



# The Effects of Coexistent Psychiatric Disorders in Patients Operated on for Acute Aortic Dissection on Postoperative Mental Health Status and on Mid-Term Time Period

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## Abstract

**Background and aims of the study:** Although relationships between ischemic heart disease and psychiatric disorders (PD) have been highlighted, a link between PD and acute aortic dissection (AAD) has not been shown. Aim of this study was to define the psychological profile of patients treated for AAD and analyze the impact of PD postoperatively and at 5-year follow-up period.

**Methods:** Two-hundred and twelve patients underwent surgery for AAD during a 9-year period, and operative mortality was 26% (n = 55/212). Of 157 survived patients, 53 (34%) (mean age 59 ± 13 years; 40 males- 75.5%), underwent psychiatric consultation postoperatively. Ascending aorta +/- arch replacement was performed in 37 patients, Bentall +/- arch replacement in 16. Data were retrospectively analyzed. Mean duration of follow-up was 32 ± 25 months.

**Results:** In 31 patients psychiatric changes were present in their medical history. Postoperatively in 25 of them a definitive diagnosis of PD (Group PD) was made in agreement of DSM-IV criteria as: major depression (n = 10), anxious-depressive syndrome (n = 5), bipolar disorder type 2 (n = 5), panic attacks (n = 2), paranoid schizophrenia (n = 1), anxiety (n = 2). Patients without a definitive psychiatric diagnosis were classified as Group non-PD (n = 28). In the postoperative period clinical manifestations of PD including delirium, persistent spatio-temporal disorientation, psychomotor agitation were evident in 20 patients (80%) in Group PD vs. 4 patients (14.8%) in Group non-PD (P < .0001). During follow-up neither deaths nor suicide attempts occurred; only 6 patients of Group PD required PD treatment (P < .0001 vs. early postoperative findings); 2 patients in Group non-PD required psychiatric medical treatment.

**Conclusion:** Our findings suggest that the incidence of postoperative psychiatric complications is higher in patients affected by preoperative PD. During follow-up freedom from PD is lower in patients who experienced postoperative PD-related complications. Since the psychiatric conditions appeared to be comfortably stable during follow-up, treatment of AAD for patients affected by PD seemed to represent the first step to detect their psychiatric disorder and to start correct medical therapy.

## Keywords

Acute aortic dissection, Aortic surgery, Psychiatric disorders, Mental health status

## Introduction

In the last years a relationship between psychiatric disorders (PD) and ischemic cardiovascular disease has been clearly shown [1-2]. PD, especially depressive disorders, represent a pathological condition with a rising epidemiological incidence; the life-time prevalence of PD ranges between 4% and 17.1% [1,3]. Depression is recognized as an independent predictor for cardiovascular mortality in the short-term period following myocardial infarction and is associated with increased cardiovascular events [4-6]. Negative effects of depression have been reported also during follow-up in patients operated of coronary artery bypass grafting [7-10]. Behavioral changes, lack of trust of the psychiatric patient in medical treatment and prevention, and pathophysiological alterations of the autonomic nervous system and hypothalamic-pituitary-adrenal axis have been considered as possible causes of the association between PD and ischemic heart disease [11-13].

Acute aortic dissection (AAD) is a catastrophic cardiovascular syndrome with an estimated incidence of 2.9 cases per 100,000 patients-years and a high mortality rate, which is about 50% at 48 hours from the onset of symptoms and 90% at one month for Type A aortic dissection [14,15]. Among the most significant risk factors for the development of this condition high arterial blood pressure, genetic predisposition, such as the presence of inherited disorders of connective (Marfan and Ehlers-Danlos syndrome), are recognized.

Although few studies have analyzed the presence of behavioral risk factors for AAD, like the abuse of cocaine or amphetamines [16-18], a link between PD and AAD has not been reported.

Clinical practice on patients admitted with A AAD diagnosis and surgically treated at our Institution has suggested that these patients constituted a particularly delicate group in terms of psychical status. Moreover, we observed that psychiatric complications such as postoperative delirium, spatiotemporal dissociation and psychomotor agitation were particularly frequent, resulting in the need of psychiatric treatment in the postoperative period. These findings have suggested the existence of a possible relation between PD and AAD, similar to that already reported for ischemic heart disease.

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**Table 1:** Preoperative and perioperative characteristics.

| Characteristic                                   | No. patients |
|--|--------------|
|  | <b>53</b>    |
| Age, years                                       | 59.2 ± 13.2  |
| Male gender, n. (%)                              | 40 (75.5)    |
| Hypertension, n. (%)                             | 51 (96)      |
| Smoking habit, n. (%)                            | 29 (55)      |
| Family history, n. (%)                           | 10 (20)      |
| Dyslipidemia, n. (%)                             | 10 (20)      |
| Diabetes mellitus, n. (%)                        | 2 (3.8)      |
| Obesity, n. (%)                                  | 13 (25.5)    |
| Substance abuse, n. (%)                          | 2 (3.8)      |
| Ascending aorta +/- hemiarch replacement, n. (%) | 27 (50)      |
| Ascending aorta + arch replacement, n. (%)       | 10 (19)      |
| Bentall operation +/- arch replacement, n. (%)   | 16 (30)      |
| Cardiopulmonary bypass time, minutes             | 152 ± 59     |
| Aortic cross-clamp time, minutes                 | 90 ± 39      |
| Hypothermic arrest, n. (%)                       | 31 (61)      |
| Circulatory arrest time, minutes                 | 32 ± 29      |
| In-ICU stay, days                                | 4 ± 2        |

ICU = Intensive Care Unit

**Table 2:** Postoperative psychiatric diagnosis.

| Psychiatric Disorder                | No. patients    |
|-------------------------------------|-----------------|
|                                     | <b>(n = 25)</b> |
| Major Depression, n. (%)            | 10 (40)         |
| Anxious Depressive Syndrome, n. (%) | 5 (20)          |
| Type 2 bipolar disorder, n. (%)     | 5 (20)          |
| Panic Attacks, n. (%)               | 2 (8)           |
| Paranoid Schizophrenia, n. (%)      | 1 (4)           |
| Anxiety, n. (%)                     | 2 (8)           |

Aim of the current study was to retrospectively detect the relation between PD and AAD, define the psychological profile of patients treated for AAD and analyze the impact of PD postoperatively and at mid-term follow-up.

## Patients and Methods

From January 2005 to October 2013 at the Cardiac Surgery Unit of the Tor Vergata University Policlinic, 212 patients were consecutively operated for Type A AAD. Mortality rate, as recorded at 30 days, was 26% (55/212).

Among the survivors 53 patients (mean age 59.2 ± 13.2 years, range 20-79 years; 40 males), who represented the object of our study, underwent psychiatric consultation for evaluation of their psychiatric profile in the early postoperative period. Data were retrospectively analyzed.

Diagnosis and type of PD were established by psychiatrists according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders Fourth Edition, American Psychiatric Association, 1994* (DSM-IV).

All patients except two (96%) were affected by recognized arterial hypertension; smoking habit was recorded in 29 patients (55%). The incidences of the other risk factors for cardiovascular diseases are reported in [table 1](#).

The study was approved by our local Institutional Review Board, which waived the need for patient consent. All preoperative and intraoperative characteristics are reported in [table 1](#).

## Surgical procedures

All the patients underwent surgery on an emergency basis. Surgical access was longitudinal median sternotomy in all the cases. Cardiopulmonary bypass was instituted through arterial cannulation of the right axillary artery in 23 cases (43%), femoral artery in 18 (34%), ascending aorta in 12 (23%). Venous drainage was obtained by cannulation of the right atrium. Myocardial protection was achieved by administration of intermittent antegrade blood cardioplegia (600

ml the first dose, 400 ml the others every 25-30 minutes).

Ascending aorta +/- hemiarch replacement was performed in 27 patients, ascending aorta + arch replacement in 10, Bentall procedure +/- arch replacement in 16.

In 31 patients circulatory arrest, moderate hypothermia (26-27°C) and selective antegrade cerebral perfusion was instituted to perform the distal anastomosis of the vascular graft for emiarch or total arch replacement.

All preoperative and intraoperative characteristics are reported in [table 1](#).

## Data collection

Diagnosis and type of PD was established by three psychiatrists according with criteria reported in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*. Psychiatric therapy was administered or changed as required in presence of postoperative acute exacerbation of PD. Follow-up was completed in 52/53 patients (mean duration 33 ± 25 months). Mental health status of every patient was investigated during a 2-month period (November-December 2013). Need for in-hospital readmission for cardiovascular causes or for treatment of PD during follow-up was also recorded at the outpatient clinic visit or by telephone interview. Freedom from PD was defined as absence of clinical manifestations of PD and when a specific therapy required for treatment of PD exacerbation was not necessary, except the use of anxiolytic drugs at low doses. During the immediate postoperative period or during follow-up sertraline or paroxetine was used for the treatment of major depression, anxious depressive syndrome or panic attacks, alprazolam was administered for the treatment of anxious depressive syndrome and anxiety, quetiapine hydrochloride (seroquel) for the treatment of bipolar disorder and schizophrenia.

## Statistical analysis

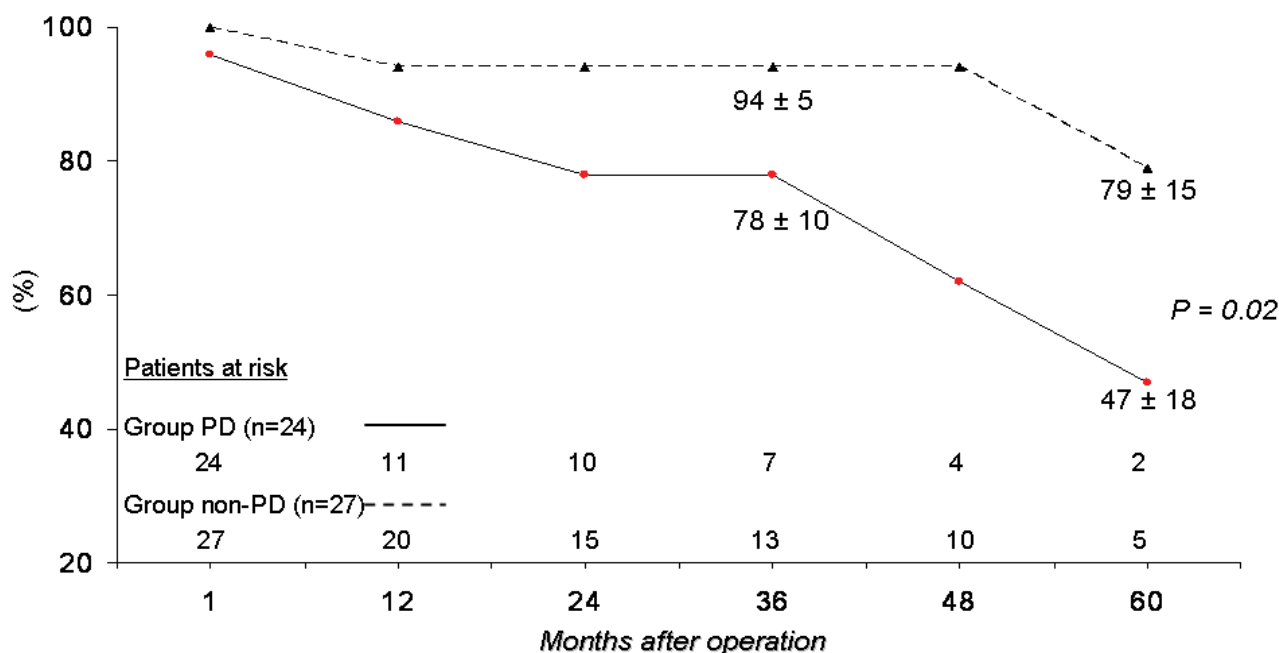
Statistical analysis was performed with Stat View 4.5 (SAS Institute Inc, Abacus Concepts, Berkeley, CA). Student's *t* test for continuous data and the  $\chi^2$  or Fisher's exact tests for categorical data were used. Seventeen preoperative and perioperative variables were analyzed including age, gender, arterial hypertension, smoking habit, family history, diabetes mellitus, dyslipidemia, obesity, substance abuse, presence and type of PD, cardiopulmonary bypass and aortic cross-clamp times, the need and the duration of circulatory arrest, type of surgical procedures, length of intensive care unit stay. Risk factors analysis to detect independent predictors for postoperative psychiatric disorders was performed using univariate analysis and the logistic regression analysis. Freedom from PD during follow-up was expressed as mean values plus or minus 1 standard deviation, and computed by using the Kaplan-Meier method; the log-rank test was used to compare event-free survival among subgroups. All other continuous values were expressed as mean plus or minus 1 standard deviation of the mean. All *P* values less than 0.05 were considered statistically significant.

## Results

### Psychiatric features and postoperative results

In 31 patients (58%) a psychiatric alteration was reported in their medical history. Of them, however, postoperatively, a diagnosis of PD was definitively made in 25 patients (47%) (Group PD) on the basis of psychiatric consultation at our unit as: major depression (n = 10), adjustment disorder with depressed mood (anxious depressive syndrome) (n = 5), type 2 bipolar disorder (n = 5), panic attacks (n = 2), paranoid schizophrenia (n = 1), anxiety without a specific psychiatric diagnosis (n = 2) ([Table 2](#)). In the other 6 patients the reported psychiatric alterations in their history did not meet criteria of PD according to *DSM-IV* classifications.

Smoking habit was more frequent in Group PD (79%) vs. Group non-PD (33%) (*P* = .001); the incidence of the other cardiovascular risk factors were similar in both Groups.



**Figure 1:** Freedom from PD during follow-up (33 ± 25 months) for Group PD vs. Group non-PD.

PD = Psychiatric Disorders

Clinical postoperative manifestations of PD including delirium, persistent spatio-temporal disorientation, psychomotor agitation were evident in 20 patients (80%) in Group PD vs. 4 patients (14.8%) in Group non-PD ( $P < .0001$ ).

The variables analyzed, as gender, sex, type of surgical procedure, duration of cardiopulmonary bypass and aortic cross clamp times, circulatory arrest, length of stay in intensive care unit were not identified as risk factors for postoperative psychiatric complications at the univariate analysis. Postoperatively, two patients in Group non-PD experienced cerebral ischemic stroke.

### Follow-up results

During the follow-up neither deaths nor suicide attempts occurred, but one patient of Group PD with a postoperative psychiatric diagnosis of anxiety showed aggressive behaviour towards his wife. At the end of follow-up only 6/24 patients of Group PD (1 patient lost at follow-up) continued to be affected by PD requiring treatment: 2 patients remained affected by major depression, 1 by paranoid schizophrenia, 1 by type 2 bipolar disorder, 1 by panic attacks, and 1 by anxiety. Therefore, the incidence of PD requiring treatment decreased from 100% in the Group PD in the postoperative period to 25% (6/24) during follow-up ( $P < .0001$ ). One patient in Group PD affected by major depression developed a primitive respiratory insufficiency requiring home oxygen therapy. The other patient affected by major depression experienced an ischemic stroke 4 months after operation. All the other patients in Group PD did not show acute clinical manifestations of PD; they were in psychiatric follow-up or required the use of anxiolytic drugs at low doses, only. Two more cases were affected by PD (major depression,  $n = 1$ , anxiety,  $n = 1$ ) in Group non-PD. Overall, freedom from PD requiring the need of psychiatric therapy at 1, 3 and 5 years was 85%, 78%, 47% in Group PD vs. 94%, 94%, 79% in Group non-PD ( $P = .02$ ) (Figure 1).

Freedom from PD at 1, 3 and 5 years in patients who showed psychiatric complications in the early postoperative period in comparison with patients who did not developed psychiatric complications is reported in figure 2.

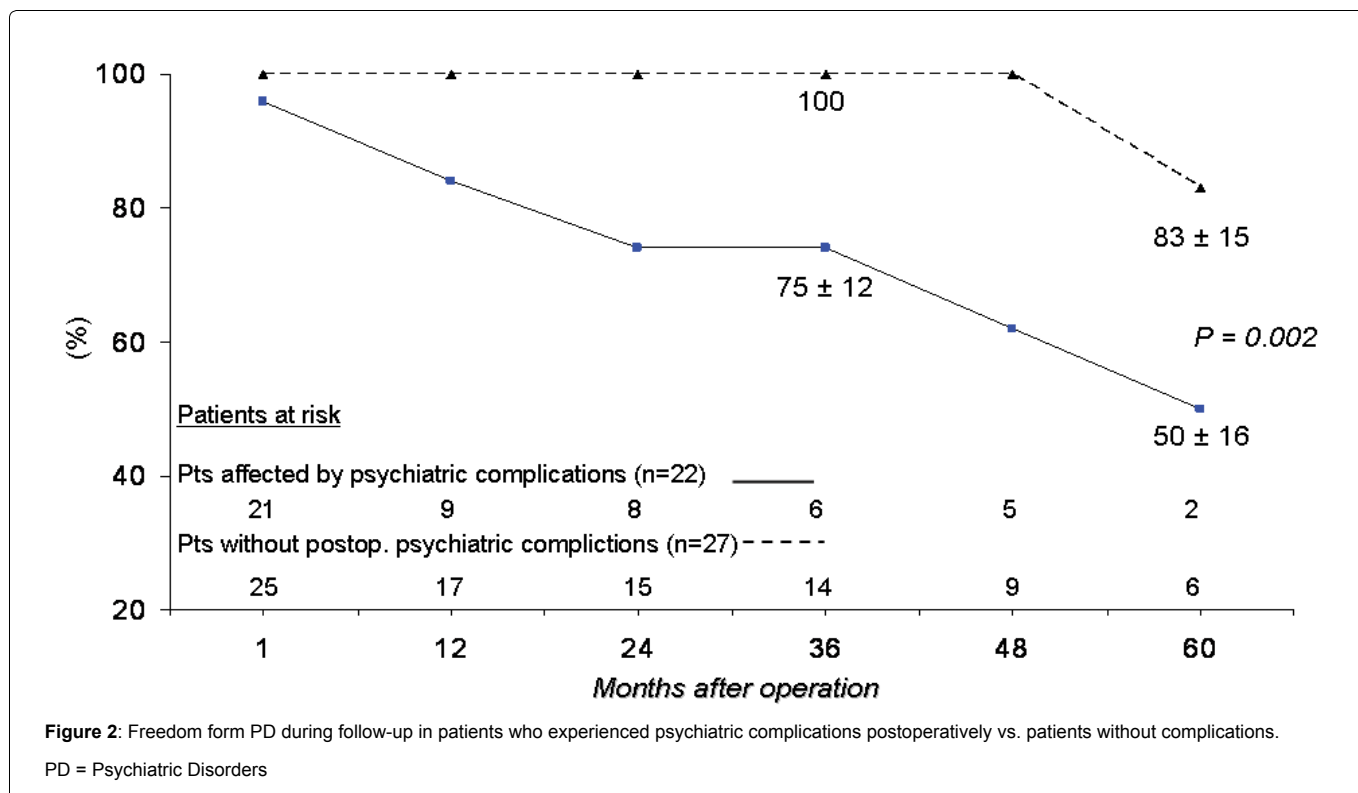
### Discussion

Major depression is highly prevalent in cardiac patients; between 15-20% of patients affected by coronary artery disease meet criteria

for Major Depression syndrome [19,20], and the rate of Major Depression in these patients is threefold higher than in the general population [21]. Patients with heart failure, atrial fibrillation, and those undergoing implantable cardioverter-defibrillator (ICD) placements are similarly at increased risk for elevated depressive symptoms and for MDD [22,23]. Finally, among patients undergoing coronary artery bypass graft surgery, approximately 15% of patients meet full Major Depression criteria on diagnostic interview [24].

In our study, we retrospectively reviewed 53 patients admitted directly to the cardiac operating room with diagnosis of AAD and treated under emergency. All the patients underwent during hospitalization in the postoperative period psychiatric evaluation aimed to highlight the presence of PD. We found a strong relation between PD and AAD: postoperatively in 47% of patients ( $n = 25$ , Group PD) a precise clinical syndrome was recognized by the consultant psychiatrists. In Group PD the incidence of postoperative psychiatric complications was about 80%. The major psychiatric disorders were major depression, anxiety-depressive syndrome and anxiety status, representing more than 70% of PD diagnosed in the postoperative period. This incidence of PD in patients affected by AAD is very high (2 to 10 times) in comparison with that observed for the general population (4-7%) and in patients with ischemic heart disease (15-30%) [19-25]. The high prevalence of psychiatric disorders and major depression we observed in patients with AAD provides further confirmation that the research in the last 20 years have shown that a psychiatric disorder, especially major depression, is not only more frequent in patients with heart disease than the general population but it can be considered as a cardiovascular risk factor, independent from the other traditional risk factors. In our series Major Depression was diagnosed in 40% of cases.

Moreover 2 patients, in whom initially diagnosis of PD was not made postoperatively, developed onset PD manifestations during follow-up. These findings seem to provide the evidence regarding our hypothesis of a strict relation between AAD and PD. The mechanisms potentially responsible for the association with acute aortic events may be related primary to pathophysiological alterations due to genetic polymorphisms of the autonomic nervous system, as found in the correlation between ischemic heart disease and PD [11], or secondary to the fact that psychiatric patients often do not take care of their health and do not control potential risk factors (i.e., do



**Figure 2:** Freedom from PD during follow-up in patients who experienced psychiatric complications postoperatively vs. patients without complications. PD = Psychiatric Disorders

not take drugs for treatment of arterial hypertension). Smith and coworkers found a strong relation between bipolar disorders and cardiometabolic morbidity (i.e. thyroid disorders, chronic pulmonary disease, arterial hypertension, diabetes mellitus): patients affected by bipolar disorders were less likely than controls to access primary-care to treat hypertension or atrial fibrillation. Similarly, Gladigau and co-worker found a strong link between severe mental illness and high incidence (from 19% to 69%) of several risk factors for cardiovascular disease, such as smoking, obesity, overweight, hypertension, diabetes, dyslipidemia, metabolic syndrome [25].

In our study we found a significantly higher incidence of smokers in Group PD in comparison with Group non-PD (79% vs. 33%,  $P = .001$ ); moreover, although without a statistically significant difference, also obesity was more frequent in Group PD (29.2% vs. 22%,  $P = .57$ ).

During a mid-term follow-up, although freedom from PD remained significantly related to the presence of PD diagnosed postoperatively (Figure 1 and Figure 2), we observed an important reduction of clinical psychiatric manifestations. In fact, only 6 patients of the 24 patients in Group PD (not including the patient lost during follow-up) continued to be affected by PD. In particular, a significant reduction of psychiatric manifestations was observed at follow-up for depressive or bipolar disorders in comparison with the immediate postoperative findings (2/24 vs. 19/24 patients,  $P < .001$ ).

The reason to justify the remission of psychiatric symptoms is not entirely clear: it would seem that hospitalization for surgery had a positive influence on the natural history of mental illness. Probably, the treatment of the aortic pathology for this group of patients has been the first step to recognize and treat both cardiovascular risk factors and psychiatric disease. During follow-up 1 patient experienced a cerebral stroke, which aggravated the pre-existing depression.

Finally, it appears very important to emphasize the complete absence of suicides in this population during follow-up period. Our preliminary data would show that surgical intervention, albeit representing an important trauma, in combination with a proper diagnostic and therapeutic way for the control of psychiatric symptoms, had had a positive impact during the psychiatric status at follow-up.

### Limitations of the study

Our observations relate to a small group of patients and the

type of study is retrospective. Therefore, further investigation will be needed to corroborate what has been highlighted. However, it should be noted that the tested sample represented approximately 30% of survived patients after AAD surgery. Moreover, the results will need confirmation with analysis of additional factors, i.e., genetic, biological and behavioral which could better explain and describe the underlying pathophysiology and relation with AAD.

In conclusion, our findings suggest that the incidence of postoperative psychiatric complications is higher in patients affected by preoperative PD. During follow-up freedom from PD is lower in patients who experienced postoperative PD-related complications. Since the psychiatric conditions appeared to be comfortably stable after surgery, treatment of AAD for patients affected by PD seems to represent a first step to detect psychiatric pathology and to start a correct medical therapy for a better control of mental health. Following these interesting preliminary results, the study is continuing in a prospective manner.

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