ORIGINAL ARTICLE

# Correlation between Pre-Stroke Frailty and Stroke Severity in Older Patients with Non-Surgical Carotid Artery Stenosis

Thon Thiraworawong, MD[1]

[1] Vascular Neurology Unit, Department of Neurology, Neurological Institute of Thailand, Bangkok, Thailand

**Objective:** To investigate the effect of frailty regarding frail versus non-frail patients with carotid artery stenosis.

**Materials and Methods:** The present study was a retrospective cohort study performed in a tertiary care setting. The study included the baseline characteristics and clinical outcomes of the participants. Univariate analysis and Cox proportional hazard regression model were used to include confounders. The primary outcome was the composite of the ischemic stroke and all-caused death in frail versus non-frail patients with carotid artery stenosis.

**Results:** The present study included 450 patients with a 1-year follow-up. Composite events occurred in 33 patients (22.0%) in the frailty with carotid artery stenosis group compared with 35 patients (11.7%) in non-frailty with carotid artery stenosis group (HR 1.92, 95% CI 1.59 to 2.37, p<0.001).

**Conclusion:** Frailty is strongly associated with unfavorable outcomes in older patients with carotid artery stenosis. Risk stratification and special consideration in frail older patients should be considered in the strategy plan of care.

**Keywords:** Frailty; Stroke; Carotid stenosis; Older; Non-surgical

Received 11 January 2024 | Revised 8 May 2024 | Accepted 14 May 2024

**J Med Assoc Thai 2024;107(7):528-34**

**Website:** http://www.jmatonline.com

Aging is a major health concern worldwide. The presence of medical advances in countries tends to result in fewer new populations and higher life expectancies for older adults. Due to the high likelihood of adverse events, these patients require a specific treatment approach. Some patients are treated with medication alone, and their symptoms are monitored.

Fried et al. introduced the frailty phenotype, which is considered the definition of frailty[1]. Frailty is defined as a clinical syndrome driven by age-related biological changes that drive the physical characteristics of frailty and, eventually, adverse outcomes. Frailty has been conceptualized as a pre-disability state. However, it can also coexist with disability. In addition, frailty is multidimensional, heterogeneous, and unstable, which distinguishes it from disability or aging alone[2,3]. Models and definitions have been proposed to operationalize frailty assessments in various settings. However, frailty assessment tools are time-consuming, require special equipment, and may be limited to stroke patients[4,5]. The FRAIL scale used to assess the frailty status is a self-reported scale that does not require activities affected by the disease itself. The FRAIL scale can be used to estimate frailty without special tools and is valid in clinical practice[6,7].

The European Society of Cardiology guidelines suggest specific recommendations for frail patients: to maintain a 130 to 140 mmHg systolic target and 80 to 90 mmHg diastolic target, if tolerated[8]. The 2018 American Heart Association/American College of Cardiology guidelines recommend that hypercholesterolemia treatment in older adults should not differ from that in younger patients[9]. Evidence-based guidelines have been published for the overall management of people aged 65 years and older with diabetes. The 2019 Endocrine Society clinical practice guideline suggests low-dose aspirin of 75 to

**Correspondence to:**

Thiraworawong T.

Vascular Neurology Unit, Department of Neurology, Neurological Institute of Thailand, Bangkok 10400, Thailand.

**Phone:** +66-2-3069899 ext. 2253

**Email:** thiraworawong.t@nit.go.th

**How to cite this article:**

Thiraworawong T. Correlation between Pre-Stroke Frailty and Stroke Severity in Older Patients with Non-Surgical Carotid Artery Stenosis. J Med Assoc Thai 2024;107:528-34.

DOI: 10.35755/jmedassocthai.2024.7.14009

162 mg/day for secondary prevention in patients aged 65 years or older with diabetes and atherosclerotic cardiovascular disease[10]. However, evidence of a correlation between frailty and carotid artery stenosis is currently limited, and the difficulty in treating carotid artery stenosis in frail patients may increase over time. This trend has yet to be investigated.

Carotid artery stenosis can lead to ischemic stroke. The current treatment guidelines suggest the use of medical therapy and carotid revascularization, for carotid artery stenosis that is high-risk of progression.

The main objective of the present study was to investigate the effect of frailty regarding frail versus non-frail patients with carotid artery stenosis who had not undergone surgical interventions by carotid endarterectomy.

## Materials and Methods

### Study design

The present study was a retrospective cohort study conducted between August 2019 and July 2022 at the Neurological Institute of Thailand. The study examined the clinical, imaging data, and clinical outcomes in older patients with symptomatic carotid artery stenosis from medical records. The present study was approved by the Institutional Review Board of the Neurological Institute of Thailand (registration number: 65047). All methods were performed in accordance with the Declaration of Helsinki.

### Study participants

Patients were included in the present study if they 1) were aged older than 65 years and 2) had symptomatic carotid artery stenosis with a degree of stenosis of 50% or more and at least 1-year follow-up. The Thai version of the FRAIL scale was used to identify frail patients. Informed consent was obtained from all participants.

Patients were excluded from the present study if they 1) had undergone surgical interventions by carotid endarterectomy, 2) had a follow-up of less than one year, 3) were unable to obtain a medical history, and 4) had carotid artery disease due to other mechanisms, such as radiation-related carotid stenosis/occlusion, Takayasu disease, or fibromuscular dysplasia.

### Data collection and definitions

The baseline characteristics of the patients included gender, age, body mass index, characteristics of carotid artery stenosis, mode of arrival to hospital, educational level, antiplatelet medication, baseline National Institutes of Health Stroke Scale (NIHSS), smoking, comorbidities, low-density lipoprotein cholesterol (LDL-C) level, HbA1c level, Charlson comorbidity index, Fazekas scale score, medial temporal lobe atrophy score. Missing data were managed especially in respect to continuous variables, which were potentially entered into regression models. The present study excluded patients with incomplete or incorrect data for the following variables, age, body mass index, NIHSS, HbA1c level, and LDL-C level.

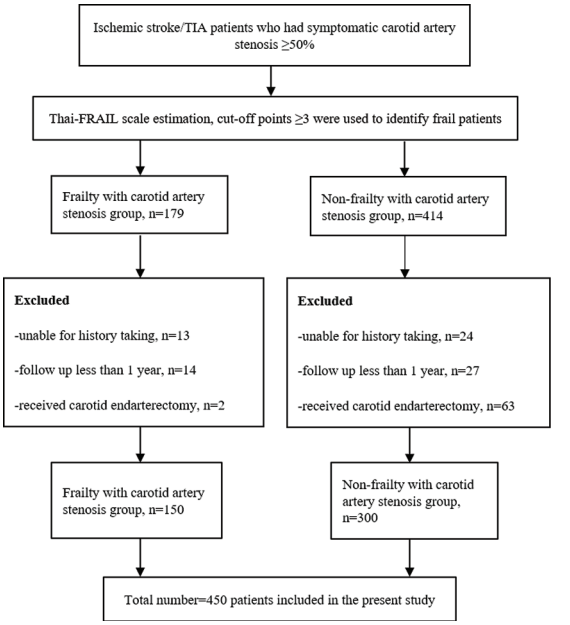


**Figure 1.** Flow diagram of the study.

Frailty was defined using the Thai version of the FRAIL scale[6], which is a 5-item questionnaire for frailty screening. The items are as follows: "fatigue", "resistance", "ambulation", "illnesses", and "loss of weight". Each item required a self-reported response rated as 1 or 0 points, depending on the presence of characteristics in each criterion. The scores range from 0 to 5, with higher scores indicating greater frailty. According to the original FRAIL scale[7], cutoff points of 3 or more (Figure 1) were used to identify frail patients.

Medication non-adherence was defined as the proportion of patients who had refill lag of more than one month during follow-up over a period of one year.

Achieve target blood pressure was defined as the proportion of patients with hypertension who had systolic blood pressure measured at each visit of less than 140 mmHg or less than 130 mmHg if

diabetic, more than 80% during follow-up over a period of one year.

Achieve target LDL-C was defined as the proportion of patients with hypercholesterolemia who had LDL-C level measured at each visit of less than 1.8 mmol/L, for more than 80% during follow-up over a period of one year.

Achieve target HbA1c was defined as the proportion of patients with diabetes mellitus who had HbA1c level measured at each visit of less than 53 mmol/mol, more than 80% during follow-up over a period of one year.

Smoking cessation was defined as the proportion of smokers discontinuing tobacco smoking within six months after the onset of ischemic stroke/transient ischemic attack.

Symptomatic carotid artery stenosis was defined as the presence of atherosclerotic narrowing of the proximal internal carotid artery by 50% or more at the level of bifurcation in patients with history of ischemic stroke/transient ischemic attack involving ipsilateral carotid territory.

Carotid artery stenosis could be diagnosed by either gadolinium-enhanced magnetic resonance angiography or contrasted computed tomographic angiography and measured by the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[11] criteria.

Recurrent ischemic stroke was defined as a first episode of neurological deficit persisting more than 24 hours with symptom localizable to the previous symptomatic carotid artery stenosis.

Recurrent transient ischemic attack was defined as a focal and localizable, such as hemispheric neurological deficit, transient ischemic attack, or monocular blindness persisting less than 24 hours with symptom localizable to the previous symptomatic carotid artery stenosis.

Death was defined as all-cause death.

### Study outcome assessment

The primary outcome of the present study was defined as the first episode of the composite events of ischemic stroke and all-cause death in frail versus non-frail patients with carotid artery stenosis.

Other secondary clinical outcomes included hemorrhagic stroke, first occurrence of ischemic stroke, and number of deaths.

A vascular neurologist (TT) evaluated the medical records of these patients. Outcome events were adjudicated by attending neurologist. Attending neurologist were blinded to the study participants' frailty status.

### Statistical analyses

A previous study[12] found that the patients who had carotid artery stenosis had an incidence death of approximately 0.6% in 30 days. However, if these patients had frailty, the incidence of death would increase to 4.9% in 30 days. The formula for sample size calculation in the present study was derived from a textbook[13]. The author estimated that a sample size of 450 patients would provide 80% power and avoid type 2 errors. Categorical variables were reported as numbers (%). Continuous variables were reported as medians with interquartile ranges. A Cox proportional hazards regression model was used to compare the relationship between the outcomes of both groups while adjusting for confounding factors. Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported. If multiple events of the same type occurred, the time until the first event was used in the model. A p-value of less than 0.05 was considered significant. All statistical analyses were performed using SPSS Statistics for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA).

## Results

The present study was a single-center, tertiary care setting. Four hundred fifty older patients (Figure 1) with carotid artery stenosis that included 190 men and 260 women with a median age of 72 years were participating (Table 1). Baseline patient characteristics are summarized in Table 1. The present study excluded patients with incomplete or incorrect data for the following variables, age, body mass index, NIHSS, HbA1c level, and LDL-C level. Nevertheless, none of the continuous variables were absent in the present study.

Table 2 shows the endpoints between frail and non-frail patients with carotid artery stenosis. Composite events occurred in 33 patients (22.0%) in the frailty with carotid artery stenosis group compared with 35 patients (11.7%) in the non-frailty with carotid artery stenosis group (HR 1.92, 95% CI 1.59 to 2.37, $p<0.001$). Figure 2 shows the survival analysis between frail patients and non-frail patients with carotid artery stenosis. All-cause death occurred in 14 patients (9.3%) in the frailty with carotid artery stenosis group compared with 12 patients (4.0%) in the non-frailty with carotid artery stenosis group (HR 2.29, 95% CI 1.45 to 2.98, $p<0.001$).

In the subgroup analyses, the author compared the primary outcomes between frail and non-frail

**Table 1.** Demographic data of the study participants

| Patient characteristics | Total (n=450) | Frail group (n=150) | Non-frail group (n=300) | p-value |
|---|---|---|---|---|
| Female; n (%) | 260 (57.8) | 92 (61.3) | 168 (56.0) | 0.531 |
| Age (years); median (IQR) | 72 (66 to 79) | 73 (66 to 80) | 71 (66 to 80) | 0.756 |
| Body mass index (kg/m$^2$); median (IQR) | 20.7 (18.3 to 22.5) | 19.8 (18.1 to 20.1) | 21.2 (18.8 to 23.4) | 0.139 |
| Carotid stenosis >70%; n (%) | 40 (8.9) | 12 (8.0) | 28 (9.3) | 0.252 |
| Mode of arrival to hospital; n (%) | | | | 0.457 |
| Private arrival | 370 (82.2) | 121 (80.7) | 249 (83.0) | |
| EMS arrival/transfer | 80 (17.8) | 29 (19.3) | 51 (17.0) | |
| Education level; n (%) | | | | 0.335 |
| Elementary school or lower | 240 (53.3) | 78 (52.0) | 162 (54.0) | |
| High school or above | 210 (46.7) | 72 (48.0) | 138 (46.0) | |
| Antiplatelet medication; n (%) | | | | 0.231 |
| Aspirin | 231 (51.3) | 79 (52.7) | 152 (50.6) | |
| Clopidogrel | 137 (30.4) | 48 (32.0) | 89 (29.7) | |
| Other | 82 (18.3) | 23 (15.3) | 59 (19.7) | |
| Baseline NIHSS; median (IQR) | 9 (7 to 12) | 9 (7 to 12) | 9 (6 to 13) | 0.563 |
| Medication non-adherence; n (%) | 20 (4.4) | 7 (4.7) | 13 (4.3) | 0.267 |
| Smoking; n (%) | 247 (54.9) | 78 (52.0) | 169 (56.3) | 0.435 |
| Smoking cessation; n (%) | 230 (93.1) | 72 (92.3) | 158 (93.5) | 0.338 |
| Hypertension; n (%) | 232 (51.6) | 76 (50.6) | 154 (51.3) | 0.531 |
| Achieve target blood pressure; n (%) | 198 (85.3) | 65 (85.5) | 133 (86.4) | 0.414 |
| Diabetes mellitus; n (%) | 237 (52.7) | 80 (53.3) | 161 (53.7) | 0.432 |
| Achieve target HbA1c; n (%) | 179 (75.5) | 61 (76.2) | 118 (73.3) | 0.589 |
| HbA1c (mmol/mol); median (IQR) | 52 (47 to 59) | 52 (48 to 59) | 52 (47 to 58) | 0.332 |
| Hypercholesterolemia; n (%) | 286 (63.4) | 92 (61.3) | 194 (64.7) | 0.356 |
| Achieve target LDL-C; n (%) | 245 (85.7) | 80 (87.0) | 165 (85.1) | 0.561 |
| LDL-C (mmol/L); median (IQR) | 1.7 (1.5 to 2.8) | 1.7 (1.5 to 2.7) | 1.7 (1.5 to 2.8) | 0.258 |
| Chronic kidney disease; n (%) | 35 (7.8) | 12 (8.0) | 23 (7.7) | 0.644 |
| Ischemic heart disease; n (%) | 80 (17.8) | 29 (19.3) | 51 (17.0) | 0.237 |
| Congestive heart failure; n (%) | 19 (4.2) | 7 (4.7) | 12 (4.0) | 0.431 |
| Chronic lung disease; n (%) | 52 (11.6) | 14 (9.3) | 38 (12.7) | 0.663 |
| Asthma; n (%) | 30 (6.7) | 9 (6.0) | 21 (7.0) | 0.534 |
| Arthritis; n (%) | 18 (4.0) | 5 (3.3) | 13 (4.3) | 0.538 |
| Cancer; n (%) | 11 (2.4) | 4 (2.6) | 7 (2.3) | 0.435 |
| Charlson comorbidity index; n (%) | | | | 0.335 |
| Summation score <5 points | 431 (95.8) | 142 (94.7) | 289 (96.3) | |
| Summation score ≥5 points | 19 (4.2) | 8 (5.3) | 11 (3.7) | |
| Fazekas scale; median (IQR) | | | | 0.685 |
| Periventricular white matter | 1 (0 to 2) | 1 (0 to 2) | 1 (0 to 2) | |
| Deep white matter | 1 (0 to 2) | 1 (0 to 2) | 1 (0 to 2) | |
| Medial temporal lobe atrophy score; median (IQR) | 1 (0 to 2) | 1 (0 to 2) | 1 (0 to 2) | 0.339 |

IQR=interquartile range; EMS=emergency medical service; NIHSS=National Institutes of Health Stroke Scale; LDL-C=low-density lipoprotein cholesterol

patients with carotid artery stenosis according to gender, age, smoking, hypertension, diabetes mellitus, hypercholesterolemia, chronic kidney disease, ischemic heart disease, congestive heart failure, chronic lung disease, asthma, arthritis, cancer, and carotid artery stenosis greater than 70% (Figure 3). The effect of frailty was observed in all subgroups.

## Discussion

An analysis comparing frail and non-frail patients with carotid artery stenosis revealed that frailty in older patients was strongly associated with poor composite outcomes.

The study participants participating in the present study were Thai. The average body mass

**Table 2.** Endpoints of frail patients versus non-frail patients with carotid artery stenosis

| Endpoints | Frail group (n=150) | Non-frail group (n=300) | HR (95% CI) | p-value |
|---|---|---|---|---|
| Composite of ischemic stroke and all-cause mortality; n (%) | 33 (22.0) | 35 (11.7) | 1.92 (1.59 to 2.37) | <0.001 |
| Median survival time (months) | 8.4 | 9.9 | | |
| Ischemic stroke; n (%) | 19 (12.7) | 23 (7.7) | 1.62 (1.12 to 2.11) | 0.014 |
| Median survival time (months) | 8.2 | 9.3 | | |
| Hemorrhagic stroke; n (%) | 0 (0.0) | 0 (0.0) | - | - |
| Median survival time(months) | - | - | - | - |
| All-cause mortality; n (%) | 14 (9.3) | 12 (4.0) | 2.29 (1.45 to 2.98) | <0.001 |
| Median survival time(months) | 8.7 | 11.1 | | |

HR=hazard ratio; CI=confidence interval

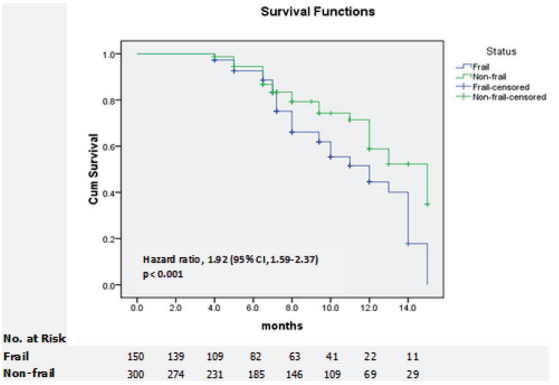


**Figure 2.** Survival analysis based on primary outcome among frail patients versus non-frail patients with carotid artery stenosis.

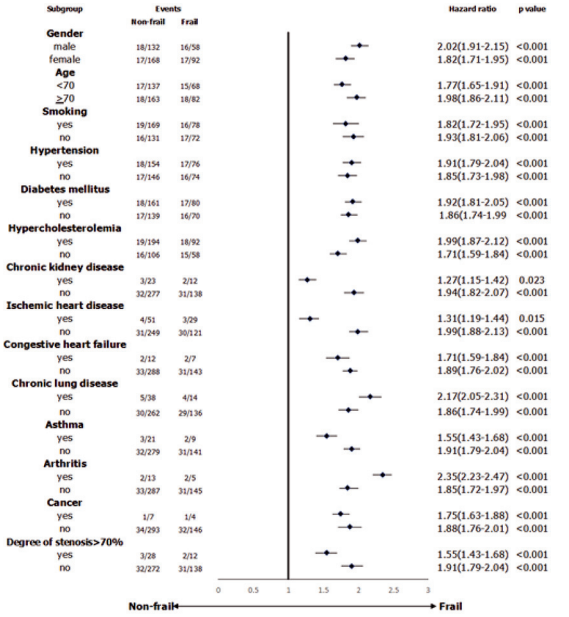


**Figure 3.** Subgroup analysis based on primary outcome in frail patients versus non-frail patients with carotid artery stenosis.

index of Asian ethnicities is lower than that of other ethnicities. According to a previous study[14], the normal range for Thai persons is 18.5 to 23 kg/m². In the present study, the body mass index of frail older patients tended to be lower than that of non-frail older patients. Additionally, frailty may indirectly impact the body mass index. Moreover, frailty can cause inflammation[15]. A previous study[16-18] showed that the loss of muscle mass, muscle anabolism, reduced muscle strength, and poor handgrip strength are linked to chronic low-grade inflammation.

Currently, clinical practice guidelines for preventing ischemic stroke in frail older patients are unclear. Medical therapy is the main treatment option for non-surgical carotid artery stenosis, especially in patients with comorbidities. In addition, most landmark clinical trials[19,20] have not included frail older patients in their research methodology. Most primary-prevention randomized controlled trials have not specifically recruited patients with frailty and have focused primarily on stroke prevention in the general population[21]. However, the subgroup analysis in the present study based on composite events showed that frailty may be predictors of unfavorable outcomes in all subgroups. Carotid endarterectomy is often not recommended in patients with severe comorbidities, particularly heart and lung diseases[22], and precautions should be taken when treating such patients. The risk of complications increases with an increased incidence of myocardial infarction[23-25].

Although a person aged older than 65 years is often defined as "elderly or older", no concrete definitions of "elderly or older" accurately characterize this patient population. The generic term "elderly or older" may lead to different interpretations according to patient status, study settings, and definitions, which is problematic for decision-making. In carotid artery

trials[26-28], older patients were referred to as those over 70, 75, or 80 years old. Older patients are at higher risk of periprocedural complications. In a previous study[29], a meta-analysis of multiple randomized controlled trials comparing carotid endarterectomy to carotid artery stenting showed that the combined risk of periprocedural stroke and death increased with age, from 3% in patients younger than 60 years, 9% in patients 75 to 79 years, and 11% in patients older than 80 years. The cutoff point for appropriate clinical caution that turns into an age-related bias is difficult to define.

## Limitation

The present study had limitations. First, the Thai version of the FRAIL scale may have some disadvantages when used to assess frailty. For instance, assessing cognitive frailty was not feasible. Cognitive frailty can indirectly affect patient outcomes, such as medication adherence and lack of stroke awareness. However, the proportion of the medical non-adherence, Fazekas scale scores and medial temporal lobe scores were low among the study participants. Patients for whom a medical history could not be obtained were excluded from the present study. Second, the frailty scale includes comorbidities that are risk factors for vascular disease. This could have an indirect effect on stroke outcomes. Third, owing to the retrospective study design and analysis of the enrolled data, unmeasured bias or uncollected confounders may have existed in the present study. However, this limitation was addressed using a regression model. In the future, it may be necessary to confirm the outcomes of the present study in a larger population or in randomized controlled studies.

## Conclusion

Frailty is strongly associated with unfavorable outcomes in older patients with carotid artery stenosis. Risk stratification and special consideration in frail older patients should be considered in the strategy plan of care.

## What is already known on this topic?

Evidence of a correlation between frailty and severity of stroke in older patients with carotid artery stenosis is currently limited.

## What does this study add?

Carotid artery stenosis can lead to ischemic stroke. Assessing frailty is more beneficial when selecting high risk older patients with carotid artery stenosis.


## Acknowledgment

The author appreciates Associate Professor Varalak Srinonprasert (Division of Geriatric Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University) for granted the use of the Thai version of the FRAIL scale.

## Funding disclosure

The present research received no external funding.


## Conflicts of interest

The author declares no conflicts of interest.

## References


1. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-56.
2. Hogan DB, MacKnight C, Bergman H. Models, definitions, and criteria of frailty. Aging Clin Exp Res 2003;15:1-29.
3. Robinson TN, Walston JD, Brummel NE, Deiner S, Brown CH 4th, Kennedy M, et al. Frailty for surgeons: Review of a national institute on aging conference on frailty for specialists. J Am Coll Surg 2015;221:1083-92.
4. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. J Gerontol A Biol Sci Med Sci 2007;62:722-7.
5. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age Ageing 2006;35:526-9.
6. SriwongWT, Mahavisessin W, Srinonprasert V, Siriussawakul A, Aekplakorn W, Limpawattana P, et al. Validity and reliability of the Thai version of the simple frailty questionnaire (T-FRAIL) with modifications to improve its diagnostic properties in the preoperative setting. BMC Geriatr 2022;22:161. doi: 10.1186/s12877-022-02863-5.
7. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012;16:601-8.
8. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021-104.
9. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of

blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. Circulation 2019;139:e1082-143.
10. LeRoith D, Biessels GJ, Braithwaite SS, Casanueva FF, Draznin B, Halter JB, et al. Treatment of diabetes in older adults: An Endocrine Society* clinical practice guideline. J Clin Endocrinol Metab 2019;104:1520-74.
11. Barnett HJM, Taylor DW, Haynes RB, Sackett DL, Peerless SJ, Ferguson GG, et al. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325:445-53.
12. Banning LBD, Benjamens S, Bokkers RPH, Zeebregts CJ, Pol RA. Role of pre-operative frailty status in relation to outcome after carotid endarterectomy: a systematic review. Ann Transl Med 2021;9:1205. doi: 10.21037/atm-20-7225.
13. Rosner B. Estimation of sample size and power for comparing two binomial proportions. In: Rosner B, editor. Fundamentals of biostatistics. 5th ed. Pacific Grove, CA: Duxbury; 2000. p. 384-5.
14. Pan WH, Yeh WT. How to define obesity? Evidence-based multiple action points for public awareness, screening, and treatment: an extension of Asian-Pacific recommendations. Asia Pac J Clin Nutr 2008;17:370-4.
15. Vandanmagsar B, Youm YH, Ravussin A, Galgani JE, Stadler K, Mynatt RL, et al. The NLRP3 inflammasome instigates obesity-induced inflammation and insulin resistance. Nat Med 2011;17:179-88.
16. Bano G, Trevisan C, Carraro S, Solmi M, Luchini C, Stubbs B, et al. Inflammation and sarcopenia: A systematic review and meta-analysis. Maturitas 2017;96:10-5.
17. Gale CR, Baylis D, Cooper C, Sayer AA. Inflammatory markers and incident frailty in men and women: the English Longitudinal Study of Ageing. Age (Dordr) 2013;35:2493-501.
18. Tuttle CSL, Thang LAN, Maier AB. Markers of inflammation and their association with muscle strength and mass: A systematic review and meta-analysis. Ageing Res Rev 2020;64:101185.
19. Côté R, Battista RN, Abrahamowicz M, Langlois Y, Bourque F, Mackey A. Lack of effect of aspirin in asymptomatic patients with carotid bruits and substantial carotid narrowing. The Asymptomatic Cervical Bruit Study Group. Ann Intern Med 1995;123:649-55.
20. King A, Shipley M, Markus H. The effect of medical treatments on stroke risk in asymptomatic carotid stenosis. Stroke 2013;44:542-6.
21. Naylor R, Rantner B, Ancetti S, de Borst GJ, De Carlo M, Halliday A, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2023 clinical practice guidelines on the management of atherosclerotic carotid and vertebral artery disease. Eur J Vasc Endovasc Surg 2023;65:7-111.
22. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004;351:1493-501.
23. Rosenfield K, Matsumura JS, Chaturvedi S, Riles T, Ansel GM, Metzger DC, et al. Randomized trial of stent versus surgery for asymptomatic carotid stenosis. N Engl J Med 2016;374:1011-20.
24. Eckstein HH, Reiff T, Ringleb P, Jansen O, Mansmann U, Hacke W. SPACE-2: A missed opportunity to compare carotid endarterectomy, carotid stenting, and best medical treatment in patients with asymptomatic carotid stenoses. Eur J Vasc Endovasc Surg 2016;51:761-5.
25. Silver FL, Mackey A, Clark WM, Brooks W, Timaran CH, Chiu D, et al. Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). Stroke 2011;42:675-80.
26. Feng Y, Bai X, Li S, Zhu F, Wang Y, Chen Y, et al. Thirty-day outcome of carotid artery stenting in elderly patients: A single-center experience. World Neurosurg 2020;138:e311-6.
27. Ahmadi R, Schillinger M, Lang W, Mlekusch W, Sabeti S, Minar E. Carotid artery stenting in older patients: is age a risk factor for poor outcome? J Endovasc Ther 2002;9:559-65.
28. Taguchi A, Sakamoto S, Okazaki T, Oshita J, Kuwabara M, Kurisu K. Safety of carotid artery stenting for elderly patients with cervical carotid artery stenosis. Interv Neuroradiol 2020;26:439-45.
29. Howard G, Roubin GS, Jansen O, Hendrikse J, Halliday A, Fraedrich G, et al. Association between age and risk of stroke or death from carotid endarterectomy and carotid stenting: a meta-analysis of pooled patient data from four randomised trials. Lancet 2016;387:1305-11.