Prediction of stroke reconvalescence after coronary bypass surgery indicated by CT scan parameters

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Abstract

Background: Stroke in the postoperative time course after heart surgery remains a serious risk. Cranial computer tomography (CCT) is the first line option to detect severe intracranial damage. However, only few data are available to predict neurological outcome. Using visual rating scales (VRSs), this study addresses reliability and effectivity to indicate neurological status and likelyhood of improvement.

Methods: In a single-center retrospective evaluation, 3719 patients underwent coronary bypass surgery. Because of a delayed recovery phase and neurologic deficits after cardiac surgery 109 patients had a cranial CT scan in the early postoperative period. The incidence of clinically relevant findings within the imaging was rated by an experienced neuroradiologist using two VRS, that is, the age-related white matter changes (ARWMCs) and the Mendes–Ribeiro visual rating scale (MRVRS). Both are computer-assisted measurement schemes to detect stroke-related intracranial damage. Follow-up was investigated with regard to clinical outcome and patient-related risk profiles.

Results: Of 109 patients with postoperative cranial CT scans due to prolonged recovery phases or proven neurological damage 44.5% had one cerebral defect in CCT imaging scans only. The others showed multiple defects. During hospital stay, 92.3% experienced neurological improvement exposing reduced ARWMC, while 7.1% had no improvement and correlating high scores. Of both scales, the ARWMC-VRS demonstrated superior accuracy and discrimination. The preoperative ejection fraction (EF), arteriosclerotic degeneration of carotid arteries, and reduced glomerular filtration rate were found to have a high correlation ($r = 0.0005$) with the latter group. In-hospital mortality of this cohort was 8.18%.

**Abbreviations:** ARWMC, age-related white matter change; AUC, area under the curve; EF, ejection fraction; GFR, glomerular filtration rate; ICC, intraclass correlation coefficient; ROC, receiver operating characteristic curves.
1 | INTRODUCTION

Postoperative stroke can vary, usually between 1.7% and 4.5%.\(^1\)\(^–\)\(^4\) A recent study demonstrated relatively low rates of stroke, finding the risk of stroke after coronary artery bypass grafting (CABG) to be 1.8%.\(^5\) Specifically nonmodifiable risk factors, such as age, have been shown to significantly impact the risk of neurological deficits. The risk of stroke increases with age: octogenarians, for example, were found to have a 9% risk of postoperative stroke within 30 days of the operation. Patients aged ≥75 years had an 8.9% risk of postoperative stroke, patients 65–74 with a risk of 3.6%, and patients <65 with a 0.9% risk.\(^6\) The occurrence of a perioperative stroke was furthermore found to have, amongst other complications, one of the strongest associations with mortality.\(^7\)\(^–\)\(^12\) The occurrence of cerebrovascular deficits following surgery, therefore, emphasizes the need for a comprehensive preoperative risk profile. Cerebrovascular accidents in the form of “silent infarcts,” that is, without any sign of neurological symptoms, may also play a role in postoperative cognitive dysfunction in CABG patients.\(^13\)\(^–\)\(^16\) It has been proposed that silent infarcts, possibly an accumulation thereof, might predispose to a decline in cognitive function. Preoperative screening may help identify patients with undiagnosed cerebrovascular disease who are at higher risk of postoperative cognitive decline.\(^17\) The recommendation obtains additional gravitas when one considers the proportion of CABG patients who have a history of preoperative stroke.\(^18\)\(^–\)\(^26\) Hospital stay, for example, was increased 2.67-fold in patients who suffered a stroke.\(^2\)\(^,\)\(^27\)

The main goal of this study was to determine the role of cranial computed tomography imaging in assessing postoperative neurological damage in patients who underwent coronary artery bypass grafting. Prognostic studies comparing different scores, providing physicians with the knowledge about expected mortality and neurological reconvalescence are an effective option, but they require a major effort.

In terms of imaging visual rating scale (VRS) are implemented by rating multiple predetermined anatomically and functionally important brain regions according to a set score for lesion severity and size. Two commonly implemented VRS, which are easily applied, quick, and accurate, include the age-related white matter change (ARWMC) VRS and the Mendes-Ribeiro VRS (MRVRS). Researchers have analyzed CCT images using different types of models to determine the prognostic strength of the models’ score of CCT images in predicting cognitive deficits. This has only been done sparingly with the ARWMC and MRVRS. For example, high ARWMC VRS scores were associated with worsening balance and gait over a 3-year study period in elderly patients. Only one study\(^21\) has to date attempted to correlate scores from the ARWMC VRS with cognitive impairment in stroke patients. Researchers found that ARWMC scores independently correlated with cognitive impairment.

In concern of our cardiosurgical patients, this study addresses the question whether VRSs can be reliably and effectively used to predict neurological outcome after hospital discharge in suspected post-CABG stroke patients. Additionally, the putative perioperative risk factors in post-CABG patients are related to neurological lesions (as measured by VRSs) and their influence on neurological outcome is studied.

2 | PATIENTS AND METHODS

Three thousand seven hundred and nineteen patients underwent CABG surgery in the time frame between 2006 and 2013. Among them 109 pts. with postoperative neurological disorders were included in the study. The study was approved by the local Ethics committee.

2.1 | Data collection

Patients were identified by searching the university clinic digital database “ORBIS.” Using advanced search criteria, the operation and procedure key codes assigned for the CABG and CCT procedures as well as the International Classification for Diseases codes given for the suspected diseases were used as measures of search inclusion. All patients meeting these criteria who were treated at the University of Marburg clinic from the years 2006 to 2013 were accepted and a total of 110 patients were included in the study. Information about comorbidities and medical history such as alcoholism, chronic obstructive pulmonary disease, asthma, renal insufficiency, arterial...
hypertension, as well as past neurological or cardiological pathologies were collected from admission write-ups. Perioperative risk factors, such as the length of time of operation, the time spent on the heart-lung machine, preoperative hematocrit, ejection fraction (EF), creatinine, and the glomerular filtration rate (GFR) were either found in the preoperatively ordered laboratory analysis results or from operation documentation records. If the GFR was not found in the records, it was calculated using the Cockroft-Gault formula. Any further missing information, such as time spent in the hospital, could also be found in the final patient discharge record. Occasionally, data concerning potential perioperative risk factors were not found in patient files or in the digital patient database. This was noted in the respective SPSS data files. Patients with missing perioperative data (N = 8) were excluded from statistical analysis concerning those specific perioperative factors. Patients who died during the course of the study (N = 9) were included in the statistical analysis. Neuropsychological assessment findings performed at the onset of neurological symptoms, and at the end of hospital stay were usually found in the consultations section of patient files. Data from neuropsychological assessments were collected and added into SPSS data files. If data was missing from paper-based patient files, it could often be found in the electronic patient records using the digital database ORBIS. A temporary log-in and password were granted for access to ORBIS with help from medical administration. CCT images were obtained in conjunction with, and with aid from the neuroradiological department.

2.2 Grading of neurological damage and implementation of the VRS

CCT images were rated by an experienced neuroradiologist using two VRS with subsequent entry and input of VRS scores and data into SPSS cells by an assistant. Both the neuroradiologist and assistant, though blind to the individual patient case files, had the background knowledge that the CCTs were from patients with neurological sequelae following CABG. Following the first assessment of CCTs using both VRS, a second assessment was performed in a similar manner 2 months later. Grading and input of scores into SPSS using both the ARWMC and MRVRS took approximately 2 min per patient. The ARWMC VRS (Figure 1) assesses five different brain regions: the frontal, parieto-occipital, temporal, infratentorial, and the basal ganglia. The basal ganglia include the globus pallidus, thalamus, insula, striatum, and internal/external capsule. The basal ganglia score was determined as follows: 0 = no lesions, 1 = one focal lesion (≥5 mm), >1 focal lesion, and confluent lesions. Lacunes were defined as well-defined areas of size ≥2 mm. All other regions were, with the logic that they anatomically belong to the white matter and are dissimilar to the basal ganglia region, evaluated slightly differently: 0 = no lesions, 1 = focal lesions, 2 = beginning confluence of lesions, 3 = diffuse involvement of the entire region. White matter lesions were ill-defined and moderately hypodense areas of ≥5 mm. So as to have a frame of reference for the CCT slice angulation for each region, examples of CCT images with their recorded scores for lesions were examined from published literature. All five brain regions were graded separately in the left and right brain hemispheres. Scores given for each region or hemisphere were added together to get a total score. A maximum total score for each hemisphere was 15, a maximum total score for each region when including both hemispheres was 6, and a total maximum score when including all hemispheres and regions was 30. The MRVRS (Figure 2) was implemented by assessing four different anatomical regions: the anterior frontal, posterior frontal, parietal, and occipital regions. In each region, any lesions were graded by the extent of the lesion (0 = normal, 1 = periventricular only, 2 = periventricular and deep white, 3 = extending out to the subcortical white matter “full thickness”) and severity of the lesion (0 = normal, 1 = mild, 2 = moderate, 3 = severe). Examples of scoring of lesions with CCT using the MRVRS were taken from studies to have context. The scores for extent and severity of lesions were then multiplied to give a regional score, regional scores were then added together to give a

**FIGURE 1** Scoring system 1: age-related white matter change (ARWMC)

- The ARWMC (Age-Related White Matter Change) assesses five different brain regions:
- The frontal, parieto-occipital, temporal, infratentorial and basal ganglia
- Score: White matter score: 0 = no lesion, 1 = focal lesions, 2 = beginning confluence of lesions, 3 = diffuse involvement of the entire region
- The basal ganglia include the globus pallidus, thalamus, insula, striatum, and internal/external capsule.
- Basal ganglia score: 0 = no lesion, 1 = one focal lesion ≥5 mm, >1 focal lesion or confluent lesion
total score. The maximum possible score for each region is 9, and the maximum total score for the MRVRS is 36. The left and right brain hemispheres were not graded separately, as with the ARWMC VRS.

2.3 | Organization of patient data

All assessments recorded by neurologists subsequent to the onset of neurological symptoms and immediately before hospital release were documented and entered into SPSS data files. By comparing neurological assessments performed immediately after the onset of symptoms with the neurological assessments taken from neurologists at the end of hospital stay, we were able to determine the degree of neurological reconvalescence. We divided the patient population into two groups: those with "no improvement" and those with "some improvement" at final neurological assessment. The number of neurological deficits for each patient was compiled by taking the sum of individual neurological deficits noted by medical staff during their assessments at the end of hospital stay. These data were also entered in SPSS cells, allowing an analysis of the number of neurological deficits in the study population. Detailed records of pathological neurological symptoms noted during neurological assessments at the end of hospital stay were found in patient files. The score of neurological deficits corresponded to the number of individually noted neurological impairments each patient had (e.g., facial nerve paralysis + sensory loss in arm = 2). This enabled us to determine any association between the number of neurological deficits and a VRS.

2.4 | Statistical analysis

Patient data were documented and entered into cells of the statistical software package SPSS (Statistical Product and Service Solutions), which was also used to organize patient data and for statistical analyses. Differences were considered nonsignificant if the value $p > .05$, and were considered significant if $p < .05$. The data was checked to determine if it had a normal distribution. Because the data was often found to have a non-normal distribution, nonparametric statistical tests were frequently used. Intrarater reliability for the ARWMC and MRVRS was computed by determining the intraclass correlation coefficient (ICC). The ICC proved to be an appropriate test for this inquiry as it described the similarity in scoring the VRS produced with multiple applications. For the ICC, a representation of the intrarater reliability, a value of one demonstrated the highest possible value, and a value of zero the lowest possible. The presence of any correlation between the number of neurological defects and the ARWMC score was verified using Spearman’s rho ($\rho$, rank correlation coefficient), a measure of nonparametric correlation between two variables (values range from $-1$ to $+1$, with the value 0 indicating no correlation). To investigate the statistical dependence between two variables, as in this case, Spearman's rho was a fitting test. The Pearson correlation test, a measure of nonparametric correlation between two variables (values ranging from $-1$ to $+1$, and the value 0 indicating no correlation), was used to investigate if an association existed between the number of neurological defects (as noted during neurological assessments at end of hospital stay) and the Mendes–Ribeiro score. To establish if the number of neurological deficits was associated with patients found in a stratified ARWMC total score, cross-tabulation, Pearson's $\chi^2$ test, and Kendall's tau-b rank correlation coefficient (a nonparametric test used to measure any association between two variables) were implemented. To ascertain if an association between two neurological assessment groups ("no improvement" and "some improvement") with the ARWMC score existed, the Kolmogorov–Smirnov test was used to determine if the ARWMC total score had a normal distribution. As it did not, no t-test could be used to determine if there was a difference in the two groups. Instead, the nonparametric Mann–Whitney U-test was used to distinguish any difference in the ARWMC score of the two groups. The Mann–Whitney U-test was an appropriate test for
distinguishing if, for example, higher ARWMC scores were associated with the “no improvement” group. To determine if there was an association between the dichotomized ARWMC Score and the neurological assessment cross tabulation was used. Because of the dichotomous categorization and the nonparametric nature of the data, analysis of the contingency tables was done with Pearson’s $\chi^2$ and Fisher’s exact test. These tests were also used to determine if any Mendes–Ribeiro score >0 was significant in determining neurological assessment. To ascertain if basal ganglia damage, as assessed with the ARWMC VRS, was associated with neurological deficits, the nonparametric correlation was determined using Spearman-Rho. The nonparametric Mann–Whitney U-test and Wilcoxon W-test were used to verify if an association existed between the neurological assessment groups and basal ganglia damage as assessed with the ARWMC VRS. The same tests were used to determine if an association existed between the neurological assessment groups and the ARWMC and MRVRS. Additionally, receiver operating characteristic (ROC) curves were able to determine which VRS was more accurate. The ability of a ROC curve to discriminate the accuracy of a test was viewed as significant if the $p < .05$ and the area under the curve (AUC) was greater than 0.5. To establish which quantitative perioperative factors were associated with neurological assessment groups, the Pearson $\chi^2$ test and the Fisher’s exact test were used. To determine the influence of quantitative perioperative factors on neurological outcome ROC curves were applied. For statistical purposes, some quantitative perioperative factors, such as degree carotid stenosis, were described as present or not present. For example, carotid stenosis was deemed significant, and therefore present, as of ≤50%. To confirm if any quantitative perioperative factors were associated with either the ARWMC or MRVRS, Spearman’s rank correlation coefficient (Spearman Rho) was used to measure the nonparametric correlations (because the total scores were not distributed normally). To determine which quantitative perioperative factors were not associated with the total ARWMC and Mendes–Ribeiro scores the nonparametric Mann–Whitney test was used.

3 | RESULTS

The characteristics of the study population are shown in Table 1. The ARWMC VRS was performed twice by an experienced neuroradiologist with all patient CCT images over a 2-month period. The intrarater reliability was computed by comparing the results from the first and second ARWMC VRS assessments. The ICC was 0.978 (an ICC of 1 is the highest possible value). The $p$-value was found to be significantly different ($p < .0005$). The boxplots seen in Figure 3 represent the two temporally distinguishable ARWMC total score VRS assessments. Both boxplots are similar, with multiple outliers. The outliers for both assessments are, with one exception, the same. The number of outliers illustrates how the highest results in both instances of analysis were due to the same patients (Table 2).

To determine where incongruity within the total score might exist, the first assessment regional scores and second assessment regional scores were also compared. All regional scores except for one had ICC values above 0.900, and all had significantly different

| Table 1 | Baseline characteristics of the study population |
|----------|----------------------------------|
| Variable                               | N = 109 |
| Age (mean ± SD)                         | 70.8 ± 9.5 |
| Alcoholism                              | (6) 5.5% |
| Aortic valve replacement                | (37) 33.9% |
| Arteriosclerosis of the carotid arteries | (46) 42.2% |
| Asthma                                  | (5) 4.6% |
| CAD (1, 2, or 3 vessel disease)         | (9) 8.3%, (29) 26.6%, (71) 65.1% |
| CCT finding: old infarct                | (8) 7.3% |
| COPD                                    | (31) 28.4% |
| Creatinine                              | 1.18 ± 0.74 |
| Deaths (no neurological reason)         | 9 |
| Decompensated cardiac failure           | (66) 60.6% |
| Diabetes                                | (39) 35.8% |
| Elective surgery                        | (72) 66.1% |
| Gender: female                          | (40) 36.7% |
| GFR                                     | 63.2 ± 26.5 |
| Hematocrit                              | 0.344 ± 0.0575 |
| Hypercholesterolemia                    | (87) 79.8% |
| Hypertonus                              | (104) 95.4% |
| Ischemia time on HLM                    | 67.1 ± 26.4 |
| Mitral valve replacement                | (10) 9.2% |
| Operation time                          | 244.9 ± 73.2 |
| PAD                                     | (19) 17.4% |
| Parkinsons disease                      | (3) 2.8% |
| PFO                                     | (6) 5.5% |
| Preoperative EF                         | 51.7 ± 16.6 |
| S/p cerebrovascular insult              | (21) 19.3% |
| S/p myocardial infarct                  | (23) 21.1% |
| Smoker                                  | (38) 34.9% |
| Time on bypass                          | 115.1 ± 47.6 |
| Time spent in hospital                  | 30.2 ± 20.6 |

Note: Details are presented in alphabetical order. For further statistical analysis of perioperative data, see Table 5.

Abbreviations: CAD, coronary artery disease; CCT, cranial computer tomography; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; GFR, glomerular filtration rate; HLM, heart lung machine; PAD, pulmonary artery disease; PFO, patent foramen ovale.
p-values (p < .000). The region with the lowest ICC value was the basal-ganglia region, which had an ICC value of 0.878. The intrarater reliability for the MRVRS, which was also performed twice over a 2-month period, was also found for the total score as well as the regional total scores. The ICC score for the total score was 0.988, with a significant p-value: p < .0005. The lowest ICC score for the regional totals was 0.812, all other regions having an ICC above 0.952 (1 being the highest possible value), also with a significant p-value (p < .0005). A positive Spearman Rho’s (0.2) association with a significant p-value (p = .04, two-tailed) was found correlating the number of neurological defects patients had with the ARWMC VRS.

FIGURE 4 illustrates the percentage of patients with the number of neurological deficits they incurred. In comparison, a positive correlation was found (r = 0.198) between the number of neurological defects in patients and the MRVRS, with a significant p-value (p = .022, one-tailed). Additionally, any association between the number of neurological deficits and a stratified ARWMC total score (patients with the score 0 [none], scores 1–10 [mild-to-moderate], and scores >10 [severe]) was investigated. Upon analysis using Kendall’s tau-b, a positive correlation coefficient was found (0.144), however, the p-value was not significantly different (p = .113). The nonparametric Spearman-Rho was used to determine if basal ganglia damage, as assessed with the ARWMC Scale, is associated with the number of neurological deficits. The correlation coefficient was found to be 0.142, with a nonsignificant p-value (two-sided) of .149.

Additionally, this study attempted to find any association between the two neurological assessment groups, “no improvement” and “some improvement,” with basal ganglia damage using the ARWMC VRS. A significant difference was found between the basal ganglia ARWMC scores in the groups “no improvement” and “some improvement.” Using the nonparametric Mann–Whitney test, the “no improvement” group was shown to be associated with higher rated scores for basal ganglia damage than the “some improvement” group. The results were significant, with a two-sided p-value of .046.

Furthermore, we attempted to determine if an association existed between two ARWMC groups (score >0 and 0) with the dichotomized neurological assessments (“no improvement” and “some improvement”). It was found using χ² tests, cross-tabulation, and Fischer’s exact test, that there is an association between the dichotomized ARWMC score and the neurological assessment (p = .002).

3.1 | Neurological improvement categorized by ARWMC scores

In Figure 5, one sees that the neurological assessment group with “some improvement” included 92.86% of patients who received an ARWMC score of 0, while the “no improvement” group included only 7.13% of patients with a score of 0.

Similarly, cross-tabulation, Pearson χ² tests, and Fischer’s exact test were used to assess if an association existed between the two Mendes–Ribeiro groups (score >0 and 0) and the neurological assessment groups “no improvement” and “some improvement”. A score >0 was significant in determining “no improvement during neurological assessment” (p < .0005). All neurological assessments were stratified into two groups, “no improvement” and “some improvement”, to determine any association with the total ARWMC score. An association was found using a nonparametric Mann–Whitney test, with a significant p-value (p < .0005), between the ARWMC score and the neurological assessment. In the “no improvement” group: the mean was 4.1, the median was 4, and the standard deviation was 2.4. In the “some improvement” group: the
mean was 1.7, the median was 1, and the standard deviation was 2.8. This indicates that the ARWMC score can predict the degree of neurological reconvalescence.

### 3.2 Neurological outcomes and their respective ARWMC VRS scores

The two boxplots in Figure 6 show that the group "no improvement at final neurological assessment" has higher ARWMC values. Using the nonparametric Mann–Whitney U-test and Wilcoxon W tests, the total scores of the ARWMC and MRVRS were both found to predict neurological assessment before discharge. High scores for both scales predicted "no improvement," while low scores predicted "some improvement." In addition, the ARWMC VRS was more accurate than the MRVRS. All results were significantly different from 0: \( p < .000 \). In addition, ROC-Curves were used to determine which VRS was more accurate and was able to discriminate better. The higher the AUC value is to its maximum "1," the better its accuracy and discrimination. AUC values that are \( \leq 0.5 \) are negative predictors, while those >0.5 are positive predictors.

The ARWMC VRS AUC was found to be 0.858 \( (p < .000) \), while the AUC of the MRVRS was 0.681 \( (p = .005) \). Both results showed AUC results that are significant at the >0.5 level of probability (Table 3, Figure 7).

### 3.3 ROC curve analysis of ARWMC and MRVRS

Using the stratified neurological assessment groups ("no improvement" and "some improvement"), we were also able to discern if any associations existed with qualitative perioperative factors. To determine the influence of qualitative perioperative factors on neurological outcome the Pearson \( \chi^2 \) test and the Fischer’s exact test were used (Table 4 for summary of significance levels). Only the presence of arteriosclerosis in the carotid arteries, an example of a qualitative perioperative factor, was found to be significantly associated with the neurological assessment \( (p < .028) \). Similarly, quantitative perioperative factors were also compared with the two neurological groups (Table 5). To determine the influence of quantitative perioperative factors on neurological outcome, ROC curves were used again. The preoperative EF was found to have a significant association with the "no improvement" group. The ROC curve (Figure 8) shows an AUC of 0.660 \( (p = .012) \) and a standard deviation of 0.059. The GFR was also found to have a significant association with the "no improvement" group. The ROC curve (Figure 8) has an AUC of 0.361, indicating a negative predictive value \( (p = .027) \).

| Table 2 | Overview of \( p \)-values obtained from \( \chi^2 \) tests performed as associative analysis |
|---|---|
| **Perioperative factors** | **\( p \)-value** |
| Alcoholism | .178 |
| Aortic insufficiency | .175 |
| Aortic stenosis | .602 |
| Aortic valve replacement | .435 |
| Arteriosclerosis of the carotid arteries | .028* |
| Asthma | .668 |
| Chronic kidney disease | .478 |
| COPD | .477 |
| Decompensated cardiac failure | .188 |
| Diabetes | .177 |
| Elective/emergency operation | .258 |
| Endocarditis | .514 |
| Gender | .219 |
| Hypercholesterolemia | .172 |
| Hypertonus | .267 |
| Intracardial thrombus | .541 |
| Mitral insufficiency | .588 |
| Mitral stenosis | .288 |
| Mitral valve replacement | .314 |
| PAD | .515 |
| Parkinsons disease | .698 |
| Patent foramen ovale | .143 |
| S/p cerebrovascular insult | .165 |
| S/p myocardial infarct | .076 |
| Smoker | .546 |
| Tricuspid insufficiency | .115 |
| Tricuspid stenosis | .134 |

Note: Associative analysis of qualitative perioperative factors. For all patients in the neurological assessment groups after CABG surgery each single mark is compared between the "no improvement" and "some improvement" postoperative time course. Because of a different spectrum of neurological deficits (see Figure 4) and multiple associated factors in case history each mark was compared despite the additional factors coincidentally present. Therefore, a vary grouping exist. Abbreviation: CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; PAD, pulmonary artery disease. *significant value.
3.4 | Quantitative perioperative factors and the ARWMC or MRVRS

Spearman’s rank correlation coefficient was used to determine if any association existed between the quantitative perioperative factors and either the ARWMC or MRVRS. No quantitative perioperative factors were significantly associated with either the ARWMC or MRVRS scores (Table 5). Nonparametric testing was used for associative analysis of qualitative perioperative factors with the two VRS groups. Because the total scores were not distributed normally, the nonparametric Mann–Whitney test was used instead of the t-test. Multiple qualitative perioperative factors were found significantly to predict higher scores with the ARWMC VRS: status post cerebrovascular insult (ARWMC $p = .005$), emergency operation (ARWMC $p = .034$), and concurrent mitral valve replacement (ARWMC $p = .019$). The only significant perioperative factor for the Mendes–Ribeiro $p$-value was Status post cerebrovascular insult ($p = .003$) (Table 6).
**Figure 6** Boxplot representation of the "no improvement" and "some improvement" neurological outcomes and their respective ARWMC VRS scores. ARWMC, age-related white matter change; VRS, visual rating scale.

**Table 3** Parameters for the receiver operating characteristic curves (ROC) - AUC (see Figure 7)

| Test result variable(s) | AUC  | Standard error | Asymptotic sig. | Asymptotic 95% confidence interval Lower limit | Upper limit |
|-------------------------|------|----------------|-----------------|-----------------------------------------------|-------------|
| ARWMC VRS               | 0.858| 0.044          | 0.000           | 0.772                                         | 0.943       |
| MRVRS                   | 0.681| 0.065          | 0.005           | 0.553                                         | 0.810       |

Note: ROC curve analysis of ARWMC and MRVRS in predicting neurological assessment groups "no improvement" and "some improvement."

Abbreviations: ARWMC, age-related white matter change; AUC, area under the curve; MRVRS, Mendes-Ribeiro VRS; ROC, receiver operating characteristic curves; VRS, visual rating scale.

**Figure 7** Sensitivity and specificity of the ARWMC and Mendes–Ribeiro VRS in predicting the measure of neurological assessment. ARWMC, age-related white matter change; VRS, visual rating scale.
4 | DISCUSSION

4.1 | Reliability of the VRS

Both interrater and intrarater reliability has been shown to have moderate-excellent agreement for the ARWMC VRS. A strong intrarater agreement indicates that the repeated evaluation of images by the same evaluator remains constant over time and dependably produces the same results. Multiple studies investigating intrarater agreement revealed an ICC values of 0.94, the lowest ICC value found in a study was 0.84. Our results support the assertion that intrarater reliability with the ARWMC VRS is high.

Our analysis showed high intrarater reliability using several statistical tests for the ARWMC VRS. The intrarater reliability for the ARWMC VRS was calculated using results from two consecutive ARWMC VRS assessments. The ICC was 0.978 (an ICC of 1 being the highest possible value), demonstrating an excellent intrarater agreement. ICC values were also calculated for regional areas to determine if these were homogeneous with statistical analysis producing significantly different p-values (p < .000) for all regions. All regions, except for the basal ganglia region, had ICC values above 0.900. The region with the lowest intrarater agreement was the basal ganglia region, which had an ICC of 0.878. Similarly, the intrarater reliability for the MRVRS was calculated. Here, the ICC was 0.988 with a significant p-value: p < .0005, indicating an extremely high intrarater agreement as well.

### Table 4

Summary of AUC, standard error, and p-values obtained from ROC-curve analysis

| Perioperative factors | AUC   | Standard error | p-value |
|-----------------------|-------|----------------|---------|
| BMI                   | 0.608 | 0.062          | .091    |
| Hematocrit            | 0.465 | 0.061          | .573    |
| Ischemia time on HLM  | 0.570 | 0.064          | .288    |
| Age                   | 0.545 | 0.064          | .478    |
| Preoperative EF       | 0.660 | 0.059          | .012*   |
| Creatinine            | 0.572 | 0.064          | .251    |
| GFR                   | 0.361 | 0.061          | .027*   |
| Operation time        | 0.562 | 0.058          | .320    |
| Time on bypass        | 0.537 | 0.062          | .579    |
| CCT postoperative day execution | 0.524 | 0.062 | .701 |
| Time spent in hospital| 0.524 | 0.063          | .704    |

Abbreviations: AUC, area under the curve; CCT, cranial computer tomography; EF, ejection fraction; GFR, glomerular filtration rate; HLM, heart lung machine; ROC, receiver operating characteristic curves. *significant value.

### Table 5

Summary of correlation coefficient scores and p-values obtained from Spearman’s rank correlation coefficient analysis

| Perioperative factors | ARWMC VRS | MRVRS | p-value | ARWMC VRS | MRVRS | p-value |
|-----------------------|-----------|-------|---------|-----------|-------|---------|
| BMI                   | 0.008     | 0.107 | .286    | 0.008     | 0.107 | .286    |
| Hematocrit            | −0.015    | 0.003 | .975    | −0.015    | 0.003 | .975    |
| Ischemia time on HLM  | 0.101     | 0.020 | .843    | 0.101     | 0.020 | .843    |
| Age                   | 0.086     | 0.043 | .661    | 0.086     | 0.043 | .661    |
| Preoperative EF       | −0.015    | −0.094| .353    | −0.015    | −0.094| .353    |
| Creatinine            | 0.004     | −0.102| .301    | 0.004     | −0.102| .301    |
| GFR                   | −0.465    | 0.005 | .960    | −0.465    | 0.005 | .960    |
| Operation time        | 0.128     | 0.185 | .060    | 0.128     | 0.185 | .060    |
| Time on bypass        | 0.036     | 0.067 | .513    | 0.036     | 0.067 | .513    |
| CCT postoperative day execution | −0.026 | 0.021 | .834    | −0.026 | 0.021 | .834    |
| Time spent in hospital| −0.070    | −0.097| .330    | −0.070    | −0.097| .330    |

Note: No quantitative perioperative factors were significantly associated with either the ARWMC or MRVRS scores having correlation to neurologic disorders.

Abbreviations: ARWMC, age-related white matter change; CCT, cranial computer tomography; EF, ejection fraction; GFR, glomerular filtration rate; HLM, heart lung machine; MRVRS, Mendes-Ribeiro VRS; VRS, visual rating scale.

4.2 | VRSs fully reflect neurological deficits

We also wanted to determine if an association exists between the degree of neurological dysfunction and the score patients received from the ARWMC and MRVRS after surgery. The extent of neurological dysfunction was described in terms of the total number of individual neurological deficits (e.g., facial nerve paralysis, dysphagia, hemiparalysis) patients had. A positive Spearman Rho’s (0.2) association with a significant p-value was found, suggesting that higher ARWMC scores (indicating greater histological brain damage) were associated with more neurological deficits of patients. The MRVRS also had a positive correlation with a significant p-value (p = .022). Grouping of the ARWMC scores was then done to determine if a stratification of ARWMC scores, as has been done in multiple studies, is correlated with neurological outcome. The number of neurological deficits was found to be associated with stratified ARWMC groups (patients with the score 0 [none], scores 1–10 [mild-to-moderate], and scores >10 [severe]). A positive Kendall’s tau-b association (0.144) was found, however, the p-value was not significantly different (p = .113). Subsequently,
patients were stratified into two groups ("no improvement" and "some improvement") based upon their neurological recovery during their hospital stay. A strong association between these groups and the ARWMC score was found. Patients who had no neurological improvement during the course of their hospital stay were associated with having higher ARWMC scores. For example, the "no improvement" group had a much higher mean (4.1) and median (4) ARWMC score than the "some improvement" group, which had a mean of 1.7 and median of 1 (p < .0005). These results support the view that the ARWMC VRS, a representation of the histological damage incurred after a stroke, can predict the neurological outcomes of patients.

Furthermore, a dichotomized ARWMC score (>0 and 0) also demonstrated a positive correlation with the two neurological assessment groups "no improvement" and "some improvement." For example, only 7% of patients who received an ARWMC score of "zero" were included in the "no improvement" group, whereas 93% of all "zero" ARWMC scores were included in the "some improvement" group. Additionally, of the patients in the "no improvement" group, 93% had an ARWMC score >0. The ARWMC VRS has been repeatedly been shown to accurately represent histological brain damage. Researchers found the scale to correlate well with the degree of cognitive impairment. Our results, therefore, support this conclusion with the addendum that our results were specific to intra- and postoperative CABG patients. The basal ganglia region warranted closer investigation because of its unique pathohistological findings.

The basal ganglia region was the region with the highest number of minor neurological defects. This study's patient demographic, which has a high percentage of comorbidities, represents a population with a high risk for vascular disease. This appears to most adversely affect the basal ganglia region. We initially suspected that the high quantity of minor defects would not associate with the presence of neurological symptoms, as these defects tend to commonly appear in the population. However, the nonparametric Mann-Whitney test found that the "no improvement" group was associated with higher rated ARWMC scores for basal ganglia damage than the "some improvement" group. The MRVRS does not take into account the basal ganglia region. For the MRVRS, an association was found between two Mendes–Ribeiro groups (score >0 and 0) and the neurological assessment groups "no improvement" and "some improvement." A score >0 was significant in determining "no improvement during neurological assessment" (p < .0005). Results from statistical correlational tests indicate that both the ARWMC and MRVRS are useful in predicting neurological outcomes of patients. High scores for both scales were associated with "no improvement," while low scores were associated with "some improvement." To determine which VRS was more accurate and able to discriminate better, ROC-Curves were used. The higher the AUC value is to its maximum value "1," the better its accuracy and discrimination. AUC values that are ≤0.5 are negative predictors, while those >0.5 are positive predictors. Both scales showed AUC

![ROC-Curve of preoperative Ejection Fraction](image1)

| Area    | Std. Error | Asymptotic Sig. | Asymptotic 95% Confidence Interval |
|---------|------------|-----------------|-----------------------------------|
| 0.660   | 0.059      | 0.012           | 0.545                             |

![ROC-Curve of Glomerular Filtration Rate (GFR)](image2)

| Area    | Std. Error | Asymptotic Sig. | Asymptotic 95% Confidence Interval |
|---------|------------|-----------------|-----------------------------------|
| 0.361   | 0.061      | 0.027           | 0.242                             |

FIGURE 8 Perioperative quantitative risk factor preoperative ejection fraction (EF), glomerular filtration rate (GFR), and association with neurological assessment. ROC, receiver operating characteristic curves.
TABLE 6 Summary of ARWMC and MRVRS p-values from nonparametric statistical analysis

| Perioperative factors                      | ARWMC VRS p-value | MRVRS p-value |
|-------------------------------------------|-------------------|---------------|
| Gender                                    | .153              | .889          |
| PAD                                       | .938              | .613          |
| Mitral insufficiency                      | .912              | .437          |
| Mitral stenosis                           | .362              | .846          |
| Tricuspid insufficiency                    | .382              | .398          |
| Tricuspid stenosis                        | .425              | .476          |
| Aortic insufficiency                      | .340              | .333          |
| Aortic stenosis                           | .160              | .236          |
| Endocarditis                              | .087              | .459          |
| S/p cerebrovascular insult                | .005*             | .003*         |
| Parkinsons disease                        | .379              | .663          |
| Alcoholism                                | .866              | .798          |
| Hypertonus                                | .371              | .663          |
| COPD                                      | .549              | .125          |
| Smoker                                    | .666              | .250          |
| Arteriosclerosis of the carotid arteries   | .096              | .861          |
| Asthma                                    | .519              | .711          |
| Chronic kidney disease                    | .515              | .257          |
| S/p myocardial infarct                    | .435              | .259          |
| Decompensated cardiac failure            | .770              | .843          |
| Patent foramen ovale                      | .438              | .202          |
| Intracardial thrombus                     | .218              | .815          |
| Elective/emergency operation              | .034*             | .805          |
| Aortic valve replacement                  | .798              | .802          |
| Mitral valve replacement                  | .019*             | .437          |
| Diabetes                                  | .235              | .564          |
| Hypercholesterolemia                      | .588              | .455          |

Note: Probing the efficiency of both VRS, multiple qualitative perioperative factors were found significantly to predict higher scores with the ARWMC VRS: status post cerebrovascular insult (ARWMC p = .005, emergency operation (ARWMC p = .034), and concurrent mitral valve replacement (ARWMC p = .019). The only significant perioperative factor for the Mendes–Ribeiro p-value was Status post cerebrovascular insult (‘p = .003). Abbreviations: ARWMC, age-related white matter change; COPD, chronic obstructive pulmonary disease; MRVRS, Mendes–Ribeiro VRS; PAD, pulmonary artery disease; VRS, visual rating scale. *significant value.

results that were >0.5 with significantly different from zero p-values. However, the AUC for the ARWMC VRS was higher (0.858) than that for the MRVRS was (0.681), indicating is the more accurate procedure.

4.3 Perioperative factors and neurological assessment

The stratified neurological assessment groups ("no improvement" and "some improvement") were also used to discern if any associations with qualitative perioperative factors were present. The presence of arteriosclerosis in the carotid arteries, an example of a qualitative perioperative factor, was found to be associated with the neurological outcome (p < .028). Similar results have been published, for example, in a study which investigated stroke rates among patients who underwent CABG and who were screened for carotid stenosis that found that higher stenosis grade, particularly >70%, was associated with higher stroke rates. Importantly, one should note that higher stenosis rates may not be directly linked with higher stroke rates or neurological outcome, as higher carotid stenosis rates may also be associated with worse concomitant disease pathology. If higher grade carotid stenosis rates are truly associated with higher stroke rates or worse neurological outcome, one should consider if preoperative carotid endarterectomy (CEA), carotid stenting, or a combined CABG with CEA or stenting would improve neurological outcomes. Trials suggest that while no great difference in in-hospital mortality exists, concurrent coronary artery stenting, which is rarely done, may result in lower rates of stroke as compared to CEA. A 62% increased risk of postoperative stroke was found in patients with concurrent CEA and CABG as opposed to patients who underwent carotid artery stenosis (CAS) with only CABG. Other qualitative perioperative factors that were investigated in this study were not found to be significantly associated with the neurological outcome groups in this study (Table 6). While multiple studies have investigated CABG perioperative risk factors and their association with postoperative stroke, studies concerning risk factors and postoperative CABG neurological outcome are sparse. A study completed in 2012 found that certain perioperative factors such as diabetes, emergency surgery, and lung disease were associated with postoperative risk of encephalopathy. This study was limited by the somewhat small patient population (n = 77). A study conducted at Johns Hopkins used various types of neurological assessments and attempted to determine what perioperative factors could be influential at 1 month and at 1 year. Measured 1 year postoperatively, low systolic blood pressure 24 h after the operation was associated with improved visual perception and psychomotor speed, and longer postoperative hospital stay was associated with worse language skills. The presence of diabetes predicted at 1 month postoperatively a worse psychomotor speed and ast 1 year worse executive function. Interestingly, alcoholism was found to predict an improved visual memory after year. Cognitive decline following CABG has been widely investigated, and the general consensus supports its presence. However, the extent and frequency of cognitive dysfunction following CABG are inconsistently listed in literature. This could be due to the wide variation in criteria used in assessing cognitive dysfunction. This wide variation in results suggests that the most appropriate assessment for determining neurological dysfunction has not yet been identified. This impairs
other studies have supported this assertion. Creatinine levels were discussed in relation to cerebral ischemia. GFRs also had a significant association with hypercholesterolemia, prior myocardial infarct, and cigarette smoking. Previous stroke, pulmonary artery disease, and CAS were associated with a higher risk of stroke. Multiple other possible risk factors, including gender, prior hypertension, diabetes mellitus, congestive heart failure, and chronic renal failure, were inconsistently shown to be predictive. Advanced age and prolonged cardiopulmonary bypass time were found to be associated with an increased risk of perioperative stroke. Our analysis of quantitative perioperative factors was also compared with the neurological assessment groups to determine if these had any influence in determining neurological outcome. ROC-curve analysis found that the preoperative EF had a significant association with the neurological outcome "no improvement" group. The ROC curve (Figure 8) shows an AUC of 0.660 (p = .012) and a standard deviation of 0.059. This unexpected finding suggests that patients with higher preoperative EF had a higher risk of having a poor neurological outcome, while patients with lower preoperative EF levels were less likely to have a worse neurological outcome. The question remains if reduced blood flow in brain has a protective effect. The concept of cerebroprotection has been widely used in place of neuroprotection. Intensive studies on the cellular signaling pathways involved in ischemic conditioning have improved the mechanistic understanding of tolerance to cerebral ischemia. GFRs also had a significant association (p = .027) with the "no improvement" group. The ROC curve (Figure 8) revealed an AUC of 0.361, indicating a negative predictive value. Higher GFR levels predicted better neurological outcome, while lower levels predicted worse neurological outcomes. This result is supported by other studies, which have shown that renal dysfunction and lower GFR levels are associated with increased long-term risk of stroke. The other quantitative perioperative factors in our study were not found to have a significant association with the cognitive outcome groups (Table 5). The AUC found using ROC curves was 0.608 for BMI (p = .091), suggesting a positive but nonsignificant tendency of BMI as a risk factor. Studies have produced oxymoronic results, some suggest that BMI acts as a protective factor, others finding it may be a risk factor. While this study found no effect of creatinine levels on neurological outcome, other studies have supported this assertion. Creatinine levels were found to impact executive function at both 1 month and 1 year. The impact of preoperative anemia in CABG surgery has been debated as well. Multiple studies have shown that it is not directly linked to an increase in the risk of stroke or mortality in CABG patients, with some authors suggesting that any increased risk may be attributable to blood transfusion. The same quantitative perioperative factors were also taken and compared to the ARWMC and MRVRS total scores. Nonparametric testing and associative analysis found no significant associations. Qualitative perioperative factors were also compared with the ARWMC and MRVRS total scores. Multiple qualitative perioperative factors were found to predict higher scores: Status post cerebrovascular insult (ARWMC p = .005, Mendes–Ribeiro p = .003), emergency operation (ARWMC p = .034), and mitral valve replacement (ARWMC p = .019). While other studies have shown that these variables have an impact on the risk of stroke after CABG, or on neurological outcome, statistical comparison of these factors with the ARWMC or MRVRS was not to be found in the literature, and is, if at all, limited and remains to be clarified.

The CCT scans performed at the onset of neurological symptoms and assessed using these VRSs predict, neurological outcome. In addition, patients with "no improvement" and "some improvement" at final neurological assessment upon hospital dismissal were found to differ significantly with regard to their ARWMC score: the "no improvement" group showed a score of 4.1 ± 2.4 while the "some improvement" group obtained a score of 1.7 ± 2.8 (p < .0005). Further stratification of ARWMC and Mendes–Ribeiro scores into those of >0 and 0 and comparison with the "no improvement" and "some improvement" groups, both scales demonstrated an association between scores >0 and the "no improvement" group. Patients with score of 0 were more likely to have "some improvement" at the time of dismissal.

Using ROC curves the discrimination and accuracy strength of each VRS were found. The ARWMC VRS AUC was found to be 0.858 (p < .000), while the AUC of the MRVRS was found to be 0.681 (p = .005), indicating that the ARWMC VRS is superior in this regard. Of note was that high quantities of minor defects occurred in the basal ganglia region. These defects appear to be uniformly found in this patient demographic. Basal ganglia damage was found to be associated with end-of-hospital-stay neurological outcome. A history of cerebrovascular insult (ARWMC p = .005, Mendes–Ribeiro p = .003), emergency CABG operation (ARWMC p = .034), and concurrent mitral valve replacement (ARWMC p = .019) were associated with higher VRS scores. Qualitative and quantitative, potential perioperative risk factors including carotid stenosis, preoperative EF, and GFR were found to be significantly associated with the neurological outcome groups. Both VRSs were found to be appropriate, discriminating scales for the analysis of CCT images in stroke patients. When applied at the onset of neurological symptoms both scales are, to a certain extent, able to predict neurological reconvalescence upon hospital dismissal. Of both scales, the ARWMC VRS demonstrated superior accuracy and discrimination. The use of the ARWMC VRS in the post-CABG operational setting in patients with suspected stroke can provide physicians with insightful information toward the progression of neurological dysfunction.

4.5 Limitations and outlook

Our study represents an approach in which we investigated the neurological disturbances after cardio surgical inter vention s, attempted to classify them, and thus provide a tool in the hands of
the treating physicians to make prospective decisions in intensive care treatment. For our CT data evaluation, an experienced neuroradiologist cooperated with our team and supported the study. The essential skills of a neuroradiologist are necessary for introducing the scoring system in CT scan analysis but can be continued by intensive care specialists. Moreover, the target of the study should not be misunderstood. These scores are not useful in identifying patients at neurological risk per se. It could be useful in evaluating symptoms’ progression, but mainly the scores appear helpful in identifying the likelihood of symptoms’ remission. For establishing the scores as effective tool in treatment finding the helpful in identifying the likelihood of symptoms’ progression, but mainly the scores appear effective tool in treatment finding the helpful in identifying the likelihood of symptoms’ progression. The essential skills of a neuroradiologist are necessary for introducing the scoring system in CT scan analysis but can be performed by intensive care specialists. Moreover, the target of the study should not be misunderstood. These scores are not useful in identifying patients at neurological risk per se. It could be useful in evaluating symptoms’ progression, but mainly the scores appear helpful in identifying the likelihood of symptoms’ remission. For establishing the scores as effective tool in treatment finding the helpful in identifying the likelihood of symptoms’ progression.
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