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Preoperative Cognition Predicts Clinical Stroke/TIA and Mortality After Surgical Aortic Valve Replacement in Older Adults

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Abstract

Background: Stroke and death remain risks of surgical aortic valve replacement (SAVR). Preoperative cognitive screeners repeatedly show that reduced scores predict postoperative outcome, but less is known about comprehensive neuropsychological measures predicting risk. This study had two aims: 1) investigate whether preoperative cognitive measures predicted postoperative clinical stroke/transient ischemic attack (TIA) and mortality in older adults undergoing SAVR, and 2) identify the best predictors within a comprehensive cognitive protocol.

Methods: 165 participants aged 65+ with moderate-to-severe aortic stenosis completed preoperative cognitive measures assessing memory, attention, language, visuospatial abilities, and executive functions. Postoperative stroke evaluations were conducted by trained stroke neurologists preoperatively and 1, 3, and 7 days postoperatively, and mortality outcomes were obtained by report and records. Logistic regressions were conducted to evaluate preoperative cognitive predictors of clinical stroke/TIA within one week of surgery and mortality within one year of surgery.

Results: Multivariate models showed measures of delayed verbal memory recall (Hopkins Verbal Learning Test-Revised [HVLT-R] Delayed Recall; OR=0.86; 95% CI 0.74 – 0.99) and visuospatial

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skills (Judgment of Line Orientation [JOLO]; OR=0.95; 95% CI 0.90 – 1.01) predicted clinical stroke/TIA within one week of surgery, $R^2 = .41$, $p < .001$, $f^2 = .69$. Measures of naming ability (Boston Naming Test [BNT]; OR=0.88; 95% CI 0.80 – 0.96), verbal memory recall (HVLT-R Delayed Recall; OR=1.23; 95% CI 0.99 – 1.51), visual memory recall (Rey Complex Figure Delayed Recall; OR=0.90; 95% CI 0.80 – 1.00), medical comorbidities (Charlson Comorbidity Index; OR=1.71; 95% CI 1.22 – 2.65), and sex (OR=2.39; 95% CI 0.90 – 7.04) were significant predictors of death within one year of surgery, $R^2 = .68$, $p < .001$, $f^2 = 2.12$.

Conclusions: Preoperative cognitive measures reflecting temporal and parietal lobe functions predicted postoperative clinical stroke/TIA within one week of SAVR and mortality within one year of SAVR. As such, cognitive measures may offer objective and timely indicators of preoperative health, specifically vulnerabilities in cerebral hypoperfusion, that may inform intervention and/or intensive postoperative monitoring and follow-up after SAVR.

Keywords

aortic valve stenosis; aortic valve replacement; cognition; stroke; mortality; neuropsychology

Introduction

Older adults undergoing open-heart procedures, such as surgical aortic valve replacement (SAVR), remain at elevated risk for stroke and mortality, with stroke/transient ischemic attack (TIA) reported in 2%−19% of cases and silent acute cerebral infarcts on MRI reported in approximately 60% of cases (Daneault et al., 2011; Messé et al., 2014). Mortality rates following isolated SAVR procedures range from 5%−7% (Paradis et al., 2014; Vasques et al., 2012). Previous literature has identified neurological disorders (OR=4.8), age (OR=1.02), and having other medical comorbidities (e.g., carotid stenosis [OR=1.81], diabetes [OR=1.60], hypertension [OR=0.81], renal failure [OR=0.67], and hypothyroidism [OR=0.63]) as risk factors that predict postoperative stroke following SAVR (Sultan et al., 2020; Udesh et al., 2017). Similarly, age (age 61–70 HR=2.08; >70 years old HR=3.80), having other medical comorbidities (e.g., diabetes HR=1.51; renal failure HR=1.47; congestive heart failure HR=1.37), and clinical stroke after SAVR significantly predict mortality following SAVR (Higgins et al., 2011; Messé et al., 2014). Identifying patients at greatest risk for stroke and death may improve postoperative outcomes, inform prevention or intervention strategies, aid in surgical decision making, and reduce healthcare burden. Thus, consistent with the priorities of the American College of Surgeons focused on optimal preoperative assessment of geriatric surgical patients (Mohanty et al., 2016), this study investigated whether (and which) preoperative cognitive measures improve prediction of negative outcomes among older adults following SAVR.

Preoperative cognitive measures administered by trained clinicians at the bedside yield objective and sensitive scores reflecting even mild perturbations of brain function (Lezak et al., 2012). In fact, preoperative cognitive measures, and particularly those assessing memory and attention, have been used to predict negative surgical outcomes (e.g., delirium, increased length of hospital stay, and cost of care) in a wide range of populations (Millar et al., 2001; O’Reilly-Shah et al., 2019; Oresanya et al., 2014; Robinson et al., 2012). SAVR, despite its relatively high-risk profile relative to other cardiac procedures (e.g., SAVR 5%−7% mortality vs. coronary artery bypass grafting [CABG] 3%−5%; Paradis et al., 2014), has been studied infrequently and generally using only brief cognitive screeners (O'Reilly-Shah et al., 2019; Robinson et al., 2012), which may not be sensitive enough to detect preoperative mild cognitive difficulties that could reflect increased vulnerability to postoperative stroke/TIA or death.

This study investigated the hypothesis that cognitive test scores would predict postoperative stroke and mortality, even after accounting for demographic factors and medical comorbidities. because they are objective, sensitive, and current indicators of brain function and general health. Participants included a cohort of older adults who were recruited for a parent study on the incidence and impact perioperative stroke and post-operative cognitive decline. Participants were administered a comprehensive battery of cognitive tests that evaluated a range of cognitive abilities before and after surgery. Results of the parent study showed this cohort experienced a high incidence of perioperative embolic strokes (Massaro et al., 2016; Messé et al., 2014) but among the participants who survived and completed the study, the large majority demonstrated intact, cognitive outcomes at one year (Giovannetti et al., 2019). In the current study, we expected that worse performance on preoperative cognitive measures would significantly predict postoperative clinical stroke/TIA within one week and mortality within one year following SAVR in older adults. A second aim was to explore which specific cognitive measures would best predict risk for negative postoperative outcomes to inform the most efficient and streamlined use of testing in practice.

Material and Methods

Data were collected for a parent study on stroke and cognition in older adults undergoing SAVR (R01HL084375; PI - T. Floyd), which was approved by the University of Pennsylvania Institutional Review Board. The parent study was designed and powered to prospectively investigate the incidence and impact of clinical stroke/TIA and silent radiographic cerebral infarction (Messé et al., 2014) and post-operative cognitive changes (Giovannetti et al., 2019; Massaro et al., 2016; Messé et al., 2014). All participants provided informed consent and were compensated to participate in the parent study. The current study is a retrospective analysis of the archived data from the parent study.

Participants

This study included surgery participants from the parent study (Giovannetti et al., 2019; Massaro et al., 2016; Messé et al., 2014). Surgery participants were fluent English speakers aged 65 years or older recruited from two University of Pennsylvania Health System hospitals between April 2008 and September 2012. The anesthetic and surgical procedures for each participant were determined by the clinical team. Participants were not recruited if they had a history of past cardiac surgery, carotid stenting or endarterectomy within the prior six weeks, active psychiatric disorder, severe sensory/motor/cognitive impairment, or major neurological disease/disorder. One hundred ninety-three individuals enrolled, but 28 participants were excluded for the following reasons: suspected cognitive impairment based on a screening test (MMSE < 23; n=3); refused or failed to obtain any baseline cognitive testing (n=15); did not ultimately undergo surgery (n=4); or were lost to follow (n=6).

The final sample included 165 participants. The 28 participants who were excluded were significantly older (*M*=78, *SD*=6.92) than those who were included (*M*=75.54, *SD*=5.93) in the final sample ($t(191)= -1.98$, $p=.049$, $d = -.41$). There were no group differences in other demographic or clinical data (all *t*s<1.76, all *p*s>.08). Because 15 of the 28 excluded participants did not have any cognitive data, differences in cognitive tests scores were not examined.

Procedures

Participants completed questionnaires and cognitive tests before SAVR and again at 4–6 weeks and 9–12 months after surgery. For this study, only the preoperative questionnaires and cognitive measures were analyzed as predictors of postoperative stroke and mortality. Stroke was evaluated with a postoperative MRI of the brain (diffusion-weighted imaging [DWI]) and serial neurologic evaluations that were conducted over a seven-day period following surgery. Mortality was tracked over a one-year period following surgery.

Predictors of Stroke and Mortality

Demographic and Clinical Data—Using self-report questionnaires and chart review, the following variables were obtained before surgery: age; sex; education; race/ethnicity; medical comorbidities (i.e., Charlson Comorbidity Index [CCI]; Charlson et al., 1987); body mass index (BMI), which has been used as a measure of physical frailty (Hubbard et al., 2010); and mood (i.e., Geriatric Depression Scale; Yesavage et al., 1982). For this study, because some conditions on the CCI were exclusion criteria (e.g., dementia, hemiplegia) or were examined independently (e.g., history of stroke/TIA), the CCI was computed as the unweighted sum of 9 conditions, including pulmonary disease, connective tissue disease, liver disease, renal disease, congestive heart failure, hypertension, HIV/AIDS, peripheral vascular disease, diabetes.

Cognitive Protocol—The preoperative cognitive protocol included a brief cognitive screening measure of global cognition (Mini Mental Status Examination [MMSE]) and ten cognitive variables across five cognitive domains: memory, language, visuospatial skills, executive function, and attention/working memory (Giovannetti et al., 2019). The measures and variables, described in Table 1, were selected to assess cognitive abilities as recommended in consensus guidelines (Brandt, 1991; Lamar et al., 2002; Murkin et al., 1995).

Clinical Stroke/TIA within 7 Days of Surgery—Trained stroke neurologists performed neurologic examinations preoperatively and 1, 3, and 7 days postoperatively. MRI of the brain occurred within 1 week after surgery on a 1.5 Tesla Siemens Magnetom Avanto (Siemens, Erlangen, Germany) or GE Signa Excite (GE Medical Systems, Milwaukee, WI) scanner as described elsewhere (Messé et al., 2014). Participants were classified as having had a clinical stroke/TIA if they demonstrated new focal neurologic symptoms during the neurologic evaluations consistent with a vascular territory and without an alternative explanation at any postoperative examination. For some participants (n=3), focal neurologic symptoms were only transitory (i.e., TIA). Individuals were classified as not having a clinical stroke/TIA if they demonstrated no new symptoms of clinical stroke/TIA regardless of whether they showed acute cerebral lesion(s) on DWI-MRI.

Acute Cerebral Lesions on MRI Obtained within 7 Days of Surgery—The volume of acute cerebral ischemic lesions observed on MRI, regardless of clinical symptoms, was analyzed as a secondary stroke outcome. Acute cerebral lesions were defined as hyperintensities on DWI sequences, with matching hypointensities on apparent diffusion coefficient maps. T2-fluid attenuated inversion recovery MRI images were reviewed to rule out artifacts. Two trained readers blinded to background data independently read the scans (interrater reliability, κ=0.93; Massaro et al., 2016). A radiologist resolved discrepancies. Acute cerebral lesions were manually segmented with a viewing and segmenting tool (MRIcron, http://www.nitrc.org/projects/mricron) and quantified for each participant (lesion number, total lesion volume).

Mortality within One Year of Surgery—Mortality information was collected at 4–6 weeks post-surgery and again at 9–12 months by informant report or death records.

Statistical Analyses

Analyses were conducted in R Studio Version 1.2.5033, SPSS Version 28.0.1.0, and Mplus Version 8.2. Descriptive analyses were performed for all study variables, and *t*-tests/Mann-Whitney *U* tests or Chi-square tests were used to compare baseline demographic and cognitive measures between those who suffered a postoperative clinical stroke/TIA within one week of surgery compared to those who did not and between those who died versus survived within one year of surgery.

Logistic regressions were conducted in Mplus Version 8.2 using full information maximum likelihood (FIML) to address missing data. FIML fits statistical models based on all observed data and thus permits inclusion of all participants, even those with missing data. Logistic regression assumptions (i.e., linearity, independence of errors, multicollinearity) were evaluated prior to regression analyses. Then, logistic regressions were performed using Bayesian methods to evaluate predictors of clinical stroke/TIA (i.e., stroke/TIA vs. no stroke/TIA) within 7 days of surgery and mortality (i.e., died vs. survived) within one year of surgery. Bayesian estimators are recommended over traditional, maximum likelihood approaches for small samples and outcomes that have a low base rate, as Bayesian approaches do not require the assumptions for large sample theory and instead assume that estimates may have a non-normal posterior distribution (van de Schoot et al., 2014). As prediction is highly dependent on priors with Bayesian estimation and given the dearth of literature evaluating similar models, the default settings in Mplus for priors for categorical outcomes (0, 5) and predictors (0, infinity) were used for the regression analyses. To evaluate model fit, the variance accounted for (R^2) by the predictors, as well as the Bayesian posterior predictive p-values, which assess to what extent the observed model in the current sample fits with expected population parameters and for which values closer to .5 indicate good model fit (Gelman, 2013; Meng, 1994), were considered. Separate analyses were conducted considering prediction for (a) a cognitive screener (i.e., MMSE) and (b) a comprehensive cognitive protocol, in both cases controlling for demographic and physical health variables. Final logistic regression models included measures from a comprehensive neuropsychological battery. Odds ratios and 95% Confidence Intervals were computed for each independent variable in the multivariate logistic regression models. Bivariate Spearman's rank-order correlations were used to examine associations between participant variables (i.e., demographics, cognitive measures) and total acute cerebral lesion volume. All results were considered significant at $p<.05$.

Results

Demographics and Clinical Characteristics

Participant characteristics and performance on preoperative cognitive measures are summarized in Table 2. Participants with cognitive impairment and neurological disorders (e.g., dementia) were not recruited; consequently, average neuropsychological test scores (shown in Table 2) were all within normal limits for older adults. The participants in this study were all older people undergoing SAVR because of severe aortic stenosis, indicating that they all had significant cardiovascular disease and symptoms of aortic stenosis (e.g., shortness of breath, fatigue); nevertheless, they differed in the extent to which they demonstrated other medical comorbidities on the CCI, which ranged from 0 – 5 out of 9 possible comorbid conditions.

Postoperative Stroke/TIA

Serial neurological exams showed 29 participants (17.6%) suffered an acute clinical stroke (n=26) or TIA (n=3) within the first seven days following surgery. A total of 114 participants received postoperative inpatient MRI, and 67 participants with MRI showed an average of 1.88 new lesions (range = 0 – 34) with an average total infarct volume of 1278.9mm^3 (range = 0 – 55,871.22mm^3).

Participants with Postoperative Clinical Stroke/TIA vs. Participants without Postoperative Clinical Stroke/TIA within 7 Days of Surgery—As shown in Table 3, participants with postoperative stroke/TIA obtained significantly lower scores on measures of language/naming (i.e., Boston Naming Test [BNT]), verbal episodic memory (i.e., Hopkins Verbal Learning Test – Revised [HVLT-R] Delayed Recall), visuospatial abilities (i.e., Judgment of Line Orientation [JOLO]), and executive function (i.e., Trail Making Test B-A).

Multiple Regression Model Predicting Postoperative Clinical Stroke/TIA—There was no evidence for multicollinearity, as tolerance statistics ranged from .59 - .90 and the variance inflation factor (VIF) statistics ranged from 1.11 – 1.68. As shown in Table 4 (Model 1), a measure of delayed memory recall (HVLT-R Delayed Recall) and a measure of visuospatial perception (JOLO) significantly predicted postoperative stroke/TIA within one week of surgery. Model fit and classification accuracy statistics indicated that the model accounted for a significant portion of the variance ($R^2 = .41$, $p<.001$, $f^2=.69$) with good model fit (Bayesian posterior predictive p-value = .529).

Note that MMSE was not significant in the multivariate model, indicating that the HVLT-R and JOLO significantly predicted clinical stroke/TIA within one week of surgery even after considering prediction from the MMSE. Additionally, ancillary analyses including only the MMSE demonstrated that the MMSE alone did not significantly predict stroke/TIA within one week of surgery ($B = -0.080$, $SE = 0.005$, $p = 0.09$).

Correlates of Total Lesion Volume—Results of bivariate Spearman correlations between total acute infarct lesion volume and predictor variables are reported in the Supplementary Materials. Lower scores on a measure of attention/working memory (Digit Span Test) were significantly associated with larger total lesion volumes. No other demographic/clinical variable or neuropsychological test score was significantly associated with total infarct volume.

Mortality

A total of thirteen participants died within one year following surgery (7.9% mortality). Nine participants died within 4–6 weeks after surgery, and four participants died between 6 weeks and a year of surgery.

Participants who Died within One Year of Surgery vs. Participants who Survived—As shown in Table 5, participants who died after surgery had significantly more medical comorbidities (CCI) and lower scores on the cognitive screener (MMSE). Additionally, compared to those who survived, participants who died had significantly worse baseline language performance (BNT, Animal Fluency), verbal episodic memory (HVLT-R Delayed Recall), attention/working memory (Digit Span Test), and executive function (TMT B-A).

Multiple Regression Models Predicting Mortality—As shown in Table 6 (Model 2), sex, a measure of medical comorbidities (CCI), and measures of visual spatial memory (Rey Long Delay), confrontation naming (BNT), and delayed memory recall (HVLT-R Delayed Recall) significantly predicted postoperative mortality. Model fit and classification accuracy statistics indicated that the model accounted for a significant portion of the variance ($R^2 = .68$, $p < .001$, $f^2 = 2.12$) with good model fit (Bayesian posterior predictive p-value = .529). Specifically, the results indicated that male sex, more medical comorbidities, and lower scores on the BNT, HVLT-R, and Rey Long Delay were associated with mortality.

The MMSE was not significant in the multivariate model, indicating that the BNT, HVLT-R, Rey Complex Figure Test, Charlson Comorbidity Index, and sex significantly predicted mortality within one year of surgery even after considering prediction from the MMSE. Additionally, ancillary analyses including only the MMSE demonstrated that the MMSE alone did not significantly predict mortality within one year of surgery ($B = -0.120$, $SE = 0.006$, $p = 0.06$).

Discussion

Cognitive measures significantly predicted postoperative stroke/TIA and mortality in older adults following SAVR, whereas a brief cognitive screener (MMSE), as well as clinical/

demographic variables, such as age, BMI, and self-reported history of stroke/TIA did not consistently predict negative surgical outcomes. Cognitive measures, which are objective and may be obtained just before surgery, may yield accurate measures of current brain function and health, particularly vascular health (Snyder et al., 2021), which is critical for surgical outcomes. Additionally, most cognitive measures yield a range of scores, even within a relatively homogeneous population (i.e., older adults with chronic cardiovascular disease), offering a low-cost, non-invasive method for identifying meaningful variability within a high-risk sample.

Multivariate models showed that a measure of delayed memory recall (HVLT-R Delayed Recall) and a measure of visuospatial perception (JOLO) were the best predictors of clinical stroke/TIA. Measures of visual spatial memory (Rey Long Delay), confrontation naming abilities (BNT), and delayed memory recall (HVLT-R Delayed Recall), along with sex and a measure of medical comorbidities (Charlson Comorbidity Index), were the best predictors of mortality. Specifically, the odds of postoperative stroke/TIA in the 7-day postoperative period increased by 16% with each item not recalled on the HVLT-R Delayed Recall measure, and by 5% with each incorrect item on the JOLO, independent of baseline performance on all other cognitive measures. Additionally, each detail not recalled on Rey Long Delay Free Recall was associated with 11% increased odds of death within one year of surgery, and each incorrectly named or omitted item on the BNT was associated with an increased odds of death within one year of surgery by 14%, independent of baseline performance on all other cognitive measures. Risk of death within one year of surgery also increased by 1.71 times for each unit increase on the CCI and was 2.39 times more likely for men relative to women. Although the HVLT-R Delayed Recall measure also significantly predicted death within one year of surgery in the multivariate model, the estimate was not in the expected direction. Specifically, univariate analyses showed that the HVLT-R Delayed Recall was significantly lower among participants who died within one year of surgery (medium to large effect size) but prediction in the multivariate model was positive. Although findings from tests of multicollinearity were within the acceptable range, the HVLT-R Delayed Recall score was moderately correlated with several other test scores, suggesting that these intercorrelations may have led to suppression effects. Nevertheless, correlations among cognitive tests and their errors are not unexpected, and suppressor variables account for outcome-irrelevant variations among predictors, improve the predictive power of the model, and in this case, likely contributed to the large amount of variance accounted for in the model (Akinwande et al., 2015). In sum, relative to demographic and clinical/vascular risk factors that have been reported in prior studies of stroke and death following SAVR (Higgins et al., 2011; Messé et al., 2014; Sultan et al., 2020; Udesh et al., 2017), cognitive test scores demonstrated similar odds ratios, and thus, may be particularly useful in determining risk in demographically homogeneous populations (e.g., among older adults) or when medical records are incomplete or unavailable.

It was somewhat surprising that measures of executive function and processing speed were not significant predictors of postoperative outcomes, as executive function abilities are most commonly associated with cerebrovascular disease in older adults. In this relatively homogeneous sample of older people with chronic cardiovascular disease, measures of executive function might not be sufficiently sensitive to detect differences in severity of impairment (see Larrabee 2014). Results showed that measures of temporal cortical functions (i.e., delayed recall and language/naming abilities) may have greater sensitivity in detecting more severe cerebrovascular disease or possibly a secondary preclinical neurodegenerative disease that places individuals with chronic cardiovascular disease at greater risk for poor surgical outcomes in this sample. Tests of delayed recall and naming abilities are associated with function of left temporal cortical regions (i.e., BNT; left temporal cortex [Baldo et al., 2013]; HVLT-R Delayed Recall [Squire et al., 2002]; medial temporal cortex), and tests of visuospatial functions (JOLO) suggested posterior temporal parietal regions (Tranel et al., 2009). Thus, the results of the cognitive tests implicate vascular watershed regions (Massaro et al., 2016; Wiggins et al., 2020) and may reflect preoperative vulnerabilities of poor brain/vascular health in a high-risk sample. Although mechanisms remain unknown and data regarding the location of new acute lesions were not examined, future studies should seek correspondence with brain imaging. Nevertheless, our results imply that cognitive measures of linguistic/naming, delayed recall, and visuoperceptual abilities may be best suited to screen older cardiac patients for poor surgical outcomes.

Analyses of acute infarcts on MRI showed that worse attention/working memory abilities (Digit Span Test) were modestly associated with greater total volume of acute (postoperative) lesions. The Digit Span Test is considered a test of attention and working memory that relies on functioning of the frontal-parietal cortex, a watershed region. Thus, baseline attention/working memory abilities may reflect patients’ vulnerability to new, non-lethal cerebrovascular emboli after surgery (e.g., possibly due to chronic hypoperfusion; Snyder et al., 2021). However, the clinical relevance of acute cerebral lesions remains controversial, and in the present sample, acute lesions were observed in the majority of patients who survived without cognitive difficulties (i.e., “silent” lesions; Giovannetti et al., 2019).

Several study limitations are worth noting. First, participants were recruited from an established heart valve disease program that accepts complicated surgical cases; outcomes may have differed in a multiple-site study that included hospitals with less experience in SAVR and fewer complicated cases. Second, based on the parent study, only 6% of the eligible recruitment pool was non-White (Messé et al., 2014), limiting generalizability to more diverse populations with more medical comorbidities due to known health disparities in the US. Along this line, tests of naming ability, such as the BNT, may not be appropriate for people who are not native English speakers. Further, the BNT includes some items that are outdated and/or inappropriate for use with people who identify as Black, regardless of their native language; therefore, a more up-to-date naming test or a modified version of the BNT using a freely replaceable item or modified scoring is strongly recommended in future studies with more diverse participants (Byrd et al., 2021; Salo et al., 2022). Third, data on surgical complications, measures of cardiovascular function, and the exact cause of death were not collected, though nearly 70% of those who died (i.e., 9/13) did not survive the surgery or the recovery period. Future studies should consider the utility of preoperative neuropsychological tests for predicting surgical complications and the utility of cardiovascular function metrics in predicting risk, as well as obtain detailed data on cause of death. Fourth, our study was a retrospective analysis of a parent study that was not designed to investigate mortality outcomes. As such, our results should be interpreted as preliminary and should be used to guide future, larger prospective studies that include classification accuracy statistics. Fifth, six participants were lost to follow-up and though they shared similar characteristics to participants who died, mortality outcome could not be definitively coded.

Finally, over the past five to ten years, aortic valve replacement procedures have been more frequently performed via a minimally invasive, catheter-based procedure (i.e., transcatheter aortic valve replacement, TAVR), particularly for the treatment of severe, symptomatic aortic stenosis in patients with intermediate surgical risk (Still et al., 2018). Recent studies investigating national trends of SAVR and TAVR procedures have demonstrated that TAVR procedures have increased steadily over the past decade, though SAVR procedures are still being performed and the number of SAVR procedures per year has remained relatively constant (Clark et al., 2022). In fact, SAVR remains the most effective valve replacement option for a variety of situations, including, for example, among patients younger than 65 years of age who will likely need a subsequent valve replacement later in life, patients at high risk for a permanent pacemaker, patients with rheumatic heart disease, and patients of low surgical risk given its durability (Still et al., 2018). Additionally, TAVR and SAVR have been shown to have similar survival (i.e., mortality) and stroke rates in some populations (Gleason et al., 2018). Though the results of one recent TAVR study were consistent with our results and showed preoperative scores on the Clock Drawing Test, a visuospatial measure associated with posterior cortical functions, significantly predicted length of hospital stay and hospital cost following TAVR (Wiggins et al., 2021), further investigation is required to determine whether risk factors for death and stroke are the same following SAVR versus TAVR (Smith et al., 2011).

Regarding strengths, our study is one of the few examining outcomes among older adults undergoing SAVR; because our sample was at such high-risk of negative outcomes, and these outcomes were assiduously and prospectively ascertained, we were able to study mortality and stroke in a relatively small sample of 165 participants. The cognitive protocol was administered and scored by a team led by a clinical neuropsychologist, stroke outcomes were obtained by serial evaluations conducted by neurologists with expertise in stroke and included MRI of the brain, and mortality outcomes were evaluated over the course of one year; thus, predictors and outcomes were carefully and comprehensively measured. Finally, neuropsychological predictors were intended to be feasible for rapid assessment of risk at the bedside.

In conclusion, our results add to the accumulating literature demonstrating the utility of neuropsychological assessment in surgical settings (Berger et al., 2018; Wiggins et al., 2021) and more broadly beyond the surgical arena, particularly compared to brief cognitive screeners (e.g., MMSE) or other indicators of brain or overall health (e.g., BMI, history of stroke/TIA), given that these did not independently predict negative post-operative outcomes (Donders, 2020; Watt & Crowe, 2018). The importance of post-surgical assessment has been illustrated in numerous papers on post-operative cognitive decline (e.g., Giovannetti et al., 2019; Price et al., 2008), but our study demonstrates the utility of neuropsychological assessment at the pre-surgical timepoint for people over age 65. Pre-surgical cognitive testing, particularly testing of language, episodic memory, and visuospatial abilities (i.e., temporal and parietal lobe functions), offers an objective, current, and efficient (i.e., easy to obtain at the bedside) indicator of current brain health (e.g., chronic hypoperfusion) that predicts negative outcomes of surgery among older adults. Preoperative measures of language (i.e., confrontation naming) and delayed recall abilities should be included as part of routine pre-operative care to facilitate treatment planning and guide more intensive surgical or post-operative monitoring. Investigators developing rapid, digital cognitive assessment tools for the presurgical arena (e.g., Amini et al., 2019; Arias et al., 2020; Wiggins et al., 2021) should include measures of posterior cortical functions to facilitate prediction of surgical outcomes in older people.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Availability Statement:

The data that support the findings of this study are available from the corresponding author, T.G., upon reasonable request.

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Table 1.

List of neuropsychological tests and test descriptions

Domain	Test	Description	Outcome Variable (possible range)
Global Cognition	Mini-Mental Status Examination (MMSE)	30-point screening questionnaire assessing orientation, short-term memory, attention, short-term recall, and language	Total correct (0 – 30)
Verbal Memory	Hopkins Verbal Learning Test- Revised (HVLT-R Delay Recall)	12-word list administered over 3 learning trials, followed by a delay trial after 25 minutes	Total correct (0 – 12)
Visual Spatial Memory	Rey Complex Figure (Rey Long Delay)	complex geometric design presented for copy (see below); recall assessed by asking participant to draw the figure from memory 20 minutes later (delayed recall)	Accuracy of delayed recall (0 – 36)
Naming	Boston Naming Test (BNT Total Score)	line drawings of objects/animals are presented individually for naming	Total correct (0 – 60)
Verbal Fluency	Animal Fluency	as many animal names as possible must be generated in 60 seconds	Total number of words (0 – no upper limit)
Visuospatial Perception	Judgment of Line Orientation (JOLO)	angled lines must be matched to the orientation of angles presented in an array of multiple choices	Total correct (0 – 30)
Executive Function	Trail Making Test- Part B-Part A	a line must be drawn to connect a series of numbers or alternating numbers and letters	Total completion time (0 – 300 sec)
Attention/Working Memory	Digit Span Test (Forward + Backward)	increasing lengths of number sequences must be repeated in forward and reverse order	Total correct (0 – 30)

Table 2.

Demographic characteristics and raw cognitive test performance scores of sample (N=165).

Characteristic	Mean (SD) / Median (range)
Age (years)	75.5 (5.9)
Sex (% Female)	37
Education (years)	13.9 (3.0)
Race (% White)	94.5
Past stroke or transient ischemic attack (%)	12.7
Medical comorbidities (Charlson Comorbidity Index)[c]	1.0 (0 – 5)
Body Mass Index[c]	28.8 (17.2 – 52.9)
Geriatric Depression Scale[a,c]	2.0 (0 – 20)
Mini-Mental Status Examination[b]	27.7 (1.6)
Rey Complex Figure Long Delay Free Recall	14.1 (6.0)
Boston Naming Test (BNT)[c]	55.0 (22 – 60)
Animal Fluency total	18.2 (5.0)
HVLT-R Delayed Recall total	7.3 (2.5)
Judgment of Line Orientation (JOLO) total	20.7 (5.6)
Trail Making Test – Part A (time to completion)[c]	46.0 (22 – 213)
Trail Making Test – Part B (time to completion)[c]	109.0 (51 – 301)
Trail Making Test – B-A[c]	63.0 (−2 – 256)
Digit Span Test – Forward total	9.5 (1.9)
Digit Span Test – Backward total	6.1 (2.4)
Digit Span Test Total	15.54 (3.77)

[a] Maximum = 30 (worst).

[b] Maximum = 30 (best).

[c] Median (range) reported for variables not normally distributed.

Table 3.

Differences between participants who had a postoperative clinical stroke/TIA within one week of surgery vs. those who did not.

Characteristic	Stroke (n = 29)	No Stroke (n = 136)	Test Statistic	*p* Value	Effect Size
Age (years)	77.0 (5.6)	75.2 (6.0)	$t = -1.47$	.14	$-.30^{\wedge}$
Sex (% Female)	44.8	35.3	$X^2=0.93$	.33	$-.08^{\wedge\wedge\wedge}$
Education (years)	13.8 (2.5)	13.9 (3.0)	$t=0.19$	.85	$.04^{\wedge}$
Race (% White)	89.7	95.6	$X^2=1.63$	.20	$-.10^{\wedge\wedge\wedge}$
Past stroke/TIA(%)	24.1	10.3	$X^2=4.12$	.06	$0.16^{\wedge\wedge\wedge}$
Medical Comorbidities (Charlson Comorbidity Index)^{c}	2.0 (0 – 4)	1.0 (0 – 5)	$U=1673$	.19	$-0.10^{\wedge\wedge}$
Body Mass Index^{c}	29.3 (17.2 – 37.8)	28.8 (23.3 – 52.9)	$U=1825.5$	.53	$-0.05^{\wedge\wedge}$
Geriatric Depression Scale^{a,c}	4.0 (0 – 14)	2.0 (0 – 20)	$U=1748.5$	.57	$-0.04^{\wedge\wedge}$
Mini-Mental Status Examination^{b}	27.3 (1.9)	27.8 (1.5)	$t=1.33$	.19	$.27^{\wedge}$
Rey Complex Figure Long Delay Free Recall	12.2 (5.7)	14.5 (6.0)	$t=1.76$	.08	$.39^{\wedge}$
Boston Naming Test (BNT)^{c}	51.5 (32 – 59)	55 (22 – 60)	$U=1269$	**.01** **	$-0.21^{\wedge\wedge}$
Animal Fluency	16.6 (5.5)	18.5 (4.8)	$t=1.86$	.06	$.40^{\wedge}$
HVLT-R Delayed Recall	5.9 (2.4)	7.6 (2.5)	$t=3.33$	**.00** **	$.68^{\wedge}$
Judgment of Line Orientation (JOLO)	18.1 (5.3)	21.3 (5.6)	$t=2.73$	**.01** **	$.58^{\wedge}$
Trail Making Test – B-A^{c}	88.0 (44 – 245)	59.0 (−2 – 256)	$U=921.5$	**<.001** ***	$-0.28^{\wedge\wedge}$
Digit Span Test Total	14.44 (2.98)	15.78 (3.89)	$t=1.68$	.10	$.36^{\wedge}$

Values are expressed as mean (SD) or %.

$^{*}p < .05$.

$^{**}p < .01$.

$^{***}p < .001$.

[a] Maximum = 30 (worst).

[b] Maximum = 30 (best).

[c] Median (range) reported for variables not normally distributed.

Effect sizes:

$^{\wedge}$Cohen’s d (.2 = small; .5 = medium; .8= large)

$^{\wedge\wedge}$Probability of superiority (<0.44 or >0.55 = small; <0.36 or >0.64. = medium; <0.29 or >0.71 = large)

$^{\wedge\wedge\wedge}$Phi (.1 = small; .3 = medium; .5 = large)

Table 4.

Logistic regression model predicting postoperative clinical stroke/TIA within one week of surgery.

	B (SE)	β	Odds Ratio (95% CI)	p value
Model 1				
Age	0.006 (0.002)	0.025	1.01 (0.97, 1.05)	.40
Sex	−0.172 (0.028)	−0.063	0.84 (0.44, 1.82)	.31
Education	0.050 (0.005)	0.109	1.05 (0.94, 1.19)	.19
Past stroke or TIA	0.598 (0.030)	0.155	1.82 (0.84, 3.77)	.06
Charlson Comorbidity Index	0.021 (0.008)	0.020	1.02 (0.83, 1.27)	.42
BMI	−0.029 (0.002)	−0.110	0.97 (0.92, 1.03)	.15
GDS	−0.038 (0.003)	−0.113	0.96 (0.89, 1.03)	.16
MMSE	0.084 (0.006)	0.101	1.09 (0.93, 1.27)	.14
Rey Complex Figure Long Delay Free Recall	0.017 (0.002)	0.078	1.02 (0.95, 1.08)	.28
BNT	−0.034 (0.002)	−0.149	0.97 (−.92, 1.02)	.11
Animal Fluency	0.014 (0.003)	0.053	1.01 (0.95, 1.09)	.36
HVLT-R Delayed Recall	**−0.156 (0.005)**	**−0.297**	**0.86 (0.74, 0.99)**	**.01** *
JOLO	**−0.050 (0.002)**	**−0.215**	**0.95 (0.90, 1.01)**	**.04** *
Trail Making Test (B-A)	0.003 (0.0002)	0.153	1.00 (0.998, 1.01)	.10
Digit Span Test	−0.021 (0.004)	−0.060	0.98 (0.89, 1.07)	.34

Note: $R^2 = .41$, $p < .001$, $f^2 = .69$.

* $p < .05$.

Table 5.

Differences between participants who died within one year of surgery vs. those who survived.

Characteristic	Died (n = 13)	Survived (n = 152)	Test Statistic	*p* Value	Effect Size
Age (years)	76.6 (6.4)	75.4 (5.9)	t= −.68	.50	−.20[^]
Sex (% Female)	30.8	37.5	X^2=2.33	.77	−.04[^^^]
Education (years)	12.4 (2.4)	14.0 (3.0)	t=1.82	.07	.57[^]
Race (% White)	100	94.1	X^2=8.14	1.0	−.07[^^^]
Past stroke/TIA(%)	15.4	12.5	X^2=0.09	.67	0.02[^^^]
Medical Comorbidities (Charlson Comorbidity Index)[c]	2.0 (1 – 4)	1.0 (0 – 5)	U=571	**.01**[*]	−.29[^^]
Body Mass Index[c]	28.5 (17.2 – 33.9)	29.0 (21.6 – 52.9)	U=831	.34	.42[^^]
Geriatric Depression Scale[a,c]	4.0 (0 – 16)	2.0 (0 – 20)	U=813.5	.33	−.41[^^]
Mini-Mental Status Examination[b]	26.5 (2.0)	27.8 (1.5)	t=2.98	**.00**[**]	.86[^]
Rey Complex Figure Long Delay Free Recall	10.4 (5.4)	14.4 (6.0)	t=1.93	.06	.66[^]
Boston Naming Test (BNT)[c]	48 (26 – 55)	55 (22 – 60)	U=330.5	**.00**[**]	.17[^^]
Animal Fluency	14.6 (3.3)	18.4 (5.0)	t=2.12	**.04**[*]	.77[^]
HVLT-R Delayed Recall	5.8 (2.2)	7.4 (2.5)	t=2.26	**.03**[*]	.65[^]
Judgment of Line Orientation (JOLO)	17.8 (7.4)	20.9 (5.4)	t=1.78	.08	.56[^]
Trail Making Test – B-A[c]	149.5 (33 – 256)	62 (−2 – 245)	U=393.5	**.02**[*]	.20[^^]
Digit Span Test Total	13.11 (4.14)	15.70 (3.71)	t=2.01	**.046**[*]	.69[^]

Values are expressed as mean (SD) or %.

[*] $p < .05$.

[**] $p < .01$.

[a] Maximum = 30 (worst).

[b] Maximum = 30 (best).

[c] Median (range) reported for variables not normally distributed.

Effect sizes:

[^] Cohen's d (.2 = small; .5 = medium;.8= large)

[^^] Probability of superiority (<0.44 or >0.55 = small; <0.36 or >0.64. = medium; <0.29 or >0.71 = large)

[^^^] Phi (.1 = small; .3 = medium; .5 = large)

Table 6.

Logistic regression models predicting postoperative mortality within one year of surgery.

	B (SE)	β	Odds Ratio (95% CI)	p value
Model 2				
Age	0.006 (0.002)	0.018	1.01 (0.94, 1.07)	.42
Sex	**0.871 (0.042)**	**0.234**	**2.39 (0.90, 7.04)**	**.04**[*]
Education	0.016 (0.007)	0.018	1.02 (0.87, 1.23)	.47
Past stroke or TIA	−0.156 (0.044)	−0.028	0.86 (0.28, 2.25)	.42
Charlson Comorbidity Index	**0.539 (0.015)**	**0.354**	**1.71 (1.22, 2.65)**	**<.001**[**]
BMI	−0.082 (0.005)	−0.215	0.92 (0.81, 1.05)	.11
GDS	0.007 (0.004)	0.016	1.01 (0.91, 1.12)	.46
MMSE	0.068 (0.009)	0.057	1.07 (0.84, 1.35)	.29
Rey Complex Figure Long Delay Free Recall	**−0.106 (0.005)**	**−0.338**	**0.90 (0.80, 1.00)**	**.03**[*]
BNT	**−0.125 (0.003)**	**−0.389**	**0.88 (0.80, 0.96)**	**<.001**[**]
Animal Fluency	0.067 (0.006)	0.186	1.07 (0.91, 1.22)	.20
HVLT-R Delayed Recall	**0.211 (0.008)**	**0.289**	**1.23 (0.999, 1.51)**	**.03**[*]
JOLO	0.003 (0.003)	0.009	1.00 (0.92, 1.10)	.49
Trail Making Test (B-A)	0.006 (0.0003)	0.182	1.01 (1.00, 1.01)	.09
Digit Span Test	−0.049 (0.005)	−0.102	0.95 (0.83, 1.07)	.26

Note: $R^2 = .68$, $p < .001$, $f^2 = 2.12$.

[*] $p < .05$

[**] $p < .001$.