Mechanical prosthetic valve disease is related with an increase in depression and anxiety disorder

Yasemin Turker¹, Kurtulus Ongel², Mehmet Ozaydin³, Yasin Turker⁴, Funda Yildirim Bas⁵, Mehmet Akkaya⁶

¹Family Medicine Center, Duzce, ²University of Katip Celebi, Faculty of Medicine, Department of Family Medicine, İzmir, ³University of Suleyman Demirel, Faculty of Medicine, Department of Cardiology, Isparta, ⁴Duzce University, Faculty of Medicine, Department of Cardiology, Duzce, ⁵University of Suleyman Demirel, Faculty of Medicine, Department of Family Medicine, Isparta, ⁶Bezm-i Alem University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey

ABSTRACT

Aim Patients with organic disease can present with psychiatric symptoms. We hypothesized that since patients with prosthetic heart valve require frequent hospital followup and are at higher risk for complications, the incidence of depression and anxiety is higher in these patients.

Methods This cross-sectional study prospectively studied 98 consecutive patients with mechanical prosthetic heart valve. All patients fulfilled prosthetic heart valve evaluation form, Beck Depression Inventory (BDI) and Hamilton Anxiety Scale (HAS). Complete blood count, basic metabolic panel and echocardiogram results were collected for all the patients.

Results Using the BDI, there were 26 patients (27%) with no depression, 20 (20%) with mild depression, 38 (39%) with moderate, 4 (4%) with severe and 10 (10%) patients with very severe depression. Average score was 18.3±11.4 on BDI and 19.1±11.1 on HAS. The depression level was positively associated with prothrombin time (p<0.001) and international normalized ratio (INR) level (p<0.001). Hamilton Anxiety Scale was significantly correlated with comorbidities (r: 0.344; p=0.002), blood transfusion (r: 0.370; p<0.001), obesity (r: 0.319; p=0.007) and Beck Depression Scale was correlated with comorbidities (r: 0.328; p=0.002), in patients with prosthetic heart valve disease.

Conclusion Patients with prosthetic heart valve have higher prevalence of depression and higher scores of anxiety and depression. Early recognition and appropriate treatment of depression and anxiety may decrease the morbidity in prosthetic heart valve disease. Besides, use of new oral anticoagulant agents that do not need INR check, could decrease anxiety and depression in the future.

Keywords: anxiety, depression, heart valve diseases, comorbidities, prothrombin time, international normalized ratio.
INTRODUCTION

Patients with organic disease can present with psychiatric symptoms. Depression is the most common psychiatric disorder accompanying organic disorders and is a significant clinical syndrome affecting both mortality and morbidity in those patients (1). Among the patients with organic disorders, the prevalence of major depression was found to be 5-10% in inpatients and 9-16% in outpatients (2). Patron et al. found that 48% patients were depressed any time during their life after cardiac surgery (e.g. heart valve surgery, coronary artery bypass graft) (3). Mechanical prosthetic heart valves are commonly used nowadays for the treatment of heart valve diseases with proven utility for increasing life expectancy and quality of life. Patients with prosthetic heart valves constitute 28% of the population with heart valve disease and they need to take anticoagulation therapy lifelong and international normalized ratio (INR) level check at regular intervals. Besides, these patients may develop structural heart disease over time (4).

We hypothesized that since patients with prosthetic heart valve require frequent hospital follow-up and are at higher risk for complications, the incidence of depression and anxiety is higher in these patients.

PATIENTS AND METHODS

Study design

The study was designed as cross-sectional and the patients with mechanical prosthetic heart valve, aged 18 or older, who were admitted to the Cardiology Outpatient Clinic, University of Suleyman Demirel, Faculty of Medicine, between March 2008 and August 2009, were consecutively enrolled. With a tolerance of 5% error, assuming alpha 0.05 and beta 0.20, it was found that 100 patients would be sufficient to detect a significant difference. Patients with mental retardation were excluded and all patients gave informed written consents.

All patients completed prosthetic heart valve evaluation form, Beck Depression Inventory (BDI) and Hamilton Anxiety Scale (HAS). In prosthetic heart valve evaluation form the data including patient’s age, gender, type of prosthetic valve, procedure date, need for repeated procedure, smoking status, comorbidities (hypertension, obesity, diabetes, chronic renal failure), history of bleeding, transfusion, cerebrovascular accident, myocardial infarction, congestive heart failure, pulmonary disease or gastrointestinal disease were collected. Patients’ recent complete blood count, basic metabolic panel and echocardiogram results were collected too.

Beck Depression Inventory

The Beck Depression Scale (BDS) is one of the most common scales used for assessment of mood disorders and depression, created by Aaron Beck in 1961 (5). It consists of 21 questions, 15 for emotional and 6 for somatic symptoms and filled by the patient. In BDS, scoring ranges from 0-3 on each question. The total score is calculated by summation of all the patient’s responses, so the maximum possible sum is a score of 63. Higher scores on the scale indicate a greater level of depressive symptoms, BDS 0-11 indicates no depression, 12-26 mild depression, 17-29 moderate depression, 30-39 severe depression and above 40 indicates very severe depression (5).

Hamilton Anxiety Scale

The Hamilton Anxiety Scale measures the severity of anxiety level and symptom distribution. It is a 14-item test including mood and somatic symptoms administered by an interviewer. Each item is rated on a five-point Likert-type scale ranging from 0-4, so the sum of the score range is between 0-56. The patients must complete the test within 72 hours from the admission (6).

The study protocol was approved by the Ethics Committee of Suleyman Demirel University and all subject signed written consent forms.

Statistical analysis

Measured values are reported as mean ± standard deviation (minimum-maximum values). One-way ANOVA, Kruskal Wallis, chi-square test and student test were used to compare group differences where appropriate. Spearman correlation test was used to identify correlation between continuous variables. Differences were considered significant at a p value of < 0.05.

RESULTS

In the study 98 patients (54% males, n=53) with prosthetic heart valve presenting to Cardiology Outpatient Clinic were enrolled. The past dura-
of the surgery for heart valve was 7.89 ± 5.7 years (1-25 year) before they were included into the study (Table 1). According to the BDS, there were 26 (27%) patients with no depression, 20 (20%) with mild depression, 38 (39%) with moderate, four (4%) with severe and 10 (10%) patients with very severe depression. Average score was 18.3 ± 11.4 on BDS and 19.1 ± 11.1 on HAS.

Table 1. Characteristics of study participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No (%) of patients/value at current visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>98</td>
</tr>
<tr>
<td>Age, years</td>
<td>53.6±10.9</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>54 (54.5)</td>
</tr>
<tr>
<td>AVR</td>
<td>10 (10%)</td>
</tr>
<tr>
<td>MVR</td>
<td>75 (77%)</td>
</tr>
<tr>
<td>AVR and MVR</td>
<td>13 (13%)</td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td>18.3±11.4</td>
</tr>
<tr>
<td>No depression</td>
<td>26 (27)</td>
</tr>
<tr>
<td>Mild depression</td>
<td>20 (20%)</td>
</tr>
<tr>
<td>Moderate depression</td>
<td>38 (39%)</td>
</tr>
<tr>
<td>Severe depression</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Very severe depression</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Hamilton Anxiety Scale</td>
<td>19.1±11.1</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>3 (3)</td>
</tr>
<tr>
<td>CHF</td>
<td>2 (2)</td>
</tr>
<tr>
<td>COAH</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>19 (19.4)</td>
</tr>
<tr>
<td>Gingival bleeding</td>
<td>15 (15.3)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>8 (8%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>29 (30%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8 (8%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>9 (9)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>26 (26.5)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>19 (19.4)</td>
</tr>
<tr>
<td>Atrial flutter</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Premature atrial contraction</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Premature ventricular contraction</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

AVR, aort valve replacement; MVR, mitral valve replacement; COAH, chronic obstructive pulmonary disease; CHF, congestive heart failure.

Of those 98 patients, eight (8%) were 33-40, 31 (31%) 41-50, 36 (37%) 51-60, 13 (13%) 61-70 and 10 (10%) were 71-80 years of age. A comparison of patients by age groups did not show difference for either BDS (p=0.520) or HAS (p=0.469).

Medical history of the patients was significant for cerebrovascular accident in three (3%) patients, congestive heart failure and chronic obstructive pulmonary disease in two (2%) patients each. Four patients had gastrointestinal bleeding, 19 had epistaxis and 15 patients had gingival bleeding after the surgery. Eight patients had received blood transfusion due to anemia or bleeding. Among the cardiac risk factors, hypertension was present in 29 (30%) patients, diabetes mellitus in eight (8%) and obesity in nine (9%) patients. Arrhythmia was detected in 26 patients, 19 had atrial fibrillation, one had atrial flutter, five had premature atrial contraction and one had premature ventricular contraction.

Table 2 showed the comparison between depression level on BDS and patients complete blood count (CBC), coagulation parameters, fasting glucose, renal function test and echocardiographic findings. The depression level was positively correlated with prothrombin time and INR level. Prothrombin time was longer than expected in patients with mild and moderate depression (36±12.4 vs. 39±11.7, respectively), whereas it was shorter than expected in patients with very severe depression (21.8±8.2) (Table 2). Patients with severe depression were also found to have lower than expected INR levels (Table 2). However, BDS was not significantly correlated with prothrombin time (p=0.446) and INR (p=0.919) (in correlation analysis).

Table 2. Comparison between depression level and laboratory and echocardiographic data

<table>
<thead>
<tr>
<th>Depression level</th>
<th>Hb (g/dL)</th>
<th>Glucose (mg/dL)</th>
<th>PT (sec)</th>
<th>INR</th>
<th>BUN (mg/dL)</th>
<th>Cr (mg/dL)</th>
<th>EF (%)</th>
<th>LA (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (n = 26)</td>
<td>12.6 ± 1.6</td>
<td>108 ± 71</td>
<td>37.5 ± 8.6</td>
<td>2.64 ± 8.6</td>
<td>215 ± 6.1</td>
<td>6.19 ± 3.3</td>
<td>60.3 ± 2.5</td>
<td>44.9 ± 5.9</td>
</tr>
<tr>
<td>Mild (n = 20)</td>
<td>13.1 ± 1.0</td>
<td>90 ± 11</td>
<td>36 ± 2.0</td>
<td>2.09 ± 2.0</td>
<td>172 ± 3.6</td>
<td>3.3 ± 6.4</td>
<td>54.5 ± 2.0</td>
<td>44.5 ± 4.5</td>
</tr>
<tr>
<td>Moderate (n = 38)</td>
<td>13.3 ± 1.3</td>
<td>93 ± 1.7</td>
<td>39 ± 1.7</td>
<td>3.19 ± 2.5</td>
<td>211 ± 6.9</td>
<td>6.4 ± 6.9</td>
<td>58.4 ± 2.5</td>
<td>46.3 ± 4.7</td>
</tr>
<tr>
<td>Severe (n = 4)</td>
<td>13 ± 1.2</td>
<td>96 ± 1.7</td>
<td>28.5 ± 2.1</td>
<td>3.3 ± 2.0</td>
<td>17 ± 1.7</td>
<td>6.9 ± 4.6</td>
<td>62.5 ± 2.5</td>
<td>47 ± 1.7</td>
</tr>
<tr>
<td>Very severe (n = 10)</td>
<td>108 ± 2.0</td>
<td>21.8 ± &lt; 5.8</td>
<td>21.8 ± &lt; 5.8</td>
<td>6.1 ± 0.9</td>
<td>1.7 ± 0.3</td>
<td>4.04 ± 0.9</td>
<td>8.2 ± 0.04</td>
<td>41.2 ± 1.7</td>
</tr>
<tr>
<td>p</td>
<td>0.462</td>
<td>0.474</td>
<td>&lt;</td>
<td>0.001</td>
<td>0.535</td>
<td>0.021</td>
<td>0.001</td>
<td>0.110</td>
</tr>
</tbody>
</table>

EF, ejection fraction; Hb, hemoglobin; INR, international normalized ratio; LA, left atrium diameter; PT, prothrombin time; Cr, creatinine.

The depression levels were also compared with patients’ demographic and clinical features (Table 3). Patients with comorbidities accompanying prosthetic heart valve had more advanced degree of depression (p=0.005). Similarly, chronic gastrointestinal disease was correlated with very severe stage of depression (p=0.001). Other parameters did not show significant difference.

Patients with chronic diseases accompanying prosthetic heart valve were more depressive according to BDS (22.5 ± 13.3 vs. 14.9 ± 7.9;
p = 0.001) and more anxious according to HAS (23.2 ± 11.7 vs. 15.0 ± 9.4; p = 0.001) than patients without comorbidities. The presence of hypertension was associated with higher scores for both depression (24.9 ± 10.2 vs. 16.7 ± 10.6; p = 0.01) and anxiety (24.9 ± 10.2 vs. 16.7 ± 10.6; p = 0.01). There was no significant difference between patients with and without diabetes for depression (p=0.272) and anxiety (p = 0.842). Gender difference, history of repeat procedure, cerebrovascular accident, congestive heart failure and smoking status were also not in correlation to depression and anxiety.

History of bleeding by itself was not associated with depression and anxiety. However, while depression score was not different between patients with and without blood transfusion (p=0.235) due to anemia or bleeding, patients with transfusion history were more anxious (32 ± 4.2 vs. 17.9 ± 10.8; p < 0.001). Similarly patients with obesity were more anxious than non-obese ones (27.77 ± 7.83 vs. 18.24 ± 11.09; p=0.014).

Patients with arrhythmia had similar depression scores compared to the patients without arrhythmia. Although the difference did not reach statistical significance, patients with arrhythmia tended to be more anxious than those without it (22.7 ± 12.7 vs. 17.8 ± 10.2; p=0.054). The presence of gastrointestinal disease in the patients was correlated with both high depression (45 ± 10.0 vs. 17.8 ± 10.8; p=0.001) and anxiety (39 ± 10.0 vs. 18.7 ± 10.8; p=0.01) scores.

The Hamilton Anxiety Scale was significantly correlated with comorbidities (r: 0.344; p=0.002), blood transfusion (r: 0.370; p<0.001), obesity (r: 0.319; p=0.007) and the Beck Depression Scale (r: 0.660; p<0.001) in patients with prosthetic heart valve disease. The Beck Depression Scale was correlated with comorbidities (r: 0.328; p = 0.002) in patients with prosthetic heart valve disease. The Hamilton Anxiety Scale was not significantly correlated with PT (p=0.423) and INR (p =0.789).

The type of heart valve surgery were aortic valve replacement (AVR) for 10 (10%) patients, mitral valve replacement (MVR) for 75 (77%) patients and both AVR and MVR for 13 (13%) patients. Table 4 showed the comparison between type of heart valve surgery and clinic and laboratory data. There were no significant differences in HAS, depression level and BDS between AVR, MVR and AVR and MVR.

**DISCUSSION**

In the present study, the level of depression and anxiety in patients with prosthetic heart valve and its relationship with the demographic and clinical features was investigated. A significant association between depression level and prothrombin and INR levels was found. The level of depression was more severe in patients having comorbidities and gastrointestinal disease. Besides, hypertensive patients were more anxious and depressive compared to non-hypertensive ones. Patients who had blood transfusion and obesity were more anxious.

Chronic diseases are long-term diseases that may cause psychiatric problems in their course (7-9).
Depression and anxiety disorder are the most common psychiatric diseases occurring in patients with somatic diseases and they usually coexist (10). Worsening in the quality of life, functional disability and direct biological effects of organic diseases are the main reasons for development of depression (11). Several studies have reported increased prevalence of depression and anxiety in patients with chronic disease as compared to patients without chronic disease (12-16). It was determined that patients undergoing heart operation experienced such physical and psychological problems as decrease in appetite, sleep disturbances, fatigue and activity intolerance, anxiety and depression within six months of being discharged (17). In our study, 27% of the patients with prosthetic heart valve did not have depression measured by the Beck Depression Inventory. In a study done by Bahar et al., age was reported to be correlated with higher anxiety and depression scores (15). On the contrary, Munir et al. found that majority of patients with anxiety and depression were aged between 20-49 years (18). In the present study, we did not find significant difference in neither the Beck Depression Inventory nor Hamilton Anxiety Scale by patient’s age.

Female gender has been shown to be a risk factor for the development of depression. Some studies have demonstrated that women have higher average depression scores than males (19-20). Gilmour et al. found that females with depression had a higher risk for the development of heart disease while males did not (21).

The relationship between psychiatric disorders and irritable bowel syndrome has been subject of interest for a long time (22). It has been shown that patients with irritable bowel syndrome have a higher incidence of depression and anxiety disorder (23). In addition, patients with depression have also been reported to have higher incidence of gastrointestinal disease (24). Coexistence of depression and irritable bowel syndrome has been attributed to increased sympathetic activity. Our results are in accordance with previous studies, showing that patients with gastrointestinal diseases were more depressive and anxious. These patients were also more likely to be in “very severe depression group” in the Beck Depression Inventory groups.

This study demonstrated a significant relationship between the depression levels and the prothrombin time and INR levels. Longer prothrombin time than expected in patients with mild and moderate depression was found, whereas it was shorter than expected in patients with severe depression. Additionally, INR levels were lower than expected in the very severe depression group. These findings may indicate that patients with more depression and anxiety have lower sense of responsibility to protect themselves from possible complications that may occur due to prosthetic heart valve disease. It is reasonable to think that these patients do not have regular prothrombin time and INR check and hence cannot reach target values.

In the present study, the prevalence of depression and anxiety was higher in patients with comorbidities accompanying prosthetic heart valve disease. Besides, the level of depression was more severe in these patients compared to patients without comorbidities. Patients with chronic diseases are known to be more depressive and anxious (13,15,16). Since the study participants had chronic heart disease, comorbidities with this challenging heart problem make them more depressive and anxious.

A meta-analysis reported a significantly higher risk for the development of hypertension in patients with high psychological stress levels. Moreover, it was claimed that this risk is comparable to well-known risk factors for the development of hypertension such as obesity and lack of physical activity (25). Supporting the literature, patients with hypertension in this study were more depressive than without hypertension using the Beck Depression Inventory. The Hamilton Scale anxiety scores were also higher in patients with hypertension.

Patients requiring blood transfusion following bleeding or due to anemia experienced intense anxiety in this study. Since patients with prosthetic heart valve need frequent follow-ups over a long period of time, the need for admission to the hospital for blood transfusion probably makes them more aggressive and anxious.

Several studies have demonstrated high prevalence of depression and anxiety in patients with obesity (26,27) pointing that in obese individuals, impaired body image and body dissatisfaction were observed, which might contribute to the development of anxiety and depression in this population. However, no correlation was reported between obesity and a level of anxiety and depression. In our study, there was no difference in respect to depression between obese and non-
obese patients whereas obese patients were found to feel more anxious.

Prevalence of anxiety and depression is very common in patients with ischemic heart disease (28). Persistent symptoms of anxiety and depression increased substantially the risk of death in patients with ischemic heart disease (29). Patients with organic disease with major depressive disorder have longer in-hospital stays, fail to comply with treatment of the disease and medication they are prescribed, and have increased mortality and morbidity rates. Similar correlation is also found in patients with anxiety. Van Hout et al. reported that presence of anxiety disorder increases mortality in men, however, mortality in women is not increased (30). Garfield et al. reported that anxiety disorders, major depressive disorder, and co-occurring anxiety and major depressive disorder are associated with incident heart failure in large cohort (31).

The depression and anxiety scores were not significantly different among the prosthetic valve type in this study. Relatively lower depression and anxiety detection in patients with both AVR and MVR may be associated with their younger age.

There are several limitations of the present study. The number of patients across the different depression categories is unbalanced (only four patients in severe depression), therefore, a more balanced sample size across the depression categories would potentially allow for more robust comparison between these groups. The other limitation of study was that there was no control group of healthy individuals. Finally, patients did not have pre-surgery measurements of depression and anxiety level to compare the difference between pre and post surgery changes.

In conclusion, it is crucial to identify depression and anxiety disorders of the patients with mechanical prosthetic valve disease, which can play an important role in treatment planning, and helps physicians predict the indication for treatment modalities and good long-term outcomes. Early recognition and appropriate treatment of depression and anxiety may decrease the morbidity in prosthetic heart valve disease. Besides, use of new oral anticoagulant agents that do not need INR check, could decrease anxiety and depression in the future.

FUNDING

No specific funding was received for this study.

TRANSPARENCY DECLARATIONS

Competing interest; none to declare.

REFERENCES