Therapeutics and Clinical Risk Management

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Brain Frailty on Neuroimaging Beyond Chronological Age Is Associated with Functional Outcome After Endovascular Thrombectomy in Patients with Anterior Large Vessel Occlusion

Jinrui Li[1,2,*], Junting Chen[3,4,*], Kailin Cheng[3,5], Jianxia Ke[1,5], Jintao Li[1,5], Jia Wen[3,5], Xiaoli Fu[1,5,*], Zhu Shi[1,3,5,*]

[1]Department of Neurology and Stroke Center, Dongguan People's Hospital, Southern Medical University, Dongguan, Guangdong, People's Republic of China; [2]Department of Neurology, Nanyang Central Hospital, Henan Province, Nanyang, Henan, People's Republic of China; [3]Postgraduate School, Guangdong Medical University, Zhanjiang, Guangdong, People's Republic of China; [4]Department of Neurology, Houjie Hospital, Guangdong Medical university, Dongguan, Guangdong, People's Republic of China; [5]Department of Neurology, The 10th Affiliate Hospital, Southern Medical University, Dongguan, Guangdong, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xiaoli Fu, Email cocofuxiaoli@163.com; Zhu Shi, Email sound_shi@126.com

Background: Current guidelines have not recommended an upper age limit for endovascular thrombectomy (EVT) in patients with large vessel occlusion (LVO) stroke. However, elder age links to an increased risk of poor outcome. This study aimed to investigate the efficacy of EVT in elderly versus non-elderly patients and determine the respective factors of poor outcome.

Methods: Three hundred and two consecutive patients with LVO-stroke who underwent EVT were included, and we used sensitivity analysis with restricted cubic spline to define 75 years as the inflexion point. Participants were thus dichotomized into elderly (≥75 years) and non-elderly (<75 years) groups. Brain frailty on neuroimaging was evaluated using the global cortical atrophy (GCA) scale and the Fazekas scale for white matter lesions (WML). The primary outcome was 3-month functional outcome, and the secondary outcomes were EVT efficacy and safety.

Results: Elderly patients had significantly higher incidences of hypertension, diabetes mellitus, atrial fibrillation, and more severe GCA and WML. The rate of good outcome in elderly patients was 32%, significantly lower than non-elderly patients (54%, $p<0.001$). There was no difference in terms of reperfusion (89% vs 93%, $p=0.363$) and intracranial hemorrhage (38% vs 41%, $p=0.826$) between two groups. In elderly patients, high degree of GCA (OR 1.15, 95% CI 1.02–1.30, $p=0.012$) and moderate/severe WML (OR 5.88, 95% CI 1.47–23.50, $p=0.015$) independently predicted 3-month poor outcomes.

Conclusion: GCA and WML play pivotal roles for the functional outcomes in elderly patients undergoing EVT for LVO-stroke, providing valuable and practical information for early prediction of long-term prognosis.

Keywords: stroke, endovascular thrombectomy, prognosis, elderly, brain frailty

Introduction

Large vessel occlusion (LVO) represents a substantial proportion, nearly 29–38%, of all acute ischemic strokes,[1,2] and is the predominant subtype leading to disability and mortality, accounting for 61.6% of post-stroke dependency and 95.6% of post-stroke mortality.[3] Endovascular thrombectomy (EVT) significantly improves the prognosis of LVO stroke and has become the standard care for patients with anterior circulation LVO.[4,5] However, extrapolation of these evidences from randomized clinical trials (RCT) to elderly patients remains challenging[6–8] because elderly patients were excluded or underrepresented in previous RCT studies. On the other hand, the proportion of elderly patients eligible for EVT is expected to substantially increase due to the continuing trend of global population aging.

Received: 18 October 2024
Accepted: 7 February 2025
Published: 18 February 2025

There is no consensus definition of the elderly, with the minimum age for classification typically ranging between 65 and 70 years. According to the National Institute on Aging consensus, the elder was further subdivided into "young-old" (65–74 years) and "old-old" (≥75 years).[9] Although chronological age per se has been recognized as a determinant for post-stroke disability and mortality after EVT,[10–12] biological age seems to play a more crucial role. Brain frailty, in terms of cortical neuronal atrophy (GCA) and white matter lesions (WML), was indicated as a better neuroimaging indicator of biological age influencing the long-term recovery after stroke.[13,14] Although EVT was recommended as eligible for all age groups,[11] chronological age has not displayed a linear association with functional outcomes. For the elderly, further priority should be directed towards long-term functional recovery and quality of life, instead of periprocedural survival. A meta-analysis of 3456 patients showed that LVO patients with moderate-to-severe WML were at increased risk for disability and mortality after EVT,[15] and the ESCAPE-NA1 post-hoc study reported that LVO patients with severe GCA had worse 90-day functional outcomes after EVT.[16] Currently, however, there are no data on comparative studies integrating chronological age and brain frailty structural parameters representing biological age.

In this study, we first analyzed the association between chronological age and long-term functional outcomes in acute stroke patients treated with EVT for anterior LVO. Furthermore, we evaluated the association of GCA and WML with the efficacy and safety of EVT procedures, as well as the long-term functional outcome. Finally, the differential effects of GCA and WML in the context of chronological age stratification were additionally compared.

Methods

Study Population

This was a retrospective observational study that was approved by the ethics committee of Dongguan People's Hospital (KYKT2022-066) and conformed to the Declaration of Helsinki, and all patients or relatives provided informed consent for data collection.

From a prospectively compiled database of our university hospital, we enrolled consecutive patients undergoing EVT for acute anterior LVO stroke from January 2018 to February 2023. All included patients were treated according to our institution's stroke protocol, which is based on the latest international guidelines.[17] Patients were assessed by a stroke specialist upon admission, and intravenous thrombolysis was performed if symptoms presented within a 4.5-hour time window. Patients suspected of LVO received multimodal CT screening, and EVT eligibility was determined by the stroke center's neurointerventional surgeons based on DAWN or DEFUSE-3 criteria.[4,18] EVT was performed using approved EVT devices and techniques such as stent retrievers, large-bore aspiration catheters, or a combination of both, at the discretion of the attending neurosurgeon.

The following were the inclusion criteria: (1) age > 18 years; (2) proximal anterior circulation large vessel occlusion involving the intracranial internal carotid artery, the first segment of the middle cerebral artery (M1), or both; (3) premorbid mRS ≤ 2; and (4) baseline Alberta Stroke Program Early Computed Tomography Score (ASPECTS) > 6. The exclusion criteria were as following: (1) occlusion of posterior circulation vessels; (2) evidence of recent intracranial hemorrhage; (3) presence of severe systemic illnesses, such as malignant tumors, significant renal insufficiency, cardiac insufficiency, and other conditions; (4) other etiologies of cerebral white matter lesions including infection, inflammatory demyelinating diseases and degenerative diseases of the central nervous system; (5) poor imaging quality or missing follow-up data.

Data Collection

Clinical data, including patient demographics, risk factors, lab tests, EVT procedural details, and follow-up outcomes were retrieved from an electronic medical record system and collected by experienced neurologists using a standardized table. Picture Archiving and Communication Systems (PACS) were used to evaluate the LVO site, infarction territory, collateral circulation grading, reperfusion status (modified Thrombolysis in Cerebral Infarction) mTICI grade, and the presence of intracranial hemorrhage. We assessed pretreatment collateral circulation grade of each patient on brain angiography before performing EVT according to the American Society for Interventional and Therapeutic

Neuroradiology /American Society of Interventional Radiology (ASITN/SIR) criteria.[19] ASITN/SIR score of 3–4 was defined as good collaterals, 1–2 moderate collaterals, and 0 poor collaterals.

Evaluation of GCA and WML

Baseline non-contrast computed tomography (CT) scans were used to assess GCA and WML. Brain atrophy was assessed using the GCA scale.[20] This scale systematically evaluated the extent of brain atrophy in 13 different regions of the brain. Firstly, the expansion status of cortical sulci in the frontal lobe, parietal lobe, and temporal lobe were evaluated with GCA. Secondly, the ventricular GCA scores were used to assess the ventricular dilatation in the frontal lobe, parietal lobe, temporal lobe, and the third ventricle. Each assessment region was assigned a score ranging from 0 to 3. GCA 0 indicated no cortical atrophy, GCA 1 indicated mild atrophy (sulcal widening), GCA 2 indicated moderate atrophy (brain volume loss), and GCA 3 indicated severe atrophy (severe knife blade atrophy). The overall GCA scores ranged from 0 (no atrophy) to 39 (maximum atrophy) and were further divided into cortical GCA scores (ranging from 0 to 18) and ventricular GCA scores (ranging from 0 to 21). In order to investigate the contributions of regional brain atrophy, the sum of atrophy scores for the frontal, parietal, temporal lobes, and ventricular regions in both hemispheres was calculated. Additionally, the Evans' index was a measurement of the maximum width of the frontal horns divided by the internal width of the cranium.[21] Both diameters were measured on the same CT scan image. The severity of white matter lesions was assessed using the Fazekas scale as described previously.[22]

The anonymous offline analysis of the baseline CT scans was performed by an experienced neuroradiologist (XF) and a stroke specialist (GL). Both readers were blinded to all clinical information. Image quality was first scored by two reviewers on a scale of 1–3 (1=poor, 2=pass, 3=good). Images rated as 1 by any reviewer due to severe motion artifacts or low signal-to-noise ratio were excluded. There was good agreement in the degree of GCA (κ=0.828) and WML (κ=0.883). In any event of disagreement, a third senior stroke expert (ZS) determined the final interpretation.

Definition of Outcomes

The primary outcome was the 3-month functional outcome assessed using the modified Rankin Scale (mRS). An mRS score of 0 to 2 was considered as a favorable functional outcome.

The secondary outcomes included post-procedural reperfusion based on mTICI, ICH and malignant cerebral edema (MCE). ICH was determined by the presence of hyperintensity on follow-up CT immediately after EVT. If the hyperintensity on the CT could not be distinguished from contrast leakage, a follow-up CT was conducted, and the persistent hyperintensity after 24 hours was recorded as ICH. A symptomatic ICH (sICH) was defined as the presence of ICH on CT, along with neurological worsening (increase of ≥4 in NIHSS score). MCE was defined by the presence of all the following criteria:[23] (1) acute infarction with hypodensity of ≥50% of the middle cerebral artery territory, (2) signs of brain swelling such as sulcal effacement or compression of the lateral ventricle, (3) midline shift at the septum pellucidum >5 mm with effacement of the basal cisterns within 7 d post-EVT, and (4) neurological deterioration (increase of ≥4 in NIHSS score).

Statistics

Statistical analysis was performed using SPSS 22.0 (IBM SPSS Statistics, Chicago, IL, USA). Continuous variables were expressed as means ± standard deviation or medians (interquartile range) and qualitative variables were expressed as numbers (percentage). Normality of distributions was evaluated using histograms and the Shapiro–Wilk test. Continuous variables were compared between younger geriatric group and older geriatric group using *t*-test or nonparametric Mann–Whitney *U*-test, and chi-square test as appropriate. Univariate and multivariate logistic regressions were used to determine independent predictors of poor outcome at 3-month defined by mRS scores of 3–6 in accordance with our previous statistical analyses. A p-value<0.05 was considered significant.

Results

During the study period, 404 patients with acute ischemic stroke underwent EVT and 75 cases were excluded due to the presence of infarcts in the posterior circulation. The following patients were further excluded: 13 patients with systemic

complications such as tumors, severe infections, cardiac, renal failure or other definite causes of cerebral WML; 5 patients with bilateral LVO; 2 patients with pre-admission mRS scores≥2; 1 patient with admission ASPECT scores of 5; and 6 patients with missing or incomplete follow-up data. Three hundred and two patients were included in the final analysis (Figure 1). Among the patients included, the mean age was 64.2±12.8 years with 207 (68.5%) being male. The average cortical GCA score was 3.2±3.5, the average ventricular GCA score was 4.8±4.4, and the overall GCA score was 8.0±7.3. A total of 33% of participants were classified as moderate /severe WML. Two hundred and seventy-seven (91.2%) patients achieved successful reperfusion, while 122 (40.1%) patients experienced ICH, 36 (11.9%) experienced sICH and 76 (25.1%) exhibited MCE. At 3-month follow-up, 147 (48.7%) cases demonstrated favorable outcomes and 40 (13.2%) cases died.

First, we compared the proportions of patients with good versus poor outcomes across chronological age intervals (per 10 years). There was a tendency for higher proportion of poor outcomes at 3-month follow-up with increasing age. Elderly patients aged ≥70 years demonstrated a poor outcomes rate exceeding 50%, while those ≤70 years had a rate below 50% (Figure 2A). To further explore the effect of age on outcomes, sensitivity analysis was carried out utilizing restricted cubic splines without predefined cut-off criteria, and a dose–response relationship was observed between chronological age and poor outcomes (p for overall=0.003; p for non-linearity=0.697) (Figure 2B). The risk of poor outcomes increased steadily until age 75 years; after age 75 years, there was a more pronounced tendency for poor outcomes. Based on the inflection point on RCS plot, we thereafter divided the patients into an elderly group (age ≥75 years; n=74) and a non-elderly group (age < 75 years; n=228).

Compared to the non-elderly group, the elderly group patients were more likely to be females (49% vs 26%, $p<0.001$) and had higher proportions of risk factors including hypertension (80% vs 54%, $p<0.001$), diabetes (34% vs 23%,

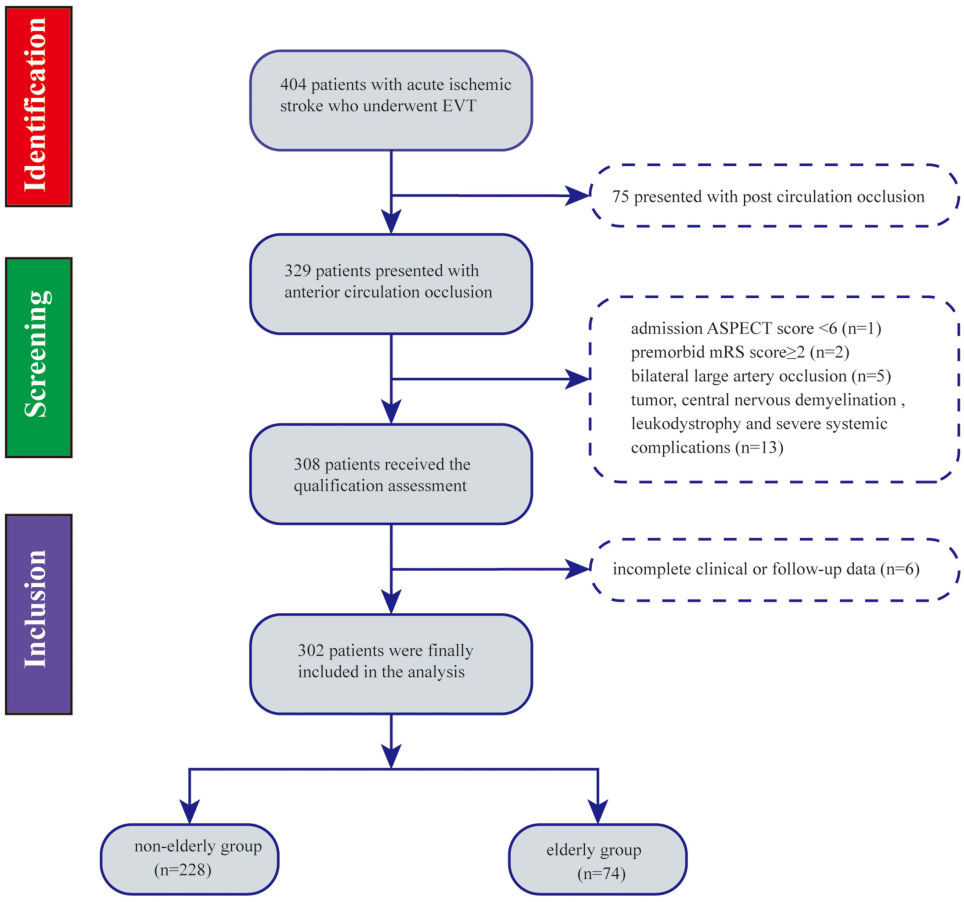

Figure 1 The flow chart of study participants.

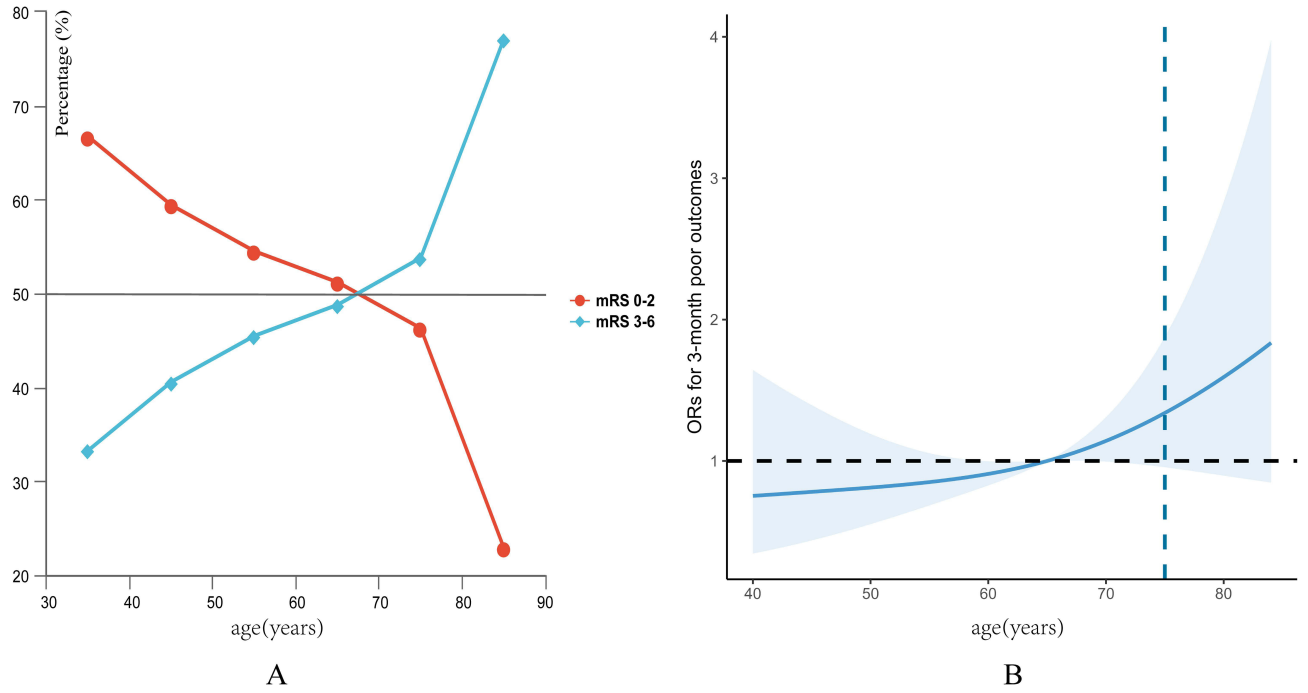

Figure 2 (**A**) Distribution of proportion of stroke patients with 3-month follow-up outcomes across different age intervals (per decade). (**B**) Restricted cubic spline showing the non-linear association of chronological age with 3-month functional disability. Blue lines indicated the cut-offs we applied.

p=0.060), and atrial fibrillation (61% vs 30%, *p*<0.001). The elderly patients also exhibited significantly higher NISS scores (16.0±7.3 vs 13.5±5.5, *p*=0.012) and systolic blood pressure (SBP) [151 (138,171) vs 144 (128,160) mmHg, *p*=0.008]. Furthermore, cardioembolic (CE) causes were mainly found in the elderly group (58%), while large artery atherosclerosis (LAA) was the primary etiology in the non-elderly group (59%). There were no significant differences observed between the two groups regarding occlusion sites, procedural parameters, anesthesia approaches and collateral circulation grading (Table 1).

There were significant differences in the severity of brain atrophy between the non-elderly and elderly groups (cortical GCA: 2.1±2.4 vs 6.9±3.8, *p*<0.001; ventricular GCA: 3.5±3.7 vs 8.8±3.9, *p*<0.001; overall GCA: 5.5±5.5 vs 15.7±6.9, *p*<0.001). In the non-elderly group, no significant differences were observed in WML and GCA between patients with favorable versus unfavorable outcomes. However, in the elderly group, patients with unfavorable outcome

Table 1 Comparison of Clinical Characteristics and Outcomes of the Study Population Stratified According to Age < 75 years Versus Age ≥ 75 years

	Non-Elderly Group (<75 year) n=228	**Elder Group (≥75 years) n=74**	***p*-value**
Demographic and risk factors			
Age (mean±SD)	59±10	80±4	<0.001
Male (n, %)	169 (74)	38 (51)	<0.001
Hypertension (n, %)	123 (54)	59 (80)	<0.001
Diabetes mellitus (n, %)	52 (23)	25 (34)	0.060
Atrial fibrillation (n, %)	68 (30)	45 (61)	<0.001
Smoking (n, %)	85 (37)	22 (30)	0.238

(*Continued*)

https://doi.org/10.2147/TCRM.S498094

Table 1 (Continued).

	Non-Elderly Group (<75 year) n=228	Elder Group (≥75 years) n=74	*p*-value
Current stroke characteristics			
NIHSS (mean±SD)	13.5±5.5	16.0±7.3	0.012
ASPECT (mean±SD)	8.9±1.3	9.0±1.1	0.736
SBP, mmHg, (M, IQR)	144 (128,160)	151 (138,171)	0.008
DBP, mmHg, (M, IQR)	86 (76,96)	83 (74,97)	0.216
TOAST classification (n, %)			
ICAS	134 (59)	29 (39)	0.001
CE	77 (34)	43 (58)	
UN	17 (8)	2 (3)	
Occlusion sites (n, %)			0.895
ICA	77 (34)	28 (38)	
MCA-1	96 (42)	29 (40)	
MCA-2	31 (14)	10 (14)	
Tandon	23 (10)	6 (8)	
Treatment characteristics			
OTP, min, (mean±SD)	415±301	333±270	0.009
PTR, min, (mean±SD)	92±43	99±60	0.812
iv thrombolysis (n, %)	87 (38)	21 (28)	0.127
Type of anesthesia (n, %)			
General anesthesia	136 (60)	39 (53)	0.293
Sedation	92 (40)	35 (47)	
ASTIN/SIR scale (n, %)			
Good (3–4)	88 (39)	32 (43)	0.478
Poor (0–2)	140 (61)	42 (57)	
Outcomes 3-month mRS			
mRS 0–2, n (%)	123 (54)	24 (32)	0.001
Death, n (%)	29 (13)	20 (27)	0.004
mTICI scales			
0–2a, n (%)	17 (8)	8 (11)	0.363
2b-3, n (%)	211 (93)	66 (89)	
Hemorrhagic transformation			
ICH, n (%)	94 (41)	28 (38)	0.826
sICH, n (%)	27 (12)	9 (12)	0.975
MCE, n (%)	59 (26)	17 (23)	0.617

Abbreviations: OTP, time from onset to groin puncture; PTR, time from groin puncture to re-perfusion; NIHSS, NIH Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; SBP, systolic blood pressure; DBP, diastolic blood pressure; MCE, malignant cerebral edema; mTICI, modified treatment in cerebral ischemia score; ICH, intracranial hemorrhage.

Table 2 Multi-Variable Logistic Regression Analysis of 3-month Functional Outcome According to Non-Elderly (Age < 75 Years) Versus Elderly Patients (Age ≥ 75 Years)

	Non-Elderly Patients (<75 years) n=228			Elder Patients (≥75 years) n=74		
3-Month mRS	**0–2 (n=123)**	**3–6 (n=105)**	***p*-value**	**0–2 (n=24)**	**3–6 (n=50)**	***p*-value**
Cerebral frailty						
WMH			0.147			0.004
None/mild (0–2), n (%)	98 (80)	75 (71)		15 (63)	14 (28)	
Moderate/severe (3–6), n (%)	25 (20.3)	30 (29)		9 (38)	36 (72)	
Brain atrophy						
Evans index (M, IQR)	0.26 (0.24,0.28)	0.26 (0.25,0.29)	0.121	0.28 (0.25,0.30)	0.28 (0.25,0.28)	0.643
Cortical GCA, (mean±SD)	1.68±1.91	2.50±2.75	0.055	3.29±2.39	8.6±3.13	<0.001
Ventricle GCA, (mean±SD)	3.15±3.44	3.84±3.94	0.310	4.92±2.81	10.66±2.77	<0.001
Total GCA, (mean±SD)	4.84±4.86	6.34±6.12	0.153	8.21±4.16	19.26±4.72	<0.001

Abbreviations: WMH, white matter hyperintensity; GCA, global cortical atrophy.

exhibited higher burden of WML and GCA compared to those with favorable outcome. (cortical GCA: 3.29±2.39 vs 8.6 ±3.13, p<0.001; ventricle GCA: 4.92±2.81 vs 10.66±2.77, p<0.001; total GCA: 8.21±4.16 vs 19.26±4.72, p<0.001; moderate/severe WML: 38% vs 72%, p=0.004) (Table 2 and Supplement Figure 1).

In terms of efficacy and safety of EVT procedure, no significant differences were observed between elderly versus non-elderly group. Both groups showed similar rates of revascularization (mTICI 2b/3) (89% vs 93%, *p*=0.063), ICH (38% vs 41%, *p*=0.826), sICH (12% vs 12%, *p*=0.975), and MCE (23% vs 26%, *p*=0.617). However, patients in the elderly group exhibited a significantly lower proportion of favorable outcomes at 3 months compared to the younger geriatric group (32% vs 54%, *p*=0.001), with a significantly higher mortality rate (27% vs 13%, *p*=0.001) (Table 1 and Supplement Figure 2).

Multivariable logistic regression was conducted separately in elderly versus non-elderly groups to compare risk factors of 3-month poor outcomes. Interestingly, we observed that the risk factors influencing poor outcomes in elderly group differed from those in non-elderly group. First, NHISS score was identified as independent risk factors for both groups (non-elderly group: OR 1.085, 95% CI 1.026–1.147, *p*=0.004; elderly group: OR 1.129, 95% CI 1.026–1.242, *p*=0.013). Poor collateral circulation was found to be an independent risk factor solely in non-elderly patients, showing no significant association in elderly patients (non-elderly group: OR 2.276, 95% CI 1.242–4.173, *p*=0.008; elderly group: OR 0.666, 95% CI 0.196–2.264, *p*=0.515). In contrast, moderate/severe WML was identified as an independent factor for poor outcome in elderly group, whereas it exhibited no significant association in non-elderly group (non-elderly group: OR:1.34, 95% CI 0.67–2.69, p=0.41; elderly group: OR:5.88, 95% CI: 1.47–23.50 p=0.015) (Figure 3).

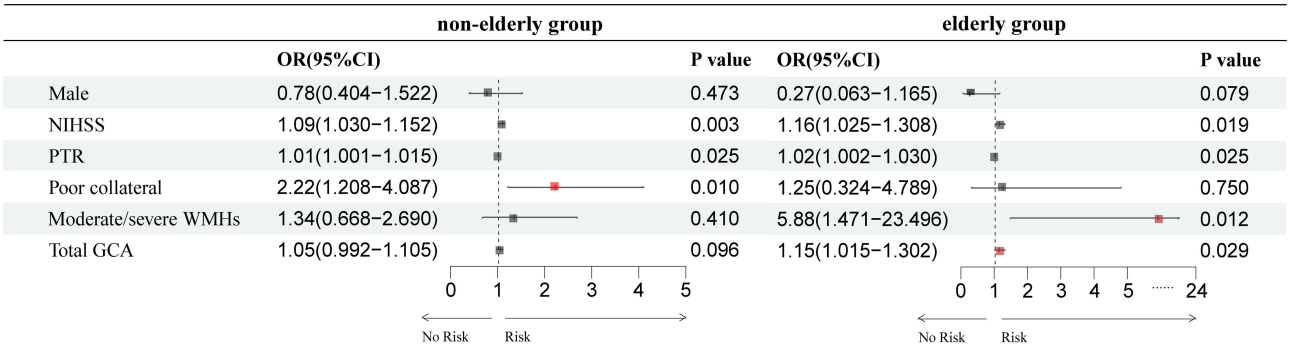

Figure 3 Forest plot of the odds ratio (OR)s of predictors for 3-month adverse functional outcome after stroke in elderly patients versus non-elderly patients.

https://doi.org/10.2147/TCRM.S498094

Discussion

The main findings of this study included: (1) There were no significant differences in efficacy and safety of EVT for anterior LVO stroke between elderly and younger patients, but higher risk for 3-month outcome and mortality was observed in elderly patients. (2) A chronological age of 75 years was found to be a significant inflection point for functional prognosis following endovascular therapy (EVT) in this study, with distinct prognostic factors for each age group. Good collateral circulation was an independent predictor of favorable outcomes in patients <75 yrs, while in those ≥75ys, brain frailty neuroimaging indicators were associated with poor outcomes.

A national registry study from 2012 to 2019 in the United States reported a substantial increase in elderly patients aged ≥80 years undertaking EVT treatment.[12] The NIHSS and chronological age are critical predictors of clinical outcomes, and age per se should not be a barrier to EVT eligibility. Although clinical evidence demonstrated that successful reperfusion and ICH complications after EVT in elderly patients were comparable to those observed in the non-elderly, ranging from 61% to 88% with sICH incidence of 20% to 35%, the proportion of 3-month favorable outcome varied between 20% and 40%,[12,24–27] significantly lower than the non-elderly population. Our results were consistent with prior findings: the elderly patients in our study had a remarkable lower proportion of favorable outcomes (32%) compared to non-elderly patients, despite comparable reperfusion rates. Beyond chronological age, factors associated with physiological age seem to more profoundly affect the long-term prognosis of elderly patients.

In most RCTs evaluating the efficacy of EVT, the upper age limit for safety inclusion was 80 years; however, this exclusion criterion has been being consistently surpassed in real-world clinical cohort studies. With aging, brain tissue undergoes characteristic structural changes, including cortical atrophy and white matter integrity disruption, as observed in neuroimaging. Furthermore, these neuroimaging changes do not seem to follow a linear pattern with advancing chronological age. In our study, sensitivity analyses established 75 years as the inflection point, illustrating the remarkable impact of advanced physiological age on long-term prognosis.

In the univariate analysis, elderly patients had a higher prevalence of risk factors including hypertension, diabetes, and atrial fibrillation, as well as more severe stroke symptoms. A possible explanation is that increased chronological age may be associated with a higher burden of comorbidities and more severe cerebrovascular lesions. A further important characteristic of elderly patients was the enhanced neuroimaging evidence of brain frailty, with a greater incidence of moderate-to-severe cerebral WML and increased severity of GCA. However, after adjusting for potential confounding factors, the prognostic influences varied between the two age groups. For the non-elderly group, prolonged PTR time and poor collateral circulation were associated with poor outcomes; whereas in elderly patients, increased WML and GCA scores were independently associated with poor outcomes. In both age groups, higher NIHSS scores served as a common risk factor for poor outcomes.

Prior studies reported that in patients undergoing EVT for LVO-stroke, those with moderate-to-severe WML had worse prognosis at 3 months;[15,28,29] contrary findings have also been reported.[30–32] Because of the different age profiles of study populations included in previous researches, the non-linear correlation between chronological age and WMH development may be one plausible explanation. In addition, Benali et al reported that severe brain atrophy was also associated with an increased risk of poor outcomes following EVT in the post hoc analysis of the ESCAPE-NA1 trial.[16] WMH and GCA indicated the degree of cerebral white matter and cortical degeneration, respectively, offering a more complete evaluation of brain frailty. In our study, we found that the GCA score and WML significantly influenced the functional outcome of the elderly patients. In contrast, no significant correlations were observed in the non-elderly patients.

WML and GCA were used as accessible-neuroimaging indicators for brain structural frailty after stroke.[33] Brain frailty undermined individual's ability to adapt and recover and could be influenced by aging and various atherosclerotic comorbidities.[34,35] WML and GCA are more common in elderly population, with an exponential increase with advanced aging.[36,37] We observed a significant association between moderate/severe GCA and WML with 3-month poor outcomes after EVT in elderly patients, but not in the non-elderly patients, which might be attributed to the declining reserve capacity of brain structures in the elderly.

Our study had some limitations. First, it was a single-center retrospective study with a moderate sample size, the effect of selection bias, including race, region, and eligibility criteria, should be taken into account when generalizing the

findings. Second, the GCA scale was employed in our study, based on cranial CT scans, to evaluate brain atrophy. However, the impact of cerebral edema following ischemia might lead to an underestimation of GCA in the affected hemisphere.[38] Third, the brain frailty encompasses more alterations than GCA and WML, such as cognitive reserve, vascular reactivity, and hemodynamics, etc. Therefore, further studies are warranted to explore the influence of brain frailty on stroke recovery in elderly population.

Conclusion

GCA and WML play pivotal roles for the functional outcomes in elderly patients undergoing EVT for LVO-stroke, providing valuable and practical information for early prediction of long-term prognosis.

Data Sharing Statement

The datasets analyzed during the current study are not publicly available due to patients' privacy protection, but anonymous data are available from the corresponding author on reasonable request.

IRB Ethics Statement

The study complied with the Helsinki Declaration and the study protocol was approved by the Institutional Review Board if Dongguan People's Hospital (KYKT2022-066; Dec 1, 2022). All patients gave written informed consent.

Acknowledgment

We would like to thank the participants of our stroke registry study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by Guangdong Basic and Applied Basic Research Fund (2021B1515120089). The sponsor was not involved in the design, methods, subject recruitment, data collections, analysis, or preparation of the paper.

Disclosure

All authors declare no conflicts of interest in this work.

References

1. Lakomkin N, Dhamoon M, Carroll K, et al. Prevalence of large vessel occlusion in patients presenting with acute ischemic stroke: a 10-year systematic review of the literature. *J Neurointerv Surg*. 2019;11(3):241–245. doi:10.1136/neurintsurg-2018-014239
2. Smith WS, Lev MH, English JD, et al. Significance of large vessel intracranial occlusion causing acute ischemic stroke and TIA. *Stroke*. 2009;40(12):3834–3840. doi:10.1161/STROKEAHA.109.561787
3. Malhotra K, Gornbein J, Saver JL. Ischemic strokes due to large-vessel occlusions contribute disproportionately to stroke-related dependence and death: a review. *Front Neurol*. 2017;8:651. doi:10.3389/fneur.2017.00651
4. Olthuis SGH, Pirson FAV, Pinckaers FME, et al.; MR CLEAN-LATE investigators. Endovascular treatment versus no endovascular treatment after 6–24 h in patients with ischaemic stroke and collateral flow on CT angiography (MR CLEAN-LATE) in the Netherlands: a multicentre, open-label, blinded-endpoint, randomised, controlled, Phase 3 trial. *Lancet*. 2023;401(10385):1371–1380. doi:10.1016/S0140-6736(23)00575-5
5. Yang P, Zhang Y, Zhang L, et al.; DIRECT-MT Investigators. Endovascular thrombectomy with or without intravenous alteplase in acute stroke. *N Engl J Med*. 2020;382(21):1981–1993. doi:10.1056/NEJMoa2001123
6. Mehta A, Fifi JT, Shoirah H, et al. National trends in utilization and outcome of endovascular thrombectomy for acute ischemic stroke in elderly. *J Stroke Cerebrovasc Dis*. 2021;30(2):105505. doi:10.1016/j.jstrokecerebrovasdis.2020.105505
7. Lai YJ, Peng SH, Lai WJ, et al. Predictors of 30-day mortality after endovascular thrombectomy for large vessel occlusion in the elderly. *Interv Neuroradiol*. 2023;29(1):37–42. doi:10.1177/15910199211069259
8. Sudre J, Venditti L, Ancelet C, et al. Reperfusion therapy for acute ischemic stroke in older people: an observational real-life study. *J Am Geriatr Soc*. 2021;69(11):3167–3176. doi:10.1111/jgs.17394

9. Yancik R. Cancer burden in the aged: an epidemiologic and demographic overview. *Cancer*. 1997;80(7):1273–1283. doi:10.1002/(SICI)1097-0142(19971001)80:7<1273::AID-CNCR13>3.0.CO;2-4
10. Jiang X, Wang J, Hu Y, et al. Is endovascular treatment still good for acute ischemic stroke in the elderly? A meta-analysis of observational studies in the last decade. *Front Neurosci*. 2024;17:1308216. doi:10.3389/fnins.2023.1308216
11. Rezai MK, Dalen I, Advani R, et al. Thrombectomy in large vessel occlusion stroke-Does age matter? *Acta Neurol Scand*. 2022;146(5):628–634. doi:10.1111/ane.13691
12. Adcock AK, Schwamm LH, Smith EE, et al. Trends in use, outcomes, and disparities in endovascular thrombectomy in US patients with stroke aged 80 years and older compared with younger patients. *JAMA Netw Open*. 2022;5(6):e2215869. doi:10.1001/jamanetworkopen.2022.15869
13. Benali F, Singh N, Fladt J, et al. ESCAPE-NA1 investigators. mediation of age and thrombectomy outcome by neuroimaging markers of frailty in patients with stroke. *JAMA Netw Open*. 2024;7(1):e2349628. doi:10.1001/jamanetworkopen.2023.49628
14. Umarova RM, Gallucci L, Hakim A, Wiest R, Fischer U, Arnold M. Adaptation of the concept of brain reserve for the prediction of stroke outcome: proxies, neural mechanisms, and significance for research. *Brain Sci*. 2024;14(1):77. doi:10.3390/brainsci14010077
15. Fan H, Wei L, Zhao X, et al. White matter hyperintensity burden and functional outcomes in acute ischemic stroke patients after mechanical thrombectomy: a systematic review and meta-analysis. *Neuroimage Clin*. 2024;41:103549. doi:10.1016/j.nicl.2023.103549
16. Benali F, Fladt J, Jaroenngarmsamer T, et al. Association of brain atrophy with functional outcome and recovery trajectories after thrombectomy: post Hoc analysis of the ESCAPE-NA1 trial. *Neurology*. 2023;101(15):e1521–e1530. doi:10.1212/WNL.0000000000207700
17. Jadhav AP, Desai SM, Jovin TG. Indications for mechanical thrombectomy for acute ischemic stroke: current guidelines and beyond. *Neurology*. 2021;97(20 Suppl 2):S126–S136. doi:10.1212/WNL.0000000000012801
18. Albers GW, Marks MP, Kemp S, et al.; DEFUSE 3 Investigators. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378(8):708–718. doi:10.1056/NEJMoa1713973
19. Higashida RT, Furlan AJ, Roberts H, et al.; Technology Assessment Committee of the American Society of Interventional and Therapeutic Neuroradiology; Technology Assessment Committee of the Society of Interventional Radiology. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. *Stroke*. 2003;34(8):e109–37. doi:10.1161/01.STR.0000082721.62796.09
20. Wahlund LO, Westman E, van Westen D, et al.; From the Imaging Cognitive Impairment Network (ICINET). Imaging biomarkers of dementia: recommended visual rating scales with teaching cases. *Insights Imaging*. 2017;8(1):79–90. doi:10.1007/s13244-016-0521-6
21. Zhou X, Xia J. Application of Evans index in normal pressure hydrocephalus patients: a mini review. *Front Aging Neurosci*. 2022;13:783092. doi:10.3389/fnagi.2021.783092
22. Fazekas F, Chawluk JB, Alavi A, Hurtig HI, Zimmerman RA. MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. *AJR Am J Roentgenol*. 1987;149(2):351–356. doi:10.2214/ajr.149.2.351
23. Kimberly WT. Predicting malignant cerebral edema after large hemispheric stroke. *Neurocrit Care*. 2020;32(1):84–85. doi:10.1007/s12028-019-00841-1
24. Alawieh A, Starke RM, Chatterjee AR, et al. Outcomes of endovascular thrombectomy in the elderly: a 'real-world' multicenter study. *J Neurointerv Surg*. 2019;11(6):545–553. doi:10.1136/neurintsurg-2018-014289
25. Meyer L, Alexandrou M, Flottmann F, et al.; German Stroke Registry–Endovascular Treatment (GSR-ET) †. Endovascular treatment of very elderly patients aged ≥90 with acute ischemic stroke. *J Am Heart Assoc*. 2020;9(5):e014447. doi:10.1161/JAHA.119.014447
26. Viticchi G, Potente E, Falsetti L, et al. Efficacy and safety of reperfusion treatments in middle-old and oldest-old stroke patients. *Neurol Sci*. 2022;43(7):4323–4333. doi:10.1007/s10072-022-05958-4
27. Ahmetović H, Jerković A, Vidaković MR, Košta V. The comparison of mechanical thrombectomy and symptomatic therapy on early outcome of acute ischemic stroke in patients older than 80 years: a retrospective cohort study. *Clin Neurol Neurosurg*. 2022;221:107378. doi:10.1016/j.clineuro.2022.107378
28. Derraz I, Abdelrady M, Ahmed R, et al. Impact of white matter hyperintensity burden on outcome in large-vessel occlusion stroke. *Radiology*. 2022;304(1):145–152. doi:10.1148/radiol.210419
29. Boulouis G, Bricout N, Benhassen W, et al. White matter hyperintensity burden in patients with ischemic stroke treated with thrombectomy. *Neurology*. 2019;93(16):e1498–e1506. doi:10.1212/WNL.0000000000008317
30. Mechtouff L, Nighoghossian N, Amaz C, et al. White matter burden does not influence the outcome of mechanical thrombectomy. *J Neurol*. 2020;267(3):618–624. doi:10.1007/s00415-019-09624-2
31. Eker OF, Rascle L, Cho TH, et al. Does small vessel disease burden impact collateral circulation in ischemic stroke treated by mechanical thrombectomy? *Stroke*. 2019;50(6):1582–1585. doi:10.1161/STROKEAHA.119.025608
32. Atchaneeyasakul K, Leslie-Mazwi T, Donahue K, Giese AK, Rost NS. White matter hyperintensity volume and outcome of mechanical thrombectomy with stentriever in acute ischemic stroke. *Stroke*. 2017;48(10):2892–2894. doi:10.1161/STROKEAHA.117.018653
33. Rabinstein AA, Albers GW, Brinjikji W, Koch S. Factors that may contribute to poor outcome despite good reperfusion after acute endovascular stroke therapy. *Int J Stroke*. 2019;14(1):23–31. doi:10.1177/1747493018799979
34. Chandra RV, Leslie-Mazwi TM, Oh DC, et al. Elderly patients are at higher risk for poor outcomes after intra-arterial therapy. *Stroke*. 2012;43(9):2356–2361. doi:10.1161/STROKEAHA.112.650713
35. Dąbrowski J, Czajka A, Zielińska-Turek J, et al. Brain functional reserve in the context of neuroplasticity after stroke. *Neural Plast*. 2019;2019:9708905. doi:10.1155/2019/9708905
36. Garnier-Crussard A, Bougacha S, Wirth M, et al. White matter hyperintensities across the adult lifespan: relation to age, Aβ load, and cognition. *Alzheimers Res Ther*. 2020;12(1):127. doi:10.1186/s13195-020-00669-4
37. Prins ND, Scheltens P. White matter hyperintensities, cognitive impairment and dementia: an update. *Nat Rev Neurol*. 2015;11(3):157–165. doi:10.1038/nrneurol.2015.10
38. Jaroenngarmsamer T, Benali F, Fladt J, et al.; ESCAPE-NA1 Investigators. Cortical and subcortical brain atrophy assessment using simple measures on NCCT compared with MRI in acute stroke. *AJNR Am J Neuroradiol*. 2023;44(10):1144–1149. doi:10.3174/ajnr.A7981