REVISTA PORTUGUESA DE CIRURGIA CARDIO-TORÁCICA E VASCULAR

CIRURGIA VASCULAR

DELIRIUM PÓS-OPERATÓRIO EM CIRURGIA VASCULAR

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Resumo

Objetivos: Este estudo teve como principais objetivos determinar a incidência de *Delirium* Pós-Operatório e identificar fatores de risco peri-operatórios nos doentes submetidos a Cirurgia Vascular. Perceber o impacto do *Delirium* Pós-operatório na duração do internamento e criar um algoritmo de atuação para estes doentes foram também objetivos deste estudo.

Material e Métodos: Estudo prospetivo observacional com inclusão de 56 doentes consecutivos submetidos a Cirurgia Vascular. Os critérios de exclusão foram a idade inferior a 18 anos, nível de consciência alterado, distúrbio psiquiátrico ou défice visual ou auditivo. Foi aplicado o teste *Mini Mental State Examination* durante a visita pré-anestésica. Os doentes com indicadores clínicos de Delirium foram avaliados com recurso ao *Confusion Assessment Method* (CAM). Os doentes foram avaliados no pós-operatório durante os 5 dias.

Resultados: A incidência de *Delirium* Pós-operatório neste estudo foi de 12,5%, maioritariamente registado entre o segundo e quinto dia de pós-operatório. Os doentes com Delirium apresentaram dor moderada a intensa. A duração do internamento foi de 21 dias nos doentes com *Delirium* e de 7 dias nos doentes que não desenvolveram Delirium (p 0.001).

Conclusões: A incidência de *Delirium* Pós-operatório neste grupo de doentes foi inferior ao previamente demonstrado noutros estudos. A incidência de *Delirium* foi superior dos doentes admitidos na Unidade de Cuidados Intensivos e a dor esteve associada ao desenvolvimento de *Delirium*, sugerido uma oportunidade de atuação pós-operatória. O desenvolvimento de *Delirium* no 2º e 5º dia de internamento reflete a necessidade de medidas preventivas e diagnósticas precoces e prolongadas. O aumento do tempo de internamento associado ao Delirium Pós-operatório e as suas implicações clínicas e económicas mostram a necessidade de implementação de estratégias.

Palavras Chave: *Delirium* Pós-operatório; Cirurgia Vascular; Confusion Assessment Method

Summary

Postoperative delirium after vascular surgery

Objectives: *The objectives of this study were to determine the incidence of Postoperative Delirium and to identify specific perioperative risk factors in patients undergoing Vascular Surgery. Other goals were to study its impact in hospital length of stay and to create an algorithm to deal with patients under suspicion of Postoperative Delirium.*

Material and Methods: *A total of 56 consecutive vascular surgery patients were prospectively evaluated. Exclusion criteria were age less than 18, dementia, abnormal level of consciousness, psychiatric disorder and visual or hearing impairment. Mini Mental State Examination were applied during pre-anesthetic visit. In patients with clinical indicators of delirium the Confusion Assessment Method was applied. Patients were assessed during 5 days after surgery.*

Results: *The overall incidence of delirium was 12,5%, developped mostly by the second to fifth postoperative day. Patients with delirium presented moderate to severe pain. Patients who received combined general and regional anesthesia didn't develop delirium. The median hospital length of stay was 21 in patients with delirium and 7 days in patients without (p 0.001).*

Conclusions: *The overall incidence of postoperative delirium was lower than previously reported. The incidence of delirium was higher in ICU patients and pain was associated with postoperative delirium suggesting the opportunity to control postoperative factores. The development of delirium in the second and fifth day indicated the need for early and more prolonged preventive and diagnosing measures. Clinical and costly considerations of prolonged hospital stay shown in this cohort warrant strong debate strategies to be applied.*

Keywords: *Postoperative Delirium, Vascular Surgery, Confusion Assessment Method*

INTRODUCTION

Delirium is defined as an acutely altered and fluctuating mental status with features of impairment of attention and lack of awareness to the environment. The fifth edition of the Diagnostic and Statistical Manual (DSM-5) has revised the diagnostic criteria of delirium.[1]

Delirium is a common and deleterious complication following surgery and anesthesia.[2] It is associated with longer length of stay in Intensive care unit (ICU) as well as in hospital, higher mortality, higher costs and poor cognitive and functional outcomes.[3]

The incidence of Delirium is widely variable and depends on patients characteristics, risk factors and type of surgery. For General Surgery the incidence of Postoperative Delirium is reported from 5-15%, ranging up to 65% for patients with hip fractures.[4] In intensive care setting Delirium occurs in up to 80%.5 Vascular patients, who usually are older and with several cardiovascular comorbidities, are at a significantly higher risk for developing postoperative delirium.[6,7] Among the various types of surgery, open abdominal aortic aneurysm repair is recognized as a particularly high-risk procedure.[6]

Clinical history and physical examination are the golden standards for diagnosis of Delirium. Instruments such as Confusion Assessment Method (CAM), often associated with Mini-Mental State Exam (MMSE), are available for diagnosis of Delirium. A version of CAM suitable for assessment of patients connected to a mechanical ventilator (CAM-ICU) has been developed and validated. Several other instruments are available for diagnosis of delirium and others for rating delirium severity.[8]

Many predisposing and precipitating factors contribute for the development of Postoperative Delirium. There are few studies with focus on vascular patients.[6,7,9,10,11]

As a perioperative specialist, the anesthesiologist plays a crucial role acting in the preoperative period through the identification of risk factors; during surgery using preventive strategies; and in the postoperative setting monitoring, diagnosing and treating Postoperative Delirium.

Currently, data about Postoperative Delirium in vascular patients is lacking. Therefore, the objectives of this study were to determine the incidence of Postoperative Delirium and to identify specific perioperative risk factors in patients undergoing vascular surgery. Other goals were to study its impact in hospital length of stay and to create an algorithm to deal with patients under suspicion of Postoperative Delirium.

MATERIAL AND METHODS

The study protocol was approved by the hospital's ethics committee. All patients gave their written informed consent to take part in the study. Patient data was processed and electronically stored according to the declaration of Helsinki - Ethical principles for medical research involving human subjects.

Between December 2014 and February 2015 a total of 56 consecutive vascular surgery patients were prospectively evaluated. Exclusion criteria were: age less than 18, dementia (MMSE <25), abnormal level of consciousness, psychiatric disorder and visual or hearing impairment. Elective and emergent cases were included.

Mini Mental State Examination was applied on the day before surgery, during pre-anesthetic visit, to patients with 65 or more years.

Clinical indicators referred in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) were assessed. In those patients with clinical indicators of delirium, diagnosis was confirmed using the CAM or CAM-ICU in the Post-Anesthesia Care Unit and during hospital stay. Patients were assessed in the postoperative period for 5 days.

Predisposing factors (individual factors that determine a patient's vulnerability) such as demographic data, malnutrition, history of tobacco, alcohol and drugs abuse, atrial fibrillation, diabetes mellitus and stroke/transient ischemic attack were collected. Precipitating factors (related to external noxious stimuli or insults) were also evaluated and these included infections, anaemia, type and urgency of surgery, admission to an intensive care unit and pain scores. Data directly related to anesthesia such as anesthesia technique, duration and premedication was collected.

Eligible surgical procedures included open and endovascular aortic repair, carotid surgery, peripheral bypass surgery, amputation procedures and percutaneous endovascular interventions. They were divided in four categories: carotid surgery, open supra and infrainguinal surgery, endovascular supra and infrainguinal surgery and other surgeries. Regional anesthesia was composed of spinal block, combined sequential spinal epidural anesthesia, peripheral nerve block and local anesthesia with sedation.

STATISTICS

Assuming that the proportion of subjects with postoperative delirium after vascular surgery was 25% (+-10%), a sample of 56 subjects provided a 95% confidence interval and 90% statistical power for an estimated population of 200 subjects.

A descriptive analysis was first conducted for all variables of interest. Frequencies and proportions were calculated for categorical data and mean, median, standard deviation for continuous data. Chi-square test was used to compare differences in categorical variables such as comorbilities, benzodiazepine premedication, type and urgency of surgery, anesthetic technique and pain scores. Hospital length of stay was analyzed by using the Mann-Whitney test.

For statistical analysis, the significance level considered was 0,05 and IBM SPSS Statistics version 22 was used.

RESULTS

A total of 56 patients were included in this study. The overall incidence of delirium was 12,5% (7 patients) (95% CI

Table 1 **Predisposing and precipitating factors data of participants (n = 56).**

Predisposing and precipitating factors	Delirium n=7 (%)	No delirium n=49 (%)	p value
Preoperative			
Age			
Mean	63±9	66±9	0.20
Advanced age (≥ 65 years)	3 (43%)	30 (61%)	
Patient Habits			
Smoking	5 (71%)	21 (43%)	0.12
Alcohol abuse	2 (29%)	6 (12%)	0.20
Comorbidities			
Diabetes mellitus	3 (43%)	25 (51%)	0.29
Stroke	0	4 (8%)	0.58
Atrial fibrillation	1 (14%)	3 (6%)	0.35
Anemia	3 (43%)	34 (92%)	0.13
Infection	1 (14%)	6 (12%)	0.42
Pre-medication			
Benzodiazepine	4 (57%)	47 (96%)	0.01

= 6,19-23,62). The mean age of patients developing postoperative delirium was 63±9 years versus 66±9 years in patients not developing postoperative delirium. There were 44 men and 12 women. Six of the 7 patients who developed postoperative delirium were men (85.7%).

Patients with delirium had history of tobacco and alcohol abuse, atrial fibrillation and a diagnosed infection more frequently than patients without delirium. However there was no statistically significant difference between these two groups (Table 1). The mean body mass index was 24 and 5 patients were obese but this wasnt related with a higher incidence of delirium. The majority of patients (92%) were premeditated with benzodiazepines and only 4 patients developed postoperative delirium.

None of the 5 patients submitted to carotid surgery developed delirium. Postoperative delirium developed more often after endovascular supra and infra-inguinal surgery (42,9%) but there was no statistically significant difference regarding the type of surgery between the two groups (Table 2). Only one patient underwent urgent surgery and didn't have postoperative delirium.

The mean anesthesia duration was 201 minutes (maximum of 480 minutes and a minimum of 45 minutes). A total of 34 (60.7%) patients received general anesthesia, 17 (30.4%) regional anesthesia and 5 (8.9%) combined general and regional anesthesia. The types of anesthesia are presented in Table 2. Regional anesthesia techniques were performed such as spinal block (n 8), combined sequential spinal epidural anesthesia (n 4), peripheral nerve block (n 3) and local anesthesia with sedation (n 2). The rate of postoperative delirium was higher in general anesthesia group (n 5; 71.4%) and none of the patients who received combined anesthesia developed delirium.

Admission to an intensive care unit occurred in 8

Table 2 **Intra and Postoperative predisposing and precipitating factors data of participants (n = 56).**

Predisposing and precipitating factors	Delirium n=7 (%)	No delirium n=49 (%)	p value
Intraoperative			
Type of surgery			0,51
Carotid	0	5 (10%)	
Open supra and infra-inguinal	2 (29%)	21 (43%)	
Endovascular supra and infra-inguinal	3 (43%)	15 (31%)	
Others	2 (29%)	8 (16%)	
Type of Anesthesia			0,65
General	5 (71%)	29 (60%)	
Regional	2 (29%)	14 (29%)	
Combined General + Regional	0	5 (10%)	
Postoperative			
ICU admission	2 (29%)	6 (12%)	0,20
Pain intensity			0,72
no pain	0	5 (10%)	
mild pain	3 (43%)	22 (45%)	
moderate pain	3 (43%)	19 (39%)	
severe pain	1 (14%)	3 (6%)	

(14.3%) cases. There was no difference in the incidence of postoperative delirium between patients who were admitted in an intensive care unit and those who were admitted in an postoperative recovery unit (2 vs 5 patients, respectively). Regarding postoperative pain scores, 4 (57.1%) patients with delirium presented moderate to severe pain and 3 (42.9%) mild pain. Patients with no pain after surgery (n 5, 8.9%) didn't develop postoperative delirium.

Delirium was diagnosed on the first postoperative day in 3 (42,9%) patients. An equal number of patients developed delirium on the fifth postoperative day. In one (14,3%) case diagnosis was made during the second day after surgery.

The median hospital length of stay was 21 (P25:15; P75:27) and 7 (P25:3; P75:19.5) days in patients with and without delirium, respectively (p 0.001) (Figure 1).

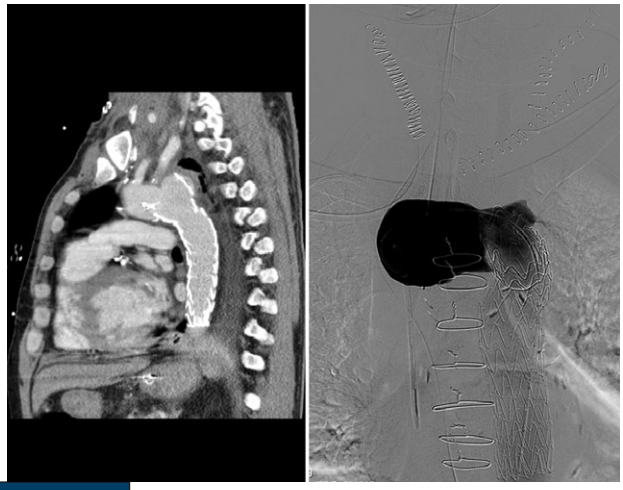

Figure 1

The average length of stay in patients with Postoperative Delirium was higher (median 21 days, P25:15; P75:27) than in patients without Delirium (median 7 days, P25:3; P75:19.5) (p=0,037).

DISCUSSION

The overall incidence of postoperative delirium was 12.5%, which was lower than previously reported.[7,9,10] Only Sugimoto M. 11 study with patients who underwent open abdominal aortic aneurysm surgery reported similar incidence. Other studies with surgical vascular patients reported an incidence of delirium between 19,4%[10] and 39,2%.[7]

Patients undergoing vascular surgery have been described as at increased risk of developing delirium since they have advanced age, coexistent cerebrovascular disease and are mostly male.[12,13] The lower incidence of postoperative delirium in this study can be explained by different preoperative conditions. The authors excluded patients with dementia or abnormal level of consciousness because preoperative cognitive impairment has been shown to be a risk factor for postoperative delirium.[14] Patients included in this study were younger than in other series[7,9,10,11] Age ≥70 years old was described as a significant predictor of postoperative delirium in previous studies.[11] In Sasajima's[9] study involving bypass surgery for chronic ischemia older patients (≥80 years old) had higher incidence of delirium. Only Schneider et al.[15] included patients of younger age (53-84 years old). Comorbidities known as risk factors for delirium development were evaluated in this study but were not statistically significant for delirium development. Only four patients had cerebrovascular disease.

Administration of benzodiazepines is consistently and strongly associated with an increased burden of delirium. However, for emergence delirium this remains controversial.[16] For highly anxious patients or patients with alcohol or benzodiazepine use disorders benzodiazepines can be added, but particular care should be taken in elderly patients. In this study, benzodiazepines were administered as a preoperative medication in most patients but only 4 developed delirium. Among patients who develop postoperative delirium, benzodiazepine premedication occurred in 57% and may play important contributor to delirium. This requires further studying, even though the limited number of patients evaluated needs to be taken into account when analysing these results.

Postoperative delirium appears to be strongly influenced by the severity of the surgical insult. For example, in otolaryngological surgery the reported incidence of postoperative delirium is 12% while in major abdominal and cardiac surgeries is 50 and 51% respectively.[16] Contrary to other studies different types of surgery were included, from carotid surgery to open abdominal aortic aneurysm repair.[17] As expected none of the patients submitted to carotid surgery developed delirium. Open surgery was most frequently performed but the incidence of delirium was higher in patients submitted to endovascular surgery (43% vs 29%). Other surgeries which include amputations and peripheral revascularization have the same incidence of Delirium than open vascular surgery. This could be explained by the associated systemic atherosclerosis and the frail condition of patients with critical limb ischemia which puts them at risk for developing delirium after surgery.[9,16] As most surgeries were elective and patients have been managed to ensure optimal physical status the postoperative delirium rate could be lower than in acutely ill patients.

The influence of anesthesia as risk factor for the development of postoperative delirium remains uncertain. Previous investigations couldnt prove a higher incidence of delirium in patients who received general anesthesia when compared to other types of anesthesia.[18,19] Likewise, this study was unable to establish a link between the type of anesthesia and the development of postoperative delirium. Patients who received combined general and regional anesthesia didn't develop delirium. This result could be a bias considering the low proportion of this type of anesthesia.

Eight patients were admitted in the ICU after surgery. In concordance with the literature the incidence of delirium in ICU patients (25%) was higher than non-ICU patients (14.6%).[20]

Increased pain and pain management strategies after surgery are independently associated with the development

of postoperative delirium.[21] In this sample, patients with no postoperative pain didn't develop delirium. Similarly to previous reports[21], 57% of the patients with delirium had moderate to severe pain which is associated with greater chances of developing delirium. Inadequate postoperative pain control is a predictor of the development of postoperative delirium and strategies to optimize postoperative pain control, preferably with nonopioid pain medications and regional techiques, will prevent delirium.

Delirium is usually diagnosed during the early postoperative days and symptoms are often worse at night. In this study most patients developed delirium in the second and fifth day indicating the need for early and more prolonged monitoring and diagnosing measures.

The median duration of hospital stay was significantly higher in the delirium group (21 vs 7 days). Cognitive impairment has been associated with longer hospital stays.[17,20,22] These results suggest an association between delirium and length of stay. Co-morbidity and higher costs associated with prolonged hospital stay shown in this cohort warrant strong debate regarding diagnostic and therapeutic strategies to be applied.

Several limitations of this study warrant comment. First of all the etiology of delirium is multifactorial and some potential confounding factors were not accounted. Secondly some subgroups of patients known to be at increased risk of delirium, such as patients with dementia or abnormal levels of consciousness, were not included. Furthermore, we might have missed the hypoactive type of delirium and the real incidence of delirium in surgical vascular patients may be underestimated.

An intervention program has been described to have the ability to reduce the incidence, severity and duration of delirium. After this study, Anesthesiologists and Psychiatrics implemented a delirium prevention protocol using a combined nonpharmacologic and pharmacologic strategy.

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