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Revascularization for asymptomatic carotid artery stenosis improves balance and mobility

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Abstract

Objective: Balance and mobility function worsen with age, more so for those with underlying chronic diseases. We recently found that asymptomatic carotid artery stenosis (ACAS) restricts blood flow to the brain and might also contribute to balance and mobility impairment. In the present study, we tested the hypothesis that ACAS is a modifiable risk factor for balance and mobility impairment. Our goal was to assess the effect of restoring blood flow to the brain by carotid revascularization on the balance and mobility of patients with high-grade ACAS (≥70% diameter-reducing stenosis).

Methods: Twenty adults (age, 67.0 ± 9.4 years) undergoing carotid endarterectomy for high-grade stenosis were enrolled. Balance and mobility assessments were performed before and 6 weeks after revascularization. These included the Short Physical Performance Battery, the Berg

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Balance Scale, the Four Square Step Test, the Dynamic Gait Index (DGI), the Timed Up and Go test, gait speed, the Mini-Balance Evaluation Systems Test (Mini-BESTest), and the Walking While Talking complex test.

Results: Consistent with our previous findings, patients demonstrated reduced scores on the Short Physical Performance Battery, Berg Balance Scale, DGI, and Timed Up and Go test and in gait speed. Depending on the outcome measure, 25% to 90% of the patients had scored in the impaired range at baseline. After surgery, significant improvements were observed in the outcome measures that combined walking with dynamic movements, including the DGI ($P = .02$) and Mini-BESTest ($P = .002$). The proportion of patients with Mini-BESTest scores indicating a high fall risk had decreased significantly from 90% (n = 18) at baseline to 40% (n = 8) after surgery ($P = .02$). We used Pearson's correlations to examine the relationship between balance and mobility before surgery and the change after surgery. Patients with lower baseline DGI and Mini-BESTest scores demonstrated the most improvement after surgery ($r = -0.59$, $P = .006$; and $r = -0.70$, $P = .001$, respectively).

Conclusions: Carotid revascularization improved patients' balance and mobility, especially for measures that combine walking and dynamic movements. The greatest improvements were observed for the patients who had been most impaired at baseline.

Keywords

Asymptomatic carotid artery stenosis; Balance; Mobility; Revascularization

One in four older adults aged ≥65 years will fall each year.[1] Falls and fall-related injuries are a significant public health concern because of their frequency, the associated loss of functional independence, and the costs of treatment.[2,3] In addition, 10% to 20% of falls are associated with serious injuries such as fractures or head trauma and can result in death.[4] Nonfatal fall-related injury results in an estimated $31.3 billion in treatment-related expenses.[3] Although the cause of falls is multifactorial, declines in balance and mobility are major contributors.[5] Balance and mobility dysfunction are significant predictors of falls, disability, institutionalization, and death.[6,7] Several disease states contribute to the decline in function. However, some of the impairments could be reversible and, therefore, offer an opportunity to prevent or reduce fall-related morbidity.[8] Thus, understanding the mechanisms that underlie the decline in function is essential for developing interventions that will improve balance and mobility and decrease the incidence of resultant falls.

Asymptomatic carotid artery stenosis (ACAS) affects ~10% of older adults.[9] Evidence has suggested that 40% to 50% of older adults with ACAS have cognitive dysfunction.[10,11] We have also found that individuals with ACAS have a greater decline in mobility and report higher fall rates than older adults without carotid stenosis.[10,12] Our studies have demonstrated that ACAS is associated with cerebral hypoperfusion.[10] Thus, it is plausible that flow restriction secondary to luminal narrowing from the carotid plaque will lead to impaired cerebral perfusion with resultant cognitive and mobility declines. Furthermore, improvement in middle cerebral artery flow after carotid revascularization has been associated with improved cognitive performance.[13] Given that cognitive and mobility function are inherently linked, we believe that similar improvement in mobility function could be seen with carotid revascularization. With the strong association between cognitive and mobility function,[14,15] we hypothesized that balance and mobility performance would improve 6 weeks after revascularization in individuals with high-grade ACAS of ≥70%.

METHODS

A total of 110 patients scheduled to undergo carotid endarterectomy were screened. Of the 110 patients, 48 meet the inclusion and exclusion criteria, and 20 agreed to participate in the present study. The patients were recruited from the Baltimore Veterans Affairs Medical Center and the University of Maryland Medical Center. Balance and mobility function was assessed in all patients using objective, standardized, and validated tests 1 month before and 6 weeks after surgery. The university institutional review board approved the present study, and the included patients provided written informed consent. All patients were confirmed to be receiving appropriate antiplatelet and lipid-lowering therapy, with adequate blood pressure and blood glucose control before surgery. Most of the recruited patients had been receiving appropriate risk factor modification therapy, as outlined, before enrollment. Thus, minimal changes in medical management were required. All consecutive patients were screened, and those who had fulfilled the inclusion and exclusion criteria and agreed to participate were enrolled. The study exclusion criteria included a history of stroke or transient ischemic attack, occlusion of the index carotid artery, occlusion or high-grade stenosis of the opposite (nonindex) carotid artery, severe medical illness that would interfere with the evaluations, and carotid revascularization not planned.

The order of the balance and mobility tests was the same before and after surgery, with scoring performed within 24 hours. The total testing time varied from 30 to 45 minutes among the patients owing to interindividual variability in the completion time of those tests without time limits. The study tests included the Short Physical Performance Battery (SPPB), Berg Balance Scale (BBS), Four Square Step Test (FSST), Dynamic Gait Index (DGI), Timed Up and Go (TUG) test, Mini-Balance Evaluation Systems Test (Mini-BESTest), and Walking While Talking complex (WWT_c) test. The patients' gait speed was also assessed. The SPPB comprises three items that assess gait velocity, static balance, and lower extremity strength.[6] Each item within the battery is scored on a scale of 0 to 4, with a total maximum score of 12. The short-form BBS measures the ability to maintain balance during a series of predetermined positions that alter the base of support.[16] The individual items within the test are scored on a scale of 0 to 4, with a total maximum score of 28. The four-item DGI assesses the ability to modify balance while walking in the presence of external demands (walking on a level surface, changes in walking speed, walking with horizontal head turns, and walking with vertical head turns).[17] The scale ranges from 0 to 3, with a total maximum score of 12. A higher score on the SPPB, BBS, and DGI indicates better balance. The TUG test assesses functional mobility by evaluating the time taken for the patient to rise from a chair, walk 3 m, turn around, return to the chair, and sit down.[18] A lower time indicates better performance. The Mini-BESTest, a comprehensive measure that assesses anticipatory postural adjustments, reactive postural control, sensory orientation, and dynamic gait, has an item scale that ranges from 0 to 3, with a maximum score of 28 and higher scores indicating better balance performance.[19] The WWT_c assesses a patient's ability to walk with divided attention and was performed at a usual walking pace with and without a cognitive task. The patients were instructed to walk 20 ft, turn around, and walk back 20 ft to the starting point at their usual walking pace.[20] The patients performed two trials, one without a cognitive task and one with a cognitive task. For the cognitive task, patients were asked to recite alternating letters of the alphabet starting at the letter “n.” The WWT_c time to complete the task is presented. WWT_c errors represent the number of incorrect responses while reciting alternating letters (ie, reciting two consecutive letters in the alphabet). A faster walking time and fewer errors indicate better performance with the WWT_c.

Each of these outcome measures has established impaired score thresholds (age-related normative values or established thresholds predictive of falls or mobility impairment). The fall risk cutoff for the DGI is a score <10.[17] For the Mini BESTest, the cutoff is a score of ≤ 23 for those aged 60 to 69 years and ≤22 for those aged 70 to 79 years.[21] The cutoff for the FSST is >15 seconds for someone who has already experienced multiple falls.[22] Individuals with a gait speed of <1.0 m are considered more likely to fall and to have a greater risk of adverse health-related outcomes.[23,24] A time of >33 seconds for the WWT_c has 95.6% specificity for identifying individuals more likely to fall.[20] The average number of errors for the WWT_c is two.[25] The normative cutoff values reported for older adults for the short-form BBS score is 20.61, with lower scores indicating poor balance.[16] The cutoff for the TUG test is 8 seconds for those aged 60 to 69 years and 9 seconds for those aged 70 to 79 years.[26] For the cutoff scores with two values according to age (ie, the Mini-BESTest and TUG test), we used the reported values for the oldest age group. Finally, individuals are considered to have a disability in mobility when the SPPB score is ≤10.[27]

Statistical analysis.

The data are reported as the mean ± standard deviation, median, 25th and 75th percentiles, and minimum and maximum values and were analyzed using SPSS for Windows, version 22.0 (IBM Corp, Armonk, NY). Dependent Student’s *t* tests were used to evaluate the differences between the baseline (preoperative) and postoperative results for the balance and mobility measures (ie, SPPB, BBS, FSST, DGI, TUG test, Mini-BESTest, WWT_c time, WWT_c errors). Box and whisker plots of the clinical outcome measures are presented for the balance and mobility measures at baseline and 6 weeks postoperatively. Histograms were created of the baseline and post-operative values to indicate the number of individuals who scored in the impaired range (ie, considered to have a risk of falling or impaired mobility or with scores less than the age-related normative values). McNemar’s test was used to compare the frequency of patients impaired at baseline against the frequency of patients impaired postoperatively. A two-tailed *P* value of <.05 was interpreted as indicating statistical significance.

RESULTS

Baseline clinical features.

The mean age of the patients was 67.0 ± 9.4 years. Almost one half were women (45%), and more were African American (30%) than in the U.S. distribution (Table I). Data for the WWT_c and WWT_c errors were missing for one patient who could not speak. None of the patients had vertebral artery occlusive disease. No patient died or experienced stroke or transient ischemic attack, cranial nerve injury, or bleeding or required revision surgery. The median length of hospital stay was 2 days.

Baseline mobility scores and frequency of impairment.

The mean scores for each mobility function measure were plotted to determine their frequency and distribution (Fig 1). Before surgery, all the participants, except for three, had had a gait speed greater than the value classified as a risk of frailty (>0.80 m/s). The reported age-related normative scores or established thresholds predictive of falls were used to quantify the proportion of patients who had performed at an impaired level at baseline.[16,17,21–28] The distribution of the scores and the frequency of patients with impairment varied across the tests. However, most of the tests identified a subgroup of individuals with impaired mobility or a high risk of falling. At baseline, no patients with impairment were identified using the FFST and WWT_c time (Fig 1 and Table II). For the remainder of the tests, 25.0% to 90.0% of the patients were classified as impaired at baseline, depending on the test (Fig 1). The Mini-BESTest demonstrated the greatest frequency of impaired patients, with 90% classified as having a risk of falling compared with the DGI, which classified 35% as having a risk of falling.

Change in functional status after revascularization.

The DGI ($P = .021$) and Mini-BESTest ($P = .002$) scores improved significantly after carotid artery revascularization (Fig 2). The SPPB ($P < .28$) and BBS ($P < .43$) scores improved numerically; however, the differences did not reach statistical significance. Next, we computed the proportion of patients who had performed at an impaired level at 6 weeks postoperatively using the same reported normative scores to classify impairment at baseline (Fig 3).[16,17,21–28] As at baseline, the distribution of scores and frequency of patients with impairment varied across the tests. After surgery, almost all the test scores demonstrated a decrease in the proportion of patients classified as having impairment (range, 0%−70%). Compared with baseline, the proportion of patients with impairment after surgery was significantly reduced using the Mini-BESTest (baseline, 90%; postoperatively, 40%; $P = .02$; Table II). Only the gait speed showed an increase in the proportion of patients with impairment post-operatively (baseline, 55%; postoperatively, 70%). No other balance and mobility outcome measures were significant.

DISCUSSION

To the best of our knowledge, we have demonstrated for the first time that carotid artery revascularization can be beneficial for balance and mobility dysfunction in patients with high-grade (≥70% diameter-reducing) ACAS at 6 weeks after revascularization. Improvements were more significant for the tests involving walking with external demands. This is noteworthy because these tests reflect real-world tasks essential to maintaining independent community mobility. Thus, we have shown that some aspects of balance and mobility performance will improve for patients with ACAS within as few as 6 weeks after revascularization.

Most studies of patients with ACAS have focused on impaired cognition. Given the interdependency of mobility and cognitive function,[14,15] which reflects the shared central neural mechanisms, we investigated the effects of ACAS on balance and mobility. The multifactorial processes necessary for balance, mobility, and cognitive function are controlled by similar regions of the brain (ie, frontal and prefrontal lobe-related networks).[29] Because similar areas of the brain are used, it is no surprise that individuals with cognitive impairment will also perform poorly on mobility tests.[30] We also found that individuals with ACAS and impaired balance and mobility had lower cognitive scores.[12] However, not all cognitive domains are equally associated with mobility. Superior performance on balance and mobility tests parallels better performance on executive function, memory, and processing speed assessments.[31] Executive function, attention, and fine motor coordination have also been reported to improve after carotid artery revascularization.[32–34] Further studies are needed to understand the interconnectedness between mobility and cognitive impairment and the mechanisms that link the two processes in those with ACAS. This will assist in the development of interventions to mitigate these impairments, which is essential for alleviating the burden of disability.

Cerebral perfusion is a likely mechanism through which balance and mobility improvements were mediated after carotid artery revascularization. Compelling evidence is available to suggest that cognitive function is associated with cerebral perfusion.[10,35–37] In longitudinal studies, reduced cerebral blood flow has been associated with worsening gait speed, memory, and executive function in those with diabetes.[38] Evidence has suggested that patients with ACAS will have cerebral hypoperfusion, which normalizes after revascularization.[39,40] Given the relationship between mobility and cognition, and the changes in cognition and cerebral perfusion after surgery,[41] it is reasonable that a similar mechanism would lead to changes in balance and mobility. Further research is necessary to explore the exact mechanism that revascularization targets to improve balance and mobility.

Other mechanisms that could negatively affect balance and mobility for patients with ACAS include inflammation, silent brain infarction, and intracranial atherosclerosis.[42,43] Elevated inflammatory markers in adults with chronic obstructive pulmonary disease, congestive heart failure, and high cardiovascular risk have been associated with impaired mobility.[44] Systemic inflammation impairs cerebral vasoregulation and accelerates declines in executive function, activities of daily living, and gait in older adults with diabetes.[45] Interleukin-6 and C-reactive protein are associated with decreased functional connectivity in the frontal and parietal regions in older adults with diabetes.[46] More importantly, interleukin-6 is associated with a lower blood oxygen level-dependent signal in the left middle frontal gyrus when working memory demand increases.[46] This suggests that systemic inflammation might contribute to impaired balance and mobility. Chronic inflammation results in sarcopenia and muscle weakness, which is known to affect balance and mobility negatively.[47] However, it is unlikely that a reversal of sarcopenia and muscle weakness would occur as rapidly as 6 weeks after surgery without active and intense physical therapy. A more direct effect of inflammation on cerebral microglia can also result in mobility declines, although this mechanism is thought to be mediated through chronic cerebral hypoperfusion.[48,49] Thus, both inflammation and perfusion might interact to contribute to declines in mobility function. Fixed silent brain infarctions and intracranial atherosclerotic lesions are also known to be associated with cognitive decline[50] and mobility function declines.[51] Silent infarctions, reported in ~20% of those with ACAS, predominately affects the basal ganglia,[52] which, along with the cerebral cortex and cerebellum, are important neural pathways for balance and mobility.[53] Silent infarctions have also been associated with an abnormal gait.[54] However, these non-modifiable risk factors would not be expected to respond to carotid artery revascularization.

The Mini-BESTest classified 90% of the study patients into an impaired (fall risk) category. The Mini-BESTest measures multiple aspects of balance control, including anticipatory control, reactive control, sensory orientation, and dynamic gait, and might be more sensitive to detecting a fall risk. Our results suggest that more sensitive balance and mobility outcome measures that specifically target the expected impairments in those with ACAS will be essential for identifying patients with impaired performance at baseline and those patients more likely to benefit from therapeutic interventions. We used the same measures in our previous study and found they were sensitive enough to detect group differences among patients with moderate-grade vs high-grade vs no stenosis. In that study, we found that patients with stenosis who demonstrated cognitive and mobility declines were 2.86 times more likely to fall compared with adults without stenosis.[12] Also, the patients with the greatest impairment in balance and mobility were more likely to show the greatest improvements at 6 weeks after surgery. Most patients scored well on the SPPB at baseline and, therefore, did not demonstrate a measurable change after surgery. High SPPB scores indicate a higher functioning patient population that is less likely to be limited in activities of daily living (ADLs) or have a risk of frailty. Although we did not assess ADLs or frailty, our patients' gait speed (range, 0.7–1.2 m/s) did not place them at risk of frailty (<0.80 m/s)[55] or dependency in ADLs (<0.55 m/s), except for three patients.[56] Balance and mobility function are components of several frailty indexes currently being evaluated for use as risk stratification tools before surgery and in general clinical care. Our results have indicated that some of the frailty scores might actually improve after carotid revascularization. It is evident that not all balance and mobility measures in the present study were impaired. Potentially, these measures (ie, FSST and WWT_c time) were not altered, might require longer postoperatively to show changes, or were not sensitive enough to detect an impairment at baseline. Thus, we would not have expected to find improvements in those measures after surgery.

The absence of a control group was a limitation, although withholding surgery to create such a group would have been unethical. Owing to the relatively small number of patients included and the selection criteria, a treatment selection bias could have been present. The patients enrolled in the present study might have had a greater propensity to experience increases in balance and mobility function and those not selected might have been be less likely to show such changes. Potentially, confounders could have been present, such as the interactions with the research staff, that might underlie the balance and mobility improvements. However, the balance and mobility tests administered in the present study are commonly used and have been reported to have excellent testeretest reliability, ranging from 0.84 to 0.97, in older adults, indicating the stability of scores for intervals as brief as 1 to 4 weeks.[16,26,57,58] A large sample size would be necessary to definitely ascertain the benefits of carotid revascularization on balance and mobility dysfunction.

CONCLUSIONS

Preserving mobility and balance function is vital for ADLs and for maintaining injury-free independence for older adults. Thus, approaches that can effectively mitigate declines in mobility and balance function are critically important for the aging population. It is becoming increasingly apparent that ACAS is associated with declines in mobility and balance. The results from the present study suggest benefits to balance and mobility dysfunction can be attenuated by 6 weeks after carotid artery surgery. This could indicate that ACAS is a modifiable risk factor for mobility decline in the elderly. Those individuals with the greatest impairments in balance and mobility showed the largest improvements in function after surgery. The next step is to determine why some balance and mobility measures improved after surgery and other domains did not change. Finally, understanding the underlying mechanisms that drive the changes in function are necessary for developing other therapeutic approaches for those patients not recommended for surgery.

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ARTICLE HIGHLIGHTS

- **Type of Research:** A repeated measure design
- **Key Findings:** Individuals with asymptomatic carotid stenosis with diameter reduction ≥70% performed better on some balance and mobility measures after revascularization.
- **Take Home Message:** Asymptomatic carotid artery stenosis is associated with impaired mobility and cognition and a greater fall risk.

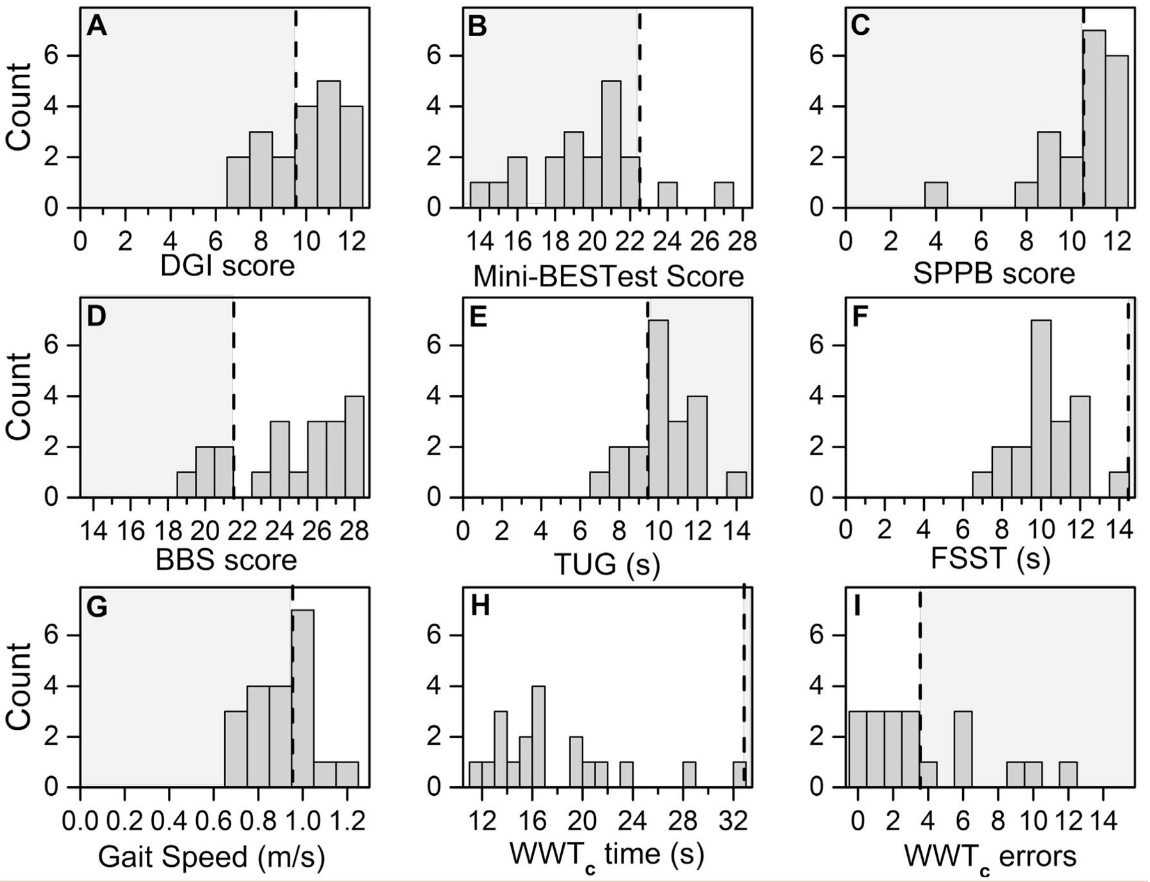

Fig 1.

Frequency graphs of mobility function assessments at baseline for patients with high-grade asymptomatic carotid artery stenosis (ACAS). **A**, Dynamic Gait Index (*DGI*) score. **B**, Mini-Balance Evaluation Systems Test (Mini- BESTest) score. **C**, Short Physical Performance Battery (*SPPB*) score. **D**, Berg Balance Scale (*BBS*) score. **E**, Timed Up and Go (*TUG*) time. **F**, Four Square Step Test (FSST) time. **G**, Gait speed. **H**, Walking While Talking complex (WWT_c) time. **I**, WWT_c errors. The *gray area* demarcated by the *black dotted line* represents the values below the age-related normative scores (BBS, TUG), indicating mobility disability (SPPB), or indicating a high fall risk (DGI, Mini-BESTest, FSST, gait speed, WWT_c time and errors).

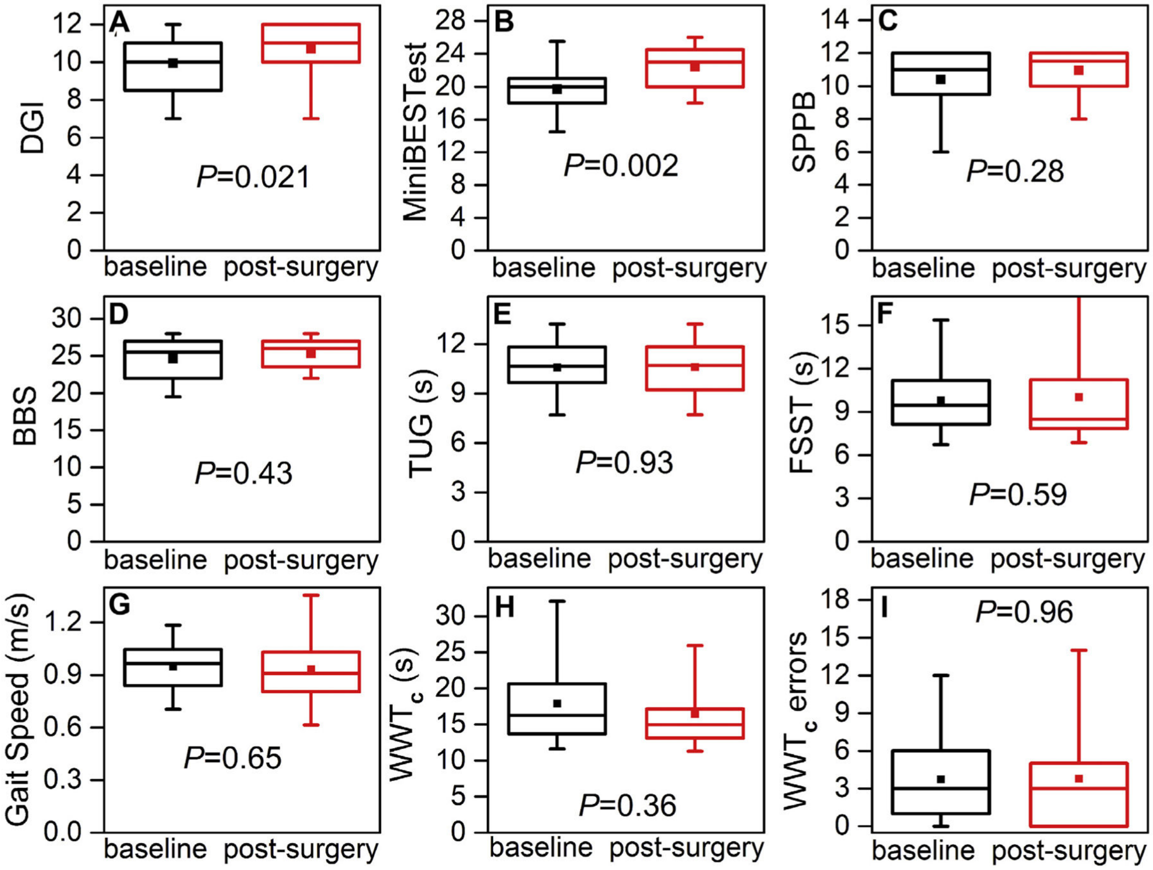

Fig 2.

Boxplots of mobility function assessments for patients with high-grade asymptomatic carotid artery stenosis (ACAS) at baseline (*black boxes*) and 6 weeks after carotid endarterectomy (*red boxes*). **A**, Dynamic Gait Index (*DGI*). **B**, Mini-Balance Evaluation Systems Test (Mini-BESTest). **C**, Short Physical Performance Battery (*SPPB*). **D**, Berg Balance Scale (*BBS*). **E**, Timed Up and Go (*TUG*) test. **F**, Four Square Step Test (*FSST*). **G**, Gait speed. **H**, Walking While Talking complex (WWT_c) time. **I**, WWT_c errors. *Horizontal line in box* indicates the median; top line of box, upper quartile (75th percentile); bottom line of box, lower quartile (25th percentile); filled square, mean; and *vertical lines (ends of whiskers),* minimum and maximum values. *P* values computed using paired *t* tests.

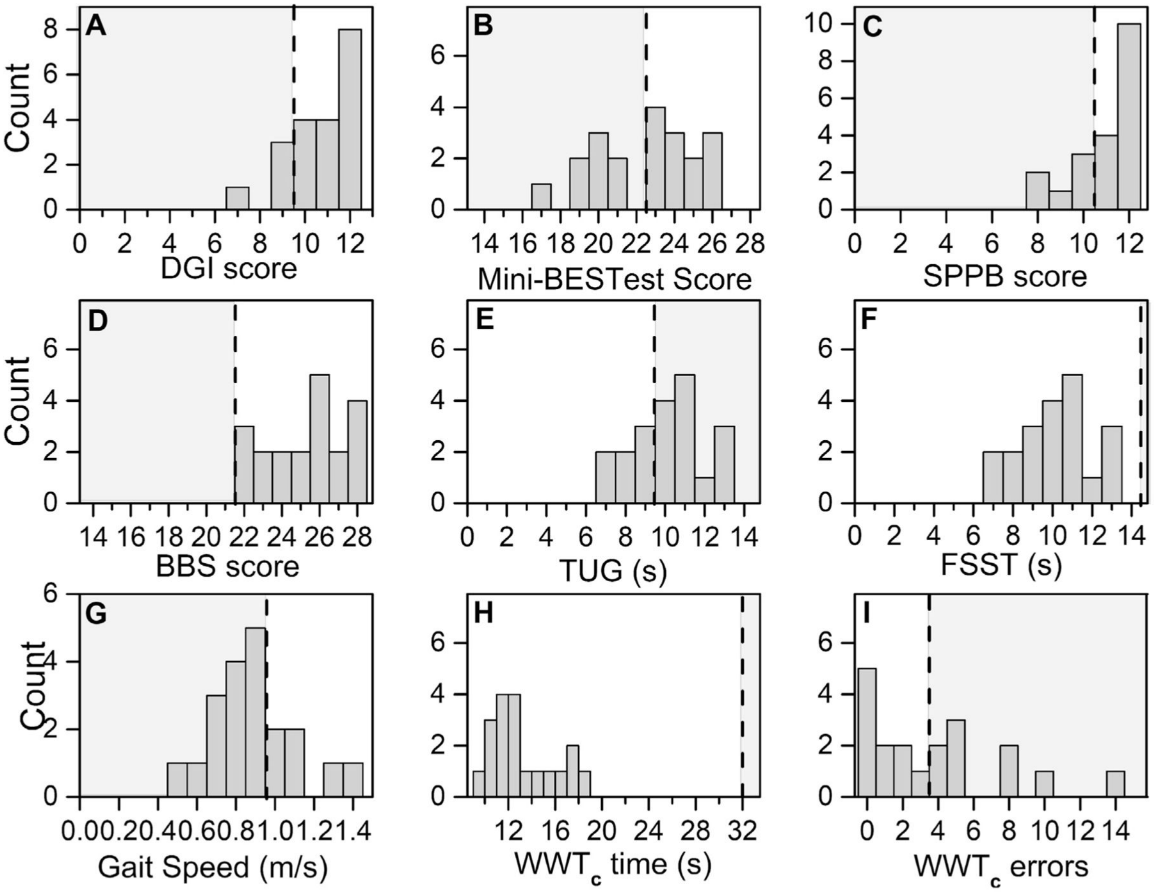

Fig 3.

Frequency graphs of mobility function assessments after carotid endarterectomy for patients with high-grade asymptomatic carotid artery stenosis (ACAS). **A**, Dynamic Gait Index (*DGI*) score. **B**, Mini-Balance Evaluation Systems Test (Mini-BESTest) score. **C**, Short Physical Performance Battery (*SPPB*) score. **D**, Berg Balance Scale (*BBS*) score. **E**, Timed Up and Go (*TUG*) time. **F**, Four Square Step Test (*FSST*) time. **G**, Gait speed. **H**, Walking While Talking complex (*WWT*$_c$) time. **I**, WWT$_c$ errors. The *gray area* demarcated by the *black dotted line* represents the values below age-related normative scores (BBS, TUG), indicating mobility disability (SPPB), or indicating a high fall risk (DGI, Mini-BESTest, FSST, gait speed, WWT$_c$ time and errors).

Table I.

Clinical patient characteristics (n = 20)

Characteristic	Mean ± SD or No. (%)
Age, years	67.0 ± 9.4
Female sex	9 (45.0)
African-American race	6 (30.0)
Coronary artery disease	10 (50.0)
Diabetes mellitus	11 (55.0)
Hypertension	19 (95.0)
Dyslipidemia	18 (90.0)
Smoking	14 (70.0)
Stenosis, right	12 (60.0)
Peak systolic velocity, cm/s	437.0 ± 142.0

SD, Standard deviation.

Table II.

Proportion of patients with impairment on balance and mobility measures (n = 20)

	Patients with impairment, %		
Balance and mobility measure	**Baseline**	**Postoperatively**	***P* value**[a]
Dynamic Gait Index	35.0	20.0	.38
Mini-BESTest	90.0	40.0	.02
Short Physical Performance Battery	35.0	30.0	.9
Short-form Berg Balance Scale	25.0	0.0	.06
Timed Up and Go test	75.0	65.0	.53
Four Square Step Test	0.0	0.0	1.0
Gait speed	55.0	70.0	.45
Walking While Talking complex			
Time	0.0	0.0	1.0
Errors	45.0	40.0	.9

Mini-BESTest, Balance Evaluation Systems Test.

[a] Using the McNemar test.