

The impact of cognitive dysfunction on mid- and long-term mortality after vascular surgery

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Research article

Keywords: vascular surgery, perioperative risk factors, cognitive dysfunction, Mini Mental State Examination, social support, psychosocial factors

Posted Date: August 24th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-42677/v1>

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Version of Record: A version of this preprint was published on January 13th, 2021. See the published version at <https://doi.org/10.1186/s12877-020-01994-x>.

Abstract

Background: In the last decades prior studies noted the importance of frailty which is a frequently used term in perioperative risk evaluation. We investigated frailty syndrome as the psychological and socioeconomic elements of the human being. The aim of this study was assessing the importance of these factors for mortality after vascular surgery.

Methods: In our prospective, observational study (ClinicalTrials.gov Identifier: NCT02224222) we examined 164 patients who underwent an elective vascular surgery between 2014 and 2017. At the point of admission they filled out a questionnaire, in this way the patients' cognitive functions, depression and anxiety, social support and self-reported life quality were mapped. We used Cox regression and Kaplan-Meier method for relative risk calculation and survival analyses. Propensity score matching was performed to analyze the difference between patient and control, nation-wide population cohort. Effects of psychosocial factors on long term mortality were defined as primary outcome.

Results: The patients mean age were 67.05 years (SD: 9.49 years). One out of four patients had some kind of cognitive impairment measured by Mini Mental State Examination with modified, more sensitive cut-off values. In univariate Cox regression higher MMSE score was associated decreased risk for all-cause mortality (OR: 0.883, 95% CI: 0.802-0.973, $p=0.012$). After clusters were created according to MMSE score relative risks were calculated. Even mild cognitive dysfunction could increase risk for long term mortality (AHR: 1.634, 95% CI: 1.118-2.368, $p=0.009$).

Conclusion: Even mild cognitive dysfunction measured by the MMSE preoperatively could be an important risk factor for mortality after vascular surgery.

Background

In the preoperative period, it would be ideal to identify all potential risk factors, which could cause adverse events and/or negatively influence the outcome. Frailty-syndrome is an age-related, multi-dimensional state of decreased physiologic reserve which results in diminished resiliency and increased vulnerability of patients. Frailty has been proven to be an excellent predictor of unfavorable health outcomes in the older surgical population. [1] It has been studied intensively for the past two decades, and it seems that frail patients receiving surgery have significantly worse short- and mid-time survival compared to the non-frail patient population. [2, 3]

According to the modern and comprehensive definition, frailty is a medical syndrome with multiple causes and contributors, characterized by diminished strength and endurance and reduced physiological function, leading to increased vulnerability for adverse health outcomes such as functional decline and early mortality. [4] This general concept contains all the factors which have serious effect on mortality and quality-adjusted life years.

The clinical experience shows that some other, routinely not evaluated factors could influence postoperative outcome. Frailty refines former risk stratification, based on clinically measured and anamnestic data, enabling a more precise assessment of the length and difficulty of healing and recovery after surgery. Traditionally, older age, lower educational level, current smoking, current use of postmenopausal hormone therapy, certain ethnicity, unmarried state, clinical depression, or use of antidepressants and intellectual disability are mentioned as the most important predictors for frailty. [5–8] As it appears from the list, frailty risk factors can be basically divided into two main groups. In this current article, over the traditional score systems we focus on factors including intellectual, mental, social and psychological aspects.

Objectives

This study aimed to preoperatively identify the most important psychological and social variables which can influence postoperative outcome in patients undergoing vascular surgery.

The primary endpoint was overall mortality while secondary endpoints were defined as one- and two-year survival. A comparison between our vascular surgery patient population and a representative, control population cohort was also performed to identify the potential difference in the aspect of the psychosocial attitude.

Methods

Study design, Setting, Participants

This study was approved by the Regional Ethics Committee (TuKEB 250/2013) and registered on ClinicalTrials.gov (NCT02224222). The inclusion criteria were as follows: age over 18 years, Hungarian citizenship and elective vascular surgery. Exclusion criteria were

pregnancy, legal incapacity or considered to have limited capability to understand the study procedures and ethical consent. All clients were capable of making decisions regarding their participation in this study and accordingly their written consent was obtained. A study nurse, a medical student or a doctoral school fellow invited patients to participate in the study during their outpatient anesthesiology visit. Baseline questionnaires were fulfilled 5–30 days before surgery. After signing the informed consent 199 adult patients were enrolled prospectively at the Department of Vascular Surgery of the Heart and Vascular Center of Semmelweis University, in Budapest between September 2014 and August 2017. Thirty-two patients were excluded because of cancellation surgery. Three patients withdrew their consent. Finally, data of 164 patients were used for statistical analysis.

Definitions and measurements (variables and data sources and grouping)

A wide range of clinical and psychosocial factors was assessed as potential determinants of outcome. Clinical factors included perioperative laboratory parameters (blood counts, renal function, ion levels, etc.), intraoperative parameters (operation time, cross-clamp time, blood loss, need for transfusions and fluid balance medications), postoperative parameters (blood loss, medications, etc.), outcomes, incidence and quality of postoperative complications (major cerebrovascular or neurological event; acute or chronic heart failure defined as pulmonary edema, atrial fibrillation, arrhythmias, cyanosis, metabolic disorders, need for inotropes, respiratory failure; infection; acute renal failure /need for renal replacement therapy/; length of mechanical ventilation; length of ICU and in-hospital stay and in-hospital mortality). The American Society of Anesthesiologist risk score (ASA score) [9], and the Vascular Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (Vascular POSSUM) [10–13] were calculated, too. The vascular-POSSUM consists of two parts, a physiological and an operative score. The physiological part includes age and major vital parameters (cardiac, renal, hematological and neurological function) and the operative part focuses on intraoperative blood loss, peritoneal contamination, possible malignancy and the length and urgency of the procedure.

Psychosocial factors

Psychosocial and demographic anamnestic data were collected as e.g. age, gender, living conditions, smoking, alcohol consumption and education. Then participants were asked to fulfill out many questionnaires measuring psychosocial factors: the Beck Depression Inventory (BDI), the Spielberger State- and Trait Anxiety Inventory (STAI-S, STAI-T), the Mini Mental State Examination (MMSE), the Geriatric Depression Scale, the Somatic Symptom Severity Scale, the Devins Illness Intrusiveness Rating Scale, the Caldwell Social Support Dimension Scale, and specific parts of the Hungarostudy Query (a representative national study of 2013, used as control group, measuring health status, illnesses, bio-psycho-social background and health-related quality of life /HRQ/).

For mapping, the cognitive function Mini-Mental State Examination (MMSE) was applied. MMSE is a well-established inventory to screen cognitive deficits and signs of dementia. It contains simple questions and problems in many areas including auto- and allopsychic orientation, short term memory, arithmetic computation such as the decreasing serial sevens, language use, and comprehension, as well as basic visual-motor skills. The questionnaire scored 0 to 30. Cut-off values are 23, 18 and 9 signs for mild, moderate and severe cognitive impairment, respectively. [14, 15] To detect the mildest cognitive impairment modified cut-off values were used according to a paper published earlier. [16] In this study, the cut-off value 27 and below was used to detect mild and 23 and below for severe cognitive impairment.

Patients were asked to estimate self-reported happiness and satisfaction using a 1 to 10 scale. These self-reported parameters were reported earlier as an important aspect of determining long-term mortality of healthy adult volunteers. [17]

The State-Trait Anxiety Inventory (STAI) was used for the characterization of the anxiety of patients. The inventory consists of two parts, the STAI-S and the STAI-T axis. The first 20 questions refer to the transitional emotional status evoked by a stressful situation (STAI-S), as e.g. a hospital admission or a surgical intervention. The STAI-T score reflects personal differences in chronic anxiety susceptibility. Each group is scored 20 to 80 calculated from answers which are four-level Likert items. [18, 19] The STAI as a high reliability and validity test is well documented in the Hungarian population.[20] (STAI T and S Cronbach's α = 0.638 and 0.763, respectively)

The Beck Depression Inventory (BDI) was used for affective disorders,. The BDI, a 21-item questionnaire, is an established tool for depression screening with each item evaluating a symptom of depression, such as bad mood, pessimistic outlook, feelings of guilt and loss of appetite. Each item contains four sentences indicating the degree of severity for that particular symptom. Answers are four-level Likert items; the whole inventory is scored 0 to 60.[21–23] Validity and reliability of the BDI are also well-documented in the Hungarian population. [24] (Cronbach's α = 0.787)

The Geriatric Depression Scale is a yes-or-no question-based, 30-item inventory for the assessment of depression occurring in the older population. In our set, the short form of the GDS was used which includes 15 questions. Every question is scored either 0 or 1, the sum is normal between 0 and 9. [25] (Cronbach's $\alpha = 0.704$)

The Somatic Symptom Severity Scale (Patient Health Questionnaire – PHQ15) refers to different symptoms as e.g. gastrointestinal dysfunction, dizziness, chest pain and dyspnea. It is calculated by assigning scores of 0, 1 and 2 to the response categories of “not at all”, “bothered a little”, and “bothered a lot” for all 13 somatic symptoms. Also, 2 items from the mood module (fatigue and sleep) are scored 0 (“not at all”), 1 (“several days”) or 2 (“more than half the days” or “nearly every day”). We did not use questions regarding pain caused by menstruation or dysmenorrhea for better comparability. Thus the inventory is scored from 0 to 28. Scores of 5, 10, and 15 represent cut-points for low, medium, and high somatic symptom severity, respectively. [26–28] (Cronbach's $\alpha = 0.730$)

The Devin's Illness Intrusiveness Rating Scale measures the effect of illness on different social issues. The 13-item questionnaire was introduced to screen for illness-induced disruptions of lifestyle, activities and interests that can compromise with psychosocial well-being and can contribute to emotional distress in chronic diseases. Answers are seven-level Likert items; the inventory is scored from 13 to 91. [29, 30] (Cronbach's $\alpha = 0.854$)

For analysis of the patient's social web structure, the Caldwell Social Support Dimension Scale was used. This is a novel version of the Social Support Questionnaire published originally in 1987. [31] The intensity of different interpersonal relationships and supports, such as direct relatives, neighbors, workmates and friends are represented in the query. After the first summary of scores, a distinct familial (parents, spouse, grandparents, children and other relatives) and non-familial (neighbor, schoolmate, workmate, other social or sacral company) support score was created. Answers are a four-level Likert item. [32–34] (Cronbach's $\alpha = 0.570$)

Finally, the shortened form of the Athens Insomnia Scale Inventory (AIS-5) was also recorded to detect mild or severe insomnia. The cut-off score of the AIS-5 is ≥ 4 , which is related to potential insomnia. [35] (Cronbach's $\alpha = 0.630$)

The data were compared to the Hungarostudy (HS) population. Free-access, nationally representative, face-to-face household surveys are conducted in Hungary every 10 years, for the last time in 2013 ($n = 2,000$). [36, 37] The Hungarostudy is built up from the inventories listed above, it contains the BDI, STAI, CSSDS, Devin's Illness Intrusiveness Rating Scale, PHQ15 and AIS over basic questions about age, sex, education, marital status, religion, physical status. In HS further questions was about smoking, drinking alcoholic beverages and some about the income of the participant. In our inventory, a shorter form from HS 2013 was used, in this manner, the two populations became comparable. Identical questions were compared by using the propensity score matching method.

Outcomes

The primary outcome of the study was overall mortality. As a secondary outcome, one year and two-year mortality were examined.

Statistical analysis

Descriptive statistics (mean, standard deviation, median and interquartile range) were calculated for all continuous variables. Means and SDs were used in the case of normal distribution, the Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to ascertain the type of distribution. For categorical variable χ^2 -test was used, for continuous variable non-parametric tests were used, with the Mann Whitney U test as default. Categorical variables were calculated from continuous scales, with well-proved cut-off values. Univariate and multivariable logistic regression (Cox regression) models were also performed. The Kaplan-Meier analysis with log-rank and the Breslow tests were used to investigate differences in short and mid-term survival analyses. $P < 0.05$ was considered statistically significant. For statistical analysis the IBM SPSS Statistics 24.0 (SPSS Inc., Chicago, Illinois) with R plugin (version 3.2.1) for PS matching was used.

A propensity-matched analysis was performed for comparative analysis of the vascular population and the Hungarian patient cohort. During the propensity score matching pairs were generated from the HS representative group and the vascular surgical group according to age, gender and place of living. Balance on baseline covariates between the treated and control groups were evaluated using absolute standardized differences. A value less than 0.1 was considered as an acceptable standardized bias. As the pairs were created identical questions were compared to analyze the difference in psychological attitude and social state between a general and surgical population.

Results

Descriptive and outcome data

Data of 164 patients were analyzed. The mean age of the population was 67.05 years, (SD \pm 9.49) and 35.97% of the patients were female. In the postoperative period 20.73% of the patients were admitted to the ICU, the median length of stay was 1.5 days (IQR 1.0–2.0). The median length of the surgical ward stay was 6.0 days (IQR 5.0–9.0 days). During the follow-up time (1,312 days, IQR: 924-1,582 days) 42 patients (25.61%) died, the 30-day mortality was 0.61% (1 patient) and the 1-year mortality was 4.88% (8 patients). The vascular POSSUM score was slightly higher in the non-survived group [16 points (IQR: 14.00–18.00) vs. 17 points (IQR: 15.00–22.00), $p = 0.025$]. The non-survived group had more previous vascular surgeries (43.44% vs. 66.67%, $p = 0.009$). With regard to laboratory parameters lower hemoglobin and non-pathological higher CRP levels were observable in those who died during the follow-up. In the non-survival patients, the occurrence of previous stroke (16.39% vs. 26.19%, $p = 0.162$) and psychiatric disorders (4.10% vs. 7.14%, $p = 0.068$) tended to be higher, compared to surviving patients.

Table 1
Preoperative variables and overall mortality

All patients (n = 164, 100%)									
Survivors (n = 122, 74.39%)									
Non-survivors (n = 42, 25.61%)									
Preoperative Variables	Count	Percentages within survivors	Mean/Median	Standard Deviation/IQR	Count	Percentages within non-survivors	Mean/Median	Standard Deviation/IQR	p value ^b
Gender	male	77	63,1%		28	66,7%			0,679
Age			66,9	10,0			67,6	8,0	0,874
BMI			27,5	4,7			26,0	3,8	0,092
ASA	1	1	0,8%		0	0,0%			0.783 ^c
	2	46	37,7%		10	24,4%			
	3	72	59,0%		29	70,7%			
	4	3	2,5%		2	4,9%			
Vascular POSSUM ^a			16,0	(14,0–18,0)			17,0	(15,0–22,0)	0,025
Ischemic Heart Disease	43	35,2%			15	35,7%			0,956
Myocardial infarction	23	18,9%			5	11,9%			0,302
Diabetes Mellitus	35	28,7%			19	45,2%			0,049
Obesity	31	25,4%			5	11,9%			0,068
Hypertension	108	88,5%			34	81,0%			0,214
CABG	10	8,2%			4	9,5%			0,791
Neoplasia	28	23,0%			10	23,8%			0,909
Psychiatric disorder	5	4,1%			3	7,1%			0,430
Previous vascular surgery	53	43,4%			28	66,7%			0,009
Stroke or TIA	20	16,4%			11	26,2%			0,162
COPD	25	20,5%			14	33,3%			0,092
Thyroid disorder	7	5,7%			2	4,8%			0,811
Hemoglobin (g/l)			140,3	14,6			129,8	19,7	0,020
Platelet number (G/l)			235,4	81,0			251,9	111,9	0,632
Glomerular filtration rate (ml/min/1.73 m ²)			84,4	13,6			86,2	10,2	0,537
C reactive protein (mg/L)			3,0	(1,2–6,2)			12,4	(4,5–33,5)	< 0.001

a = not normally distribution

b = Pearson chi square test for categorical variables and Man-Whitney U test for continuous variables

c = Kolmogorov-Smirnov Z test

We compared the study population with the Hungarostudy patients. After propensity score matching (adjusting participants to age, gender and place of living), 159 pairs were created. The vascular surgery patients cohort visited health care facilities more frequently over the last year (26.6% vs. 11.8%, $p < 0.001$). The patient cohort had more intensive social support [CSSDS scores were 20 (15.00–23.00) vs. 23 (19.00–27.00), $p < 0.001$ for the population group and the patient cohort, respectively]. Table 1. shows the comparison between the HS population and the surgical group before propensity matching. Table 2. shows the socio-economical comparison between the population of Hungarostudy Survey and our vascular surgery population after propensity score matching.

Table 2
Comparison between the propensity score matched pairs (Hungarostudy vs. vascular surgery group, n = 159 pairs)

		Hungarostudy group				Vascular surgery group				p value
		Count	Percentages within HS	Median	IQR	Count	Percentages within vascular surgery group	Median	IQR	
No medical contact - last year*		42	26,6%			18	11,8%			< 0,001
Actual bodily pain*		85	53,5%			85	53,5%			0,545
Self-reported health condition (1–10)				3	(3,0–4,0)			3	(3,0–3,0)	0,471
Patient Health Quality				21	(16,0–26,0)			20	(17,0–24,0)	0,637
Life satisfaction (1–10)				7	(5,0–8,0)			7	(5,0–8,0)	0,472
Happiness (1–10)				7	(5,0–8,0)			7	(5,0–9,0)	0,119
In-hospital-days - last year				0	(0,0–0,0)			1	(0,0–10,0)	< 0,001
Alternative health care - last 3 years*		4	2,5%			18	11,3%			0,002
Caldwell Social Support Dimension Scale				20	(15,0–23,0)			23	(19,0–27,0)	< 0,001
Caldwell Social Support Dimension Scale - family				10	(8,0–12,0)			12	(10,0–15,0)	< 0,001
Caldwell Social Support Dimension Scale - other				9	(7,0–12,0)			10	(7,0–13,0)	0,001
Smoking	Never	74	46,5%			23	14,7%			< 0,001
	Used to smoke	44	27,7%			80	51,3%			
	Active smoker	41	25,8%			53	34,0%			
Physical exercise/week				5	(4,0–7,0)			2	(0,0–6,0)	< 0,001
Other, non-sport physical activity/week				3	(1,0–4,0)			1	(1,0–4,0)	< 0,001
Drinking alcoholic beverages (1–5)				2	(1,0–4,0)			2	(1,0–3,0)	0,310
Not religious*		50	32,1%			75	47,2%			0,024
Financial difficulties*		28	18,2%			19	11,9%			0,083

* = categorical variable, chi square test were used for statistics, on continuous variable Mann-Whitney U test were used

Main results

Significant correlation between MMSE score and patient's age was not verifiable (Pearson $R^2 = -0.075$, $p = 0.340$), and the age was not an independent risk factor for mortality (HR: 1.012, 95% CI: 0.980–1.045, $p = 0.465$). The minimum of MMSE score was 18 points, maximum was 30 points.

According to the traditional MMSE categories (normal range 24 points and above) 11.59% of the patients had cognitive impairment. As a novel cut-off value of MMSE (normal range 27 points and above) was used, the prevalence of cognitive dysfunction increased to 25.00%.

The Kaplan Meier analysis was performed for survival, the curves are shown in Fig. 1. Part A is a summary of used categories. On Fig. 1/B the conventional cut-off value was applied, on Fig. 1/C the more sensitive, modified cut-off value was applied as a definition of cognitive dysfunction. All MMSE categories created the way described above were significantly different from the point of view of survival. (log-rank p-values in Fig. 1, each at the matching Kaplan-Meier curve).

Each worse MMSE clusters - created as described in Figure.1/A - were associated with increased risk of long-term mortality adjusted to vascular POSSUM (HR: 1.659, 95% CI: 1.129–2.439, $p = 0.001$).

Figure 1. Different type of clustering according to MMSE score and long term mortality

Analyzing risk for mortality Cox regression was used. Higher MMSE score had protective effect on all-cause mortality (OR:0.883, 95%CI: 0.802–0.973, $p = 0.012$). The cohort with cognitive dysfunction (MMSE score ≤ 24 points) had higher risk for mortality adjusted to vascular POSSUM (OR: 2.918, 95% CI: 1.380–6.170, $p = 0.005$).

Other analyses

Self-rated parameters (happiness, satisfaction, current health status) were lower in the non-survival group. In the case of happiness, the result was significant (median = 8.0 IQR: 5.0–10.0 vs. 6.0 IQR: 5.0–8.0, $p = 0.046$), furthermore in the case of satisfaction the significance was not reached, but the correlation seems obvious (median = 7.0 IQR: 5.0–8.0 vs. 6.0 IQR: 5.0–7.0, $p = 0.122$).

BDI, GDS and STAI-T and S scores were not significantly different between the non-survival and survival groups. Similarly, the Patient Health Quality 15 and the Caldwell Social Support Dimension Scale showed no significant effect on the aspect of survival.

Short and mid-time outcomes (one- and two years survival which was defined as secondary outcomes) did not show significant correlation with the result of the psychological or sociological questionnaire.

Discussion

Key findings

In our prospective study, we examined several preoperative psychological and sociological factors to determine risk factors which can influence postoperative mortality. Several reports have shown that poor functional status and physical frailty give rise to worse postoperative mortality. [38] According to our findings cognitive dysfunction measured by the MMSE score caused worse mid- and long-time survival. For the classification of cognitive functions we used a different cut-off system on MMSE score to detect cognitive disabilities in a more precise way.[16] The traditionally created and the modified cut-off value cognitive impairment group (MMSE score below 24 in traditionally and below 27 in modified, respectively) were associated with worse survival.

In contrast, the preoperative cognitive deficit did not influence the direct postoperative period or the short time survival in a significant way. On the other hand, patients with a mild cognitive deficit (MMSE score 24–26) have a slightly different risk in comparison with patients without cognitive dysfunction (MMSE score 27–30) after approximately 1,000 days of follow-up time. The highest risk for mortality was linked to patients with MMSE scores equal or lower than 23 points.

Prior studies that have noted the importance of depression and anxiety suggest that these mental problems have a heavy effect on short and mid-term survival. [39, 40] However, these data suggest that depression severity is an important risk factor, our current dataset could not prove a strong relationship between the observed BDI, GDS or STAI Score systems from the point of view of primary and secondary outcomes. Morin et al. have recently published an article where they conclude that depression severity is the predictive factor over cognitive dysfunction and physical frailty. [41] Our earlier results had shown negative correlation of anxiety severity in the short time

survival in patients with cardiac surgery. [40] According to our recent findings we could hypothesize the negative effect of cognitive impairment mostly in the mid- and long term-survival in vascular surgical patients.

The other aim of our study was to compare the vascular surgical population to the general, healthy population. The present results are significantly different in several major respects. After propensity score matching the analysis clearly shows lower mobility, decreased physical activity and more frequent smoking in the vascular surgical population. (Table 2.) Several papers have emphasized the importance of social support in different clinical contexts. [42–45] One unanticipated finding was that vascular surgical patients had higher self-reported, social support score. Our finding suggests that people with (vascular) surgical or any other kinds of health problems receive higher social support or at least they feel so.

Limitations of the study

A main limitation of the conducted study is the relatively small sample size. In some aspects, we did not have an adequate number of participants to obtain the appropriate statistical power. However, in the case of psychological and sociological topics, tendencies have a crucial role, too. The single-center experience makes us more careful during the interpretation of our findings.

Conclusion

The purpose of the current study was to determine a novel kind of preoperative risk factor based on the patients' psychological and sociological parameters. After an extended analysis we found a significant relationship between the patients' preoperative cognitive dysfunction and worse long-term mortality. To assess the cognitive impairment MMSE was used with modified cut-off values to obtain a more sensitive estimation. As far as the future is concerned our findings suggest applying cognitive mapping to estimate postoperative mortality risk more accurately. The presented data suggest appreciating the preoperative existing mildest cognitive impairment as a potential risk factor for increased mid- and long-term mortality after vascular surgery.

During the analysis of the socioeconomic ambience the vascular surgery group reported significantly higher social support than the general control group measured by the Caldwell Social Support Dimension Scale.

Abbreviations

AHR	adjusted hazard ratio
AIS	Athens Insomnia Scale
ASA	American Society of Anesthesiology
BDI	Beck Depression Inventory
BMI	body mass index
CABG	coronary artery bypass grafting
COPD	chronic obstructive pulmonary disease
CRP	C reactive protein
CSSDS	Caldwell Social Support Dimension Scale
GDS	Geriatric Depression Scale
HS	Hungarostudy
ICU	intensive care unit
IQR	interquartile range
MMSE	Mini Mental State Examination
PHQ	Patient Health Questionnaire 15
SD	standard deviation
STAI	State Trait Anxiety Inventory
TIA	transient ischemic attack
Vascular POSSUM	Vascular Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity

Declarations

Ethical Approval and Consent to Participate

Study was approved by Scientific Research Ethics Committee, Semmelweis University, Budapest. Approval number is 250/2013. All clients were capable of making decisions regarding their participation in this study and accordingly their written consent was obtained.

Consent for publication

The authors give their consent for information to be published in BMC Geriatrics. (BGTC-D-20-00679R1, A., Szabó). All authors understand that the information will be published without their name attached, but that full anonymity cannot be guaranteed. All authors understand that the text and any pictures or videos published in the article will be freely available on the internet and may be seen by the general public. The pictures, videos and text may also appear on other websites or in print, may be translated into other languages or used for commercial purposes. All authors have been offered the opportunity to read the manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Role of funding source

The present study did not receive any funding.

Authors contributions:

ASza - data analysis and interpretation, drafting the article and final approval of the version to be published

NC - data collection, critical revision of the article and final approval of the version to be published

AN - data collection, critical revision of the article and final approval of the version to be published

KT - data collection

CE - data collection

DD – statistical analysis and final approval of the version to be published

AS - data collection and critical revision of the article

BM - critical revision of the article and final approval of the version to be published

JG - critical revision of the article and final approval of the version to be published

ASze - conception and design of the work, data analysis and interpretation, critical revision of the article and final approval of the version to be published

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

Acknowledgments

The authors thank the employees of vascular surgical ward of Heart and Vascular Center, Semmelweis University, Budapest.

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Figures

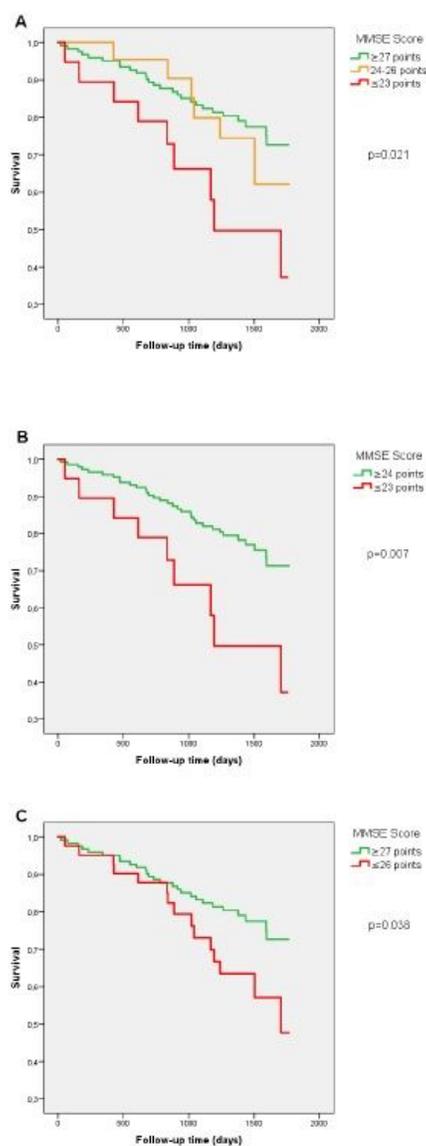


Figure 1

1. KM curve: MMSE categories and mortality: A. MMSE groups: 27 and above, 24-26, 23 and below B. MMSE groups: 24 and above, 23 and below (traditional cut-off value) C. MMSE groups: 27 and above, 26 and below (modified cut-off value)

