Archives of Clinical & Experimental Surgery

Original Article

Arch Clin Exp Surg 2015;4:202-207

doi:10.5455/aces.20150108115200

Effects of psychiatric disorders on Type A acute aortic dissection pathogenesis and analysis of follow-up results

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ABSTRACT

Aims: A connection between psychiatric disorders (PDs) and Type A acute aortic dissection (AAD) has not been shown. The aim of this study was to define the psychological profile of patients treated for AAD, and to analyze the prevalence of PDs in their medical histories, in the immediate postoperative period, and at a mid-term follow-up.

Patients and Methods: From March 2005 to October 2014, 240 consecutive patients underwent surgery for AAD. 60 patients (mean age 60 ± 13 years; 43 males) underwent psychiatric consultation postoperatively, and they represent the subjects of our retrospective study. Ascending aorta ± arch replacement was performed in 43 patients, whereas the Bentall procedure ± arch replacement was performed in 17. Data were retrospectively analyzed. Follow-ups were completed in 59 patients (mean duration 35 ± 23 months).

Results: PDs were present in the medical histories of 34 patients. Postoperatively, in 28 cases, a definitive diagnosis of PD (group PD) was made in agreement with the diagnostic and statistical manual of mental disorders-IV criteria, including: Major depression (n = 13), anxious-depressive syndrome (n = 6), bipolar disorder Type 2 (n = 4), panic attacks (n = 2), paranoid schizophrenia (n = 1), and anxiety (n = 2). 32 patients without a definitive psychiatric diagnosis were classified as Group non-PD. In the postoperative period, clinical manifestations of PDs, including delirium, persistent spatio-temporal disorientation, and psychomotor agitation were evident in 22 patients (78%) in group PD versus 8 patients (25%) in group non-PD ($P < 0.0001$). During follow-up, only one death for non-cardiac reasons occurred in group PD. There were no suicides; only 10 patients of group PD required PD treatment ($P < 0.0001$ vs. early postoperative findings); 4 patients in group non-PD required PD treatment.

Conclusion: Our findings suggest a strong relationship between PD and AAD. Because the psychiatric conditions appeared to be largely stable after surgery, treatment of AAD for patients affected by PDs seemed to represent the first step to detect their PDs and to start an appropriate medical therapy.

Key words: *Acute aortic dissection, aortic surgery, psychiatric disorders*

Introduction

The relationship between psychiatric disorders (PDs) and ischemic cardiovascular disease has been clearly shown in the last decade [1,2]. PDs, especially depressive disorders, represent a pathological condition with a rising epidemiological incidence; the lifetime prevalence of PDs ranges between 4% and 17.1% [1,3]. Thus, about 12% of women and 8% of men will

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Received / Accepted : *December 01, 2014 / January 08, 2015*

experience a major depressive episode during their lifetime. Depression is recognized as an independent predictor for cardiovascular mortality in the short-term period following myocardial infarction, and it is associated with an increased risk of cardiovascular events and heart failure [4-6]. Negative effects of depression have also been reported during follow-ups in patients undergoing coronary artery bypass grafting [7-10].

This phenomenon could be explained by several reasons: First, the behavioral changes of psychiatric patients, which could result in a lack of trust in medical treatment and prevention, could increase the prevalence of cardiovascular risk factors, such as hypertension and smoking. Second, pathophysiological alterations of the autonomic nervous system and hypothalamic-pituitary-adrenal axis that present in the pathogenesis of PDs can influence the cardiovascular system, increasing heart rate and blood pressure, which are well-known major risk factors for cardiovascular events [11-13]. Third, patients affected by PDs may receive therapies that increase the heart rate, electrocardiogram, and diastolic blood pressure [14].

Acute aortic dissection (AAD) is a catastrophic cardiovascular syndrome with an estimated incidence of 2.9 cases per 100,000 patient-years and a high mortality rate [15,16], which is about 50% at 48 h from the onset of symptoms, and 90% at 1 month, if surgically untreated [15,16]. Among the most significant risk factors for the development of this condition are high arterial blood pressure and genetic predisposition, such as the presence of inherited disorders of connective tissue, e.g., Marfan and familial syndromes.

Although few studies have analyzed the presence of behavioral risk factors for AAD, such as the abuse of cocaine or amphetamines [17-19], a link between PDs and AAD has not been reported. Clinical practice on patients admitted with an AAD diagnosis and surgically treated at the Cardiac Surgery Unit of the Tor Vergata University Policlinic has suggested that these patients constitute a particularly delicate group in terms of psychological status. Moreover, we observed that psychiatric complications, such as postoperative delirium, spatiotemporal dissociation, and psychomotor agitation, were particularly frequent, resulting in the need for psychiatric treatment in the postoperative period. Shiraishi et al. [20] reported an incidence of neurological dysfunction up to 16% in the postoperative period in 104 patients operated on for aneurysms or dissections of the thoracic aorta.

These findings suggest the existence of a possible relationship between PDs and AAD, similar to that already reported for ischemic heart disease.

The aim of the current study was to retrospectively detect the relationship between PDs and AAD, define the psychological profiles of patients treated for AAD, and analyze the impact of PD postoperatively and at mid-term follow-ups.

Patients and Methods

From January 2005 to October 2014 at the Cardiac Surgery Unit of the Tor Vergata University Policlinic, 240 patients were consecutively operated on for Type A AAD. The in-hospital mortality rate was 26% (62 patients).

Among the survivors, 60 patients (mean age 60.6 ± 13.2 years, range 20-84 years; 43 males), who represented the subjects of our study, underwent psychiatric consultation for evaluation of their psychiatric profiles 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

Table 1. Peri-operative characteristics.

Variables	*n*=60
Age, years	60.6±13.2
Male gender, *n* (%)	43 (72)
Hypertension, *n* (%)	57 (95)
Smoking habit, *n* (%)	30 (50)
Family history, *n* (%)	12 (20)
Dyslipidemia, *n* (%)	12 (20)
Diabetes mellitus, *n* (%)	2 (3.)
Obesity, *n* (%)	15 (25)
Substance abuse, *n* (%)	2 (3.3)
Ascending aorta±hemiarch replacement, *n* (%)	31 (52)
Ascending aorta+arch replacement, *n* (%)	12 (20)
Bentall operation using a composite tubular graft prosthesis±arch replacement, *n* (%)	17 (28)
Cardiopulmonary bypass time, minutes	154±60
Aortic cross-clamp time, minutes	88±37
Hypothermic arrest, *n* (%)	37 (62)
Circulatory arrest time, minutes	32±25

Statistical Manual of Mental Disorders Fourth Edition, American Psychiatric Association, 1994 (DSM-IV).

All but three patients (95%) were affected by recognized arterial hypertension; a smoking habit was recorded in 30 patients (50%). 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.

Having observed that patients affected by AAD not infrequently had a history of PDs and postoperative complications, often requiring psychiatric therapies, during the last 3 years, we systematically conducted a postoperative psychiatric evaluation of all patients. Data from the last period and those previously collected were retrospectively analyzed and constituted the sample of the current study.

Surgical Procedures

All the patients underwent surgery on an emergency basis. Surgical access was via a longitudinal median sternotomy in all cases. Cardiopulmonary bypass was initiated through arterial cannulation of the right axillary artery in 23 cases (38.3%), the femoral artery in 23 cases (38.3%), and ascending aorta in 14 cases (23.4%). Venous drainage was obtained by cannulation of the right atrium. Myocardial protection was achieved by administration of intermittent anterograde blood cardioplegia or single-dose custodiol cardioplegia.

Ascending aorta ± hemiarch replacement was performed in 31 patients (51.6%), ascending aorta + arch replacement in 12 (20%), Bentall procedure ± arch replacement in 17 (28.4%) (Table 1).

In 37 patients (61.6%), circulatory arrest, moderate hypothermia (25-26°C), and selective anterograde cerebral perfusion were used to perform the distal anastomosis of the vascular graft for hemiarch or total arch replacement.

Data Collection

Diagnosis and type of PD were established by three psychiatrists according to the criteria reported in the DSM-IV. Psychiatric therapy was administered or changed as required in the presence of postoperative acute exacerbation of PDs. Follow-ups were completed in 59/60 patients (mean duration 35 ± 23 months). The mental health status of every patient was investigated during a 2-month period (September-October 2014). The need for in-hospital readmission for cardiovascular causes or for treatment of PDs during follow-up was also recorded at the outpatient clinic visit or by telephone interview. Freedom from PD was defined as the absence of clinical manifestations of PDs and when a specific therapy required for treatment of PD exacerbation was not necessary, except for the use of anxiolytic drugs at low doses. During the immediate postoperative period or during follow-up, the specific therapies used for the treatment of major depression and anxious depressive syndrome or panic attacks were sertraline or paroxetine; for the treatment of anxious depressive syndrome and anxiety alprazolam was also used; and for the treatment of bipolar disorder and schizophrenia, quetiapine hydrochloride (Seroquel) was used.

Statistical Analysis

Statistical analysis was performed with Stat View 4.5 (SAS Institute Inc., Abacus Concepts, Berkeley, CA, USA). The Student's t-test was used for continuous data and the X2 or Fisher's exact tests were used for categorical data. Risk factor analysis to detect independent predictors for postoperative PDs was performed using univariate analysis, i.e, including the preoperative and intraoperative variables reported in Table 1, and the logistic regression analysis. Freedom from PD during follow-up was expressed as mean values ± 1 standard deviation, and computed 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 means ± 1 standard deviation of the mean. All $P < 0.05$ were considered statistically significant.

Results

Psychiatric Features and Postoperative Results

A psychiatric alteration was reported in the medical histories of 34 patients (56.6%). A postoperative diagnosis of PD was definitively made in 28 out of 60 patients (46%) (group PD) on the basis of psychiatric consultation at our unit, and included: major depression (n = 13), adjustment disorder with depressed mood (anxious depressive syndrome) (n = 6), Type 2 bipolar disorder (n = 4), panic attacks (n = 2), paranoid schizophrenia (n = 1), and anxiety without a specific

psychiatric diagnosis (n = 2). In the other six patients, the reported psychiatric alterations in their histories did not meet the criteria of PD according to the DSM-IV classifications.

Smoking habit was more frequent in group PD (80%) vs. group non-PD (33%) (P = 0.001); the incidences of the other cardiovascular risk factors were similar in both groups.

Clinical postoperative manifestations of PDs, including delirium, persistent spatio-temporal disorientation, and psychomotor agitation were evident in 22 patients (78.5%) in group PD versus 8 patients (25%) in group non-PD (P < 0.001).

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

Follow-up Results

During the follow-up, one death for a non-cardiac reason occurred; there were no suicides. One patient of group PD with a postoperative psychiatric diagnosis of anxiety showed aggressive behavior towards his wife. Only 10/28 patients in group PD (1 patient was lost at follow-up) continued to be affected by PDs requiring treatment: 5 patients remained affected by major depression, 1 by paranoid schizophrenia, 1 by type 2 bipolar disorder, 1 by panic attack, and 2 by anxiety. Therefore, the incidence of PDs requiring treatment decreased from 100% in group PD in the postoperative period to 35% (10/28) during follow-up (P < 0.001). One patient in group PD affected by major depression developed a primitive respiratory insufficiency requiring home oxygen therapy. Another 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 PDs; they were in psychiatric follow-up or required the use of anxiolytic drugs at low doses only. Four more cases were affected by PDs (major depression, n = 1, anxiety, n = 1) in group non-PD. Therefore, freedom from PDs requiring the need for psychiatric therapy at 1 and 5 years was 85% and 45%, respectively, in group PD vs. 94% and 80%, respectively, in group non-PD (P < 0.05) (Figure 1).

Freedom from PDs at 1 and 5 years in patients who showed psychiatric complications in the early postoperative period in comparison with patients who did not develop psychiatric complications was 96% and 50%, respectively, versus 100% and 84% (P < 0.01), respectively (Figure 2).

Discussion

In our study, we retrospectively reviewed 60 patients admitted directly to the cardiac operating room with a diagnosis of AAD in an emergency setting. All the patients underwent during hospitalization in the postoperative period psychiatric evaluation that aimed to highlight the presence of PDs. We found a strong relationship between PDs and AAD: Postoperatively, in 46% of patients (n = 28, group PD), a precise clinical syndrome was recognized by the consultant psychiatrists. In group PD, the incidence of postoperative psychiatric complications was 78%. The major PDs were

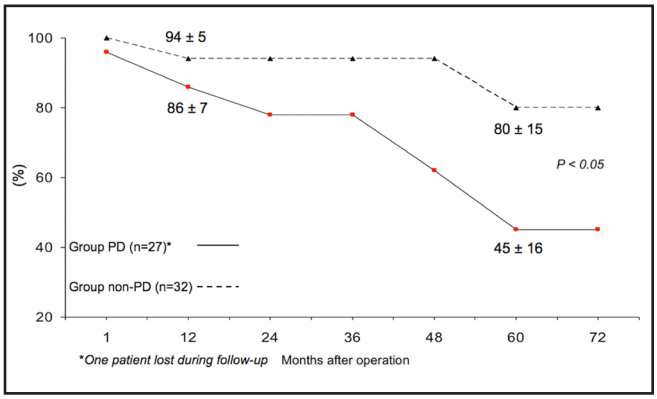

Figure 1. Freedom from psychiatric disorders (PDs) during follow-up (33 ± 25 months) for group PD versus group non-PD.

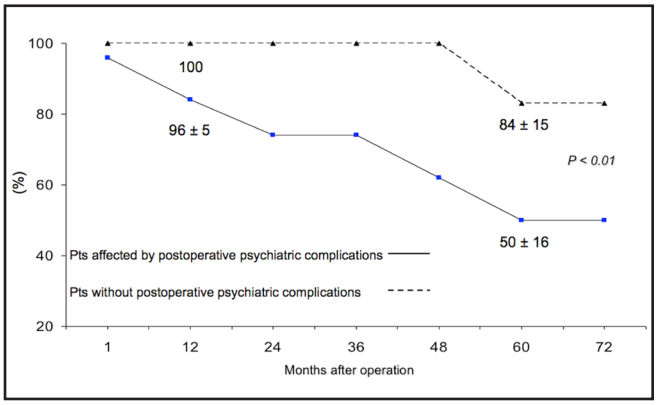

Figure 2. Freedom from psychiatric disorders during follow-up in patients who experienced psychiatric complications postoperatively versus patients without complications.

major depression, anxiety-depressive syndrome, and anxiety status, representing more than 70% of PDs diagnosed in the postoperative period. This incidence of PDs in patients affected by AAD is very high (2-10 times higher) compared with that observed for the general population (4-7%) and in patients with ischemic heart disease (15-30%) [1-3,16,21]. In our clinical practice, for patients affected by cardiac diseases apart from AAD, the need for postoperative psychiatric consultation was rare, i.e, <5% of the patient population admitted at our institution in the last 2-year period.

Moreover, four patients for whom an initial diagnosis of PD was not made post-operatively, developed PD manifestations during follow-up. These findings seem to provide evidence supporting our hypothesis of a strict relationship between AAD and PDs. The mechanisms potentially responsible for the association of PDs with AAD may be related primarily to pathophysiological alterations due to genetic polymorphisms of the autonomic nervous system, as found in the correlation between ischemic heart disease and PDs [11], or secondarily to the fact that psychiatric patients often do not take care of their health and do not control potential risk factors for cardiovascular diseases, i.e, they do not take drugs for the treatment of arterial hypertension. Smith and coworkers found a strong relation between bipolar disorders and cardiometabolic morbidity (e.g., thyroid disorders, chronic pulmonary disease, arterial hypertension, and diabetes mellitus): Patients affected by bipolar disorders were less likely than controls to access primary care to treat hypertension or atrial fibrillation [22]. Similarly, Gladigau and et al. found a strong link between severe mental illness and a high incidence (from 19% to 69%) of several risk factors for cardiovascular disease, such as smoking, obesity, overweight, hypertension, diabetes, dyslipidemia, and metabolic syndrome [21].

In our study, we found a significantly higher incidence of smokers in group PD in comparison with group non-PD (80% vs. 33%); moreover, obesity was more frequent in group PD than in group non-PD (30% vs. 22%, respectively), although this difference was not statistically significant.

During a mid-term follow-up, although freedom from PDs remained significantly related to the presence of PD diagnosed postoperatively (Figures 1 and 2), we observed an important reduction in clinical psychiatric manifestations. In fact, only 10 patients of the 27 patients in group PD (not including the patient lost during follow-up) continued to be affected by PDs. In particular, a significant reduction in psychiatric manifestations was observed at follow-up for depressive or bipolar disorders in comparison with the immediate postoperative findings (2 patients out of 23 at follow-up vs. 19 out of 24 in the postoperative period, $P < 0.001$).

The reason for 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 was the first step in recognizing and treating both cardiovascular risk factors and their psychiatric disease. During the follow-ups, one patient experienced a cerebral stroke, which worsened their pre-existing depression.

Finally, it appears very important to emphasize the complete absence of suicides in this population during the follow-up period. Our preliminary data showed that surgical intervention, albeit in response to a significant trauma, in combination with a proper diagnostic and therapeutic way for controlling psychiatric symptoms, had a positive impact on the psychiatric status in the mid-term period of follow-up.

Limitations of the Study

Our observations relate to a relatively small sample of patients, and the type of study is retrospective. Therefore, further investigation will be needed to corroborate our results. However, it should be noted that the tested sample represented approximately 30% of patients surviving AAD surgery.

Our findings suggest a strong relationship between PDs and AAD. Because the psychiatric conditions appeared to be largely stable after surgery, treatment of AAD for patients affected by PDs represents a first step in detecting psychiatric pathologies and in starting a correct medical therapy to better control mental health. Following these interesting, preliminary results, for a more accurate evaluation of the incidence of PDs in patients affected by AAD, as well as their mental health status during follow-up after cardiac surgery, this study is continuing in a prospective manner.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Frasure-Smith N, Lespérance F, Talajic M. Depression following myocardial infarction. Impact on 6-month survival. JAMA 1993;270:1819-25.
2. Halaris A. Comorbidity between depression and cardiovascular disease. Int Angiol 2009;28:92-9.
3. Pizzi C, Santarella L, Manfrini O, Chiavaroli M, Agushi E, Cordioli E, et al. Ischemic heart disease and depression: An underestimated clinical association. G Ital Cardiol (Rome) 2013;14:526-37.
4. Rumsfeld JS, Ho PM. Depression and cardiovascular disease: A call for recognition. Circulation 2005;111:250-3.
5. Frasure-Smith N, Lespérance F, Talajic M. Depression and 18-month prognosis after myocardial infarction. Circulation 1995;91:999-1005.
6. Lespérance F, Frasure-Smith N, Juneau M, Théroux P. Depression and 1-year prognosis in unstable angina. Arch Intern Med 2000;160:1354-60.
7. Mallik S, Krumholz HM, Lin ZQ, Kasl SV, Mattera JA, Roumains SA, et al.Patients with depressive symptoms have lower health status benefits after coronary artery bypass surgery. Circulation 2005;111:271-7.
8. Pignay-Demaria V, Lespérance F, Demaria RG, Frasure-Smith N, Perrault LP. Depression and anxiety and outcomes of coronary artery bypass surgery. Ann Thorac Surg 2003;75:314-21.
9. Connerney I, Shapiro PA, McLaughlin JS, Bagiella E, Sloan RP. Relation between depression after coronary artery bypass surgery and 12-month outcome: A prospective study. Lancet 2001;358:1766-71.
10. Blumenthal JA, Lett HS, Babyak MA, White W, Smith PK, Mark DB, et al. Depression as a risk factor for mortality after coronary artery bypass surgery. Lancet 2003;362:604-9.
11. Pizzi C, Manzoli L, Mancini S, Bedetti G, Fontana F, Costa GM. Autonomic nervous system, inflammation and preclinical carotid atherosclerosis in depressed subjects with coronary risk factors. Atherosclerosis 2010;212:292-8.
12. Carney RM, Blumenthal JA, Stein PK, Watkins L, Catellier D, Berkman LF, et al. Depression, heart rate variability, and acute myocardial infarction. Circulation 2001;104:2024-8.
13. Murr C, Ledochowski M, Fuchs D. Chronic immune stimulation may link ischemic heart disease with depression. Circulation 2002;105:e83.
14. Eker SS, Akkaya C, Cangur S, Yuvank U, Sarandol A, Kirli S. The effects of reboxetine and venlafaxine on ECG variables in depressed patients. Bull Clin Psychopharmacol 2011;21:11-7.
15. Tsai TT, Nienaber CA, Eagle KA. Acute aortic syndromes. Circulation 2005;112:3802-13.
16. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr, et al. Guidelines for the diagnosis and management of patients with thoracic aorta disease. Circulation 2010;121:e266-369.
17. Daniel JC, Huynh TT, Zhou W, Kougias P, El Sayed HF, Huh J, et al. Acute aortic dissection associated with use of cocaine. J Vasc Surg 2007;46:427-33.
18. Westover AN, Nakonezny PA. Aortic dissection in young adults who abuse amphetamines. Am Heart J 2010;160:315-21.
19. Swalwell CI, Davis GG. Methamphetamine as a risk factor for acute aortic dissection. J Forensic Sci 1999;44:23-6.
20. Shiraishi M, Ohki S, Muraoka A, Aizawa K, Sakano Y, Kaminishi Y, et al. Analysis of perioperative factors for neurological dysfunction in patients with thoracic aortic surgery. Arch Clin Exp Surg 2013;2:141-8.
21. Gladigau EL, Fazio TN, Hannam JP, Dawson LM, Jones SG. Increased cardiovascular risk in patients with severe mental illness. Intern Med J 2014;44:65-9.
22. Smith DJ, Martin D, McLean G, Langan J, Guthrie B, Mercer SW. Multimorbidity in bipolar disorder and undertreatment of cardiovascular disease: a cross sectional study. BMC Med 2013;11:263.