

## Predicting postoperative delirium after vascular surgical procedures

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*Objective:* The objective of this study was to determine the incidence of and specific preoperative and intraoperative risk factors for postoperative delirium (POD) in electively treated vascular surgery patients.

*Methods:* Between March 2010 and November 2013, all vascular surgery patients were included in a prospective database. Various preoperative, intraoperative, and postoperative risk factors were collected during hospitalization. The primary outcome variable was the incidence of POD. Secondary outcome variables were any surgical complication, hospital length of stay, and mortality.

*Results*: In total, 566 patients were prospectively evaluated; 463 patients were 60 years or older at the time of surgery and formed our study cohort. The median age was 72 years (interquartile range, 66-77), and 76.9% were male. Twenty-two patients (4.8%) developed POD. Factors that differed significantly by univariate analysis included current smoking (P = .001), increased comorbidity (P = .001), hypertension (P = .003), diabetes mellitus (P = .001), cognitive impairment (P < .001), open aortic surgery or amputation surgery (P < .001), elevated C-reactive protein level (P < .001), and blood loss (P < .001). Multivariate logistic regression analysis revealed preoperative cognitive impairment (odds ratio [OR], 16.4; 95% confidence interval [CI], 4.7-57.0), open aortic surgery or amputation surgery (OR, 14.0; 95% CI, 3.9-49.8), current smoking (OR, 10.5; 95% CI, 2.8-40.2), hypertension (OR, 7.6; 95% CI, 1.9-30.5) and age  $\geq$ 80 years (OR, 7.3; 95% CI, 1.8-30.1) to be independent predictors of the occurrence of POD. The combination of these parameters allows us to predict delirium with a sensitivity of 86% and a specificity of 92%. The area under the curve of the corresponding receiver operating characteristics was 0.93. Delirium was associated with longer hospital length of stay (P < .001), more frequent and increased intensive care unit stays (P = .008 and P = .003, respectively), more surgical complications (P < .001), more postdischarge institutionalization (P < .001), and higher 1-year mortality rates (P = .0026).

*Conclusions*: In vascular surgery patients, preoperative cognitive impairment and open aortic or amputation surgery were highly significant risk factors for the occurrence of POD. In addition, POD was significantly associated with a higher mortality and more institutionalization. Patients with these risk factors should be considered for high-standard delirium care to improve these outcomes. (J Vasc Surg 2015;62:183-9.)

Postoperative delirium (POD), which is characterized by a disturbance of consciousness with reduced ability to focus, sustain, or shift attention is a common medical complication after surgery.<sup>1</sup> Symptoms of POD generally arise shortly after surgery and usually persist for a few days. In some cases, however, they can last up to several weeks.<sup>2</sup> POD is associated with longer intensive care unit (ICU) stay, longer hospital stay, higher hospital costs, increased postdischarge institutionalization, and increased 30-day mortality. Even longterm effects, such as persistent functional decline and death,

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have been associated with POD.<sup>3</sup> The incidence of POD after noncardiac surgery varies from 5.1% to 52.2%, with the highest incidences among elderly patients.<sup>4-9</sup> With an aging population, the number of elderly patients undergoing surgery is growing, and this will continue to increase over time.<sup>10</sup> Consequently, the incidence of POD will most likely increase in the coming years. Various studies focusing on POD demonstrated that vascular patients are at increased risk for development of POD compared with other surgical patients, particularly after open aortic surgery.<sup>4,5</sup> Because of fluctuating symptoms, the presence of an acute confusional state may be unnoticed, leading to a delay in diagnosis and treatment. Also, clinical subtypes such as hypoactive delirium, which is more common in elderly patients and is associated with a worse prognosis, are frequently misconstrued.<sup>2,9,11</sup> Because proactive geriatric consultation in combination with prophylactic low-dose haloperidol may reduce the incidence, severity, and duration of POD in high-risk postoperative patients, identifying those patients at risk is important.<sup>12</sup> Although the pathogenesis of POD remains poorly understood, it is considered a heterogeneous, multifactorial disorder with risk factors such as advanced age, preoperative cognitive impairment, cardiac surgery, and renal insufficiency.<sup>3,4,7,13-16</sup> However, because of varying sample

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sizes and heterogeneity, it is still unclear which factors are the strongest predictors, particularly in a high-risk group such as vascular surgery patients.<sup>17</sup>

In 2010, a noninterventional, nonrandomized, singlearm prospective study was set up at our center to gain insight into the etiology of POD after vascular surgery. The aim of this study was to identify individual preoperative and intraoperative risk factors associated with POD after elective vascular surgery.

## METHODS

Design of the study. Between March 2010 and November 2013, a total of 566 consecutive vascular surgery patients who were operated on in an elective setting were prospectively evaluated. Current literature has shown that patients older than 60 years are most at risk for the occurrence of POD.<sup>3</sup> Because this study focuses primarily on independent risk factors for delirium, we limited the age of participants to  $\geq 60$  years. At the time of surgery, 463 patients (81.8%) were 60 years or older and were further assessed. Preoperative evaluation was performed by the anesthesiologist at the preoperative assessment clinic. All patients gave oral informed consent. For this study, the Medical Ethical Committee granted an official dispensation for the Dutch law regarding the patient-based medical research (WMO) obligation. Patient data were processed and electronically stored according to the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. Inclusion criteria were patients undergoing open or endovascular aortic repair, peripheral bypass surgery (including short jump graft in case of peripheral aneurysms and interventions on carotid, vertebral, and subclavian arteries), arteriovenous shunt surgery, percutaneous interventions, and different types of amputation surgery. Exclusion criteria were patients undergoing percutaneous interventions without placement of a stent, which was considered a minimally invasive intervention with no or very short hospital admission. Type of anesthesia, perioperative monitoring, and postoperative analgesia were at the discretion of the anesthesiologist. On the basis of anesthetic technique, patients were divided into general, regional, and local anesthesia groups. No further distinction was made between types of medication. Conscious sedation was not provided in the last two groups. Postoperatively, all patients who underwent open aortic repair were admitted to the ICU. They then were transferred to the surgical ward as soon as possible. After carotid interventions, patients were admitted to either the ICU or the recovery room for the first 24 hours. All other patients recovered on the surgical ward. Patients undergoing percutaneous interventions could be discharged home after 4 hours of strict bed rest if there were no signs of any complication. Missing data were complemented by review of the computerized hospital registry and charts. The primary outcome variable was the incidence of POD. Secondary outcome parameters were hospital length of stay, ICU admittance, ICU length of stay, type of care facility after discharge, and 1-year mortality.

POD. The method of POD assessment has been described previously by our group.<sup>18</sup> In short, observation of patients during hospital admission was done by nurses specially trained to recognize behavioral changes related to delirium. The Delirium Observation Screening scale score was also obtained in all patients (surgical and nonsurgical) three times a day.<sup>19</sup> With a Delirium Observation Screening scale score >3, the geriatrician was consulted to confirm the diagnosis of POD according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, criteria.<sup>1</sup> Patients who developed delirium underwent a comprehensive physical examination with additional laboratory testing to identify a possible underlying cause for delirium, such as sepsis, electrolyte imbalance, or pharmacologic abnormalities, and were treated if necessary. According to the standardized hospital protocol, haloperidol was the medical treatment of choice for symptom control, supplemented by benzodiazepines if necessary.

Clinical data selection. Factors were selected on the basis of known risk factors for the occurrence of POD.<sup>17</sup> Preoperative collected data included age, gender, body mass index (weight in kilograms/height in meters squared), American Society of Anesthesiologists (ASA) score, smoking status (current smokers and former smokers), and laboratory tests (level of hemoglobin and C-reactive protein [CRP]). Comorbidity, based on the previous medical history, was determined by the Charlson Comorbidity Index.<sup>20</sup> The Charlson Comorbidity Index is a weighted score that predicts the 1-year mortality of a patient based on coexisting medical conditions and age. Special attention was given to presence of hypertension, diabetes mellitus, cerebrovascular disease, chronic obstructive pulmonary disease, depression, cognitive impairment, and impaired renal function because these factors are known to increase the risk of POD.<sup>17</sup> Renal function was expressed as the estimated glomerular filtration rate, with values  $<60 \text{ mL/min} \times 1.73 \text{ m}^2$ indicating impaired renal function. As preoperative cognitive impairment and depression are known risk factors for POD, these were also measured with the Groningen Frailty Indicator (GFI) and further used for risk assessment for POD. The GFI is a simple questionnaire consisting of 15 items, classified in 8 separate groups, consistent with the domains of functioning. This questionnaire was routinely obtained in all vascular surgery patients at the outpatient clinic by specially trained nurses. The GFI has already been proven to predict POD after vascular surgery.<sup>18</sup> Depression was scored on the basis of the 4-item psychosocial item; scores  $\geq 1$  were considered indicative for depression. Cognitive function was divided into current complaints about memory and history of POD. Cognitive impairment was determined by a score of  $\geq 1$ . Intraoperative predictors were type of surgery, type of anesthesia, duration of surgery, and estimated blood loss. Surgical complications were classified according to the Clavien-Dindo classification of surgical complications.<sup>21,22</sup>

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