T.).

## Uncertainty Analysis

Deterministic and probabilistic sensitivity analyses were conducted to assess parameter uncertainty. Scenario analyses were conducted to assess the impact of removing patients who did not achieve mTICI 2b-3, and to assess the impact of achieving mTICI 2c-3 in the first pass.

## RESULTS

There were 823 patients from the Irish National Thrombectomy Service Database (from 2016–2019) that met the inclusion criteria, of which 631 received 1–3 passes and 192 received  $\geq 4$  passes during MT. Baseline characteristics were mostly well-balanced between the groups (Table 1). Patients in the 1–3 passes group were older (mean [SD] age 70.7 [13.7] versus 68.3 [15.0] years) and had higher mean (SD) pre-procedure Alberta Stroke Program Early CT Score (8.54 [1.32]

**Table 1. Baseline Demographics and Procedural Characteristics**

	1–3 passes n=631	≥4 passes n=192	Total n=823	P value
Demographics				
Sex, n (%)				0.230
Male	327 (51.8%)	90 (46.9%)	417 (50.7%)	
Age				0.040
Mean (SD)	70.7 (13.7)	68.3 (15.0)	70.2 (14.1)	
Clinical characteristics				
Occlusion location, n (%)				0.004
ICA carotid T/L	99 (15.7%)	41 (21.4%)	140 (17.0%)	
ICA cervical	64 (10.1%)	33 (17.2%)	97 (11.8%)	
MCA, M1	401 (63.5%)	96 (50.0%)	497 (60.4%)	
MCA, M2	67 (10.6%)	22 (11.5%)	89 (10.8%)	
Collateral score, n (%)				0.256
<50%	64 (11.6%)	27 (15.4%)	91 (12.6%)	
50–75%	149 (27.1%)	39 (22.3%)	188 (25.9%)	
75–99%	337 (61.3%)	109 (62.3%)	446 (61.5%)	
Missing	81	17	98	
Pre-procedure ASPECTS				0.012
Mean (SD)	8.54 (1.32)	8.27 (1.42)	8.48 (1.35)	
Missing	8	2	10	
NIHSS at presentation, n (%)				0.080
Mean (SD)	15.515 (5.980)	16.386 (6.052)	15.717 (6.004)	
Missing	4	3	7	
Baseline mRS, n (%)				0.357
0–2	613 (98.4%)	185 (97.4%)	798 (98.2%)	
2+	10 (1.6%)	5 (2.6%)	15 (1.8%)	
Missing	8	2	10	
Procedural characteristics				
IVT, n (%)				0.113
Yes	331 (52.6%)	88 (46.1%)	419 (51.1%)	
Missing	2	1	3	
Number of devices				
Median (min, max) [IQR]	1 (1, 4) [0]	2 (1, 5) [1]	–	
Onset to groin puncture (min)				0.829
Mean (SD)	352.8 (243.6)	357.2 (243.0)	353.8 (243.3)	
Missing	1	0	1	
Length of procedure (min)				<0.001
Mean (SD)	34.1 (23.4)	75.0 (41.0)	43.7 (33.4)	
Missing	3	0	3	

ASPECTS and collateral circulation were evaluated in-house by 1 of 4 neurointerventionalists. Collateral circulation was assessed by degree of leptomeningeal collateral supply, similar to grading system proposed by Tan et al.<sup>34</sup> This collateral grading system has been in place at Beaumont Hospital since 2016 and is agreed upon by the 4 consultant neurointerventionalists.

ASPECTS indicates Alberta Stroke Program Early CT Score; ICA, internal carotid artery; IQR, interquartile range; IVT, intravenous thrombolysis; M1, sphenoidal segment; M2, insular segment; MCA, middle cerebral artery; min, minutes; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.

versus 8.27 [1.42]), but similar proportion male (51.8% versus 46.9%) and similar National Institutes of Health Stroke Scale at presentation (mean [SD] 15.52 [5.98] versus 16.39 [6.05]). Several procedural characteristics varied between groups (Table 1). The median number of devices used in the 1–3 passes group was 1, although a median of 2 devices were used in the ≥4 passes group. Patients treated with ≥4 passes had significantly longer

procedure time and were more likely to have a proximal occlusion.

Patients in the 1–3 passes group achieved a significantly higher rate of successful reperfusion (mTICI score 2b–3) compared with patients in the ≥4 passes group (94% [92–96] versus 78% [70–84]). In multivariable regression models, the odds of achieving successful reperfusion were significantly higher for the 1–3

**Table 2. Results of Multivariable Regression Analyses for Reperfusion Probability, Functional Outcome, Time from Onset to First Reperfusion, and Number of Devices in 1–3 Passes and  $\geq 4$  Passes Groups**

Outcome*	1–3 passes	$\geq 4$ passes	Between-group comparison	P value
mTICI score 2b–3, probability (95% CI)	0.94 (0.92–0.96)	0.78 (0.70–0.84)	OR 4.7 (95% CI, 2.35–7.05)	<0.001
mRS score 0–2, probability (95% CI)	0.49 (0.44–0.54)	0.33 (0.25–0.41)	OR 2.0 (95% CI, 1.22–2.78)	<0.001
Minutes from onset to first reperfusion, mean (95% CI)	325.5 (320.5–330.5)	345.2 (335.6–355.0)	Ratio 0.94 (0.91–0.97)	<0.001

Final degree of reperfusion was evaluated in-house by 2 independent neurointerventionalists. Discrepancies were resolved by mutual consensus.

mTICI indicates modified thrombolysis in cerebral infarction; mRS, modified Rankin scale; and OR, odds ratio.

\*Adjusted for age, sex, intravenous thrombolysis, NIHSS at presentation, mRS pre-procedure, ASPECTS pre-procedure, CTA occlusion site, time from onset to groin puncture, and collateral score.

**Table 3. Safety Outcomes for 1–3 Passes and  $\geq 4$  Passes Groups**

	1–3 passes (n=631)	$\geq 4$ passes (n=192)	Total (n=823)	P value
Procedural complications, n (%)*	45 (7.1%)	29 (15.1%)	74 (9.0%)	<0.001
Distal embolus into a non-involved territory, n (%)†	8 (1.3%)	11 (5.8%)	19 (2.3%)	<0.001
Intra-procedural rupture, n (%)	9 (1.5%)	8 (4.8%)	17 (2.2%)	0.011
Missing	34	25	59	
Hemorrhage on follow-up imaging, n (%)	140 (22.2%)	70 (36.5%)	210 (25.5%)	<0.001
Mortality at 90 d follow-up, n (%)*	108 (17.1%)	46 (24.2%)	154 (18.8%)	0.029

\*Procedural complications include distal embolus into a non-involved territory, rupture, and other intra-procedural complications.

†One patient was missing distal embolus data and 3 patients were missing mortality at 90 days.

passes group compared with the  $\geq 4$  passes group after adjustment for covariates (odds ratio [OR], 4.7; [95% CI, 2.37–7.05];  $P<0.001$ ) (Table 2). Patients in the 1–3 passes group also achieved a higher rate of functional independence (mRS 0–2) as compared with patients in the  $\geq 4$  passes group (49% [44–54] versus 33% [25–41]). The odds of achieving functional independence were significantly higher for the 1–3 passes group compared with the  $\geq 4$  passes group after adjustment for covariates (OR, 2.0; [95% CI, 1.22–2.78];  $P<0.001$ ) (Table 2). There was an association between achieving a good functional outcome and higher mTICI score (Supplementary Figure S1).

Patients in the 1–3 passes group had significantly shorter time from onset to reperfusion compared with patients with  $\geq 4$  passes after adjusting for covariates (325.5 minutes [320.5–330.5] versus 345.2 minutes [335.6–355.0];  $P<0.001$ ) (Table 2).

There was a significantly higher incidence of distal embolus into a non-involved territory, intra-procedural rupture, and 90-day mortality in the  $\geq 4$  passes group compared with the 1–3 passes group (Table 3). Although there was a significantly higher incidence of hemorrhage on follow-up imaging in the  $\geq 4$  passes group compared with the 1–3 passes group.

In the sensitivity analysis which excluded patients who did not achieve final mTICI 2b–3 patients in the 1–3 passes group achieved a higher rate of functional independence (mRS 0–2) as compared with patients in the  $\geq 4$  passes group (52.1% versus 40.6%), (OR, 1.59; [95% CI, 1.01–2.50];  $P=0.045$ ).

**Table 4. Cost-Effectiveness Analysis Base Case Results (per Patient)**

	Total costs*	Total QALYs
1–3 passes	€33 529 (\$38 283.41)	0.94
$\geq 4$ passes	€36 856 (\$42 082.18)	0.75
Incremental	–€3328 (–\$3799.91)	0.19
Incremental cost-utility ratio 1–3 passes versus $\geq 4$ passes	Dominant	

QALY indicates quality-adjusted life year.

\*Analysis conducted from the perspective of the Irish public health care payer (€); costs also presented in USD equivalents.

The secondary analysis demonstrates that among patients who achieved mTICI 2c/3, the odds of achieving functional independence were significantly higher for those achieving reperfusion on the first pass compared with the  $\geq 2$  passes (OR, 1.75; [95% CI, 1.14–2.70];  $P=0.010$ ).

In the economic analysis, patients treated with 1–3 passes had 0.19 additional QALYs and lower costs (€3328; \$3800) such that 1–3 passes was dominant compared with  $\geq 4$  passes over a 5-year time horizon (Table 4). Within the hospital setting (0–90 days), mean (SD) total cost per patient was €3798 (\$4337) lower in the 1–3 passes group (€18 038; \$20 596) than for the  $\geq 4$  passes group (€21 837; \$24 933). In the long-term model, the mean (SD) total cost per patient was €471 (\$538) higher in the 1–3 passes group (€15 490; \$17 686) than that for the  $\geq 4$  passes group (€15 019; \$17 149), driven by improved survival in the

1–3 passes group. Patients treated with  $\geq 4$  passes were more likely to be in the functionally dependent or death states than patients treated with 1–3 passes at all time points in the long-term model (Supplementary Figure S2).

Deterministic and probabilistic sensitivity analyses were conducted to assess the robustness and generalizability of results. One-way sensitivity analyses which varied parameters according to the lower and upper bounds (described in Supplementary Tables S1 and S2) demonstrated that for all analyses, 1–3 passes remained dominant. The incremental cost-utility ratio was most sensitive to the number of devices used, utility for functional independence, cost of hospitalization, and the cost of devices (Supplementary Figure S3). In the probabilistic analysis, the results for all 1000 iterations were in the South-East quadrant of the cost-effectiveness plane (more effective and less costly; 1–3 passes was dominant in all iterations) (Supplementary Figure S4).

The scenario analysis where patients who did not achieve final mTICI 2b–3 were excluded demonstrated that patients successfully revascularized in 1–3 passes had 0.16 additional QALYs and lower costs (£2430; \$2775) compared with those treated with  $\geq 4$  passes. The scenario analysis where patients who achieved mTICI 2c/3 on the first pass were compared with those who achieved mTICI 2c/3 in  $\geq 2$  passes, resulted in an 0.15 additional QALYs and lower costs (£2256; \$2576).

## DISCUSSION

This study assessed the effect of the number of revascularization attempts on clinical and economic outcomes in patients with acute ischemic stroke secondary to large vessel occlusion in the Irish National Thrombectomy Service database. We found that 1–3 device passes was associated with a higher rate of successful reperfusion (mTICI 2b–3) and functional independence (mRS score 0–2), a shorter time from onset to first reperfusion, a lower rate of embolization into a new territory, reduced incidence of hemorrhage, and lower mortality compared with  $\geq 4$  passes. This finding provides further support to previous studies demonstrating the associated between increasing revascularization attempts with declining rates of reperfusion, poor functional outcome, and adverse events.<sup>17–24</sup> The sensitivity analysis which excluded patients who did not achieve mTICI 2b–3 was consistent with the primary analysis.

Among patients who achieved recanalization, a progressive linear decline in the rate of good functional outcomes with each pass has been observed,<sup>17</sup> with successful revascularization within 2 or 3 passes associated with higher rates of good clinical outcomes

compared with  $\geq 4$  passes.<sup>23,24</sup> In our secondary analysis in which patients who achieved mTICI 2c/3 were grouped into first pass or  $\geq 2$  passes, the odds of achieving successful reperfusion and functional independence were significantly higher for the first pass group compared with the  $\geq 2$  passes group.

Although research in this field is ongoing, the hypothesized mechanisms by which additional passes result in poorer outcomes include induced vascular damage and distal embolization caused by clot fragmentation.<sup>35,36</sup> As such, the potential benefits of complete reperfusion may be offset by the negative impact of multiple revascularization attempts. Our study demonstrates that the risk of adverse events is significantly decreased when the procedure is completed within 3 passes.

Emerging in vitro data have shown that clot consistency may contribute to the need for multiple passes with data demonstrating that “tough clots” requiring  $\geq 3$  passes to retrieve are more often fibrin-rich thrombi than those that are retrieved on the first 2 passes.<sup>37–40</sup> Recently the definition of the term “tough clot” has emerged as an adherent, durable thrombus that has high stiffness, generally consisting of more fibrous and less red blood cells making it resistant to endovascular thrombectomy.<sup>41</sup> MT devices or techniques which improve interaction with tough clots could facilitate more rapid and complete retrieval of such clots in fewer passes and potentially improve clinical or cost outcomes.

In the cost-effectiveness analysis, 1–3 passes was dominant compared with  $\geq 4$  passes over a 5-year time horizon, with increased QALYs and reduced costs. These findings proved to be robust and generalizable after conducting sensitivity analyses. Patients treated with 1–3 passes had higher rates of functional independence which led to both improved quality of life and lower health care resource use and cost savings. The same trend was observed when patients who did not achieve reperfusion (mTICI 2b–3) were excluded. The first pass analysis also showed improved quality of life and lower health care resource use and cost savings.

A recent study evaluated the economic impact of the first-pass effect from the perspective of health care provider and payer in the United States and several European countries.<sup>16</sup> The results indicated that the first-pass effect was associated with improved functional outcomes, shorter length of stay, and reduced procedural and hospitalization-related costs. Although first pass success remains the ultimate treatment goal<sup>42</sup>, our analysis provides evidence that optimizing the MT procedure to achieve the highest rate of successful recanalization with the fewest number of device passes is optimal for patients, also health care providers, and payers with increased odds of good

functional outcomes and lower costs. Based on our analyses, the optimized patient outcomes and cost savings associated with achieving revascularization within 3 passes suggest that investing an additional €3000 per patient to optimize the MT technique could be offset.

This study has several strengths, including the use of patient-level data for over 800 patients over the course of 4 years from the Irish National Thrombectomy Service Database which captured numerous variables, which were adjusted for in our analyses. Furthermore, we evaluated the economic impact of 1–3 passes versus  $\geq 4$  passes within a robust probabilistic state transition model with inputs and assumptions that were validated by physicians and accredited by health care authorities. The model leveraged clinical data from our registry analysis and detailed health care costing aligned with relevant costs from the Irish HIQA.

However, our findings should be interpreted in light of the following limitations. First, our analysis was powered only for the co-primary end points, namely the degree of reperfusion (mTICI score) post-procedure and functional outcome (mRS score) at 90 days. Reporting of device use within the database was aggregate and thus did not provide enough granularity to inform any additional analysis regarding line of use. Patient data were obtained from a single center, which may limit generalizability. Although the long-term costs used in the analysis were aligned with those leveraged by the Irish HIQA, they were derived from an economic analysis for atrial fibrillation. Similarly, although the health utility values used in the economic analysis were aligned with those leveraged by the 2017 Irish HIQA, they were derived from studies published 10 to 20 years ago given the lack of more recent evidence.

## CONCLUSIONS

Based on the Irish National Thrombectomy Service database, this study illustrates that the number of passes has a significant effect on both clinical outcomes and health care costs associated with acute ischemic stroke secondary to large vessel occlusion in the short and long term. Each failed revascularization attempt appears to increase the economic burden to health care payers and providers. Successful revascularization within 3 device passes is a relevant goal in the treatment of patients with acute ischemic stroke. Future research is required to elucidate the factors and methods that may increase the probability of achieving successful revascularization in the fewest number of attempts.

## ARTICLE INFORMATION

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## Supplemental Materials

Supplemental Materials

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