Endovascular Thrombectomy Beyond 24 Hours from Ischaemic Stroke Onset: A Propensity Score-Matched Cohort Study

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ABSTRACT

Background: The safety and functional outcome of endovascular thrombectomy (EVT) in the very late (VL; >24 hours) time window from ischaemic stroke onset remains undetermined.

Methods: Using data from a national stroke registry, we used propensity-score-matched (PSM) individual level data of patients who underwent EVT selected with CT perfusion or non-contrast CT/CT angiography between October 2015 and March 2020. Functional and safety outcomes were assessed in both late (6-24 hours) and VL time windows. Subgroup analysis was performed of imaging selection modality in the VL time window.

Results: We included 1150 patients [late window: 1046 (208 after PSM); VL window: 104 (104 after PSM)]. Compared to EVT treatment initiation between 6-24 hours, patients treated in the VL window had similar modified Rankin Scale (mRS) scores at discharge (Ordinal shift; common OR=1.08, 95%CI 0.69-1.47, p=0.70). No significant differences in achieving good functional outcome (mRS≤2 at discharge; 28.8% (VL) vs 29.3% (late), OR=0.97, 95%CI 0.58-1.64, p=0.93), successful reperfusion (mTICI2b-3) (p=0.77), or safety outcomes of symptomatic intracranial haemorrhage (sICH) (p=0.43) and in-hospital mortality (p=0.23) were demonstrated. In the VL window, there was no significant difference in the functional outcome amongst patients selected with perfusion versus without perfusion imaging (common OR=1.38, 95%CI 0.81-1.76, p=0.18).

Conclusion: In this real-world study, EVT beyond 24 hours from stroke onset or last known well appears feasible with comparable safety and functional outcomes to EVT initiation between 6-24 hours. Randomised trials assessing the efficacy of EVT in the VL window are warranted, but may only be feasible with a large international collaborative approach.

INTRODUCTION

Endovascular thrombectomy (EVT) for large vessel occlusion (LVO) in acute ischaemic stroke (AIS) has been proven to be effective when initiated within 6 hours of stroke onset (1). More recently, randomised controlled trials (RCT) that utilised strict inclusion criteria using advanced neuroimaging (CT perfusion or MR imaging) have demonstrated the efficacy and safety of performing EVT for selected patients presenting between 6 to 16 hours (DEFUSE-3) or 6 to 24 hours (DAWN) from the onset of stroke or last known well (2, 3). The results indicate that the presence of salvageable tissue in patients with good collateral circulation can persist well beyond 6 hours.

However, there is paucity of data on the characteristics and clinical outcomes in patients treated with EVT beyond 24 hours from stroke onset or last known well, with only four studies of modest sample sizes (between five to 34 patients) reporting outcomes in the very late (>24 hours) time window (4-7). Hence, we sought to compare the safety and functional outcomes of patients undergoing EVT in AIS in the very late time window from stroke onset or last known well with patients undergoing EVT initiated in the late (6-24 hours) time window.

METHODS

Data Source and Study Design

We performed a cohort study on prospectively collected data of patients enrolled in the Sentinel Stroke National Audit Programme (SSNAP) according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. SSNAP is a national stroke registry that includes all hospitals admitting patients presenting with acute stroke in England, Wales and Northern Ireland (covering 92% of the population of the United Kingdom, UK) (8). Overall case ascertainment in SSNAP is estimated to be over 90% of all acute stroke admissions (8). Patient data, which include demographic and clinical characteristics, treatments, and outcomes, are submitted prospectively by clinical teams using a secure web-based case report form with real-time data validation checks to ensure data quality, from the time of admission up to 6 months after stroke.

Pseudonymised individual level data of adult patients (≥18 years) presenting with AIS who received EVT between 1st October 2015 (inception of the EVT section of SSNAP) and 31st March 2020 in England and Wales were included. Patients were dichotomised according to the onset of stroke or last known well to groin puncture: (i) late EVT window (6-24 hours), and (ii) very late EVT window (>24 hours). Patients with missing discharge modified Rankin Scale (mRS) data and those presenting within 6 hours were excluded. The selection of EVT-eligible patients was at the discretion of the practitioners based on each institution's protocol. The initial imaging selection modality performed included non-contrast CT (NCCT)/CT angiography (CTA) and/or perfusion-based imaging. No specific limits were applied to the clinical inclusion criteria, including age, pre-stroke disability and baseline stroke severity on the National Institutes of Health Stroke Scale (NIHSS). Data on the parenchymal imaging findings and clot location were not available.

Outcome measures

The main functional outcome was assessed with the mRS score at ultimate hospital discharge, ranging from 0 - no symptoms to 5 – severe disability/bedridden and 6 - death. Other functional outcomes were the mRS score at 6 months, good (mRS≤2 or equivalent to the pre-stroke mRS) or excellent (mRS≤1 or equivalent to the pre-stroke mRS) functional outcome at hospital discharge and at 6 months, early neurological improvement (ENI; National Institutes of Health Stroke Scale (NIHSS) decrease ≥4 between admission and 24 hours or NIHSS 0–1 at 24 hours), early neurological deterioration (END; 24-hour NIHSS increase ≥4 from baseline), futile recanalisation [patients achieving mRS 4-6 at hospital discharge or worsening of the pre-stroke disability (mRS 4-5) despite successful reperfusion (modified thrombolysis in cerebral infarction (mTICI) score of 2b to 3). Procedural outcomes were successful reperfusion and complete reperfusion (mTICI score of 3) at the end of EVT.

Safety outcomes were in-hospital mortality, any type of intracranial haemorrhage (ICH) and symptomatic intracranial haemorrhage (sICH) defined according to European Collaborative Acute Stroke Study (ECASS) II (9) as any ICH with an increase of the NIHSS score of 4 or more within 24 hours or death. Workflow time metrics were stroke onset-to-arterial puncture, arterial puncture-to-first pass, and total procedural time (defined as arterial puncture-to-final reperfusion/angiographic run). Functional outcome measure (mRS) was assessed by a member of the Stroke team/physician at discharge and during a routinely scheduled clinical visit at 6 months, or by a specialist nurse during a follow-up telephone interview if the patient was unable to attend.

Statistical analysis

Study characteristics were summarised by the late and very late time windows using descriptive statistics for patient demographics, clinical characteristics and co-morbidities, EVT technique and time metrics. Continuous variables were expressed as means and standard deviation (SD) and categorical variables were expressed as frequencies or percentages. Comparisons of baseline variables were made using the Chi-square, Fisher's exact test or ANOVA, wherever applicable.

Propensity score matching (PSM), a reliable method of decreasing potential bias in large cohorts with multiple confounders, was conducted with a 2:1 matching of the logit of the propensity score using the nearest-neighbour (Greedy type) matching and 0.2 caliper width (10). The matching was performed without replacement, and unpaired patients not meeting the matching criteria were excluded. Each PSM-derived pair was created using the R package MatchIt. The key variables accounted for in the PSM were: age (5-year age bands from <60years to >90 years), sex, baseline stroke severity (NIHSS), pre-stroke functional status (mRS), prior administration of intravenous tissue plasminogen activator (IV-tPA) and use of perfusion imaging.

Sensitivity analysis of patients presenting with a witnessed stroke onset only (excluding last known well) and subgroup analysis, dichotomised according to the use of perfusion imaging, were performed. Since the major confounders were accounted for using PSM, univariate analyses of the outcome measures used ordinal logistic regression for the full-scale mRS; binary regression analysis for dichotomised mRS scores (good functional outcome mRS≤2, and excellent functional outcome mRS≤1), ENI, END, successful reperfusion mTICI2b-3, complete reperfusion mTICI3, any ICH, sICH, and death. Analyses of binary and ordinal outcomes were expressed as an odds ratio (OR) with a 95% confidence interval (CI). Any missing outcome data were not imputed. Two-tailed P-value of <0.05 was considered statistically significant. All analyses were conducted using StataSE 16.1 and R 4.1.0.

Ethics

SSNAP has permission to collect patient data without explicit consent, granted by the Confidentiality Advisory Group of the National Health Service Health Research Authority under Section 251. Pseudonymised data use was approved by the Healthcare Quality Improvement Partnership (HQIP) Data Access Request Group. Additional ethical approval was not sought for this study. Data access requests should be directed to SSNAP as the data provider and the HQIP as the data controller.

RESULTS

Characteristics of Study Population

A total of 4383 patients initially admitted to 123 hospitals, of which 25 are EVT-capable neuroscience centres, underwent EVT for LVO during the study period. Of these, a total of 30 patients with a lack of data on the mRS score at discharge and 3203 patients treated within 6 hours were excluded (Figure 1). 1046 patients treated 6-24 hours (late window) and 104 patients treated >24 hours (very late window) from stroke onset or last known well were included. Compared to the late window, patients treated in the very late time window had a lower baseline stroke severity (NIHSS) (12.7±7.4 vs 15.2±7.7) and were treated with IV-rtPA less frequently (19.2% vs 31.5%) (Table 1). No significant differences were observed in the remaining baseline characteristics or co-morbidities. After matching, there were 208 patients in the late window and 104 patients in the very late window, and all matched baseline characteristics were statistically similar (Table 1). The distribution of propensity scores and patients across both time windows are presented in Supplemental Figures 1 and 2 respectively.

Outcomes (After Propensity Score Matching)

When compared to EVT treatment initiation 6-24 hours from stroke onset or last known well, patients treated in the very late time window had similar mRS scores at discharge (Ordinal shift: Figure 2, Table 2; common OR=1.08, 95%CI 0.69-1.47, p=0.70). No significant difference was observed in the odds of achieving good functional outcome (mRS≤2 at discharge; 28.8% (very late) vs 29.3% (late), OR=0.97, 95%CI 0.58-1.64, p=0.93), successful reperfusion (very late: 80.0% vs late: 81.3%, p=0.77), futile recanalisation (very late (59.6%) vs late (60.5%); p=0.87), sICH (very late: 4.8% vs late: 8.0%, p=0.43) or in-hospital mortality (very late: 9.8% vs late: 14.4%, p=0.23) across both time windows (Table 2).

Sensitivity analysis

In the sensitivity analysis of patients presenting with a witnessed stroke onset only (excluding last known well), no significant differences in the mRS score at discharge following EVT treatment initiation between the very late and late time windows were demonstrated (Ordinal shift: Supplemental Table 1; common OR=1.18, 95%CI 0.67-1.55, p=0.43).

Subgroup analysis

In the very late window, there was no significant difference in the functional disability (mRS at discharge) between patients selected for EVT with versus without perfusion-based imaging (common OR=1.38, 95%CI 0.81-1.76, p=0.18) (Supplemental Table 2).

DISCUSSION

The findings in our study provide real-world data into the functional and safety outcomes of EVT treatment in patients in the very late time window. EVT performed beyond 24 hours was associated with a similar rates of functional outcome, sICH and in-hospital mortality at discharge compared to those treated between 6-24 hours from stroke onset or last known well. Based on aggregate data, our safety outcome measures (sICH 4.8%, in-hospital mortality 9.8%) were comparable to those reported in the EVT arm of the DAWN (sICH 6%, 90-day mortality 19%) (3) and DEFUSE-3 (sICH 7%, 90-day mortality 14%) (2) trials. Overall, compared to those treated in the late window, this suggests that performing EVT in the very late (>24 hours) time window appears safe and feasible, whilst achieving similar rates of functional independence (mRS≤2).

Although current guidelines recommend EVT treatment for eligible patients meeting the strict neuroimaging criteria between 6 to 24 hours from last known well, the efficacy of EVT beyond 24 hours remains undetermined. Previous case series or retrospective studies of modest sample sizes have attempted to assess the efficacy of EVT in the very late window in patients selected with advanced neuroimaging (CT perfusion or MR imaging), mirroring the inclusion criteria of the late window trials (4-7). It has been suggested that salvageable penumbra may persist beyond 24 hours and reperfusion therapy may remain beneficial in ‘slow progressors’ with a small infarct core and tenacious collateral supply (5). However, the optimal method of patient imaging selection remains uncertain and many institutions have limited access to urgent advanced imaging so select patients for EVT on the basis of visual estimation of the core infarct size (ASPECTS) and collateral status on NCCT/CTA respectively, even in the extended time windows. This may result in potentially broader and heterogeneous penumbra-core tissue characteristics compared to trial cohorts. When patients in very late time window in our study were stratified by the initial imaging modality selection, no significant differences in the functional and safety outcomes were demonstrated in patients selected using NCCT/CTA only or using

perfusion-based imaging, but these analyses are likely to be underpowered (mRS≤2 at discharge; perfusion 32.5% vs non-perfusion 26.2%). Using NCCT/CTA only to select patients for EVT in the extended time window may be a reasonable option, particularly as employing stringent perfusion-based imaging criteria of the DAWN or DEFUSE-3 trials could result in a smaller proportion of eligible patients being accepted for EVT, thereby potentially limiting the treatment impact on the overall population (11, 12). Ongoing trials using more inclusive imaging criteria are currently limited to patients presenting within the 6-24 hour window (13, 14).

It has been postulated that evolving clot composition and properties over time may render it more resistant to retrieval (15, 16). Whereas some studies have demonstrated decreasing odds of successful reperfusion (TICI2b-3) with increasing time from stroke onset to treatment, dropping to as low as 42% at 24 hours, we showed no significant difference in patients achieving successful reperfusion between the late (81.3%) and very late (80%) time windows, similar to other previous studies (2-4). This suggests that high rates of reperfusion are still achievable beyond 24 hours from stroke onset, but the rate of successful reperfusion is unlikely to be the main determinant for the lower proportion of very late window patients obtaining good functional outcome in our study; 29% mRS≤2 at discharge, which compares unfavourably with two previous smaller studies assessing EVT beyond 24 hours using advanced imaging selection criteria in which 41% (7) and 43% (4) of patients respectively achieved an independent outcome at 90 days.

The strengths of this study include its relatively large sample size of patients (n=104) treated with EVT beyond 24 hours, the national coverage of a diverse range of hospitals and MT-capable neuroscience centres, and the high case ascertainment with consecutive patient enrolment. The accuracy and high quality data within the SSNAP database results from standardised case definitions and coding

instructions, internal validation, audit trails and regular data quality reports for all participating sites (8).

There are several limitations in this study. First, due to its observational design, confounding by indication and selection bias may have influenced the results. The lack of the ASPECTS, collateral status, clot location or perfusion imaging target mismatch profiles in the registry, all key criteria in patient selection in the extended time window from stroke onset, limits the interpretation of findings due to potential underlying selection biases. However, the use of both perfusion and non-perfusion imaging selection extends the generalisability of our real-world data. Second, there was some missing data for certain outcome measures, including the mRS at 6 months. However, our primary outcome measured the mRS at hospital discharge (complete data in PSM cohort) and has been shown to correlate highly with functional outcomes at 3 months (17). Third, although there were some differences in between-group baseline characteristics, the key variables were adjusted for in the PSM analysis. In particular, the high rates of IV thrombolysis in both the late and very late time windows reflect early administration of IV thrombolysis within 4.5 hours but a significant delay in EVT due to the lack of out of hours availability in many centres. Fourth, the outcome measures, including the angiographic outcomes of vessel reperfusion, were self-assessed rather than independently evaluated by a core laboratory. Fifth, a proportion of patients included in our study presented with a best estimated onset of stroke (last known well), which may have overestimated the time since stroke onset. However, similar associations with the outcomes remained in our sensitivity analysis of patients with a witnessed stroke onset. Sixth, due to the small sample size in the study subgroups, our analyses of the secondary outcomes and subgroups are likely to have been underpowered. Last, the assessment of treatment benefit of EVT in the very late time window is precluded due to the lack of comparison to a control group of patients that underwent best medical management only. Although prospective

randomised trials are needed to confirm the treatment benefit of EVT beyond 24 hours, an RCT may not be practical due to the scarcity of patients presenting in this time period.

Conclusion

In this large real-world study, EVT in the very late time window from stroke onset or last known well appears safe without any significant increase in safety outcomes of sICH or mortality, and may be considered in selected patients presenting beyond 24 hours. Randomised trials assessing the efficacy of EVT in the very late time window are warranted, but may only be feasible with a large international collaborative approach.

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TABLES

Table 1: Table of characteristics according to time from stroke onset or last known well to endovascular treatment before and after propensity score matching (PSM).

	Before PSM			After PSM		
Feature	**6-24 hours n (%) or mean±SD**	**>24 hours n (%) or mean±SD**	**P value**	**6-24 hours n (%) or mean±SD**	**>24 hours n (%) or mean±SD**	**P value**
	Socio-demographics					
Sample size	1046	104		208	104	
Sex (male)	554 (53.0)	60 (57.7)	0.35	128 (61.5)	60 (57.7)	0.43
Age: <60 years	322 (30.7)	41 (39.4)	0.24	83 (39.9)	41 (39.4)	0.62
60-69	197 (18.8)	22 (21.1)		40 (19.2)	22 (21.1)	
70-79	295 (28.2)	20 (19.2)		55 (26.4)	20 (19.2)	
80-89	207 (19.7)	19 (18.2)		27 (12.9)	19 (18.2)	
>90 years	25 (2.3)	2 (1.9)		3 (1.4)	2 (1.9)	
	Baseline characteristics					
NIHSS on admission	15.2±7.7	12.7±7.4	**0.001**	12.0±7.0	12.7±7.4	0.45
Pre-stroke disability (mRS)	0.5±0.9	0.5±0.9	0.83	0.4±0.9	0.5±0.9	0.63
IV Thrombolysis	330 (31.5)	20 (19.2)	**0.009**	50 (24.0)	20 (19.2)	0.28
Perfusion Imaging	378 (36.1)	43 (41.3)	0.29	76 (36.5)	43 (40.9)	0.41
Contact Aspiration	285 (26.2)	29 (27.8)	0.88	61 (29.3)	29 (27.8)	0.87
StentRetriever	165 (15.7)	15 (14.4)	0.70	23 (11.0)	15 (14.4)	0.47
Contact Aspiration & StentRetriever combined	566 (54.1)	60 (57.6)	0.47	124 (59.6)	60 (57.6)	0.73
Proximal Balloon Flow Arrest	272 (26.0)	34 (32.6)	0.14	48 (23.0)	34 (33.3)	0.07
	Co-morbidities					
Hypertension	489 (46.7)	50 (48.0)	0.79	93 (44.7)	50 (48.0)	0.54
Diabetes Mellitus	140 (13.3)	11 (10.5)	0.41	27 (12.9)	11 (10.5)	0.46
Atrial fibrillation	208 (19.8)	18 (17.3)	0.52	31 (14.9)	18 (17.3)	0.45

Prior Stroke/TIA	146 (13.9)	10 (9.6)	0.21	21 (10.0)	10 (9.6)	0.88
Congestive heart failure	57 (5.4)	2 (1.9)	0.12	10 (4.8)	2 (1.9)	0.21
	Time Metrics (mins)					
Onset to Arterial Puncture	632.2±250.3	2000.9±445.1	**<0.001**	615.4±256.1	2000.9±445.1	**<0.001**
Arterial Puncture to First deployment	26.7±20.6	24.0±17.2	0.20	27.3±21.7	24.0±17.2	0.20
Arterial Puncture to End of Procedure	59.2±40.3	58.7±40.9	0.89	61.4±41.7	58.7±40.9	0.58

n = number of events, N = number of patients, SD = standard deviation, mRS = modified Rankin scale, TIA = transient ischaemic attack, NIHSS = National Institutes Stroke Severity TICI = thrombolysis in cerebral infarction, IV = intravenous, ** propensity score matched 2:1 for age, sex, baseline NIHSS, pre-stroke disability, use of intravenous thrombolysis, and use of perfusion imaging for patient selection.

Table 2: Table of outcomes dichotomised by time from stroke onset or last known well to endovascular treatment after propensity score matching in the late (6-24 hours) and very late (>24 hours) time windows.

Outcome measures	Late Window (6-24 hours) n/N (%) or median (IQR)	Very Late Window (>24 hours) n/N (%) or median (IQR)	Very Late vs Late Window	
			OR (95% CI)**	P value
mRS at discharge (Ordinal)	4 (2 – 5)	4 (2 – 5)	1.08 (0.69 - 1.47)	0.70
mRS ≤1	33/208 (15.8)	14/104 (13.4)	0.82 (0.42 – 1.62)	0.57
mRS ≤2	61/208 (29.3)	30/104 (28.8)	0.97 (0.58 – 1.64)	0.93
mRS at 6 months (Ordinal)	2 (1 – 3)	2 (1 – 3)	1.20 (0.75 – 1.98)	0.45
mRS ≤2	31/57 (54.4)	22/35 (62.8)	1.42 (0.59 – 3.35)	0.42
TICI 2b-3	169/208 (81.3)	83/104 (80.0)	0.92 (0.50 – 1.65)	0.77
TICI 3	100/208 (48.0)	49/104 (47.1)	0.99 (0.62 – 1.58)	0.97
Futile Recanalisation	126/208 (60.5)	62/104 (59.6)	0.96 (0.59 – 1.55)	0.87
ENI	79/195 (40.5)	46/97 (47.4)	1.35 (0.83 – 2.20)	0.22
END	44/195 (22.5)	16/97 (16.5)	0.66 (0.35 – 1.26)	0.21
Any ICH	19/151 (12.6)	8/71 (11.2)	0.86 (0.36 – 2.09)	0.75
sICH	10/125 (8.0)	3/61 (4.8)	0.58 (0.15 – 2.20)	0.43
In-Hospital Mortality	30/208 (14.4)	10/104 (9.8)	0.63 (0.29 – 1.34)	0.23

n = number of events, N = number of patients, OR = odds ratio, CI = confidence interval, mRS = modified Rankin scale, sICH = symptomatic intracranial haemorrhage, TICI = thrombolysis in cerebral infarction, Futile Recanalisation = mRS4-6 despite TICI2b-3 recanalisation, ENI = Early neurological improvement (NIHSS improvement by ≥4), END = Early neurological deterioration (NIHSS worsening by ≥4). ** propensity score matched 2:1 for age, sex, baseline NIHSS, pre-stroke disability, use of intravenous thrombolysis, and use of perfusion imaging for patient selection.

FIGURES

Figure 1**:** Flow chart of the patient inclusion, exclusion and outcome data for endovascular thrombectomy treatment in the late (6-24 hours) and very late (>24 hours) time windows from stroke onset or last known well.

EVT = endovascular thrombectomy, n = number of events, mRS = modified Rankin scale

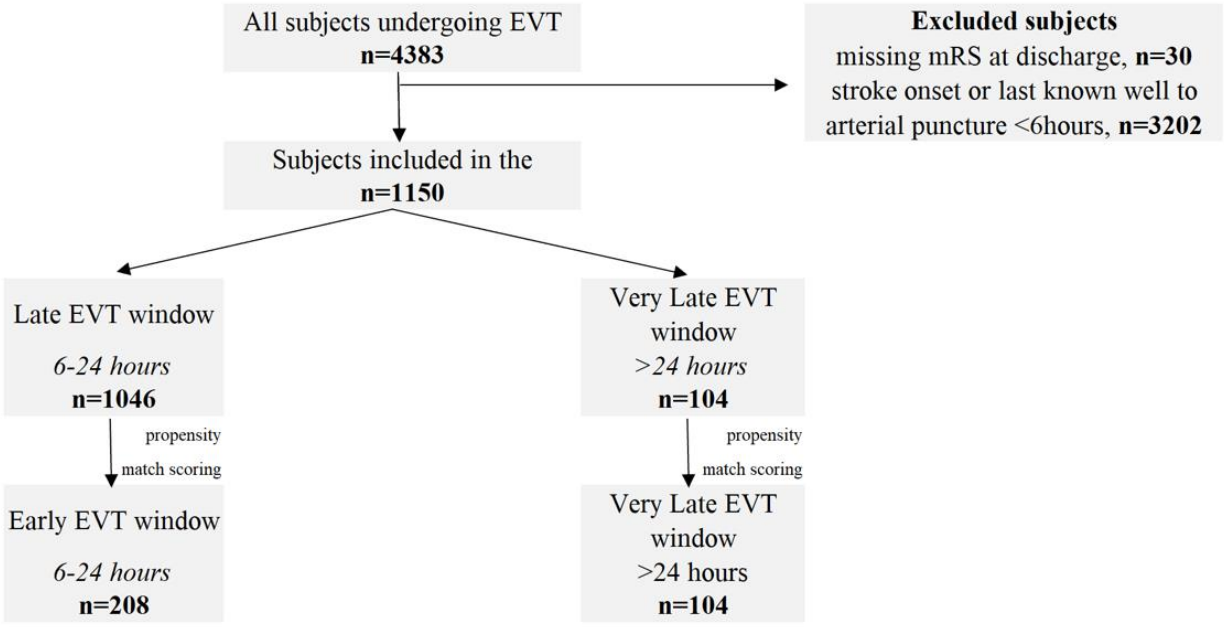
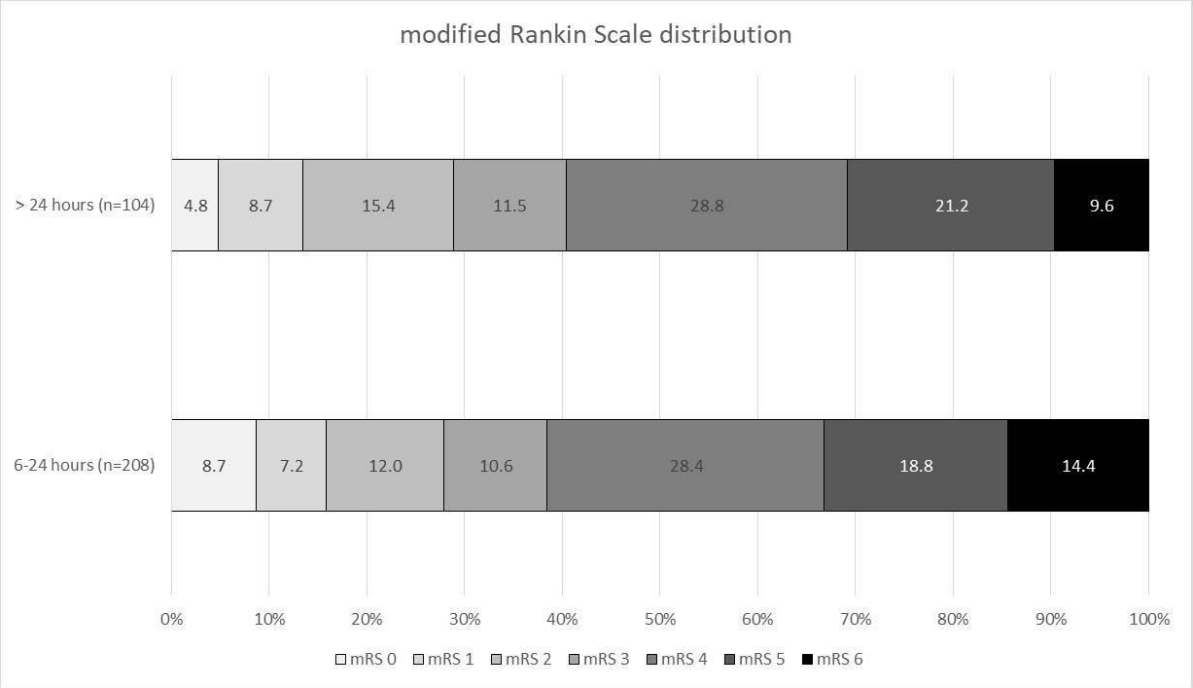


Figure 2: Distribution of the modified Rankin Scale (0 – no disability to 5 – severe disability and 6 – death) at discharge comparing EVT treatment in the late (6-24 hours) and very late (>24 hours) time windows after propensity score matching 2:1 for age, sex, baseline NIHSS, pre-stroke disability, use of intravenous thrombolysis and use of perfusion imaging for patient selection.



SUPPLEMENTAL MATERIAL

Supplemental Table 1: Table of outcomes dichotomised by time from stroke onset to endovascular treatment after propensity score matching in the late (6-24 hours) and very late (>24 hours) time windows in patients with a **witnessed stroke onset** only (excluding wake up stroke or last known well).

Outcome measures	Late Window (6-24 hours) n/N (%)	Very Late Window (>24 hours) n/N (%)	Very Late vs Late Window	
			OR (95% CI)**	P value
mRS at discharge (Ordinal)	N=115	N=71	1.18 (0.67 - 1.55)	0.43
mRS ≤2	31 (26.9)	18 (25.3)	0.87 (0.42 – 1.60)	0.57
TICI 2b-3	92 (80.0)	59 (83.1)	1.07 (0.45 – 1.93)	0.85
Futile Recanalisation	72 (62.6)	41 (57.7)	0.82 (0.45 – 1.51)	0.54
sICH *	5 (7.6)	2 (4.7)	0.58 (0.11 – 3.16)	0.53
In-Hospital Mortality	17 (14.7)	7 (9.8)	0.72 (0.29 – 1.77)	0.48

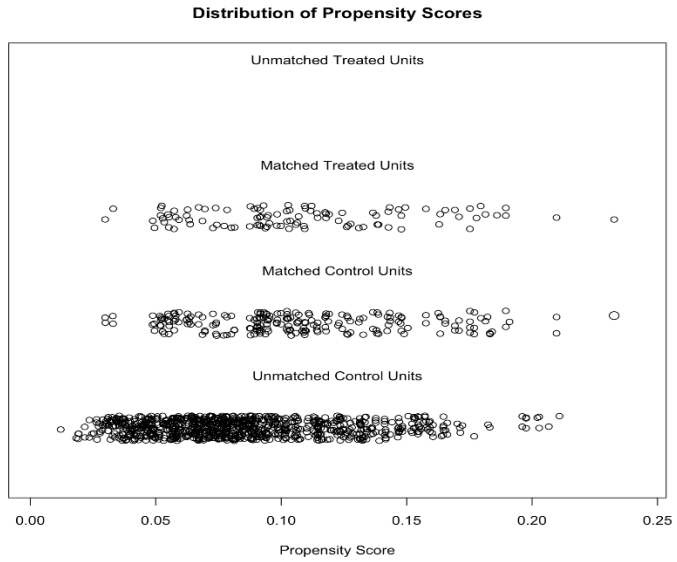
n = number of events, N = number of patients, OR = odds ratio, CI = confidence interval, mRS = modified Rankin scale, sICH = symptomatic intracranial haemorrhage, TICI = thrombolysis in cerebral infarction, Futile Recanalisation = mRS4-6 despite TICI2b-3 recanalisation. * n=65 late window group, n=42 very late window group. **propensity score matched 2:1 for age, sex, baseline NIHSS, pre-stroke disability, use of intravenous thrombolysis and use of perfusion imaging for patient selection.

Supplemental Table 2: Table of outcomes dichotomised by time from stroke onset or last known well to endovascular treatment in the very late (>24 hours) time window in patients selected **with vs without perfusion imaging**.

Outcome measures	Very Late Window n (%)		With vs Without Perfusion Imaging Selection	
	(Without perfusion)	(With perfusion)	OR (95% CI)**	P value
mRS at discharge (Ordinal)	N=61	N=43	1.38 (0.81 – 1.76)	0.18
mRS ≤2	16 (26.2)	14 (32.5)	1.35 (0.57 – 3.19)	0.48
TICI 2b-3	49 (80.3)	34 (79.1)	0.92 (0.35 – 2.43)	0.87
Futile Recanalisation	39 (63.9)	23 (53.4)	0.65 (0.29 – 1.43)	0.28
sICH *	2 (5.5)	1 (4.0)	0.70 (0.06 – 8.26)	0.78
In-Hospital Mortality	8 (13.1)	2 (4.6)	0.32 (0.06 – 1.60)	0.16

n = number of events, N = number of patients, OR = odds ratio, CI = confidence interval, mRS = modified Rankin scale, sICH = symptomatic intracranial haemorrhage, TICI = thrombolysis in cerebral infarction, Futile Recanalisation = mRS4-6 despite TICI2b-3 recanalisation * n=25 with perfusion group, n=36 without perfusion group.

Supplemental Figure 1: Distribution of the propensity scores of patients that underwent endovascular thrombectomy in the late window (6-24 hours; 'control') and very late window (>24 hours; 'treated') from stroke onset or last known well. Patients were matched 2:1 for age, sex, baseline NIHSS, pre-stroke disability, use of intravenous thrombolysis and use of perfusion imaging for patient selection.



Supplemental Figure 2: Histogram demonstration of the number of patients (frequency) with time as a continuous variable in minutes across the late (6-24 hours; left) and very late (>24hours; right) endovascular thrombectomy time windows from stroke onset or last known well to arterial puncture (after propensity score matching).