Study Protocol and Statistical Analysis Plan

Postoperative cognitive dysfunction as geriatric syndrome

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This study is reported in accordance with the STROBE guidelines.

TITLE AND ABSTRACT

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Abstract

BACKGROUND: The primary aim of this study was to determine correlations between preoperative and postoperative scores on three cognitive tests (the Mini Mental State Exam (MMSE), the Clock Drawing Test (CDT) and the Test of Gestures (TEGEST). [1,2].
METHODS: This was a prospective, monocentric, observational study that included one cohort of patients aged 65 years and older. Patients underwent acute or elective surgical operations. Preanaesthesia tests were administered. After the operation, the patients completed the same tests between the 2nd postoperative day and discharge. Preoperative and postoperative cognitive test scores were assessed [1,2].
RESULTS: This study included 164 patients. The arithmetic mean age was 74.5 years. The strongest correlations were observed between MMSE scores and TEGEST scores ($r = 0.830$ before and 0.786 after surgery, $P < .001$). To compare the MMSE and the TEGEST, the MMSE was divided into 2 categories—normal and impaired—and good agreement was found among 76.2% of the participants ($\kappa = 0.515$). If the TEGEST scoring system was changed so that scores of 4-6 indicated normal cognition and scores of 0-3 indicated cognitive impairment, the level of agreement would be 90.8%, $\kappa = 0.817$. Only 5.5 % of the patients had impaired MMSE scores and normal TEGEST scores, whereas 3.7 % of the respondents normal MMSE scores and impaired TEGEST scores [1,2].
CONCLUSION: According to our results, the TEGEST is a suitable option for assessing cognitive functioning before surgery among patients who are at risk of developing perioperative neurocognitive disorders. This study revealed that it is necessary to change the rating scale for the TEGEST so that scores of 4–6 indicate normal cognition and scores of 0–3 indicate cognitive impairment. In clinical practice, the use of the TEGEST may help to identify patients at risk of perioperative neurocognitive disorders [1,2].

INTRODUCTION

Background/rationale: The consequences of PNDs/NCDs can led to considerable changes for patients. Preanaesthesia examinations can help to identify patients at risk of PNDs/NCDs; specifically, higher Clinical Frailty Scale scores, cognitive deficits, and age over 65 years are risk factors for these disorders. Cognitive tests in preanaesthesia examinations are not

routinely performed. Study aimed to identify a quick test that is suitable for everyday clinical practice [1,2].
Objectives: This study aimed to determine whether there was consistency between preoperative and postoperative cognitive function test scores [1,2].

METHODS

Study design: Study was prospective, monocentric, observational study included one cohort of patients. The participants were recruited between October 2020 and March 2023.
Setting: The study took place in the Czech Republic at Tomas Bata Hospital in Zlin. Preoperative and postoperative testing took place in the anaesthesiology outpatient clinic or in the hospital ward [1,2].
Participants: The respondents underwent elective, semi-elective or acute surgery under general or regional anaesthesia (orthopaedic and traumatological surgeries, general and vascular surgeries, neurosurgeries, gynaecological surgeries, otorhinolaryngological surgeries, urological surgeries, eye surgeries) [1,2].
Variables: The explanatory variables were the pre- and postoperative cognitive function scores and their Clinical Frailty Scale scores (quantitative variables). The intervening variable was anaesthesia (general or regional). The response variable was the change in compatibility of the three cognitive function tests. The outcomes of the cognitive tests were the scores on the MMSE, TEGEST, and CDT before and after the operation. The Clinical Frailty Scale evaluated a patient's functional capacity before the operation. The potential preoperative confounders included distress and fear, which could affect a patient's cognitive testing performance. The potential postoperative confounders included pain and opioid treatment [1,2].
Data sources/ measurement: The data were obtained using three cognitive function tests: the Mini-Mental State Exam (MMSE), the Test of Gestures (TEGEST) and the Clock Drawing Test rated with BaJa scoring.
Bias: There was a risk of selection bias due to the way in which patients were enrolled in the study during the preanaesthesia examination. The initial indications of cognitive impairment were obtained during the preanaesthesia examination. This information may have caused patients to feel stressed, anxious or worried, thereby influencing the ir subsequent test results. There was a low risk of information bias because all patients were examined by two doctors. These two doctors did not participate in the administration of general or regional anaesthesia. The population was limited to patients undergoing surgery.
Study size: In the post hoc sample size calculation based on the results of the study, the minimum correlation coefficient for correlations between cognitive test scores was assumed to be Rho = 0.4 with a type I error rate $\alpha = 0.05$ and a test power = 0.9. The minimum sample size under these conditions is 61 respondents. Given the ordinal nature of the data, nonparametric correlations were assumed; therefore, the estimated sample size was increased by 15 %. Hence, the minimum sample size was 71 patients.
The data were processed using TIBCO STATISTICA v. 13.4.0.14.
Statistical methods: Given the ordinal nature of the data, nonparametric analyses were performed. Spearman's correlation analysis was used to examine correlations between two variables. The variables include scores on the three tests (the MMSE, TEGEST, and CDT). Differences between 2 independent samples were compared using the Mann–Whitney U test. The median, minimal, maximal, mean, standard deviation of continuous variables were calculated. Cohen's kappa coefficient was calculated to determine the level of agreement between preoperative and postoperative scores on the TEGEST, CDT and MMSE. All tests were performed at a significance level of 0.05. The statistical analyses were performed using

IBM SPSS Statistics for Windows, version 29.0. Armonk, NY: IBM Corp. Participants who were lost to follow-up and patients with missing data were excluded.

RESULTS:

Participants: A total of 203 patients participated in the study (flow diagram 1). A total of 322 potential patients were approached, 268 patients were screened, 58 patients were excluded, and 210 patients were deemed suitable for testing. A total of 203 patients agreed to participate in the study, 39 of whom were subsequently excluded (Table 1). Ultimately, this study included 164 patients. The mean age was 74.5 (± 6.6) years. The most common age among participants was 68 years old (24 respondents), followed by 70 and 81 years old (always 20 responders). The median age was 72 years.

Pain was assessed with the Numeric Rating Scale (NRS), which is simple to administer and routinely used in the hospital where the study was conducted. Scores on the NRS range from 0 to 10 points, where 0 is no pain, 1-3 indicates mild pain, 4-6 indicates moderate pain, 7-9 indicates severe pain, and 10 indicates the worst imaginable pain. Patients with severe pain (NRS score of 7 points or more) were excluded from the study.

Descriptive data: After surgery, patients were hospitalised in a standard ward or intensive care unit, depending on the nature and extent of the procedure, the patient clinical status after the operation and their complications. The decision regarding postoperative hospitalisation was made by an anaesthesiologist in consensus with the operating surgeon. All postoperative intensive care units in the hospital were under the Department of Anaesthesiology, Resuscitation, and Intensive Care. Among the 164 analysed patients, 102 were primarily admitted to the intensive care unit after surgery, 88 were still in the ICU when cognitive testing was performed, and 14 were discharged to the standard ward at the time of testing. Most of the surgeries were elective (79 %) and performed under general anaesthesia (97 %). Acute operations (21 %) were mainly performed under general anaesthesia and included vascular surgery, urological surgery and traumatological surgery. Sixty-two patients were admitted to the standard ward, and 7 patients were transferred to the ICU later in the postoperative period due to postoperative complications. The average follow-up time was 3 days after surgery [1,2].

Outcome data: The outcomes of the cognitive tests were used to divide patients into two groups. Cognitive functions were measured pre- and postoperatively using three tests (the MMSE, TEGEST and CDT). All tests were significantly correlated with one another. The correlation between the MMSE and TEGEST scores was strong ($r = 0.830$ before surgery and 0.786 after surgery, $P < .001$). The correlations of the CDT with the MMSE and TEGEST were only moderately strong. Only half of patients with a normal score on the MMSE had a normal TEGEST score. All patients who had MMSE scores indicating cognitive impairment also had TEGEST scores indicating impairment. Only 23 % of the patients with normal MMSE and CDT scores had a normal CDT score. Seven percent of patients with an MMSE score indicating mild impairment had a normal CDT score. All patients with moderate or severe impairment according to the MMSE also had CDT scores indicating impairment. Agreement between the TEGEST and the CDT was observed in 77.4 % of patients (shown in italics). The CDT indicated impairment among 17 % of the patients, but the TEGEST scores of these patients were normal. In contrast, 5.5 % of the patients with TEGEST scores indicating impairment had normal CDT scores. The Cohen kappa coefficient for the CDT and the TEGEST was $\varkappa = 0.271$, which indicated poor agreement. During the postoperative period, 43 % of the patients with a normal MMSE score had a normal TEGEST score. Five percent of the patients who had mild impairment according to the MMSE had a normal TEGEST score. All patients with moderate or severe impairment according to the MMSE had TEGEST scores indicating impairment. Only 20 % of the patients within the normal MMSE

scores had a normal CDT score. Five percent of patients with mild impairment according to the MMSE had a normal CDT score. All patients with moderate or severe impairment according to the MMSE had CDT scores indicating impairment. A total of 16.55 % of patients had CDT scores indicating impairment and normal TEGEST scores. In contrast, 5.5 % of the patients had a normal CDT and TEGEST scores indicating impairment. Cohen's kappa coefficient for these tests was $\varkappa = 0.195$, which indicated poor agreement [1,2].

Main results: The strongest correlation was observed between the MMSE and the TEGEST. To compare the MMSE and the TEGEST, the MMSE was divided into 2 categories: normal and impaired. Only 76.2% of the patients had good agreement, $\boldsymbol{\varkappa} = 0.515$. Only half of the patients with a normal MMSE score also had a normal TEGEST score. If the TEGEST score was changed (moderated), with a score of 4–6 indicating normal and a score of 0–3 representing cognitive impairment, then 90.8% of patients showed agreement.), $\boldsymbol{\varkappa} = 0.817$. This coefficient indicates excellent agreement. Only 5.5% of the patients had MMSE scores indicating impairment and normal TEGEST scores, whereas 3.7% of the respondents had normal MMSE scores and TEGEST scores indicating impairment. Postoperative measurements were analysed in a similar way. The relationships between tests when classifying the MMSE score into 2 categories (normal and impaired). Only 71.9 % of the patients agreed well, $\boldsymbol{\varkappa} = 0.419$. Only 43 % (33 out of 77) of the patients with a normal MMSE score also had a normal TEGEST score. The TEGEST was more rigorous in assessing cognitive functions. Changing TEGEST scores postoperatively showed 90.9 % of the patients had excellent agreement, $\varkappa = 0.817$. Only 4.9 % of the patients had MMSE scores indicating impairment and normal TEGEST scores, whereas 4.3 % of the patients had normal MMSE scores and TEGEST scores indicating impairment [1,2].

Other analyses: The correlations between the Clinical Frailty Scale score and cognitive test scores were calculated. 12. Spearman's correlation analysis showed that frailty was significantly correlated with cognitive test scores both before and after surgery. The strongest correlations were observed between frailty and MMSE scores ($r = -0.846$ before surgery and $r = -0.829$ after surgery, $P < .001$ for both). There was moderate correlation between frailty and TEGEST scores ($r = -0.695$ before surgery and $r = -0.677$ after surgery, $P < .001$ for both). There were also moderate correlations between frailty and CDT scores ($r = -0.521$ before surgery and $r = -0.508$ after surgery, $P < .001$ for both). All of the correlation coefficients were negative, indicating that higher (worse) scores on the Clinical Frailty Scale were associated with lower (worse) scores on the cognitive tests [1,2].

DISCUSSION

Key results and limitations: All of the cognitive tests were significantly correlated with one another. The correlation between the MMSE and the TEGEST was strong. The correlation between the CDT and the TEGEST was only moderate. Furthermore, the correlation between the MMSE and the TEGEST was observed in both the preoperative and postoperative periods. On preoperative examination, impaired cognitive function according to the MMSE was associated with impaired cognitive function according to the TEGEST. impaired cognitive function according to the TEGEST [1,2].

In contrast, only 23 % of the patients had normal scores on both the CDT and the MMSE. The reasons for this could include fear of surgery alone, anxiety during the preanaesthesia examination, inattention or a prolonged period of cognitive testing and subsequent tiredness. Seven percent of the patients who had mild impairment according to the MMSE also had a normal CDT score. The same reasons as above could be applied. The CDT was performed as a third test. All patients with moderate or severe impairment according to the MMSE also showed impairment according to the CDT [1,2].

The agreement between the TEGEST and CDT results was 77.4 %. Seventeen percent of patients showed impairment according to the CDT and had a normal TEGEST score, while 5.5 % of the patients had a normal CDT score but showed impairment according to the TEGEST. According to Cohen's kappa coefficient, there was poor agreement between these two tests [1,2].
The strongest correlation was observed between the MMSE and the TEGEST postoperatively; only 43 % of patients had normal scores on the TEGEST and the MMSE. These results may have been influenced by the use of opioids as part of postoperative analgesia, or patients may have remembered the MMSE test assignments and tasks. Patients in the Czech Republic undergo a preanaesthesia examination shortly before the actual surgery (0–14 days before the procedure). Furthermore, the surgical procedure itself or an unrecognised form of hypoactive postoperative delirium may have contributed to the poorer outcomes. resuscitation department. [1,2].
Five percent of patients who showed mild impairment according to the MMSE also had a normal TEGEST score. In the case of moderate/severe impairment, the outcomes were worse in all patients. Only 20% of the patients had normal scores on both the CDT and the MMSE; however, 5% of patients who showed mild impairment according to the MMSE also had normal scores on the CDT, while all patients who showed moderate or severe impairment according to the MMSE also showed impairment on the CDT. Only 78% of the patients showed agreement between the TEGEST and the CDT, and the kappa coefficient indicated that there was poor agreement. Due to the strong relationship between the TEGEST and the MMSE, we decided to adjust the norm of the TEGEST. If the TEGEST score norm is changed so that scores of 4–6 points indicate normal and scores of 0–3 points indicate impairment, 90.8 % of the patients showed agreement, which is an excellent degree of agreement. A similar analysis of the postoperative measurements yielded an agreement of 90.9 %. The TEGEST proved to be a suitable substitute for the MMSE in terms of serving as an indicator of cognitive function [1,2].

OTHER INFORMATION

Funding: None

SOURCES

1. STROBE PROTOCOL: The STROBE checklist is best used in conjunction with article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

2. NEKVINDOVÁ K, IVANOVÁ K, JURÍČKOVÁ L, GABRHELÍK T. *TEGEST as promising tool for assesing the risk of perioperative neurocognitive disorders*. Online. BMC Geriatrics. 2024, vol. 24, no. 713. Dostupné z.: https://link.springer.com/article/10.1186/s12877-024-05302-9?utm_source=rct_congratemailt&utm_medium=email&utm_campaign=oa_20240828&utm_content=10.1186/s12877-024-05302-9, https://doi.org.//10.1186/s12877-024-05302-9 [cited2024-08-29].

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