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Postoperative psychiatric disorders in general thoracic surgery: incidence, risk factors and outcomes

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Abstract

Objective: Postoperative psychiatric disorders (PPDs) may complicate the post-surgical outcome. We analysed the types, incidences, risk factors and outcomes of the PPDs in non-cardiac thoracic surgery patients. **Methods:** All patients (n = 100) undergoing major non-cardiac thoracic surgery from January 2004 to March 2005 were investigated prospectively. The diagnosis of PPD was made based on the *Diagnosis and Statistical Manual of Mental Disorders*. The patients were grouped into two according to the presence (group I) or absence (group II) of PPD. Data on pre-, per- and postoperative factors, and the adverse outcomes were analysed. **Results:** Eighteen patients (18%) developed PPD, including delirium in 44%, adjustment disorders in 22%, panic attack in 17%, minor depression in 11% and psychosis in 6%. The patients who developed PPD were older (58 ± 17 vs 50 ± 15 years, p = 0.05), had a longer operation time (6 ± 1 vs 5 ± 2 h, p = 0.015) and hospital stay (13 ± 9 vs 8 ± 5 days, p = 0.019). The morbidity and mortality rates were not significantly different between the groups (67% vs 46%; 11% vs 1%, respectively). The causative factors in the development of PPD were older age, longer operation time, abnormal serum chemistry values of sodium, potassium, calcium and glucose, hypoalbuminaemia, the presence of the postoperative respiratory distress and infection and blood transfusion ($p < 0.05$). **Conclusions:** PPDs are associated with adverse outcomes including a longer hospital stay, and increased morbidity and mortality rates. The identification, detection and elimination of these risk factors are recommended.

Keywords: Biochemistry; Outcomes; Postoperative care; Surgery; Complications

1. Introduction

There is little information about postoperative psychiatric disorders (PPDs) in non-cardiac thoracic surgery (NTS). PPD may complicate the post-surgical outcome, and delirium is the most investigated PPD [1—4]. In a previous study, we studied the incidence and risk factors of PPD after NTS in 432 patients [5]. Except for some other reports on delirium [1,2,6], no specific study has been designed to analyse the incidence, risk factors and outcome of PPD in patients undergoing NTS. We designed this prospective study to identify the PPDs in NTS patients, to examine the risk factors and to investigate the effect of PPDs on the post-surgical outcome.

2. Materials and methods

All patients older than 18 years (n = 100) undergoing major NTS (patients undergoing thoracotomy) in our clinic between January 2004 and March 2005 were entered into the study having provided written informed consent. Pre-, peri- and postoperative characteristics (until discharge or in-hospital death) were recorded prospectively.

The induction of the anaesthesia was performed with the combination of suphentanil (an opioid agent), pancuronium (a muscle relaxant) and either etomidate or midazolam, or both (hypnotic agents). The maintenance of the anaesthesia was provided by the continuous infusion of suphentanil, combined with either midazolam, sevoflurane (an inhalation anaesthetic) or propofol (an intravenous anaesthetic). The methods of postoperative pain management for all patients was as described in our previous study [5]: thoracic epidural catheters or intravenous patient-controlled analgesia with a duration of 3—5 days, followed by a non-steroidal anti-inflammatory drug and an opioid derivative.

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All patients were consulted by the same psychiatrician on the preoperative day, and daily for 4 days postoperatively. When PPDs were detected, a complete analysis including biochemical parameters, complete blood count and arterial blood gases was performed, and the patient was reconsulted by the same psychiatrician to initiate medical treatment. The detected types of PPD were delirium, adjustment disorders, panic attack, minor depressionand psychosis. The diagnosis was made based on the *Diagnosis and Statistical Manual of Mental Disorders* (DSM-IV) [7]. The patients were grouped into two according to the presence (group I, $n = 18$) or absence (group II, $n = 82$) of PPD. Data on three clusters of variables pertaining to preoperative predisposing factors, peri- and postoperative precipitating factors and adverse outcomes were collected.

Preoperative predisposing factors included demographic variables (age and sex), educational status (illiterate or primary, middle, high school or university graduation), characteristic of the disease (benign or malignant), active smoking (smoking during the week preoperatively), alcohol abuse (drinking despite recurrent social, interpersonal and legal problems as a result of alcohol use), co-morbidities (pulmonary, cardiac, renal, hepatic and rheumatologic disease), diabetes mellitus (either type I or II, with active treatment with insulin or oral antidiabetics), hyperlipidaemia, previous history of psychiatric disorder or surgery and chemotherapy administration. Preoperative biochemical parameters included serum chemistry values of sodium, potassium and calcium, haemoglobin level, arterial blood gas values and serum albumin levels.

The duration of the operation was the only peroperative precipitating factor. Postoperative precipitating factors included abnormal serum chemistry values (defined as sodium <130 or >150 meq l^{-1}, potassium <3.0 or >6 meq l^{-1} 1 and total calcium <8.4 or >10.2 mg dl^{-1}), abnormal blood glucose level (defined as glucose <60 or >300 mg dl^{-1}), abnormal haemoglobin level (defined as haemoglobin <13.5 or >17.5 g dl^{-1} in male patients, and <12 or >16 g dl^{-1} in female patients), hypoalbuminaemia (defined as albumin <3.5 g dl^{-1}), bed restriction, sleep deprivation, blood transfusion, respiratory distress (defined as arterial hypoxaemia PO_2 <55 mmHg on room air and hypercarbia PCO_2 >45 mmHg), infection (diagnosed when white blood cell count was greater than 12 000 mm^{-3} and postoperative fever was above 37.0 °C), medication (anti-arrhythmics, steroids and antihypertensives).

Adverse outcome variables consisted of the length of stay in the intensive care unit, the length of the hospitalisation, morbidity and in-hospital death after surgery. With regard to all factors, a statistical analysis was performed concerning 18 patients with PPD (group I) and 82 patients without PPD (group II). Continuous variables were compared using the unpaired *t*-test for normally distributed data and the Mann–Whitney *U* test for non-parametric data. Categoric variables were compared using the chi-square test and Fisher's exact test, as appropriate. Continuous data were presented as 'mean ± standard deviation'unless otherwise noted. To investigate which of the factors independently predicted PPD, a forward conditional logistic regression analysis was performed. A *p* value of less than or equal to 0.05 was considered significant.

3. Results

There were 59 male patients (59%) and 41 female patients (41%) with a mean age of 51 ± 15 years (range 15–80 years). The demographic characteristics and the surgical indications are summarised in Table 1. PPD occurred in 18 patients (18%) with a mean age of 58 ± 17 (range 25–80 years). The mean age of the patients without PPD was 50 ± 15 (range 15–75 years, $p = 0.05$). In both groups, the major indication of the surgery was a malignant disease, and the pathological type of the disease, whether benign or malignant, was not associated with the development of PPD.

All other potential preoperative predisposing factors in the development of the PPD were analysed and the results were outlined in Table 2. The ratio of the alcohol abuse was higher in group I than in group II, but the difference was not statistically significant (22% vs 7%, $p > 0.05$). About 22% of the patients in group I had previous psychiatric disorders under treatment, while the percentage in group II was 7% ($p > 0.05$). We found that only the older age was a statistically significant preoperative predictor of PPD.

Peri- and postoperative precipitating factors were analysed and the results were given in Table 3. Mean duration of the operation was higher in group I than in group II (6 ± 1 h vs 5 ± 2 h, $p = 0.015$). The patients in group I more often had abnormal serum chemistry values of sodium, potassium or calcium (61% vs 9%), hypoalbuminaemia (61% vs 2%) and abnormalities in blood glucose level (50% vs 7%), and these differences between two groups were statistically significant ($p < 0.001$ for all three parameters). The patients who developed a PPD suffered from respiratory distress, and required blood transfusion more commonly, and had a postoperative infection more often than group II patients ($p = 0.044$, $p = 0.007$, $p = 0.008$, respectively). The sleep-cycle pattern of the patients in group I had been more disturbed than group II (22% vs 7%), but the differences were insignificant ($p = 0.08$).

Table 1
Demographic variables and surgical indications of the patients.

	Group I ($n = 18$)	Group II ($n = 82$)	*p* value
Age, years (range)	58 ± 17 (25–80)	50 ± 15 (15–75)	0.05
Male/female	12/6	47/35	n.s.
Diagnosis (*n*, %)			
Malignant	13 (72%)	52 (63%)	n.s.
Lung cancer	7	29	
Lung metastases	2	11	
Mediastinal tumours	1	–	
Mesothelioma	1	8	
Oesophageal tumours	2	1	
Others	–	3	
Nonmalignant	5 (24%)	30 (37%)	n.s.
Hydatid disease	–	6	
Myasthenia gravis	–	4	
Bullous lung disease	1	4	
Tuberculosis	1	3	
Bronchiectasis	–	2	
Empyema	1	2	
Hamartoma	–	2	
PAVM	1	–	
Others	1	7	

n.s.: not significant; PAVM: pulmonary arteriovenous malformation.

Table 2
Potential preoperative predisposing factors of the development of PPD.

Factor	Group I (n = 18)	Group II (n = 82)	p value
Age (years)	58 ± 17	50 ± 15	0.05
Male/female	12/6	47/35	0.60
Educational status[a] (n)	2/3/0/5/8	6/22/11/23/20	0.23
Operation due to malignancy (n, %)	13 (72%)	52 (63%)	0.60
Smoking (n, %)	9 (50%)	39 (48%)	1.00
Alcohol abuse (n, %)	4 (22%)	6 (7%)	0.08
Chronic disease[b] (n, %)	5 (28%)	17 (21%)	0.54
Diabetes mellitus (n, %)	2 (11%)	17 (21%)	1.00
Hyperlipidaemia (n, %)	6 (33%)	18 (22%)	0.36
Previous psychiatric disease (n, %)	4 (22%)	6 (7%)	0.08
Chemotherapy administration (n, %)	3 (17%)	6 (7%)	0.20
Previous history of operation (n, %)	15 (83%)	49 (60%)	0.10
Abnormal serum chemistry values[c] (n, %)	0 (0%)	5 (6%)	0.59
Abnormal haemoglobin level[d] (n, %)	2 (11%)	4 (5%)	0.30
Abnormal arterial blood-gase values[e] (n,%)	7 (39%)	22 (27%)	0.40
Abnormal serum albumin levels[f] (n, %)	2 (11%)	5 (6%)	0.61

PPD: postoperative psychiatric disorders.
[a] Defined in order, as illiterate, primary school, middle school, high school, and university graduation.
[b] Defined as presence of any pulmonary, cardiac, renal, hepatic, and rheumatologic disease.
[c] Defined as sodium <130 or > 150 meq l^{-1}, potassium <3.0 or >6 meq l^{-1}, and total calcium <8.4 or >10.2 mg dl^{-1}.
[d] Defined as haemoglobin <13.5 or >17.5 g dl^{-1} (males), and <12 or >16 g dl^{-1} (females).
[e] Defined as hypoxaemia PO_2 <55 mmHg on room air and hypercarbia PCO_2 >45 mmHg.
[f] Defined as albumin <3.5 g dl^{-1}.

The length of the hospital stay was significantly longer when PPD developed (13 ± 9 days vs 8 ± 5 days, p = 0.019). However, no significant difference in the mean intensive care unit stay was observed (4 vs 1 days, p = 0.07). In addition to PPD, one or more complications developed in group I patients (67%), and in group II patients (46%), there was no difference between groups (p = 0.20). The complications are outlined in Table 4. The most common complication was air leak (33%) in the patients in group I, whereas atelectasis (15%) with poor clearance of the pulmonary secretions necessitating bronchoscopy, and supraventricular dysrhythmias (13%) were more common in group II. The mortality rate was 11% in group I (n = 2), while it was 1% in the other group (n = 1) (p = 0.08). The cause of death for all three patients was sepsis. Although the differences were not significant, more complications were observed in patients with PPD, and the in-hospital mortality rates were higher.

The onset of the PPD ranged from days 2 to 18 after surgery (mean 5 ± 4 days). We detected delirium in eight patients (44%), adjustment disorders in four (22%), panic attack in three (17%), minor depressive disorders in two (11%) and psychosis due to a general medical condition in one (6%). The most common signs and symptoms were agitation (78%), hallucination (44%) and confusion (22%). Appropriate medications including antipsychotics (n = 10), antidepressants (n = 9) and anxiolytics (n = 7) were given to the patients who developed PPD (some patients received multidrug therapy). Six patients (33%) responded well to the treatment; 10

Table 3
Potential per- and postoperative precipitating factors of PPD.

Factor	Group I (n = 18)	Group II (n = 82)	p value
Duration of operation (h)	6 ± 1	5 ± 2	0.015
Abnormal serum chemistry values[a] (n, %)	11 (61%)	7 (9%)	<0.001
Abnormal haemoglobin level[b] (n, %)	13 (72%)	44 (54%)	0.19
Abnormal blood glucose level[c] (n, %)	9 (50%)	6 (7%)	<0.001
Hypoalbuminaemia[d] (n, %)	11 (61%)	2 (2%)	<0.001
Respiratory distress[e] (n, %)	9 (50%)	20 (24%)	0.044
Immobilisation (n, %)	6 (33%)	18 (22%)	0.36
Sleep deprivation (n, %)	4 (22%)	6 (7%)	0.08
Blood transfusion (n, %)	16 (89%)	44 (54%)	0.007
Infection[f] (n, %)	8 (44%)	12 (15%)	0.008
Usage of anti-arrhythmics (n, %)	5 (28%)	17 (21%)	0.54
Usage of antihypertensives (n, %)	9 (50%)	24 (29%)	0.10
Usage of steroids (n, %)	5 (28%)	12 (15%)	0.18

PPD: postoperative psychiatric disorders.
[a] Defined as sodium <130 or >150 meq l^{-1}, potassium <3.0 or >6 meq l^{-1}, and total calcium <8.4 or >10.2 mg dl^{-1}.
[b] Defined as haemoglobin <13.5 or >17.5 g dl^{-1} (males), and <12 or >16 g dl^{-1} (females).
[c] Defined as glucose <60 or >300 mg dl^{-1}.
[d] Defined as albumin <3.5 g dl^{-1}.
[e] Defined as hypoxaemia PO_2 <55 mmHg on room air and hypercarbia PCO_2 >45 mmHg.
[f] Defined as blood cell count greater than 12 000/mm^3 and postoperative fever greater than 37.0 °C.

Table 4
Postoperative complications.

Complication	Group I (*n*, %)	Group II (*n*, %)
Overall incidence	12 (67%)	38 (46%)
Air leak ≥7 days	6 (33%)	5 (6%)
Atelectasis/bronchoscopy	3 (17%)	12 (15%)
Supraventricular dysrhythmias	3 (17%)	11 (13%)
Respiratory insufficiency	2 (11%)	9 (11%)
Pneumonia	2 (11%)	2 (2%)
Wound infection	2 (11%)	7 (9%)
Haemothorax	2 (11%)	5 (6%)
Pulmonary oedema	1 (6%)	–
Subcutaneous emphysema	1 (6%)	–
Vocal cord paralysis	–	2 (2%)
Liver dysfunction	–	1 (1%)
Femoral embolism	–	1 (1%)
In-hospital mortality	2 (11%)	1 (1%)

patients (56%), who had partial response, required psychiatric follow-up. Two patients (11%) died during the treatment due to sepsis.

The causative factors in the development of PPD were older age, longer operation time, abnormal serum chemistry values of sodium, potassium, calcium and glucose, hypoalbuminaemia, the presence of the postoperative respiratory distress and infection and blood transfusion ($p < 0.05$).

4. Discussion

Hackett and Weisman [8] named psychiatric complications developing during the course of the surgical treatment as 'operative syndromes'. They ranged these complications from acute psychotic episodes to problems of over-dependency and addiction, and from suicidal depression to the disruptive ward behaviour. They mentioned that a variety of problems might occur postoperatively, including a new onset or recurrent depression, mania, brief psychoses, anxiety symptoms and acute post-traumatic stress disorder.

Christodoulou and colleagues [9] investigated all the patients in the medical and the surgical clinics during 11 years. The incidence of the delirium was 11%, and those of the mood disorders including depression, psychotic disorders, adjustment disorders and anxiety disorders including panic attack were 27%, 8%, 6% and 4%, respectively. Therefore, this study did not reflect the exact incidence of the PPD, since it included the patients both in the medical and the surgical clinics. Other than our study, there is no study investigating the incidence and risk factors of the PPD in NTS. The incidence of the PPD in our study was 18%, which included delirium in 44%, adjustment disorders in 22%, panic attack in 17%, minor depressive disorders in 11% and psychosis due to a general medical condition in 6%.

Among the PPDs, delirium is the most common complication. The overall incidence of delirium is 37%, with a range of 0–74% [1,3,4]. The incidence of delirium has been reported to be 23% in cardiac surgery [10], 41% in orthopaedic surgery [11], 60% in abdominal surgery [12], 18% in gynaecologic oncological surgery [13], and 33–36% in vascular surgery [14]. The incidence of the postoperative delirium in thoracic surgery was less than 6% in our previous study [5]. The incidence has been reported to be 21% by Aakerlund and Rosenberg [6], 16% by Marcantonio and colleagues [1] and 7% by Lynch and colleagues [2]. Here in this study, the incidence of postoperative delirium was 8%, in a similar range in comparison with the previous studies.

There are some reports concerning PPDs other than delirium on overall surgical and medical patients. Depression is one of the most common psychiatric risks after hysterectomy with an incidence of nearly 8% [15]. Adjustment disorders and psychosis are the most frequently reported PPD in the patients undergoing an epilepsy surgery [16]. In the study of Giltay and colleagues [17] ($n = 8139$), postoperative psychosis developed in 2% of the patients undergoing coronary artery bypass surgery. Anxiety disorders including panic attack are found in 2% of the cancer patients [18], and may be seen in the post-surgical patients [19]. We found no specific study investigating the incidence of PPD other than delirium in NTS patients. In this study, 10% of the patients developed PPDs other than delirium.

The pathogenesis of the PPDs has been explained by several hypotheses. The cause of the early postoperative changes in the cognitive function is mostly multifactorial, including an ischaemic injury from microembolism, hypoperfusion and other factors resulting from a major surgery [20]. The physiological stress may cause a postoperative cognitive decline [21]. The pathophysiology of the delirium involves relative decreases in the muscarinic cholinergic activity, increases in the dopaminergic activity or some combination of both [22]. Delirium has been hypothesised to be a central nervous system response to the systemic inflammation during a state of blood–brain barrier compromise, and elevated levels of chemokines, which are capable of disrupting the blood–brain barrier integrity *in vitro*, may play a role in its pathogenesis [23]. An increased level of postoperative serum concentrations of S-100 β (glial) and neuron-specific enolase, which are the neurobiochemical markers of the brain damage, may be predictive in the development of the delirium after cardiac surgery [24]. The causes of the psychotic symptoms are multifactorial and are similar to those of delirium [17]. Panic attacks can occur in the context of several medical conditions such as cardiac, respiratory, vestibular or gastrointestinal disorders, and certain types of the cancer patients may be at risk for panic attacks [7]. With an increase in the sympathetic tone, hormones are released through the hypothalamic–pituitary–adrenal mechanism to cause an activation called 'fight–flight' or 'stress response' [25]. In our study, we focussed only on the predictors of PPD, and therefore, we cannot assess the mechanisms of PPD from our data.

In our previous study concerning of 432 patients, we found that the risk factors of the postoperative delirium was old age, postoperative sleep deprivation, longer operation time and markedly abnormal postoperative levels of sodium, potassium or glucose [5]. Various factors have separately influenced the development of delirium, and in general, they are divided into preoperative, intra-operative and postoperative factors [1,3]. The preoperative factors include advanced age, male sex, alcohol abuse, diabetes mellitus, mental and physical diseases, hypertension, smoking, level of education, poor functional status, markedly abnormal preoperative serum sodium, potassium, glucose or albumin level [1,3,13]. The type and duration of the surgery, the

urgency of the operation and intra-operative blood transfusion are determined as intra-operative factors [21]. Post-operative blood transfusion, infections, hypoxaemia, markedly abnormal postoperative serum sodium, potassium or glucose level, sleep deprivation and bed restriction are among the postoperative factors [6,13]. There are controversies regarding the postoperative pain and the development of the delirium. The method of the postoperative analgesia, the type of opioid and the cumulative opioid dose are not associated with an increased risk of delirium [2,21]. Alternatively, pain is an important factor [4], and increased narcotic medication above the standard regimens may cause the development of postoperative delirium [13]. In this study, we did not examine the association of the postoperative pain management with the development of PPD.

Previous researches have shown contradictory associations of ethanol use and delirium. While in some studies, there was a positive relationship between ethanol abuse and delirium [1,3], other studies have reported no such relationship [4,5]. Prior mental diseases and cognitive impairments are among the causative factors of postoperative delirium and other psychiatric disorders [3,9]. In our previous study, previous mental diseases did not affect the development of delirium [5].

In the current study, there was no significant relationship between alcohol abuse and the development of PPDs. However, patients with alcohol abuse were more common in the PPD group than in the non-PPD group (22% vs 7%, respectively). In addition, in this study, 22% of the patients who developed a PPD had a previous psychiatric impairment under treatment, but the result was not significant ($p > 0.05$). Routine screening of the cognitive functions and delirium by the psychiatrists, whenever possible not only on the admission for the surgery, but also for a longer duration before the surgery may contribute to a better preoperative mental condition for such a patient. In the presence of an alcohol abuse, nutritional support and vitamin supplementation including B vitamins and the prevention of the alcohol withdrawal using benzodiazepines may also be advised for a patient undergoing surgery.

The causative factors of postoperative psychosis are similar to that of delirium. Giltay and colleagues [17] investigated 8139 patients undergoing coronary artery bypass surgery and revealed that advanced age, preoperative renal and heart failure, dyspnoea, hypoxaemia, preoperative abnormal blood level of sodium and postoperative infection are among the risk factors in the development of the psychotic symptoms. Neurological, hormonal, metabolic disorders, hepatic or renal diseases, the abnormalities in the serum electrolyte levels and auto-immune diseases affecting the central nervous system may cause psychosis [7].

We did not investigate the risk factors separately for each type of PPD, due to the small number of the patients. However, we examined and analysed the risk factors in the development of PPD in general. Our findings demonstrated that older patients, patients with postoperative hypoalbuminaemia, abnormal postoperative blood glucose, sodium, calcium and potassium levels, the patients who developed postoperative respiratory distress and infection and the patients who required postoperative blood transfusion were at high risk of developing PPD.

Psychiatric disorders and behavioural disturbances may complicate the post-surgical outcome. Delirium increases mortality and morbidity rates [12], and prolongs hospital stay [3,12]. Post-surgical psychosis is associated with an increased rate of morbidity and mortality [17]. There is a high risk of suicidal tendencies in the patients with adjustment disorders; they may not respond to therapy and their hospital stay is prolonged [7]. In this study, we found that the hospital stay was significantly longer in the patients who developed PPD (13 days vs 8 days, $p = 0.019$). Longer hospital stay, and also ICU stay, may be a consequence of psychiatric disorders, and also can be a trigger for the development of PPD. Although the morbidity and mortality rates were higher in the patients who developed PPD, the differences were not significant in the current study ($p > 0.05$).

A wide range of psychiatric complications may occur following an NTS and they are associated with adverse outcomes including a longer hospital stay, and an increased morbidity and mortality. The identification, detection and elimination of these risk factors are recommended to prevent the occurrence of PPD.

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