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Risk factors for postoperative delirium in vascular surgery

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Abstract

The aim of this study was to identify psychiatric and somatic risk factors associated with the development, severity and duration of postoperative delirium after vascular surgery. Forty-seven patients underwent aortic, carotid artery and peripheral artery surgery. Both, surgeon and psychiatrist, monitored patients preoperatively with daily follow up. Preoperative psychiatric assessment included standardized psychopathological scales for the detection of psychiatric symptoms and cognitive deficits. We diagnosed delirium using DSM IV criteria. Delirium Rating Scale was used to estimate delirium severity. Surgical parameters included patient history, diagnoses, medication and laboratory parameters. A statistical analysis was performed using multivariate regression analyses to find factors significantly associated with delirium development, severity, and duration. Thirty-six percent of the patients developed postoperative delirium after surgery. Comparison of different parameters revealed that especially preoperative depression symptoms and perioperative transfusions/infusions had significant predictive value for the development as well as for the severity of postoperative delirium.

Keywords: Vascular surgery; Postoperative delirium; Psychiatric symptoms; Depression; Risk factors

1. Introduction

Delirium is a common medical condition, especially in elderly patients undergoing surgery. Estimates vary between 32% (range 2%–57%) and 37% (range 0% -74%) [1,2]. Recently, the incidence of postoperative delirium was found in 42% of patients who suffered from lower limb ischemia [3]. Generally, symptoms in delirious patients surface shortly after surgery and may last for a few days. In some cases, however, symptoms may persist up to several weeks [4]. The recovery process of postoperative delirium tends to be delayed due to reduced compliance to an optimal patient management. Comparison problems indicated in two metaanalyses and the observations made by several authors suggest that the prevalence of acute confusional state is often unrecognized or misdiagnosed despite the various tools available for assessing delirium and delirium severity [2,4,5], because of the fluctuating symptoms and the inadequate documentation.

Attempts to identify predictive indicators for a postoperative delirium have resulted in the description of a number of associated risk factors [3,6]. These include, among others, critical limb ischemia, age, duration of surgery and dementia in presurgical patients as well as vascular and aortic aneurysm surgery. Two additional predisposing factors that have been identified include family history of psychiatric diseases and preoperative psychological symptoms, especially depression [7].

Against this backdrop, we set out to identify a set of predictive indicators for the development of delirium after vascular surgery from both, psychological and medical perspectives. Furthermore, predictive indicators were investigated for the severity and the duration of a delirium. Our focus was directed at surgeries of carotid, main, and peripheral arteries.

2. Patients and methods

2.1. Subjects

Included were forty-seven patients (38 males, 9 females, age: mean ± SD, 66.8 ± 7.1 years; range: 53–84) admitted

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Table 1
Type of surgery performed plus number and the percentage of postoperative delirium

	Diagnosis N/%	Postoperative delirium n/N (%)
Peripheral Arterial Occlusive Disease	10/21.3	3/10 (30.0)
Aortoiliac Occlusive Disease (incl. Renal Artery Stenosis)	7/14.9	5/7 (71.4)
Infrarenal Aortic Aneurysm	12/25.5	5/12 (41.7)
Thoracoabdominal Aortic Aneurysm	4/8.5	2/4 (50.0)
Supraaortal Arterial Occlusive Disease	14/29.8	2/14 (14.3)
Total	47/100	17/47 (36.2)

to the Department of Vascular Surgery of the School of Medicine, Heinrich-Heine-University of Düsseldorf, Germany. Patient selection was performed by the operating surgeon after patients were admitted to the surgical unit. Included were patients undergoing elective surgeries that exceeded 90 min. Fourteen patients underwent carotid artery surgery, 23 had aortal surgery (abdominal aortic aneurysm, visceral, renal, iliac arterial occlusive disease) and 10 patients underwent peripheral artery surgery (Table 1). Patients gave written informed consent to the study physician. Neither the surgeon performing the operation nor the anesthesiologist in charge were informed about which patients were eligible for study participation. Although there was no random-sampling procedure to select patients, the study group comprised a representative sample of patients treated in the Department of Vascular Surgery during the study period. However, a potential selection bias has to be taken into account. Patients were also required to be German native speakers. Exclusion criteria were less invasive surgical procedures such as varicose vein operations, arteriovenous shunt operations or closure of arteriovenous fistula. The study initially comprised 60 patients. However, 13 patients dropped out of the investigation because of exitus on the second postoperative day (1), patients did not undergo surgery (9), withdrew informed consent (1), intraoperative vascular diagnosis was not found (1), and incomplete postoperative documentation (1). Recruitment took place over a three months period. The study was approved by the Institutional Review Board of the School of Medicine, University of Düsseldorf, Germany. Patients were consecutively admitted and all patients signed informed consent before entering the study. Patients received no psychiatric treatment or standardized delirium therapy by the psychiatrists who performed the examinations. A symptomatic therapy according to the clinical requirements was performed by the responsible surgeons using high and low potent neuroleptics, benzodiazepines and other medications.

2.2. Psychiatric evaluation

The psychopathological status of the patients was assessed using a battery of psychometric scales and clinical interviews. Preoperative assessment was performed by experienced psychiatrists the day before surgery. Depressive symptoms were measured with the Hamilton Depression Scale (HAMD [8]). Furthermore, Global Assessment Scale (GAS [9]), General Severity Score (ASGS), Brief Psychiatric Rating Scale (BPRS), and the Mini-Mental-State-Examination (MMSE) were used to evaluate psychosocial functioning, general psychopathological symptomatology and cognitive status [10–12]. Delirium diagnosis after surgery was based on the DSM IV criteria [13]. Delirium Rating Scale (DRS [14]) was used daily over the course of one week for estimating delirium severity. The DRS cut-off score for a delirium was 12 points. Delirium was defined according to the following criteria: mild delirium = 12 to 17 points, moderate delirium = 18 to 28 points and severe delirium = 29 to 32 points. The psychiatrists were not blind to the preoperative status of the patients.

2.3. Medical evaluation

Administration of medication, laboratory data, general and specific complications, discharge, and patient relocation were documented before and after surgery. Blood loss, infusion, blood transfusion and blood pressure together with laboratory values, i.e., hemoglobin, thrombocytes, and arterial blood gases were assessed. Standardized anesthesiological procedures with normal capnia were applied during surgery based on the anesthesia protocol and on the American Society of Anesthesiology classification (ASA-score). Patients were kept under surveillance for possible postoperative complications.

2.4. Statistical analysis

The purpose of this study was to determine factors that are predictive of a delirium after vascular surgery. Hence, multiple regression analyses were performed on all quantified variables. Our choice of the best set of variables was restricted to a reasonable amount of eight predictors since we had five times as many subjects compared to variables. We tested the hypothesis that preoperative factors (cognitive, psychopathological impairment) and perioperative factors (aortic surgery, the loss of hemoglobin, the infusion and transfusion requirements) are associated with the development of delirium after surgery. This procedure helped to find statistically the best set of eight predictors, which were then entered into a normal regression analysis to find regression coefficients. Multiple linear regression analyses were used for predicting the linear variables. We used the scores of the DRS for the criteria of the delirium severity and the number of days for the delirium duration. These scores represent linear variables. We also used the multiple regression analysis for the occurrence of delirium, which is a dichotomous variable, since the dependent variable has only two categories and the responses are split relatively evenly between these two categories (no more than 25/

Table 2
Group differences between patients with and without a postoperative delirium showing pre-, inter-, and postoperative variables*

		Without Delirium		Delirium		P
		Mean	SD	Mean	SD	
Preoperative	HAMD	1.77	2.06	5.65	5.31	0.01
	BPRS	21.13	4.13	25.12	6.10	0.01
	ASGS	0.33	0.66	1.24	1.20	0.01
	MMSE	28.73	1.78	26.71	3.31	0.03
	GAS	84.67	7.87	75.00	10.90	0.00
	Preoperative hemoglobin (g/dL)	14.18	1.34	13.50	1.80	n.s.
Intraoperative	Bloodloss (mL)	1043.6	796.64	1880.7	1405.7	n.s.
	Minimal intraoperative hemoglobin (g/dL)	11.39	2.21	9.38	2.45	n.s.
	Infusion (mL)	2931.0	988.54	4294.1	1299.7	0.00
	Autotransfusion (mL)	185	306	473	642	n.s.
	Minimal paO_2 (mmHg)	88.80	30.85	91.79	35.58	n.s.
	Sodiumbicarbonate (mL)	12.07	31.78	79.41	93.64	0.01
Postoperative	Need for transfusion (mL)	89	181	364	395	0.01
	Minimal postoperative hemoglobin (g/dL)	10.83	1.71	9.52	1.50	0.01
	Intermediate care unit (days)	1.8	1.77	2.29	1.49	n.s.

* Mean values, standard deviations, and significance of group differences. HAMD, Hamilton Depression Scale; BPRS, Brief Psychiatric Rating Scale; ASGS, General Severity Score; MMSE, Mini-Mental-State-Examination; GAS, Global Assessment Scale.

75%). Being that the results of loglinear analysis are usually quite close to those of a multiple regression analysis with a dichotomous dependent variable, our choice of method remains an adequate means of analysis [15].

3. Results

3.1. Delirium diagnosis

Postoperative delirium developed in 17 (36.2%) of the 47 patients with elective vascular surgery. Mild delirium occurred in nine patients and moderate delirium in eight patients. No patient scored more than 26 points on the DRS. In seven patients, delirium was diagnosed within the first day after surgery, in two patients within the second day, and in three patients on the third day following surgery. None of the patients developed delirium on the succeeding days (4 to 7). Symptoms lasted between one and seven days (3.0 ±1.62, ± S.D.).

3.2. Demographic, psychiatric, somatic factors, and medical outcome data

Mean age of delirious patients was 67.53 years (± 6.72). Mean age of nondelirious patients was 66.33 years (± 7.41). Postoperative delirium occurred in one of nine patients under age 60, in 13 of 25 (60–70 years), and three of 13 patients over 70 years. The ASA-score was used as a marker for mean severity of illness: No significant difference was found between nondelirious (2.8 ± 0.5) and delirious patients (2.8 ± 0.6). Twelve patients (52%) with aortic surgery (Table 1) manifested a delirium. Patients developing postoperative delirium differed significantly in their psychopathological symptomatology before surgery compared to the nondelirious patients (Table 2, Fig. 1). Furthermore, preoperative psychopathology, i.e., HAMD scores ($r=0.51$, $P=.0003$, Fig. 2), psychopathological symptoms (BPRS, $r=0.49$, $P=.0004$), psychiatric impairment (ASGS, $r=0.42$, $P=.003$), cognitive impairment and marked mental deficits (MMSE, $r=-0.34$, $P=.02$), as well as decreased psychosocial functioning (GAS, $r=-0.47$, $P=.001$) were all factors associated with a more severe (DRS) delirium after surgery. In addition, the findings demonstrated that a prolonged delirium duration coincided with increased preoperative depressive symptoms (HAMD, $r=0.49$, $P=.0005$), more general psychiatric symptoms (BPRS, $r=0.50$, $P=.0003$), and more severe psychiatric impairments (ASGS, $r=0.41$, $P=.004$), along with lower psychosocial functioning (GAS, $r=-0.39$, $P=.006$). Delirious patients required longer treatment in an intermediate care unit and showed serious complications more frequently. Increased transfusion and infusion requirements, a lower postoperative hemoglobin value, the use of sodium bicarbonate required for the equalization of an intraoperative acidic state were characteristic of the postoperative delirious patients (Table 2). Twenty percent (6 of 30) of patients that had not developed a delirium had serious complications that included respiratory insufficiency ($n=1$), congestive heart failure (3), acute renal failure (1), and cerebral seizure (1). In contrast, 41% (7 of 17) of the delirious patients indicated serious complications of ileus ($n=3$), revision (2), respiratory insufficiency (1), pneumonia (1), and acute renal failure (1).

3.3. Predictive indicators of delirium development, severity and duration

Regression analysis (Table 3) yielded four factors that were significantly associated with the development of postoperative delirium. These included preoperative depression scores

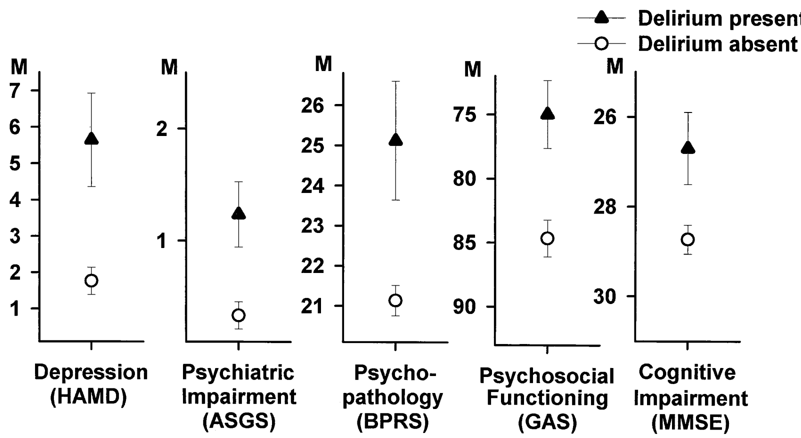

Fig. 1. Psychopathological Scales
Preoperative mean values and standard deviations for HAMD, ASGS, BPRS, MMSE, and GAS scores in patients with postoperative delirium (▲) and in nondelirious patients (○).

(*b*=0.05, *t*=3.31, *P*=.0023), cognitive dysfunction (*b*=−0.08, *t*=−3.76, *P*=.0007), amount of infusion (*b*=0.0001, *t*=2.76, *P*=.0094), and transfusion (*b*=0.0005, *t*=2.88, *P*=.0069). The squared multiple variance revealed a R^2 of 0.68.

Six variables were significantly predictive of delirium severity (R^2=0.76). These were depression, chronic obstructive lung disease (COPD), infusion, transfusion, preoperative hemoglobin, and minimal postoperative hemoglobin (Table 4, Fig. 2).

The duration of a delirium (Table 5) was best predicted by the severity of psychopathological symptoms, transfusions, hypertension, cerebral vascular disease, and preoperative hemoglobin (R^2=0.64).

After omitting the somatic items [7,9,11,12,13,14,16] from the HAMD, a significant change in the predictive value of the HAMD score was not found, neither for the development (*b*=0.07, *t*=3.42, *P*=.002), nor for the severity (*b*=1.02, *t*=3.15, *P*=.003) of a postoperative delirium. Correspondingly, a correlation analysis yielded similar significant results as with the inclusion of somatic items: Higher HAMD scores (without somatic items; *r*=0.39, *P*=.008, Fig. 2) were associated with a more severe delirium. However, including the somatic items only in the regression analysis failed to show a comparable significant predictive value of the HAMD (*b*=0.03, *t*=0.76, *P*=.45) neither for the development nor for the severity (*b*=0.71, *t*=1.07, *P*=.29) of postoperative delirium.

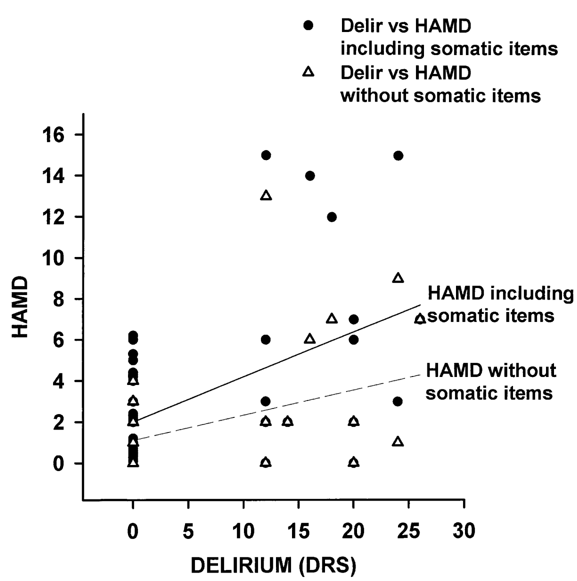

Fig. 2. Correlation Analysis
Association between the preoperative established HAMD-score (depression, on the ordinate, HAMD scores can range from 0 to 65; HAMD with and without somatic items) and the severity of postoperative delirium (DRS-Score, on the abscissa).

4. Discussion

In this investigation we have attempted to find predictive indicators for the development of postoperative delirium after vascular surgery. The findings indicate 36.2% inci-

Table 3
Parameters with significant predictive value for the development of postoperative delirium. Results of multiple regression analysis (R^2 = 0.68)

	*b**	*t***	*P****
HAMD†	0.05	3.31	0.0023
MMSE‡	−0.08	−3.76	0.0007
Transfusion (ml)	0.0005	2.88	0.0069
Infusion (ml)	0.0001	2.76	0.0094
Chronic obstructive lung disease	−0.23	−1.36	n.s.
ASA-score	−0.16	−1.51	n.s.
Normal care unit (days)	0.04	1.49	n.s.
Neurological disease	−0.04	−0.38	n.s.

* *b*, parameter estimates; ** *t*-values (*t* for H_0; Parameter = 0); *** *P*-significance value for prob > |*t*|; † HAMD, Hamilton Depression Scale; ‡ MMSE, Mini-Mental-State-Examination.

Table 4
Variables with predictive value for the severity of delirium (DRS; R^2 = 0.76)

	b	*t*	*P*
Chronic obstructive lung disease	−6.27	−2.38	0.02
Postoperative minimal hemoglobin (g/dl)	1.50	2.21	0.03
Preoperative minimal hemoglobin (g/dl)	−1.36	−2.61	0.01
HAMD*	0.86	3.90	0.0004
Transfusion (ml)	0.01	4.29	0.0001
Infusion (ml)	0.003	4.83	0.0001
Hypertension	3.22	1.56	n.s.
Impaired hearing	−1.45	−0.67	n.s.

* HAMD, Hamilton Depression Scale.

dence rate of delirium in our patient collective. Very similar results were obtained in a metaanalysis of the literature on postoperative delirium (36.8%) [2] and in a recent review of the incidence of delirium after cardiac surgery (32%) [1]. However, in our patient collective that underwent peripheral artery surgery the delirium incidence was lower than shown in another study (42%) [3]. The evidence suggests that a number of factors, both somatic and psychiatric, are associated with the development of a postoperative delirium, the severity and the duration of the delirium.

4.1. Psychiatric factors

Using multiple regression analyses, a significant association between subthreshold depression scores and the manifestation of postoperative delirium and the delirium severity emerged. The results highlighted in particular the significance of subclinical symptoms (i.e., subtle depressive symptoms) as important risk factors. Notably, the psychological items, i.e., the mood symptoms, predicted delirium, since the exclusion of somatic items did not change the significance of the predictive value of the HAMD scores. However, the inclusion of only the somatic HAMD items in the regression analysis failed to show a significant predictive value of the HAMD. Only a small number of authors have successfully confirmed a link between preoperative depressive symptoms and development of delirium following surgeries [2,7]. The analyses also showed that the risk for delirium was greatly increased in those patients with preoperative cognitive impairment (MMSE), which was indicated in the lower MMSE scores by the negative predictive b-value. A number of groups have confirmed an association between postoperative delirium and preoperative cognitive impairment (MMSE) [2,3,6]. In the current study, brain imaging was not performed so that the possibility of small vessel diseases cannot be ruled out. Furthermore, we did not analyze the correlation between preoperative vascular disease of the main cerebral arteries and the MMST.

As for the duration of the delirium, the symptoms were significantly prolonged in patients with more general psychiatric symptoms (ASGS).

Table 5
Results of multiple regression analysis: variables with predictive value for the duration of delirium (DRS; R^2 = 0.64)

	b	*t*	*P*
Cerebrovascular disease	−1.58	−3.42	0.0016
Hypertension	1.10	2.26	0.03
ASGS*	0.82	3.33	0.002
Hemoglobin <10	−0.40	−2.44	0.02
Transfusion (g/dl)	0.003	4.46	0.0001
HAMD**	0.003	0.047	n.s.
Alcohol consumption	−0.34	−0.85	n.s.
Noradrenaline (as perfusor)	1.26	1.60	n.s.

* ASGS, General Severity Score; ** HAMD, Hamilton Depression Scale.

4.2. Physiological factors

Published studies demonstrated a close link between delirium and preoperative hypertension, cerebrovascular disease and chronic obstructive lung disease [16,17]. The findings from our current study are consistent with those studies. The negative b-values for chronic obstructive lung disease and cerebrovascular disease are somewhat troubling. In fact, these patients showed a reduced risk for developing delirium. Our view is that our results are related to the heterogeneity of the patient sample, e.g., with primary and secondary diagnosis of cerebrovascular disease. A further inference is that the habituation in patients to the chronic hypocapnia and hypoxia results in a minimization of the risk and a lessening of the severity of delirium and may account for the negative predictive value in patients with chronic obstructive lung disease. The incidence of postoperative delirium in aortic diagnosis was notably high. Delirium was less frequently observed after nonaortic vascular surgery of the supra-aortal, as well as for surgery of peripheral arterial occlusive disease. One explanation may be that the expandability of surgery, meaning the dimension and the extent of the surgical procedure, may have increased the risk of delirium. In another study the authors found a twofold increase in the incidence of a delirium after aortic aneurysm surgery (46%; 16 out of 35 patients) compared to the other risk factors that are normally associated with delirium [6]. They also went on to observe that in all other nonaortic operations ($n = 841$) only 62 patients developed delirium [6]. In contrast, we discovered delirium in 52% ($n = 23$) of patients that underwent aortic surgery and in 21% ($n = 24$) of patients with nonaortic vascular surgery. The extent of surgery with an impaired oxygen supply resulting from reduced hemoglobin value of under 10 g/dL is in context with these risk factors: The lower the preoperative hemoglobin value the more severe a postoperative delirium (negative b-value). Further studies will have to establish the possible causes of negative b-value with regard to the number of days with a hemoglobin level < 10 g/dL for the duration of a delirium. Delirious patients showed reduced hemoglobin postoperatively, higher infusion and transfusion requirement, and intraoperative acidosis compensation with more sodium bicarbonate.

Indeed, transfusion requirements weighed heavily on developing delirium as well as on the severity and duration of the delirium. Recently, postoperative delirium was associated with reduced hematocrit value of less than 30% and intraoperative blood loss requiring greater number of transfusions [18]. The delirious patients in our study demonstrated a trend for greater intraoperative blood loss, with subsequent need for increased transfusions after surgery.

A number of earlier identified risk factors, which are strongly believed to be associated with postoperative delirium, included the over 70's and 80's age group, as well as the severity of preoperative illness and duration of surgery [3,6,16]. However, our study could not confirm these observations. Testing for some of the above mentioned factors, we found no association between the postoperative delirium and renal failure, coronary disease, arterial blood gases, albumin, furosemid medication anesthesia, and pain medication. Moreover, we could not relate hearing loss, alcohol, or nicotine to delirium manifestation. The discrepancies between previous findings and our results may lie in the rather unique patient sample of this study. In the current study we investigated patients that were recruited from all parts of Germany to fit the special criteria of surgery requirement. This meant that the pool of patients tended to include subjects that were also of younger ages and, as a result, tended to have reduced comorbidity.

Clearly, our study has several limitations. First, with the linear combination of eight variables (pre-, peri-, and intraoperative) we were able to explain roughly three quarters of the total variance that was associated with predicting a delirium and delirium severity after surgery, whereby approximately 30% of the variance could not be accounted for. Second, we could not isolate single psychopathological symptoms (assessment scores) directly related to the postoperative delirium. Finally, since this study was designed as a pilot study, our investigation was restricted to a limited number of patients. Since we did not perform a random selection of patients, a potential selection bias has to be taken into account. Nevertheless, it should be emphasized, that the study population is still representative for patients treated in the Department of Vascular Surgery of the University of Düsseldorf with respect to age, medication, comorbidity and surgical procedures.

One thing that is clear from the current studies of postoperative delirium is the need for extending the number of psychiatric and psychological examinations. As increased examinations are routinely conducted, it will become conceivable to isolate possible symptoms linked to the development of postoperative delirium. Also, physiological risk factors involved in delirium development could possibly be better accounted for by including other factors such as intraoperative temperature and dehydration. The latter factor has been shown to have an influential effect on the development of delirium in nonsurgical geriatric patients [19]. The factors estimated to have predictive value were determined out of the whole patient collective that underwent aortic, carotid artery and peripheral artery surgery. With an extended sample it will be necessary to differentiate between different kinds of performed surgeries.

The psychiatric and medical findings that we have described help us know with some certainty, that cognitive impairment and particularly depressive symptoms before surgery, as well as amount of perioperative infusion and transfusion requirements, play a substantial role in delirium development, accounting for the most predictive variables in delirium development and severity. Furthermore, we have demonstrated that postoperative delirium after vascular surgery occurs in more than a third of all cases, and in more than half of the patients following aortic surgery. To further clarify the issue of factors associated with delirium development it is important to determine psychiatric, surgical and anesthesia predictive parameters. It is hoped that in the course of further testing a checklist will be established that could successfully assess pre- and perioperatively the risk factors for a delirium after surgery.

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