



Research Article

Neuropsychological outcomes following endovascular clot retrieval and intravenous thrombolysis in ischemic stroke

Sam Humphrey^{1,2} , Kerryn E. Pike^{1,3,4}, Brian Long^{2,5}, Henry Ma^{6,7}, Robert Bourke², Bradley J. Wright¹ and Dana Wong¹

¹Department of Psychology, Counselling & Therapy, School of Psychology & Public Health, La Trobe University, Melbourne, Australia, ²Neuropsychology Unit, Monash Medical Centre, Melbourne, Australia, ³John Richards Centre for Rural Ageing Research, La Trobe University, Wodonga, Australia, ⁴School of Applied Psychology, Griffith Centre for Mental Health, Griffith University, Gold Coast, Australia, ⁵Neurosciences Unit, North Metropolitan Health Service, Perth, Australia, ⁶Department of Neurology, Monash Medical Centre, Melbourne, Australia and ⁷Department of Medicine, School of Clinical Sciences, Monash University, Melbourne, Australia

Abstract

Objectives: Cognitive impairment, anxiety, depression, fatigue, and dependence in instrumental activities of daily living (ADL) are common after stroke; however, little is known about how these outcomes may differ following treatment with endovascular clot retrieval (ECR), intravenous tissue plasminogen activator (t-PA), or conservative management. **Methods:** Patients were recruited after acute treatment and invited to participate in an outcome assessment 90–120 days post-stroke. The assessment included a cognitive test battery and several questionnaires. The COVID-19 pandemic led to significant disruptions in recruitment and data collection, and the t-PA and conservative management groups were combined into a standard medical care (SMC) group. **Results:** Sixty-two participants were included in the study (ECR = 31, SMC = 31). Mean age was 66.5 (20–86) years, and 35 (56.5%) participants were male. Participants treated with ECR had significantly higher National Institutes of Health Stroke Scale scores at presentation and significantly lower education. After adjusting for stroke severity, premorbid intellectual ability, and age, treatment with ECR was associated with significantly better performances on measures of cognitive screening, visual working memory, and verbal learning and memory. Participants treated with ECR also experienced less fatigue and were more likely to achieve independence in basic and instrumental ADLs. Despite this, cognitive impairment and fatigue were still common among participants treated with ECR and anxiety and depression symptoms were experienced similarly by both groups. **Conclusions:** Cognitive impairment and fatigue were less common but still prevalent following treatment with ECR. This has important practical implications for stroke rehabilitation, and routine assessment of cognition, emotion, and fatigue is recommended for all stroke survivors regardless of stroke treatment and functional outcome.

Keywords: Ischemic stroke; thrombectomy; cognition; anxiety; depression; fatigue

(Received 9 February 2024; final revision 4 September 2024; accepted 16 September 2024; First Published online 16 October 2024)

Introduction

Stroke is a leading cause of death and disability worldwide, with approximately 12 million people having a stroke each year (Feigin et al., 2021, 2022). Over half of all stroke patients will not survive, and between 24% and 49% of stroke survivors will live with some degree of ongoing disability (Carmo et al., 2015; Feigin et al., 2021, 2022). A major cause of disability after stroke is cognitive impairment, which is associated with poor long-term survival, enduring activity limitations and participation restrictions, functional dependence, and poorer quality of life (Cumming et al., 2014; Melkas et al., 2009; Nys et al., 2005; Oksala et al., 2009; Rost et al., 2022; Stolwyk et al., 2021). Post-stroke cognitive impairment is highly prevalent, with a recent meta-analysis finding an overall pooled prevalence of total post-stroke cognitive impairment of

53.4% (Barbay et al., 2018). Other conditions such as anxiety, depression, and fatigue are also common after stroke, with almost half of all stroke survivors experiencing fatigue, a quarter anxiety, and a third depression (Burton et al., 2013; Hackett & Pickles, 2014; Knapp et al., 2020; Liu et al., 2023; Paciaroni & Acciarresi, 2019). These conditions can also have a negative impact on rehabilitation, long-term outcomes, and quality of life (Acciarresi et al., 2014; Burton et al., 2013; Wijeratne & Sales, 2021).

Despite these conditions being common after stroke, little is known about how these outcomes may differ following acute stroke treatments, including endovascular clot retrieval (ECR) and intravenous tissue plasminogen activator (t-PA). Previous trials exploring the efficacy of treatment with ECR and t-PA have largely focused on degree of physical disability and independence in basic

Corresponding author: Dana Wong; Email: d.wong@latrobe.edu.au

Cite this article: Humphrey S., Pike K.E., Long B., Ma H., Bourke R., Wright B.J., & Wong D. (2024) Neuropsychological outcomes following endovascular clot retrieval and intravenous thrombolysis in ischemic stroke. *Journal of the International Neuropsychological Society*, 30: 764–776, <https://doi.org/10.1017/S1355617724000535>

© The Author(s), 2024. Published by Cambridge University Press on behalf of International Neuropsychological Society. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted re-use, distribution and reproduction, provided the original article is properly cited.

activities of daily living (bADL), with both treatments associated with reduced physical disability and greater functional independence (Emberson et al., 2014; Goyal et al., 2016). While these outcomes are important to understand, they do not provide information regarding cognitive impairment, anxiety, depression, and fatigue nor independence in instrumental activities of daily living (iADL). Previous research suggests that patients who are perceived to have good clinical outcomes with regard to physical disability continue to experience “invisible” difficulties in the areas of cognition, emotion, and fatigue, along with dependence in iADLs (Kapoor et al., 2017; Van Der Zee et al., 2013). Indeed, a recent study found that post-stroke cognitive impairment remained highly prevalent despite state-of-the-art stroke treatment (Gallucci et al., 2024). Better understanding of the nature and prevalence of these conditions following different acute treatments for ischemic stroke will enable clinicians to provide more accurate prognostic information, more effective rehabilitation, and improve the quality of life of stroke survivors.

A recent systematic review found that patients treated with ECR appear to perform better on cognitive measures compared to controls; however, heterogeneity in cognitive measures and timing of assessment precluded further analysis (De Rubeis et al., 2023). Likewise, a systematic review evaluating the effect of t-PA on post-stroke cognitive impairment also found considerable heterogeneity between studies, with the effect of t-PA on cognition remaining unclear (Broome et al., 2016). Both these reviews highlighted the paucity of studies in the area and emphasized the need for further studies to explore the impact of acute stroke treatments on cognition (Broome et al., 2016; De Rubeis et al., 2023). They also stress the need for greater consistency in cognitive measures used in stroke research (Broome et al., 2016; De Rubeis et al., 2023). Therefore, it would be useful to use measures commonly administered in neuropsychological assessments so that the findings can be translated to clinical practice. Furthermore, the reliance on general population normative data in research does not provide information on cognitive changes from estimated premorbid abilities, which may mean that high-functioning individuals are inaccurately characterized as having no cognitive impairment even if their performances have dropped significantly from baseline.

The overall aim of this study was to better inform clinicians working with stroke survivors by comparing the neuropsychological outcomes of ischemic stroke patients treated with ECR, t-PA, or conservative management. Specific aims were to investigate group differences in the following: (i) performance on cognitive tests commonly administered in neuropsychological assessments, (ii) the number of patients with impaired cognitive test performances after accounting for premorbid intellectual abilities, (iii) the presence of anxiety and depression symptoms, (iv) the presence of fatigue, and (v) independence in iADLs. Given that treatment with ECR is thought to reduce infarct volume, a known predictor of post-stroke cognitive impairment, we hypothesized that patients treated with ECR would perform better on cognitive testing compared to patients treated with t-PA and conservative management (Pendlebury & Rothwell, 2009; Samuels et al., 2023). We also hypothesized that patients treated with ECR would be more likely to achieve independence in bADLs and iADLs than those treated with t-PA and conservative management (Goyal et al., 2016). Given that anxiety, depression, and fatigue have not been thoroughly investigated following treatment with ECR, these aims were considered more exploratory.

Methods

Participants

This prospective study was conducted at Monash Medical Centre in Melbourne, Australia. Monash Medical Centre is a 640-bed teaching and research hospital in southeast Melbourne. The hospital is part of the largest public health service in the state of Victoria, providing more than 3.6 million episodes of care annually. Monash Medical Centre is one of two statewide ECR centers that provides a 24/7 service for patients across Victoria, in accordance with the statewide service protocol for ECR delivery (State of Victoria, Department of Health and Human Services, 2018). Ethics approval was obtained from the Monash Health Human Research Ethics Committee (HREC/18/MonH/96). The research was conducted in accordance with the Helsinki Declaration, and informed consent was obtained prior to participation in the study. Participants were recruited between August 2018 and February 2023. To be eligible, patients had to be at least 18 years old, admitted to Monash Medical Centre due to ischemic stroke, receive treatment within the relevant timeframe (24 hours for ECR and 4.5 hours for t-PA), and be able to provide informed consent. Patients with a history of previous stroke, brain injury, existing neurological or neurodegenerative condition, major psychiatric condition, premorbid cognitive impairment, and those with a non-English-speaking background were excluded from the study. Patients were also excluded if they had already undergone neuropsychological assessment at an inpatient or outpatient rehabilitation center, as there would likely be practice effects on cognitive testing. Patients were not randomized to treatment in this study and were recruited after they had already undergone acute stroke treatment. Therefore, patients were treated according to the Australian and New Zealand Clinical Guidelines for Stroke Management (Stroke Foundation, n.d.), which are consistent with international guidelines (Heran et al., 2024; Powers et al., 2019; Turc et al., 2019). ECR is currently only approved for patients with ischemic stroke due to large vessel occlusions in the internal carotid artery (ICA), first (M1) and second (M2) segments of the middle cerebral artery (MCA), and basilar artery (BA) as access to smaller vessels is more technically challenging due to the cerebral arteries being too narrow for endovascular devices (Przybylowski, 2014; Stroke Foundation, n.d.). Patients with less severe strokes that are not causing a disabling clinical deficit may also be ineligible for ECR (Stroke Foundation, n.d.). Hence, patients treated with ECR are more likely to have an ischemic stroke due to large vessel occlusion with greater stroke severity.

Procedure

Clinicians informed patients about the study before discharge from the stroke ward. If patients were interested in participating, the clinician obtained verbal consent for the patient to be contacted by a member of the research team in the weeks following discharge. Eligible patients were contacted via telephone and provided with further information about the study. If patients were still interested in participating, verbal consent was obtained to contact an informant to complete an AD8 Dementia Screening Interview (Galvin et al., 2005). Patients who scored ≥ 2 were considered to have premorbid cognitive impairment and were excluded from the study. An appointment to collect outcome data was then scheduled for eligible patients, and written consent was obtained at the start of the study visit. Outcome assessments were conducted with

participants in their own home or at an outpatient clinic at Monash Medical Centre, 90–120 days post-stroke. The assessments were administered by one doctoral candidate with a postgraduate qualification in clinical neuropsychology (SH) and took approximately 2–3 hours to complete.

Outcome measures

Demographic and clinical information were extracted from the medical record of each patient and included the following: age, sex, National Institutes of Health Stroke Scale (NIHSS) at presentation, premorbid modified Rankin Scale (mRS), location of occlusion, treatment type, and medical history. A summary of the outcome measures is shown in Table 1. The cognitive test battery was designed to include tests commonly administered during neuropsychological assessments and measure multiple cognitive domains including global cognition, intellectual ability, working memory, processing speed, learning and memory, visual neglect, language, and executive function. Measures were selected following review of the literature and discussions between neuropsychologists in the research team, while considering the neuropsychological test criteria recommended by the National Institute of Neurological Disorders and Stroke and Canadian Stroke Network as well as tests commonly administered in clinical practice (Hachinski *et al.*, 2006; Rabin *et al.*, 2016). Questionnaires measuring anxiety, depression, fatigue, degree of disability, BADLs, iADLs, and behavioral challenges were also administered to participants and informants. These measures were also selected following literature review and team consensus, with a particular focus on selecting measures that are valid and reliable in the stroke population.

COVID-19 disruptions

We initially aimed to complete a non-randomized three-arm parallel controlled clinical trial with a 1:1:1 ratio (ECR, t-PA, or conservative management). The trial was prospectively registered (Australian Clinical Trials Registration Number: 12619001194156) and involved the completion of two outcome assessments, three months and one year post-stroke. However, due to the COVID-19 pandemic and associated lockdown restrictions in Melbourne, we were unable to recruit participants between March and November 2020 and again between March 2021 and March 2022. Some participants were also lost to follow-up as their first outcome assessment was due to occur during a lockdown period when home visits and non-essential hospital visits were prohibited. As per the CONSERVE 2021 Statement, these significant delays in participant recruitment and data collection represent extenuating circumstances which impacted the trial (Orkin *et al.*, 2021). We therefore implemented mitigating strategies, including removing the second outcome assessment to reduce the total sample size needed for the study to be sufficiently powered. Future outcome assessments were also conducted on a home visit basis only, as non-essential clinical trials were not permitted on hospital premises. These important modifications were implemented in the early stages of the COVID-19 pandemic in March and April 2020. At that time, 16 participants had completed their first outcome assessment with only three of these participants also completing their second outcome assessment. The data from the second outcome assessments are therefore not included. The current study is now best described as an

observational study as data was only collected at one timepoint, 90–120 days post-stroke. The significant disruptions in participant recruitment and data collection also impacted our overall sample size, and the t-PA and conservative management groups were combined into a standard medical care (SMC) group to accommodate this. This is consistent with most stroke research involving ECR, which tends to combine patients treated with t-PA and conservative management into a SMC group. As the Australian and New Zealand Clinical Guidelines for Stroke Management recommend treatment with t-PA for all eligible patients while ECR is being considered (*i.e.*, bridging therapy), some participants treated with ECR were also treated with t-PA (Stroke Foundation, *n.d.*). The ECR group is therefore better classified as an ECR plus SMC group, which is being compared to a SMC alone group (*i.e.*, ECR + SMC vs. SMC), with ECR being the main focus of the current study.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 28. Missing data were handled via pairwise deletion due to a non-significant Little's missing completely at random test. To adjust for outliers, extreme values three times or more outside of the interquartile range were winsorized and replaced with the next value that was not an outlier. Statistical significance was set at a p value of < 0.01 for cognitive test data as a more conservative approach was needed to control for the inflated risk of Type 1 error associated with performing multiple comparisons within the same construct (*i.e.*, cognition). Statistical significance was set at a p value of < 0.05 for all other variables.

To compare group differences in cognitive test performances, raw scores from subtests of the Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV); Wechsler Memory Scale, Fourth Edition (WMS-IV); and Delis-Kaplan Executive Function System (D-KEFS) were converted into age-normed scaled scores ($M = 10$, $SD = 3$) using the test manuals (Delis *et al.*, 2001; Wechsler, 2009; Weschler, 2009). Sums of scaled scores from subtests of the WAIS-IV were then used to produce composite standard scores ($M = 100$, $SD = 15$) for each of the four indices and the overall quotient: Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI), Working Memory Index (WMI), Processing Speed Index (PSI), and Full-Scale Intelligence Quotient (FSIQ). Raw scores from the Test of Premorbid Function (TOPF) were converted into age-normed standard scores using the test manual (Pearson, 2009). For the remaining cognitive tests, raw scores were used for group comparisons due to relatively small numbers in the normative sample (Benedict, 1997; Culbertson & Zillmer, 2005; Kaplan *et al.*, 1983; Schmidt, 1996; Tombaugh, 1999, 2004; Wilson *et al.*, 1987). Higher scores represent better performances on all cognitive tests, except for the Trail Making Test (TMT), where raw scores reflect the time taken in seconds to complete the task (Tombaugh, 2004), and Tower of London (TOL^{DX}) Move Score, where raw scores reflect the total number of extra moves needed to complete the task (Culbertson & Zillmer, 2005). Group comparisons were conducted with independent sample t tests and are described with mean and standard deviation. Linear regression analyses were also performed to explore the effect of acute stroke treatment on cognitive test scores, adjusting for confounding variables including NIHSS at presentation, TOPF score, and age. Age was not included as a confounding variable when comparing age-normed scores on the WAIS-IV, WMS-IV, and D-KEFS. The results of the linear

Table 1. Summary of the outcome measures

Measure	Outcome	Score
Test of Premorbid Function (TOPF)	Premorbid intellectual ability	Standard score
Montreal Cognitive Assessment (MoCA)	Global cognitive screen	Raw score
Wechsler Adult Intelligence Scale, 4th Ed. (WAIS-IV)		
Verbal Comprehension Index (VCI)	Verbal intellectual ability	Standard score
Perceptual Reasoning Index (PRI)	Visual intellectual ability	Standard score
Working Memory Index (WMI)	Verbal working memory	Standard score
Processing Speed Index (PSI)	Processing speed	Standard score
Full-Scale Intelligence Quotient (FSIQ)	General intellectual ability	Standard score
Wechsler Memory Scale, 4th Ed. (WMS-IV)		
Logical Memory I	Immediate verbal memory	Scaled score
Logical Memory II	Delayed verbal memory	Scaled score
Visual Reproduction I	Immediate visual memory	Scaled score
Visual Reproduction II	Delayed visual memory	Scaled score
Symbol Span	Visual working memory	Scaled score
Rey Auditory Verbal Learning Test (RAVLT)		
Total Learning	Verbal learning	Raw score and Z-score
Delayed Recall	Verbal memory	Raw score and Z-score
Brief Visuospatial Memory Test (BVMt)		
Total Learning	Visual learning	Raw score and Z-score
Delayed Recall	Visual memory	Raw score and Z-score
Behavioral Inattention Test (BIT)		
Conventional Subtests	Visual neglect	Raw score
Boston Naming Test, 2nd Ed. (BNT)	Confrontation naming	Raw score and Z-score
Controlled Oral Word Association Test (COWAT)		
Letter Fluency (FAS)	Letter fluency	Raw score and Z-score
Category Fluency (Animals)	Category fluency	Raw score and Z-score
Trail Making Test (TMT)		
Part A	Processing speed	Time (secs) and Z-score
Part B	Cognitive flexibility	Time (secs) and Z-score
D-KEFS Color-Word Interference Test		
Color Naming	Processing speed	Scaled score
Word Reading	Processing speed	Scaled score
Inhibition	Response inhibition	Scaled score
Tower of London, Drexel University, 2nd Ed. (TOL^{DX})		
Move Score	Planning	Raw score and Z-score
Correct Score	Problem-solving	Raw score and Z-score
Hospital Anxiety and Depression Scale (HADS)		
Anxiety	Anxiety	Raw score
Depression	Depression	Raw score
Fatigue Severity Scale (FSS)	Fatigue	Raw score
Modified Rankin Scale (mRS)*	Degree of disability	Raw score
Barthel Index (BI)*	Basic ADL	Raw score
Nottingham Extended ADL Scale (NEADL)	Instrumental ADL	Raw score
Frontal Systems Behavior Scale (FrSBs)*		
Before Stroke	Behavioral challenges	T-score
After Stroke	Behavioral challenges	T-score

Note. D-KEFS = Delis-Kaplan Executive Function System, ADL = Activities of Daily Living. *Rated by informant.

regression analyses are described as unadjusted and adjusted betas (β), with corresponding 95% confidence intervals (CIs).

To compare the number of participants with impaired cognitive test scores after accounting for premorbid intellectual abilities, TOPF scores were used to produce Predicted FSIQ scores with the Advanced Clinical Solutions (ACS) software package (Pearson, 2009). Raw test scores that had not yet been standardized were converted into *z*-scores using published normative data. Cognitive test scores were considered to be impaired if they were at least one standard deviation below the Predicted FSIQ score. Cutoff scores of < 26 were used to determine impaired performances on the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), while a cutoff score of < 129 was considered an impaired performance on the Behavioral Inattention Test (BIT; Wilson et al., 1987). Participants were considered to be cognitively impaired if they

performed at least one standard deviation below their Predicted FSIQ score on two or more cognitive tests (excluding the MoCA). This criterion was adopted as it has been shown to be diagnostically accurate in a mild cognitive impairment population, and we were interested in detecting both mild and more severe cognitive changes post-stroke (Jak et al., 2009; Wong et al., 2018). Group comparisons were made using chi-square tests and Fisher's exact tests and are described as frequencies and percentages.

To compare the presence of post-stroke anxiety and depression, a cutoff score of ≥ 8 on each subscale of the Hospital Anxiety and Depression Scale (HADS) was considered to indicate the presence of anxiety or depression (Zigmond & Snaith, 1983). A cutoff score of ≥ 4 on the Fatigue Severity Scale (FSS) was considered to indicate the presence of post-stroke fatigue (Krupp et al., 1989). Cutoff scores of ≤ 2 on the modified Rankin Scale (mRS), ≥ 95 on

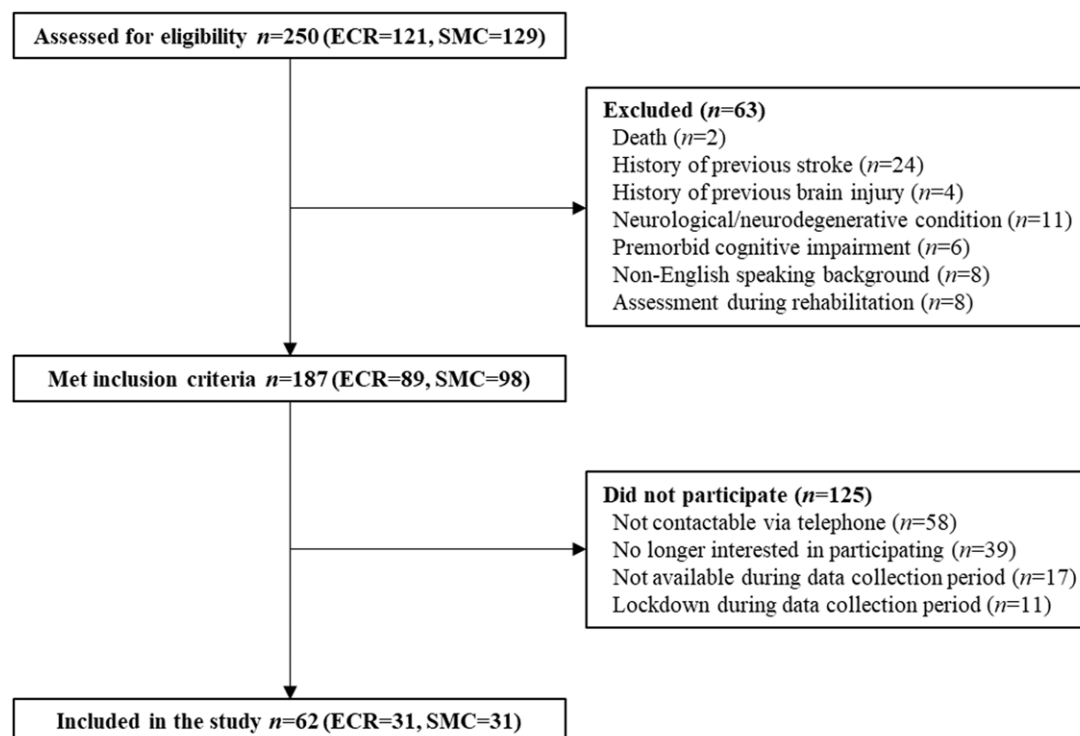


Figure 1. Flowchart of participant selection process. ECR = endovascular clot retrieval, SMC = standard medical care.

the Barthel Index (BI), and ≥ 44 on the Nottingham Extended ADL (NEADL) Scale were considered to indicate functional independence, independence in BADLs, and independence in IADLs, respectively (Mahoney & Barthel, 1965; Nouri & Lincoln, 1987; Van Swieten *et al.*, 1988). A cutoff score of ≥ 65 on the Frontal Systems Behavior Scale (FrSBe) was considered to indicate the presence of behavioral challenges (Grace & Malloy, 2001). Group comparisons of the proportion of patients exceeding these cutoffs were performed using chi-square tests and Fisher's exact tests and are described as frequencies and percentages. Logistic regression analyses were also performed to adjust for the potential influence of age, sex, education, and NIHSS at presentation on these outcomes. Age, sex, and education were not included when comparing *T*-scores on the FrSBe as these are already accounted for in the normative data. The results of the logistic regression analyses are described as unadjusted and adjusted odds ratios (OR), with corresponding 95% CIs.

Results

Patient characteristics

A total of 250 patients were screened for eligibility (Figure 1). Of these patients, 121 were treated with ECR and 129 were treated with SMC. The demographic and clinical information of all screened patients is shown in Supplementary Table 1. The only statistically significant difference between groups was NIHSS at presentation, with the ECR group having higher stroke severity. Of the 250 patients screened, 62 were included in the study (63 did not meet inclusion criteria and 125 were unwilling or unable to participate). Six patients were excluded as they were considered to have premorbid cognitive impairment (ECR = 2, SMC = 4). Eight patients were excluded as they had already undergone neuropsychological assessment during rehabilitation (ECR = 4,

SMC = 4), with the majority of these being young stroke survivors who underwent assessment in the community to guide return to work. No statistically significant differences in demographic or clinical information were identified between patients who did and did not participate (Supplementary Table 2).

Of the 62 patients who participated in the study, 31 were treated with ECR and 31 were treated with SMC. The demographic and clinical information of participants is shown in Table 2. The overall mean age was 66.5 (20–86) years, and 35 (56.5%) participants were male. Participants treated with SMC had a significantly higher level of education and slightly but not significantly higher premorbid intellectual ability than those treated with ECR. The ECR group had a significantly higher NIHSS score at presentation and significantly more large vessel occlusions than the SMC group. No other statistically significant differences were identified between treatment groups with regard to demographic or clinical information. The overall median time of participation was 104 days post-stroke (SMC = 103 days vs. ECR = 104 days, $p = 0.799$).

Cognitive tests

The results of the cognitive test performances are shown in Table 3. No statistically significant differences were identified between groups on any cognitive measure. However, after adjusting for confounding variables including stroke severity, premorbid intellectual ability, and age, the linear regression analyses (Table 4) showed that treatment with ECR was associated with better performances on measures of cognitive screening, visual working memory, and verbal learning and memory. There were no significant correlations between stroke severity and cognitive test scores, apart from TMT-A ($r = 0.30$, $p = 0.020$).

The number of participants who performed below premorbid expectation on each cognitive test is shown in Table 5. The number

Table 2. Demographic and clinical information of participants

	ECR (<i>n</i> = 31)	SMC (<i>n</i> = 31)	<i>p</i> value
Demographic information			
Age, years, mean, SD (range)	64.3 ± 16.0 (24–82)	68.8 ± 15.9 (20–86)	0.272 ^a
Male, <i>n</i> (%)	15 (48.4)	20 (64.5)	0.200 ^b
Education, years, mean, SD (range)	10.9 ± 2.3 (6–16)	12.5 ± 2.9 (7–18)	0.022^a
TOPF, SS, mean, SD (range)	98.7 ± 10.4 (81–123)	103.7 ± 12.3 (73–125)	0.087 ^a
Clinical information			
Premorbid mRS, <i>n</i> (%)			1.000 ^c
0	30 (96.8)	29 (93.5)	
1	1 (3.2)	2 (6.5)	
NIHSS, mean, SD (range)	8.5 ± 5.8 (0–21)	5.0 ± 3.9 (0–15)	0.009^a
t-PA, <i>n</i> (%)	6 (19.4)	12 (38.7)	0.093 ^b
TICI, <i>n</i> (%)			
3	22 (71.0)	–	
2C	4 (12.9)	–	
2B	5 (16.1)	–	
Left hemisphere stroke, <i>n</i> (%)	13 (41.9)	19 (61.3)	0.282 ^d
Location of occlusion, <i>n</i> (%)			<0.001^d
Internal carotid artery (ICA)			
Intracranial ICA	1 (3.2)	1 (3.2)	
ICA and M1	1 (3.2)	–	
ICA and M2	2 (6.5)	–	
Middle cerebral artery (MCA)			
First segment (M1)	15 (48.4)	–	
Second segment (M2)	10 (32.3)	8 (25.8)	
Third segment (M3)	–	3 (9.7)	
Deep branches	–	8 (25.8)	
Anterior cerebral artery (ACA)			
Second segment (A2)	–	1 (3.2)	
Posterior cerebral artery (PCA)			
Second segment (P2)	–	1 (3.2)	
Third segment (P3)	–	3 (9.7)	
Fourth segment (P4)	–	1 (3.2)	
Deep branches	–	4 (12.9)	
Basilar artery	2 (6.5)	–	
Pontine	–	1 (3.2)	

Note. ECR = endovascular clot retrieval, SMC = standard medical care, TOPF = Test of Premorbid Function, mRS = modified Rankin Scale, NIHSS = National Institutes of Health Stroke Scale, t-PA = tissue plasminogen activator, TICI = thrombolysis in cerebral infarction. ^aIndependent sample *t* test. ^bChi-square test. ^cFisher's exact test. ^dLikelihood-ratio test.

of participants presenting with impaired test performances was significantly lower in the ECR group than the SMC group on a measure of verbal memory. There were no statistically significant differences between groups in the overall number of participants who were classified as cognitively impaired (ECR = 77.4% vs. SMC = 83.9%, *p* = 0.520).

Further analysis of the cognitive test data was performed with participants treated with t-PA removed from each group (Supplementary Tables 3–5). Although measures of visual working memory and verbal learning were no longer significant after the removal of participants treated with t-PA (Supplementary Table 5), this is likely due to a lack of power given the smaller sample size (ECR = 25, SMC = 19) as effect sizes remained largely unchanged (Supplementary Table 4). Therefore, treatment with t-PA did not alter the pattern of the results in a meaningful way. There were also no statistically significant differences between groups in the overall number of participants considered to be cognitively impaired (ECR = 76.0% vs. SMC = 84.2%, *p* = 0.504).

Emotional and functional outcomes

The number of participants who achieved independence in BADLs was significantly higher in the ECR group than the SMC

Table 3. Comparison of cognitive test performances

	<i>N</i>	ECR	SMC	<i>p</i> value	Cohen's <i>d</i>
Montreal Cognitive Assessment					
Verbal Comprehension Index	61	25.6 ± 2.6	24.1 ± 3.3	0.051	0.507
Perceptual Reasoning Index	61	97.6 ± 11.6	99.7 ± 11.4	0.489	0.178
Working Memory Index	61	100.1 ± 10.4	104.0 ± 11.0	0.170	0.356
Processing Speed Index	61	100.0 ± 12.3	98.7 ± 14.2	0.685	0.104
Full-Scale IQ	61	101.4 ± 15.5	99.3 ± 13.4	0.560	0.150
Full-Scale IQ	61	99.5 ± 11.5	100.7 ± 11.4	0.674	0.108
Wechsler Memory Scale					
Logical Memory I	61	10.1 ± 2.5	9.3 ± 3.0	0.226	0.314
Logical Memory II	61	10.1 ± 2.2	8.8 ± 3.3	0.091	0.438
Visual Reproduction I	61	9.9 ± 2.3	10.9 ± 3.0	0.151	0.372
Visual Reproduction II	61	9.2 ± 3.4	8.4 ± 3.7	0.373	0.230
Symbol Span	60	10.1 ± 2.0	9.1 ± 2.7	0.110	0.419
Rey Auditory Verbal Learning Test					
Total Learning	59	43.2 ± 12.3	37.7 ± 12.5	0.090	0.449
Delayed Recall	59	8.9 ± 4.3	6.9 ± 4.2	0.079	0.466
Brief Visuospatial Memory Test					
Total Learning	59	14.9 ± 6.2	13.3 ± 7.2	0.377	0.232
Delayed Recall	59	6.5 ± 3.3	4.8 ± 3.6	0.055	0.510
Behavioral Inattention Test	59	142.7 ± 2.8	142.2 ± 3.6	0.558	0.153
Boston Naming Test					
Controlled Oral Word Association Test	61	53.6 ± 4.4	51.6 ± 7.9	0.214	0.319
Letter Fluency (FAS)					
Category Fluency (Animals)	60	31.2 ± 13.8	31.2 ± 13.8	0.978	0.007
Trail Making Test*	60	18.3 ± 4.8	17.9 ± 5.3	0.761	0.079
Part A	60	36.7 ± 12.4	42.2 ± 21.0	0.227	0.316
Part B	60	93.7 ± 38.9	124.7 ± 73.7	0.047	0.527
Color-Word Interference Test					
Color Naming	58	9.4 ± 3.3	8.8 ± 3.7	0.523	0.169
Word Reading	58	8.9 ± 3.5	10.0 ± 3.0	0.184	0.353
Inhibition	58	9.3 ± 3.8	9.7 ± 4.0	0.710	0.098
Tower of London Move Score*					
Correct Score	41	25.5 ± 19.1	26.0 ± 20.6	0.946	0.021
	41	5.7 ± 2.0	5.7 ± 2.6	0.953	0.018

Note. ECR = endovascular clot retrieval, SMC = standard medical care. *Higher scores represent poorer performance.

group (Table 6). Furthermore, the number of participants presenting with fatigue was significantly lower in the ECR group than the SMC group. No other statistically significant differences were identified between the treatment groups on any other emotional or functional outcome measures. However, after adjusting for confounding variables including age, sex, education, and stroke severity, the logistic regression analyses (Table 7) showed that treatment with ECR was associated with reduced disability, greater independence in bADLs and iADLs, and less fatigue.

Discussion

To our knowledge, this is the first study to comprehensively compare the neuropsychological outcomes of ischemic stroke patients treated with ECR and SMC using prospective methods. As hypothesized, we found that the ECR group performed significantly better on several cognitive tests compared to the SMC group. However, on an individual level, many participants treated with

Table 4. Associations between cognitive test performances and acute stroke treatment

	Unadjusted			Adjusted		
	β	95% CI	<i>p</i>	β	95% CI	<i>p</i>
Montreal Cognitive Assessment^a	1.5	−0.00 to 2.97	0.051	2.14	0.80 to 3.49	0.002
Wechsler Adult Intelligence Scale^b						
Verbal Comprehension Index	−2.04	−7.92 to 3.83	0.489	2.36	−2.02 to 6.73	0.286
Perceptual Reasoning Index	−3.80	−9.27 to 1.67	0.170	−2.31	−8.23 to 3.62	0.439
Working Memory Index	1.39	−5.42 to 8.20	0.685	4.57	−1.70 to 10.8	0.150
Processing Speed Index	2.18	−5.25 to 9.60	0.560	5.32	−2.41 to 13.06	0.174
Full-Scale Intelligence Quotient	−1.24	−7.12 to 4.64	0.674	2.47	−2.77 to 7.71	0.350
Wechsler Memory Scale^b						
Logical Memory I	0.88	−0.56 to 2.31	0.226	1.78	0.41 to 3.16	0.012
Logical Memory II	1.23	−0.21 to 2.67	0.093	1.99	0.55 to 3.43	0.008
Visual Reproduction I	−1.00	−2.38 to 0.38	0.151	−0.64	−2.14 to 0.86	0.396
Visual Reproduction II	0.81	−1.00 to 2.63	0.373	0.79	−1.21 to 2.79	0.434
Symbol Span	1.00	−0.24 to 2.24	0.110	1.62	0.42 to 2.82	0.009
Rey Auditory Verbal Learning Test^a						
Total Learning	5.54	−0.90 to 11.98	0.090	8.26	2.34 to 14.18	0.007
Delayed Recall	1.96	−0.24 to 4.16	0.079	2.60	0.39 to 4.81	0.022
Brief Visuospatial Memory Test^a						
Total Learning	1.56	−1.95 to 5.08	0.377	1.61	−1.52 to 4.74	0.306
Delayed Recall	1.75	−0.04 to 3.54	0.055	1.30	−0.41 to 3.00	0.133
Behavioral Inattention Test^a						
Conventional Subtests	0.49	−1.18 to 2.16	0.558	0.60	−1.10 to 2.31	0.481
Boston Naming Test^a	2.05	−1.24 to 5.34	0.217	3.60	0.23 to 6.97	0.037
Controlled Oral Word Association Test^a						
Letter Fluency (FAS)	−0.10	−7.22 to 7.02	0.978	2.95	−3.55 to 9.44	0.367
Category Fluency (Animals)	0.40	−2.22 to 3.02	0.761	1.10	−1.44 to 3.64	0.390
Trail Making Test						
Part A	−5.47	−14.40 to 3.47	0.225	−8.76	−16.58 to −0.94	0.029
Part B	−31.03	−61.48 to −0.59	0.046	−36.29	−66.68 to −5.90	0.020
Color-Word Interference Test^b						
Color Naming	0.59	−1.26 to 2.44	0.523	1.25	−0.62 to 3.12	0.187
Word Reading	−1.14	−2.84 to 0.56	0.184	−0.22	−1.78 to 1.35	0.783
Inhibition	−0.38	−2.41 to 1.65	0.710	0.52	−1.57 to 2.61	0.621
Tower of London^a						
Move Score	−0.43	−13.06 to 12.21	0.946	0.38	−13.52 to 14.28	0.956
Correct Score	−0.04	−1.52 to 1.44	0.953	0.19	−1.45 to 1.83	0.813

Note. ^aAdjusted for National Institutes of Health Stroke Scale (NIHSS) at presentation, Test of Premorbid Function (TOPF) score, and age. ^bAdjusted for NIHSS at presentation and TOPF score.

ECR displayed impaired cognitive test performances and were classified as cognitively impaired, suggesting that cognitive impairment may still be common among patients treated with ECR. Similarly, the ECR group was less likely to experience fatigue than the SMC group, although over half of the participants treated with ECR continued to experience fatigue, suggesting that fatigue may also be common for those treated with ECR. As expected, the ECR group was more likely to achieve independence in bADLs and iADLs. Anxiety and depression symptoms were experienced similarly by both groups. These results have important practical implications for stroke rehabilitation, and routine assessment of cognition, emotion, and fatigue is recommended for all stroke survivors regardless of acute stroke treatment and functional outcome.

After adjusting for stroke severity, premorbid intellectual ability, and age, we found that participants treated with ECR performed significantly better on measures of cognitive screening, visual working memory, and verbal learning and memory, compared to those treated with SMC. This is consistent with previous research and a recent systematic review which found that patients treated with ECR tend to perform better on cognitive testing compared to non-treated patients (De Rubeis et al., 2023). The current study therefore adds to the existing literature indicating that treatment with ECR is associated with better performances in multiple cognitive domains (López-Cancio et al., 2017; Lattanzi et al., 2020; Xu et al., 2017). However, unlike

previous studies, we did not find any significant differences between treatment groups on measures of verbal working memory, processing speed, visual learning and memory, cognitive flexibility, abstract reasoning, and response inhibition, despite using similar measures (Lattanzi et al., 2020). We also did not observe any differences on other measures including intellectual ability, visual neglect, verbal fluency, and planning and problem-solving.

There are several potential reasons for these differences between studies. Firstly, Lattanzi et al. (2020) compared patients treated with ECR and t-PA to those treated with t-PA alone, whereas only 19.4% of participants in our study received t-PA prior to undergoing ECR. There is some evidence showing the effectiveness of bridging therapy (i.e., treatment with t-PA prior to ECR) with regard to functional outcome with current stroke guidelines recommending bridging therapy for all eligible patients (Kobeissi et al., 2023; Powers et al., 2019; Wang et al., 2021). Therefore, it may well be that patients treated with bridging therapy gain more cognitive benefit as a consequence of the earlier onset of action and possible reduced time of ischemia (Kobeissi et al., 2023). We did not see this in our study due to the small number of participants who received both ECR and t-PA. However, previous studies tend to suggest that while treatment with t-PA may be associated with better cognitive performances in days after stroke, these benefits do not persist at 3- to 6-month follow-up (Broome et al., 2016). Furthermore, only 38.7% of patients in the SMC group were treated with t-PA, with no

Table 5. Number of patients performing below premorbid expectation on each cognitive test

	<i>N</i>	ECR	SMC	<i>p</i> value
Montreal Cognitive Assessment	62			
<i>n</i> impaired (%)	36	16 (51.6)	20 (64.5)	0.303 ^a
Wechsler Adult Intelligence Scale				
Verbal Comprehension Index	61			
<i>n</i> impaired (%)	5	2 (6.7)	3 (9.7)	1.000 ^b
Perceptual Reasoning Index	61			
<i>n</i> impaired (%)	8	2 (6.7)	6 (19.4)	0.255 ^b
Working Memory Index	61			
<i>n</i> impaired (%)	9	4 (13.3)	5 (16.1)	1.000 ^b
Processing Speed Index	61			
<i>n</i> impaired (%)	9	3 (10.0)	6 (19.4)	0.473 ^b
Full-Scale Intelligence Quotient	61			
<i>n</i> impaired (%)	7	1 (3.3)	6 (19.4)	0.104 ^b
Wechsler Memory Scale				
Logical Memory I	61			
<i>n</i> impaired (%)	17	5 (16.7)	12 (38.7)	0.055 ^a
Logical Memory II	61			
<i>n</i> impaired (%)	18	3 (10.0)	15 (48.4)	0.001^a
Visual Reproduction I	61			
<i>n</i> impaired (%)	12	4 (13.3)	8 (25.8)	0.221 ^a
Visual Reproduction II	61			
<i>n</i> impaired (%)	24	8 (26.7)	16 (51.6)	0.046 ^a
Symbol Span	60			
<i>n</i> impaired (%)	16	5 (16.7)	11 (36.7)	0.080 ^a
Rey Auditory Verbal Learning Test				
Total Learning	59			
<i>n</i> impaired (%)	15	5 (17.2)	10 (33.3)	0.156 ^a
Delayed Recall	59			
<i>n</i> impaired (%)	22	7 (24.1)	15 (50.0)	0.040 ^a
Brief Visuospatial Memory Test				
Total Learning	59			
<i>n</i> impaired (%)	41	19 (65.5)	22 (73.3)	0.514 ^a
Delayed Recall	59			
<i>n</i> impaired (%)	34	12 (41.4)	22 (73.3)	0.013 ^a
Behavioral Inattention Test				
<i>n</i> impaired (%)	0	0 (0.0)	0 (0.0)	
Boston Naming Test				
<i>n</i> impaired (%)	12	5 (16.7)	7 (22.6)	0.561 ^a
Controlled Oral Word Association Test				
Letter Fluency (FAS)	60			
<i>n</i> impaired (%)	21	8 (26.7)	13 (43.3)	0.176 ^a
Category Fluency (Animals)	60			
<i>n</i> impaired (%)	13	3 (10.0)	10 (33.3)	0.028 ^a
Trail Making Test				
Part A	60			
<i>n</i> impaired (%)	9	3 (10.0)	6 (20.0)	0.472 ^b
Part B	60			
<i>n</i> impaired (%)	18	6 (16.7)	12 (40.0)	0.045 ^a
Color-Word Interference Test				
Color Naming	58			
<i>n</i> impaired (%)	17	6 (21.4)	11 (37.9)	0.173 ^a
Word Reading	58			
<i>n</i> impaired (%)	9	5 (17.9)	4 (13.8)	0.730 ^b
Inhibition	58			
<i>n</i> impaired (%)	14	7 (25.9)	7 (24.1)	0.877 ^a
Tower of London				
Move Score	41			
<i>n</i> impaired (%)	7	3 (15.8)	4 (18.2)	1.000 ^b
Correct Score	41			
<i>n</i> impaired (%)	4	0 (0.0)	4 (18.2)	0.111 ^b

Note. Impaired is at least 1 SD below Predicted FSIQ. ECR = endovascular clot retrieval, SMC = standard medical care. ^aChi-square test. ^bFisher's exact test.

significant difference between the SMC and ECR groups. Therefore, it is unlikely that treatment with t-PA played a significant role in influencing the findings of our study, with this supported by further analysis with those treated with t-PA removed, which did not alter effect sizes in a meaningful way. Further research should aim to compare cognitive outcomes

between patients treated with ECR and t-PA to ECR alone as there may well be a cognitive benefit associated with bridging therapy.

The difference in location of occlusion is perhaps the most likely reason for not observing greater differences across more cognitive measures. Participants treated with ECR had significantly more large vessel occlusions than the SMC group, which is known to

Table 6. Comparison of emotional and functional outcomes

	N	ECR	SMC	p value
Hospital Anxiety and Depression Scale				
Anxiety ≥ 8				
n present (%)	62	12 (38.7)	14 (45.2)	0.607 ^b
Depression ≥ 8				
n present (%)	62	4 (12.9)	7 (22.6)	0.319 ^b
Fatigue Severity Scale ≥ 4				
n present (%)	62	16 (51.6)	25 (80.6)	0.016^b
Modified Rankin Scale ≤ 2				
n independent (%)	57	28 (96.6)	22 (78.6)	0.052 ^a
Barthel Index ≥ 95				
n independent (%)	57	27 (93.1)	20 (71.4)	0.041^a
Nottingham Extended ADL Scale ≥ 44				
n independent (%)	62	29 (93.5)	25 (80.6)	0.255 ^a
Frontal Systems Behavior Scale				
Before Stroke ≥ 65				
n present (%)	50	3 (12.0)	4 (16.0)	1.000 ^a
After Stroke ≥ 65				
n present (%)	50	7 (28.0)	9 (36.0)	0.544 ^b

Note. ECR = endovascular clot retrieval, SMC = standard medical care, ADL = activities of daily living. ^aFisher's exact test. ^bChi-square test.

Table 7. Associations between emotional and functional measures and acute stroke treatment

	Unadjusted			Adjusted		
	OR	95% CI	p	OR	95% CI	p
Hospital Anxiety and Depression Scale^a						
Anxiety	1.30	0.47–3.59	0.607	1.55	0.47–5.10	0.474
Depression	1.97	0.51–7.56	0.324	2.80	0.53–14.73	0.225
Fatigue Severity Scale^a						
	3.91	1.26–12.16	0.019	4.24	1.14–15.86	0.032
Modified Rankin Scale^a						
	7.64	0.86–68.19	0.069	125.70	2.67–5921.97	0.014
Barthel Index^a						
	5.40	1.03–28.23	0.046	28.30	2.11–379.79	0.012
Nottingham Extended ADL Scale^a						
	3.48	0.64–18.81	0.147	17.17	1.39–212.23	0.027
Frontal Systems Behavior Scale^b						
Before Stroke	1.40	0.28–7.00	0.684	2.16	0.33–14.08	0.420
After Stroke	1.45	0.44–4.78	0.545	2.14	0.54–8.41	0.278

Note. ^aAdjusted for age, sex, education, and National Institutes of Health Stroke Scale (NIHSS) at presentation. ^bAdjusted for NIHSS at presentation.

predict post-stroke cognitive impairment (Pendlebury & Rothwell, 2009; Rost et al., 2022). Therefore, the ECR group was expected to have a greater degree of cognitive impairment, but we did not observe this in our results. This is potentially due to the association between ECR and reduced infarct volume, which is also known to predict post-stroke cognitive impairment (Pendlebury & Rothwell, 2009; Rost et al., 2022; Samuels et al., 2023). Future studies exploring cognitive outcomes following different acute treatments for ischemic stroke should therefore aim to incorporate neuro-imaging to further explore the impact of final infarct volume as well as the influence of other factors such as leukoaraiosis.

Although treatment with ECR appears to be associated with better cognitive test performances than other stroke treatments, 77.4% of participants in the ECR group were classified as cognitively impaired, indicating that many of these patients continue to experience some degree of ongoing cognitive impairment. This is similar to previous research which suggests that those with relatively minor strokes still experience cognitive difficulties despite many of these patients achieving what would traditionally be considered good clinical recovery (Jokinen et al., 2015; Turner et al., 2019). This has important practical implications for stroke rehabilitation, as cognitive impairment is a major cause of ongoing disability after stroke (Rost et al., 2022). Routine screening of cognition is therefore recommended regardless of acute stroke

treatment and functional outcome, so that patients who may benefit from more comprehensive neuropsychological assessment and cognitive rehabilitation can be referred appropriately. Further assessment for high-functioning individuals should also be considered as cognitive screening may not be sensitive enough to detect mild cognitive difficulties in these individuals.

We did not find any significant differences between treatment groups with regard to anxiety or depression. This was a somewhat unexpected finding, as post-stroke anxiety and depression are thought to be related to poorer functional outcomes and cognitive impairment, both of which were more common in the SMC group (Menlove et al., 2015; Robinson & Jorge, 2016; Wijeratne & Sales, 2021). The frequency of post-stroke anxiety is estimated to range from 18.7% to 24.2% (Knapp et al., 2020), while approximately 27% of stroke survivors will experience depression (Knapp et al., 2020; Liu et al., 2023). Interestingly, the number of participants treated with ECR in our study who endorsed anxiety was higher than the overall estimated prevalence. This is potentially due to a paradoxical negative impact of increased anxiety in patients with good functional outcomes. Previous research suggests that patients with minor strokes do not receive adequate follow-up (Turner et al., 2019), including sufficient information provision, with psychoeducation and active information provision known to reduce anxiety in stroke survivors (Crocker et al., 2021; White et al.,

2014). Uncertainty about future prognosis and anxiety about the potential of further strokes may be heightened by the absence of information. This points to the need for active monitoring and anxiety management even for stroke survivors with otherwise positive outcomes.

Conversely, only 12.9% of participants treated with ECR in our study endorsed depression, less than half that of the overall estimated prevalence. There is some evidence to suggest that there is a relationship between infarct volume and depression, with the association between reduced infarct volume and ECR potentially leading to reduced depressive symptomatology in these patients (Samuels et al., 2023; Wijeratne & Sales, 2021). Further research exploring the impact of both acute stroke treatments and sub-acute care on emotional outcomes is required before any conclusions can be drawn about the effect of ECR on anxiety and depression. Other factors such as premorbid psychiatric history and social support are also important risk factors for the development of post-stroke anxiety and depression, which future studies should aim to take into consideration (Menlove et al., 2015; Robinson & Jorge, 2016).

Post-stroke fatigue was significantly lower in the ECR group compared to the SMC group. This represents a novel finding as the impact of ECR on fatigue has not been well described in the literature. The underlying mechanism of post-stroke fatigue remains poorly understood, with conflicting evidence regarding the association between fatigue and other factors such as stroke characteristics, neuroimaging, functional outcome, cognitive impairment, depression, age, sex, and education (Acciarresi et al., 2014; Paciaroni & Acciarresi, 2019; Zhan et al., 2022). Our findings suggest that acute stroke treatment may also play a role in the development of post-stroke fatigue; however, it remains unclear as to whether this is simply due to improved functional and cognitive outcomes or whether pathophysiological changes such as reduced infarct volume and neuroinflammation play a role (Paciaroni & Acciarresi, 2019).

Despite observing less fatigue in the ECR group, it was still highly prevalent among these participants, with over half of those treated with ECR endorsing post-stroke fatigue. This is consistent with Graber et al. (2019), who found that fatigue is a common symptom after ischemic stroke, even for those treated with acute reperfusion therapies who achieve good functional outcomes. Similarly, Staub and Bogousslavsky (2001) suggest that for those with excellent neurological and neuropsychological outcomes, fatigue may be the only persisting symptom, with this potentially having an ongoing negative impact on rehabilitation and quality of life (Radman et al., 2012). Improved identification, management, and treatment of fatigue remain a priority for all stroke survivors regardless of acute stroke treatment and functional outcome.

As expected, the number of participants who achieved independence in bADLs was significantly higher in those treated with ECR compared to SMC. This is consistent with previous research, which has shown that treatment with ECR is associated with significantly reduced disability and greater health-related quality of life (Goyal et al., 2016; McCarthy et al., 2019). We also found that participants treated with ECR were significantly more likely to achieve independence in iADLs compared to SMC. This is an important finding indicating that ECR not only leads to reduced disability and greater self-care but also improves participation in more complex day-to-day tasks including domestic and community activities.

The current study has several limitations which impact the generalizability of the findings, including the relatively small sample size from a single hospital site as well as the inability to

compare the outcomes of patients treated with ECR, t-PA, or conservative management as three distinct groups. We were also limited to performing the outcome measure assessments at one timepoint, 90–120 days post-stroke, which, although important to understand, does not provide information regarding the recovery trajectories of these patients. We did not screen for developmental reading difficulties, which may have impacted performance on the TOPF. While we did not exclude patients with aphasia from participating in the study, only 12 participants (19.4%) were considered to be impaired on the BNT, lower than the overall estimated prevalence of aphasia following ischemic stroke of 30% (Grönberg et al., 2022). Therefore, our recruitment process may have introduced some selection bias as it was primarily verbal and those with significant communication difficulties may have not been invited to participate by clinical staff on the stroke ward. The exclusion of those with a non-English-speaking background also limits the generalizability of the findings to patients with a culturally and linguistically diverse background. It is also important to consider that many participants in our study had quite mild strokes, as evidenced by almost all participants being able to complete a full 2–3 hour assessment. It is therefore possible that those with severe strokes and more significant disability were not invited to participate in the study, hence introducing further recruitment bias and impacting the generalizability to the broader stroke population. Further studies with larger and more diverse samples, and more communicatively accessible and inclusive recruitment processes, are still needed to determine the overall prevalence of cognitive impairment, anxiety, depression, and fatigue following different acute treatments for ischemic stroke.

Nonetheless, our study has several strengths including being the first to comprehensively assess the neuropsychological outcomes of patients treated with ECR through prospective methods. Including measures commonly used by clinicians in neuropsychological assessments means our findings are readily translatable to clinical practice, for example, by guiding test selection to detect likely areas of reduced performance or impairment (Rabin et al., 2016). Additionally, the differences between the treatment groups in stroke severity and location of occlusion are more generalizable to the wider stroke population, as current stroke guidelines recommend treatment with ECR for all eligible patients presenting with large vessel occlusions (Heran et al., 2024; Powers et al., 2019; Turc et al., 2019). It would not be practical, or ethical, to randomize patients with large vessel occlusions to different treatment groups for the purpose of cognitive assessment. We were therefore able to gain valuable insights into how acute treatments impact the neuropsychological outcomes of stroke survivors in a sample that is reflective of the real-world clinical setting. Although the differences in location of occlusion between those treated with ECR and SMC make the findings more generalizable to the wider stroke population, this does mean that interpretation of differences in cognitive function between the groups is confounded by differences in location of occlusion and cannot be solely attributed to the different acute treatments.

Conclusion

In our study, we found that treatment with ECR was associated with better cognitive and functional outcomes compared to SMC. Participants treated with ECR also experienced less post-stroke fatigue than those treated with SMC. We did not find any significant differences between groups on measures of anxiety or depression. Despite observing less cognitive impairment and

fatigue in the ECR group, these symptoms were still common for these participants (77% cognitive impairment and 52% for fatigue), indicating that cognitive impairment and fatigue continue to impact the lives of patients treated with ECR. This has important practical implications for stroke rehabilitation, and routine assessment of cognition, emotion, and fatigue is recommended regardless of acute stroke treatment and functional outcome to improve the quality of life of stroke survivors.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S1355617724000535>.

Funding statement. Sam Humphrey was supported by a Summer Foundation 2019 Allen Martin Research Scholarship.

Competing interests. None.

References

- Acciarresi, M., Bogousslavsky, J., & Paciaroni, M. (2014). Post-stroke fatigue: epidemiology, clinical characteristics and treatment. *European Neurology*, 72(5-6), 255–261.
- Barbay, M., Diouf, M., Roussel, M., Godefroy, O., & GRECOGVASC study group (2018). Systematic review and meta-analysis of prevalence in post-stroke neurocognitive disorders in hospital-based studies. *Dementia and Geriatric Cognitive Disorders*, 46(5-6), 322–334.
- Benedict, R. (1997). *Brief visuospatial memory test—revised*. Psychological Assessment Resources, Inc.
- Broome, L. J., Battle, C. E., Lawrence, M., Evans, P. A., & Dennis, M. S. (2016). Cognitive outcomes following thrombolysis in acute ischemic stroke: A systematic review. *Journal of Stroke and Cerebrovascular Diseases*, 25(12), 2868–2875.
- Burton, C. A. C., Murray, J., Holmes, J., Astin, F., Greenwood, D., & Knapp, P. (2013). Frequency of anxiety after stroke: A systematic review and meta-analysis of observational studies. *International Journal of Stroke*, 8(7), 545–559.
- Carmo, J. F. do, Morelato, R. L., Pinto, H. P., & Oliveira, E. R. A. (2015). Disability after stroke: A systematic review. *Fisioterapia Em Movimento*, 28(2), 407–418.
- Crocker, T. F., Brown, L., Lam, N., Wray, F., Knapp, P., & Forster, A. (2021). Information provision for stroke survivors and their carers. *Cochrane Database of Systematic Reviews*, 11(11), CD001919.
- Culbertson, W., & Zillmer, E. (2005). *Tower of London—Drexel university*. (2nd ed.). Multi-Health Systems.
- Cumming, T. B., Brodtmann, A., Darby, D., & Bernhardt, J. (2014). The importance of cognition to quality of life after stroke. *Journal of Psychosomatic Research*, 77(5), 374–379.
- De Rubeis, G., Ghozy, S., Fabiano, S., Pampana, E., Lanzino, G., Saba, L., & Kallmes, D. F. (2023). The Effect of Mechanical Thrombectomy on the Incidence of Poststroke Cognitive Impairment: A Systematic Review of Inhomogeneous Literature. *Cerebrovascular Diseases*, 52(6), 711–719.
- Delis, D., Kaplan, E., & Kramer, J. (2001). *Delis-Kaplan executive function system: Technical manual*. The Psychological Corporation.
- Embers, J., Lees, K. R., Lyden, P., Blackwell, L., Albers, G., Bluhmki, E., Brott, T., Cohen, G., Davis, S., Donnan, G., Grotta, J., Howard, G., Kaste, M., Koga, M., von Kummer, R., Lansberg, M., Lindley, R. I., Murray, G., Olivot, J. M., ... Hacke, W. (2014). Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: A meta-analysis of individual patient data from randomised trials. *The Lancet*, 384(9958), 1929–1935.
- Feigin, V. L., Brainin, M., Norrving, B., Martins, S., Sacco, R. L., Hacke, W., Fisher, M., Pandian, J., & Lindsay, P. (2022). World stroke organization (WSO): Global stroke fact sheet 2022. *International Journal of Stroke*, 17(1), 18–29.
- Feigin, V. L., Stark, B. A., Johnson, C. O., Roth, G. A., Bisignano, C., Abady, G. G., Abbasifard, M., Abbasi-Kangevari, M., Abd-Allah, F., Abedi, V., Abualhasan, A., Abu-Rmeileh, N. M. E., Abushouk, A. I., Adebayo, O. M., Agarwal, G., Agasthi, P., Ahinkorah, B. O., Ahmad, S., Ahmadi, S., ... Murray, C. J. L. (2021). Global, regional, and national burden of stroke and its risk factors, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. *The Lancet Neurology*, 20(10), 795–820.
- Gallucci, L., Sperber, C., Guggisberg, A. G., Kaller, C. P., Heldner, M. R., Monsch, A. U., Hakim, A., Silimon, N., Fischer, U., Arnold, M., & Umarova, R. M. (2024). Post-stroke cognitive impairment remains highly prevalent and disabling despite state-of-the-art stroke treatment. *International Journal of Stroke*, 19(8), 888–897.
- Galvin, J. E., Roe, C. M., Powlishta, K. K., Coats, M. A., Muich, S. J., Grant, E., Miller, J. P., Storandt, M., & Morris, J. C. (2005). The AD8: A brief informant interview to detect dementia. *Neurology*, 65(4), 559–564.
- Goyal, M., Menon, B. K., van Zwam, W. H., Dippel, D. W. J., Mitchell, P. J., Demchuk, A. M., Dávalos, A., Majoie, C. B. L. M., van der Lugt, A., de Miquel, M. A., Donnan, G. A., Roos, Y. B. W. E. M., Bonafe, A., Jahan, R., Diener, H.-C., van den Berg, L. A., Levy, E. I., Berkhemer, O. A., Pereira, V. M., ... Jovin, T. G. (2016). Endovascular thrombectomy after large-vessel ischaemic stroke: A meta-analysis of individual patient data from five randomised trials. *The Lancet*, 387(10029), 1723–1731.
- Graber, M., Garnier, L., Duloquin, G., Mohr, S., Guillemin, S., Ramaget, O., Piver, A., Tainturier, C., Bret-Legrand, C., Delpont, B., Blanc-Labarre, C., Guénat, J., Hervieu-Bègue, M., Ossey, G.-V., Giroud, M., & Béjot, Y. (2019). Association between fatigue and cognitive impairment at 6 months in patients with ischemic stroke treated with acute revascularization therapy. *Frontiers in Neurology*, 10, 931.
- Grace, J., & Malloy, P. (2001). *Frontal systems behaviour scale: Professional manual*. Psychological Assessment Resources, Inc.
- Grönberg, A., Henriksson, I., Stenman, M., & Lindgren, A. G. (2022). Incidence of aphasia in ischemic stroke. *Neuroepidemiology*, 56(3), 174–182.
- Hachinski, V., Iadecola, C., Petersen, R. C., Breteler, M. M., Nyenhuis, D. L., Black, S. E., Powers, W. J., DeCarli, C., Merino, J. G., Kalaria, R. N., Vinters, H. V., Holtzman, D. M., Rosenberg, G. A., Wallin, A., Dichgans, M., Marler, J. R., & Leblanc, G. G. (2006). National institute of neurological disorders and stroke–Canadian stroke network vascular cognitive impairment harmonization standards. *Stroke*, 37(9), 2220–2241.
- Hackett, M. L., & Pickles, K. (2014). Part I: Frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. *International Journal of Stroke*, 9(8), 1017–1025.
- Heran, M., Lindsay, P., Gubitz, G., Yu, A., Ganesh, A., Lund, R., Arsenault, S., Bickford, D., Derbyshire, D., Doucette, S., Ghrooda, E., Harris, D., Kanya-Forstner, N., Kaplovitch, E., Liederman, Z., Martiniuk, S., McClelland, M., Milot, G., Minuk, J., ... Shamy, M. (2024). Canadian stroke best practice recommendations: Acute stroke management, 7th edition practice guidelines update, 2022. *Canadian Journal of Neurological Sciences / Journal Canadien Des Sciences Neurologiques*, 51(1), 1–31.
- Jak, A. J., Bondi, M. W., Delano-Wood, L., Wierenga, C., Corey-Bloom, J., Salmon, D. P., & Delis, D. C. (2009). Quantification of five neuropsychological approaches to defining mild cognitive impairment. *The American Journal of Geriatric Psychiatry: Official Journal of the American Association for Geriatric Psychiatry*, 17(5), 368–375.
- Jokinen, H., Melkas, S., Ylikoski, R., Pohjasvaara, T., Kaste, M., Erkinjuntti, T., & Hietanen, M. (2015). Post-stroke cognitive impairment is common even after successful clinical recovery. *European Journal of Neurology*, 22(9), 1288–1294.
- Kaplan, E., Goodglass, H., & Weintraub, S. (1983). *Boston naming test*. (2nd ed.). Lea & Febiger.
- Kapoor, A., Lancôt, K. L., Bayley, M., Kiss, A., Herrmann, N., Murray, B. J., & Swartz, R. H. (2017). Good outcome, isn't good enough: Cognitive impairment, depressive symptoms, and social restrictions in physically recovered stroke patients. *Stroke*, 48(6), 1688–1690.
- Knapp, P., Dunn-Roberts, A., Sahib, N., Cook, L., Astin, F., Kontou, E., & Thomas, S. A. (2020). Frequency of anxiety after stroke: An updated systematic review and meta-analysis of observational studies. *International Journal of Stroke*, 15(3), 244–255.
- Kobeissi, H., Adusumilli, G., Ghozy, S., Bilgin, C., Kadirvel, R., Brinjikji, W., Heit, J. J., Rabinstein, A. A., & Kallmes, D. F. (2023). Mechanical thrombectomy alone versus with thrombolysis for ischemic stroke: A meta-analysis of randomized trials. *Interventional Neuroradiology*. 159101992311543 (Advance online publication).

- Krupp, L., Larocca, N., Muir-Nash, J., & Steinberg, A. (1989). The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of Neurology*, 46(10), 1121–1123.
- Lattanzi, S., Coccia, M., Pulcini, A., Cagnetti, C., Galli, F. L., Villani, L., Campa, S., Dobran, M., Polonara, G., Ceravolo, M. G., & Silvestrini, M. (2020). Endovascular treatment and cognitive outcome after anterior circulation ischemic stroke. *Scientific Reports*, 10(1), 18524.
- Liu, L., Xu, M., Marshall, I. J., Wolfe, C. D., Wang, Y., & O'Connell, M. D. (2023). Prevalence and natural history of depression after stroke: A systematic review and meta-analysis of observational studies. *PLOS Medicine*, 20(3), e1004200.
- López-Cancio, E., Jovin, T. G., Cobo, E., Cerdá, N., Jiménez, M., Gomis, M., Hernández-Pérez, M., Cáceres, C., Cardona, P., Lara, B., Renú, A., Llull, L., Boned, S., Muchada, M., & Dávalos, A. (2017). Endovascular treatment improves cognition after stroke: A secondary analysis of REVASCAT trial. *Neurology*, 88(3), 245–251.
- Mahoney, F., & Barthel, D. (1965). Functional evaluation: The barthel index: A simple index of independence useful in scoring improvement in the rehabilitation of the chronically ill. *Maryland State Medical Journal*, 14, 61–65.
- McCarthy, D. J., Diaz, A., Sheinberg, D. L., Snelling, B., Luther, E. M., Chen, S. H., Yavagal, D. R., Peterson, E. C., & Starke, R. M. (2019). Long-term outcomes of mechanical thrombectomy for stroke: A meta-analysis. *The Scientific World Journal*, 2019, 1–9.
- Melkas, S., Oksala, N. K. J., Jokinen, H., Pohjasvaara, T., Vataja, R., Oksala, A., Kaste, M., Karhunen, P. J., & Erkinjuntti, T. (2009). Poststroke dementia predicts poor survival in long-term follow-up: Influence of prestroke cognitive decline and previous stroke. *Journal of Neurology, Neurosurgery & Psychiatry*, 80(8), 865–870.
- Menlove, L., Crayton, E., Kneebone, I., Allen-Crooks, R., Otto, E., & Harder, H. (2015). Predictors of anxiety after stroke: A systematic review of observational studies. *Journal of Stroke and Cerebrovascular Diseases*, 24(6), 1107–1117.
- Nasreddine, Z. S., Phillips, N. A., Bäckström, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The montreal cognitive assessment, MoCA: A Brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699.
- Nouri, F., & Lincoln, N. (1987). An extended activities of daily living scale for stroke patients. *Clinical Rehabilitation*, 1(4), 301–305.
- Nys, G. M. S., Van Zandvoort, M. J. E., De Kort, P. L. M., Van Der Worp, H. B., Jansen, B. P. W., Algra, A., De Haan, E. H. F., & Kappelle, L. J. (2005). The prognostic value of domain-specific cognitive abilities in acute first-ever stroke. *Neurology*, 64(5), 821–827.
- Oksala, N. K. J., Jokinen, H., Melkas, S., Oksala, A., Pohjasvaara, T., Hietanen, M., Vataja, R., Kaste, M., Karhunen, P. J., & Erkinjuntti, T. (2009). Cognitive impairment predicts poststroke death in long-term follow-up. *Journal of Neurology, Neurosurgery & Psychiatry*, 80(11), 1230–1235.
- Orkin, A. M., Gill, P. J., Ghersi, D., Campbell, L., Sugarman, J., Emsley, R., Steg, P. G., Weijer, C., Simes, J., Rombey, T., Williams, H. C., Wittes, J., Moher, D., Richards, D. P., Kasamon, Y., Getz, K., Hopewell, S., Dickersin, K., Wu, T., ... Concato, J. (2021). Guidelines for reporting trial protocols and completed trials modified due to the COVID-19 pandemic and other extenuating circumstances: The CONSERVE 2021 statement. *JAMA*, 326(3), 257.
- Paciaroni, M., & Acciarresi, M. (2019). Poststroke Fatigue. *Stroke*, 50(7), 1927–1933.
- Pearson (2009). *Advanced clinical solutions for the WAIS-IV and WMS-IV*. Pearson Education.
- Pendlebury, S. T., & Rothwell, P. M. (2009). Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: A systematic review and meta-analysis. *The Lancet Neurology*, 8(11), 1006–1018.
- Powers, W. J., Rabinstein, A. A., Ackerson, T., Adeoye, O. M., Bambakidis, N. C., Becker, K., Biller, J., Brown, M., Demmaerschalk, B. M., Hoh, B., Jauch, E. C., Kidwell, C. S., Leslie-Mazwi, T. M., Ovbiagele, B., Scott, P. A., Sheth, K. N., Southerland, A. M., Summers, D. V., Tirschwell, D. L., & on behalf of the American Heart Association Stroke Council (2019). Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals From the American heart association/American stroke association. *Stroke*, 50(12), e344–e418.
- Przybylowski, C. J. (2014). Evolution of endovascular mechanical thrombectomy for acute ischemic stroke. *World Journal of Clinical Cases*, 2(11), 614.
- Rabin, L. A., Paolillo, E., & Barr, W. B. (2016). Stability in test-usage practices of clinical neuropsychologists in the United States and Canada over a 10-year period: A follow-up survey of INS and NAN members. *Archives of Clinical Neuropsychology*, 31(3), 206–230.
- Radman, N., Staub, F., Aboulafia-Brakha, T., Berney, A., Bogousslavsky, J., & Annoni, J.-M. (2012). Poststroke fatigue following minor infarcts: A prospective study. *Neurology*, 79(14), 1422–1427.
- Robinson, R. G., & Jorge, R. E. (2016). Post-stroke depression: A review. *American Journal of Psychiatry*, 173(3), 221–231.
- Rost, N. S., Brodtmann, A., Pase, M. P., van Veluw, S. J., Biffi, A., Duering, M., Hinman, J. D., & Dichgans, M. (2022). Post-stroke cognitive impairment and dementia. *Circulation Research*, 130(8), 1252–1271.
- Samuels, N., Compagne, K. C. J., Van Der Ende, N. A. M., Chalos, V., Konduri, P. R., Van Doormaal, P. J., Van Zwam, W. H., Majoie, C. B. L. M., Marquering, H. A., Roozenbeek, B., Lingsma, H. F., Dippel, D. W. J., & Van Der Lugt, A. (2023). Infarct volume after ischemic stroke as a mediator of the effect of endovascular thrombectomy on early postprocedural neurologic deficit. *Journal of Stroke and Cerebrovascular Diseases*, 32(2), 106906.
- Schmidt, M. (1996). *Rey auditory verbal learning test: A handbook*. Western Psychological Services.
- State of Victoria, Department of Health and Human Services (2018). *Endovascular clot retrieval for acute stroke; Statewide service protocol for Victoria*. Safer Care Victoria. <https://bettersafercare.vic.gov.au/resources/clinical-guidance/stroke-clinical-network/endovascular-clot-retrieval-protocol>.
- Staub, F., & Bogousslavsky, J. (2001). Fatigue after stroke: A major but neglected issue. *Cerebrovascular Diseases*, 12(2), 75–81.
- Stolwyk, R. J., Mihaljcic, T., Wong, D. K., Chapman, J. E., & Rogers, J. M. (2021). Poststroke cognitive impairment negatively impacts activity and participation outcomes: A systematic review and meta-analysis. *Stroke*, 52(2), 748–760.
- Stroke Foundation (n.d.). *Clinical guidelines for stroke management*. Stroke Foundation. https://files.magicapp.org/guideline/04cdab8a-c6eb-4969-b761-94fed9bd85e9/published_guideline_7404-9_4.pdf
- Tombaugh, T. (1999). Normative data stratified by age and education for two measures of verbal fluency FAS and animal naming. *Archives of Clinical Neuropsychology*, 14(2), 167–177.
- Tombaugh, T. (2004). Trail making test A and B: Normative data stratified by age and education. *Archives of Clinical Neuropsychology*, 19(2), 203–214.
- Turc, G., Bhogal, P., Fischer, U., Khatri, P., Lobotesis, K., Mazighi, M., Schellinger, P. D., Toni, D., De Vries, J., White, P., & Fiehler, J. (2019). European stroke organisation (ESO) – European society for minimally invasive neurological therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischaemic stroke endorsed by stroke alliance for Europe (SAFE). *European Stroke Journal*, 4(1), 6–12.
- Turner, G. M., McMullan, C., Atkins, L., Foy, R., Mant, J., & Calvert, M. (2019). TIA and minor stroke: A qualitative study of long-term impact and experiences of follow-up care. *BMC Family Practice*, 20(1), 176.
- Van Der Zee, C. H., Visser-Meily, J. M. A., Lindeman, E., Jaap Kappelle, L., & Post, M. W. M. (2013). Participation in the chronic phase of stroke. *Topics in Stroke Rehabilitation*, 20(1), 52–61.
- Van Swieten, J. C., Koudstaal, P. J., Visser, M. C., Schouten, H. J., & Van Gijn, J. (1988). Interobserver agreement for the assessment of handicap in stroke patients. *Stroke*, 19(5), 604–607.
- Wang, Y., Wu, X., Zhu, C., Mossa-Basha, M., & Malhotra, A. (2021). Bridging Thrombolysis Achieved Better Outcomes Than Direct Thrombectomy After Large Vessel Occlusion: An Updated Meta-analysis. *Stroke*, 52(1), 356–365.
- Wechsler, D. (2009). *Wechsler adult intelligence scale-fourth edition (WAIS-IV), Australian and New Zealand language adaptation*. NCS Pearson, Inc.
- Wechsler, D. (2009). *Wechsler memory scale-fourth edition (WMS-IV), Australian and New Zealand language adaptation*. NCS Pearson, Inc.
- White, C. L., Barrientos, R., & Dunn, K. (2014). Dimensions of uncertainty after stroke: Perspectives of the stroke survivor and family caregiver. *Journal of Neuroscience Nursing*, 46(4), 233–240.

- Wijeratne, T., & Sales, C. (2021). Understanding why post-stroke depression may be the norm rather than the exception: The anatomical and neuroinflammatory correlates of post-stroke depression. *Journal of Clinical Medicine*, 10(8), 1674.
- Wilson, B., Cockburn, J., & Halligan, P. (1987). *Behavioural inattention test*. Thames Valley Test Company.
- Wong, C. G., Thomas, K. R., Edmonds, E. C., Weigand, A. J., Bangen, K. J., Eppig, J. S., Jak, A. J., Devine, S. A., Delano-Wood, L., Libon, D. J., Edland, S. D., Au, R., & Bondi, M. W. (2018). Neuropsychological criteria for mild cognitive impairment in the framingham heart study's Old-Old. *Dementia and Geriatric Cognitive Disorders*, 46(5-6), 253–265.
- Xu, G., Dong, X., Niu, X., Zheng, G., Wang, H., Zhang, F., Li, L., & Lv, P. (2017). Cognitive function and prognosis of multimodal neuroimage-guided thrombectomy on mild to moderate anterior circulation infarction patients with broadened therapeutic window: A prospective study. *European Neurology*, 78(5-6), 257–263.
- Zhan, J., Zhang, P., Wen, H., Wang, Y., Yan, X., Zhan, L., Chen, H., Xu, N., & Lu, L. (2022). Global prevalence estimates of poststroke fatigue: A systematic review and meta-analysis. *International Journal of Stroke*, 18(9), 1387–1050.
- Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, 67(6), 361–370.