Anxiety and depression in cardiac surgery: sex and age range differences

Ansiedade e depressão em cirurgia cardíaca: diferenças entre sexo e faixa etária

La ansiedad y la depresión en la cirugía cardíaca: diferencias entre género y edad

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ABSTRACT

Objective: To investigate the association between anxiety and depression symptoms and sex and age among preoperative patients submitted to their first cardiac surgery. Methods: This is a correlational cross-sectional study, with 84 participants. The Hospital Anxiety and Depression Scale was used. Student's t-test for independent samples (sex), ANOVA (age group), and linear regression analysis were used, with a significance level of 5%. Results: Women had more anxiety and depression symptoms, with higher mean values and statistically significant differences ($p = 0.007$ and $p = 0.001$). In the regression analysis, sex was significant in the model ($p = 0.011$). Considering age, the differences regarding the presence of these symptoms were not statistically significant, either in ANOVA or in the regression analysis. Conclusion: Women had more anxiety and depression symptoms in the preoperative period of cardiac surgeries. Nurses should consider these results during the educational plan preparation for surgical patients.

Keywords: Perioperative nursing; Anxiety; Depression; Thoracic surgery.

RESUMO

Objetivo: Verificar a relação dos sintomas de ansiedade e depressão com o sexo e a idade de pacientes em pré-operatório de primeira cirurgia cardíaca. Métodos: Estudo correlacional, transversal, com 84 participantes. Utilizada a Escala Hospitalar de Ansiedade e Depressão. Realizado o teste t de Student para amostras independentes (sexo), ANOVA (idade agrupada) e análises de regressões lineares, com nível de significância de 5%. Resultados: As mulheres apresentaram mais sintomas de ansiedade e de depressão, com maiores médias e diferenças estatisticamente significantes ($p = 0.007$ e $p = 0.001$). Na análise de regressão, o sexo foi significativo no modelo ($p = 0.011$). Considerando-se a idade, as diferenças encontradas em relação à presença desses sintomas não foram estatisticamente significantes, tanto na ANOVA quanto na regressão. Conclusão: As mulheres apresentaram mais sintomas de ansiedade e de depressão no pré-operatório de cirurgias cardíacas. Esses dados devem ser considerados pelos enfermeiros ao elaborarem os planos de educação do paciente cirúrgico.

Palavras-chave: Enfermagem perioratória; Ansiedade; Depressão; Cirurgia Torácica.

RESUMEN

Objetivo: Investigar la relación de los síntomas de ansiedad y depresión con el sexo y la edad de pacientes en preoperatorio de la primera cirugía cardíaca. Métodos: Estudio correlacional, transversal, con 84 participantes. Fue utilizada la Escala Hospitalaria de Ansiedad y Depresión. Se ha realizado el teste t de Student para muestras independientes (sexo), ANOVA (edad agrupada) y análisis de regresiones lineales, con nivel de significación del 5%. Resultados: Las mujeres presentaron más síntomas de ansiedad y depresión, con mayores promedios y diferencias estadísticamente significantes ($p = 0.007$ y $p = 0.001$). En el análisis de regresión, el género fue significativo en el modelo ($p = 0.011$). Considerando la edad, las diferencias no fueron estadísticamente significantes, tanto en ANOVA, como en la regresión. Conclusión: Las mujeres presentaron más síntomas de ansiedad y depresión en el preoperatorio de cirugías cardíacas. Estos datos deben ser considerados por los enfermeros en los planes de educación del paciente quirúrgico.

Palabras clave: Enfermería Preoperatoria; Ansiedad; Depresión; Cirugía Torácica.

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INTRODUCTION

Cardiovascular diseases (CVDs) are the main cause of morbimortality in developed and developing countries. In 2008, more than 17 million deaths were due to CVDs, accounting for 30% of all deaths reported in the same period.

With progress in health technologies, many patients have their CVDs treated using minimally invasive approaches. However, some patients are still submitted to cardiac surgery, considered in many cases the only treatment option available.

Despite its potentially favorable outcome, patients waiting for cardiac surgery may feel important psychological affliction, many times resulting from fear and uncertainty related to the surgery.

In addition to the physical stressors such as the anesthesia procedure itself, patients are also exposed to psychological stressors and may show anxiety and depression symptoms.

Several studies have highlighted the importance of evaluating psycho-emotional stressors in patients waiting for cardiac surgery. Some showed a strong association between anxiety and depression symptoms and postoperative recovery from cardiac surgeries.

Anxiety and depression symptoms may cause hemodynamic alteration in the patient in the pre- and postoperative periods around cardiac surgeries, negatively affecting physiological parameters, with an impact on patient recovery.

Studies have shown a difference in the incidence of anxiety and depression symptoms in relation to sex and age. Sex was reported as a significant predictor for anxiety and depression symptoms, regardless of complicating factors such as age, marital status, education, and type of surgery.

Some studies were conducted to describe and correlate perioperative anxiety and depression symptoms in cardiac surgery patients with socio-demographic and medical variables. However, these studies only addressed patients submitted to surgical myocardial revascularization. The national and international literature presents few studies whose aim was to investigate and correlate anxiety and depression symptoms with socio-demographic and medical characteristics in patients submitted to other types of cardiac surgeries, such as valve repair.

Based on the considerations above, this study aimed to analyze the relation between the anxiety and depression symptoms and the sex and age of patients waiting for their first myocardial revascularization surgery and valve repair procedure.

METHODS

This was a correlational cross-sectional study, conducted in a university hospital in the country region of the State of São Paulo.

A consecutive and non-probability sample was comprised of subjects of both sexes, over 18 years of age, who were submitted to their first surgical myocardial revascularization and/or valve repair procedure (insertion or replacement), and who had an elective scheduling of their surgeries, between August 2013 and August 2014.

The exclusion criteria were: patients who did not present cognitive conditions to answer the questionnaires, as evaluated through the Mini-Mental State Examination (MMSE), in its adapted version in Portuguese; patients who presented clinical decompensation of cardiac disease on the day that the data were collected (presence of dyspnea, precordial pain, and/or orotracheal intubation); and patients with elective scheduling of surgery less than 12 hours in advance.

A data collection instrument was developed for participant characterization. Face and content validation were conducted for this instrument by a committee of four judges with vast experience in cardiology and cardiovascular surgery.

Each of the judges was asked to evaluate all instrument items in terms of pertinence (whether the items expressed a true relation with the study proposal) and clarity (whether the items were described in an understandable manner). If a judge evaluated an item as "not clear" or "not pertinent", there was a field for suggestions and a field to add new items.

As a result of the validation, the inclusion of the following variables was recommended: "Family monthly income (in BRL)" and "field to describe all medications prescribed on the day of data collection for subsequent analysis of psychotropic medication use."

The validated instrument was comprised of socio-demographic variables (birth date, sex, school attainment in completed grades, marital status, performance of remunerated activities, and family monthly income), and medical variables (admission date, preoperative comorbidity, prior surgery, and use of psychotropic medication during hospitalization).

The following variables: birth date; sex; admission date; preoperative comorbidity; prior surgery; and use of psychotropic medication during hospitalization were collected from medical records, while school attainment in concluded grades, marital status, performance of remunerated activities, and family monthly income were collected through individual interviews with the participants.

The participant age was calculated by subtracting the birth date from the interview date. Then, the age was categorized into five age groups: 18 to 44.9 years; 45 to 54.9 years; 55 to 64.9 years; 65 to 74.9 years; and above 75 years.

The use of psychotropic medications during hospitalization was investigated due to their potential impact on participant assessment in terms of perception of anxiety and depression symptoms.

The Hospital Anxiety and Depression Scale (HADS), in its adapted version in Portuguese, was used to evaluate the preoperative anxiety and depression symptoms. HADS was selected for being a reliable, validated, and convenient instrument to evaluate anxiety and depression symptoms,
RESULTS

In total, 137 patients were submitted to cardiac surgeries during the data collection period; 84 of these patients met the inclusion criteria and were included in the study. Table 1 shows the socio-demographic and medical data of patients, disaggregated by sex.

When comparing the study participants according to sex, no statistically significant difference was observed between male and female patients when evaluating, respectively, mean age (60 versus 56.4 years, \( p = 0.199 \)), school attainment (5.3 versus 4.9 years, \( p = 0.669 \)), and monthly income (BRL 2,296 versus 1,797, \( p = 0.400 \)).

Most participants from both groups were married. Before surgery admission, there were more active men than women, and this difference was statistically significant (\( p = 0.006 \)). Another statistically significant difference found between the groups was the use of preoperative psychotropic medication, more frequent among women than men (\( p = 0.028 \)). Women also presented arterial hypertension, dyslipidemia, overweight/obesity, and diabetes mellitus with higher frequency; however, these differences were not statistically significant (Table 1).

Table 2 shows the mean and standard deviation values of anxiety and depression symptoms, according to sex and group age.

Women presented higher mean values than men for both anxiety and depression symptoms, and these differences were statistically significant. Regarding the age group, the participants from the group of 55 to 64.9 years presented higher mean values for anxiety symptoms, followed by the group of 18 to 44.9 years, while the group of 65 to 74.9 years presented higher mean values for depression symptoms, also followed by the group of 18 to 44.9 years; however, these differences were not statistically significant.

Tables 3 and 4 show the results from the multiple linear regression analyses using as variables the responses to measurements of anxiety and depression symptoms, respectively. Regarding the relations between the variables sex and anxiety symptoms (\( p = 0.007 \)) and sex and depression symptoms (\( p = 0.001 \)), the results were statistically significant for both. The multiple linear regression model, when investigating the relation of anxiety symptoms with sex and age, was statistically significant (\( p = 0.017 \)). The two variables explained only 0.073 (7.3%) of the variance of measurement of anxiety symptoms, and sex was the only statistically significant variable in the model (\( p = 0.011 \)) (Table 3). The interpretation of this result is that one male participant would present, on average, minus 2.487 in relation to a female participant, regardless of their age, report their emotions in different ways. Then, we decided to keep the variable sex, regardless of the results from the bivariate analyses. We decided to develop a model using the forward method, in which the variables are inserted in the model one by one, according to their significance - that is, the variable sex first, then the variable age. Significance for this study was set at 5%.

The study development observed national and international ethical standards in research involving human beings. The research project was designed according to the ethical principles from the CNS Resolution 466/12, approved by the Research Ethics Committee from the Ribeirão Preto College of Nursing at the University of São Paulo (EERP-USP), on July 29, 2013, under protocol nº 191/2013.

and because it has been used in patients submitted to cardiac surgery\(^{6,7,13-15}\).

The HADS has 14 questions, seven of which evaluate the anxiety symptoms (HADS-Anxiety) and seven evaluate the depression symptoms (HADS-Depression). The scores of answers provided to each item vary from 0 to 3 and the sum from each subscale may vary from 0 to 21, where higher values indicate greater presence of anxiety and depression symptoms. These data were collected through individual interviews with the participants during hospitalization the day before the cardiac surgery.

Data analysis used the Statistical Package Social Science (SPSS), version 17.0, for Windows. A descriptive analysis was conducted for all variables.

The comparison of socio-demographic and medical characteristics of patients, disaggregated by sex, used Student's \( t \)-test for independent samples (age, family income, and school attainment) and the chi-square test (marital status, employment situation, and co-morbidity). Fisher's exact test was used with results presenting a frequency below 5, obtained from the 2x2 Contingency Tables (professionally active and use of preoperative psychotropic medications).

The comparison of mean values of anxiety and depression symptoms, as evaluated through HADS, used the Student's \( t \)-test for independent samples (sex) and ANOVA (age group).

Through the multiple linear regression technique, two analyses were conducted to investigate the relation between anxiety (dependent variable) and sex (independent variable, nominal and dichotomous) and age (independent variable, numeric) of patients, and the relation between depression (dependent variable) and sex (independent variable, nominal and dichotomous) and age (independent variable, numeric) of patients. Before conducting these analyses, we tested the possible multicollinearity between the variables that would be inserted in the adjustment of models. Although the bivariate analysis between sex and age did not identify a statistically significant difference between the groups (male and female patients), several studies have indicated women and men, regardless of their age, report their emotions in different ways. Then, we decided to keep the variable sex, regardless of the results from the bivariate analyses. We decided to develop a model using the forward method, in which the variables are inserted in the model one by one, according to their significance - that is, the variable sex first, then the variable age. Significance for this study was set at 5%.

The study development observed national and international ethical standards in research involving human beings. The research project was designed according to the ethical principles from the CNS Resolution 466/12, approved by the Research Ethics Committee from the Ribeirão Preto College of Nursing at the University of São Paulo (EERP-USP), on July 29, 2013, under protocol nº 191/2013.
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**Table 1.** Socio-demographic and medical data of patients, disaggregated by sex

<table>
<thead>
<tr>
<th>Variables</th>
<th>Male (n = 53)</th>
<th>Female (n = 31)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n)</td>
<td>% (n)</td>
<td></td>
</tr>
<tr>
<td>Married/consensual union</td>
<td>79.2 (42)</td>
<td>58.1 (18)</td>
<td>0.176**</td>
</tr>
<tr>
<td>Professionally active</td>
<td>37.7 (20)</td>
<td>9.7 (3)</td>
<td>0.006‡</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-44.9</td>
<td>11.3 (6)</td>
<td>19.4 (6)</td>
<td></td>
</tr>
<tr>
<td>45-54.9</td>
<td>22.6 (12)</td>
<td>19.4 (6)</td>
<td></td>
</tr>
<tr>
<td>55-64.9</td>
<td>35.8 (19)</td>
<td>41.9 (13)</td>
<td>0.722**</td>
</tr>
<tr>
<td>65-74.9</td>
<td>18.9 (10)</td>
<td>12.9 (4)</td>
<td></td>
</tr>
<tr>
<td>≥ 75</td>
<td>11.3 (6)</td>
<td>6.5 (2)</td>
<td></td>
</tr>
<tr>
<td>Presence of comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic arterial hypertension</td>
<td>64.2 (34)</td>
<td>74.2 (23)</td>
<td>0.342**</td>
</tr>
<tr>
<td>Smoking</td>
<td>62.3 (33)</td>
<td>61.3 (19)</td>
<td>0.929**</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>52.8 (28)</td>
<td>54.8 (17)</td>
<td>0.859**</td>
</tr>
<tr>
<td>Overweight/obesity</td>
<td>47.2 (25)</td>
<td>67.6 (21)</td>
<td>0.068**</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>35.8 (19)</td>
<td>41.9 (13)</td>
<td>0.579**</td>
</tr>
<tr>
<td>Surgery conducted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve repair</td>
<td>50.9 (27)</td>
<td>48.4 (15)</td>
<td></td>
</tr>
<tr>
<td>Myocardial revascularization</td>
<td>43.4 (23)</td>
<td>45.2 (14)</td>
<td>0.970**</td>
</tr>
<tr>
<td>Valve repair + myocardial revascularization</td>
<td>5.7 (3)</td>
<td>6.5 (2)</td>
<td></td>
</tr>
<tr>
<td>Use of preoperative psychotropic medication</td>
<td>7.5 (4)</td>
<td>25.8 (8)</td>
<td>0.028‡</td>
</tr>
</tbody>
</table>

**Chi-square test; ‡ Fisher’s exact test.**

**Table 2.** Distribution of mean values obtained from subscales of anxiety and depression symptoms, according to sex and age group

<table>
<thead>
<tr>
<th>Variables</th>
<th>HADS - Anxiety Mean (SD)</th>
<th>HADS - Depression Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (n = 31)</td>
<td>7.3 (4.9)</td>
<td>6.2 (4.9)</td>
</tr>
<tr>
<td>Male (n = 53)</td>
<td>4.7 (3.6)</td>
<td>3.3 (3.1)</td>
</tr>
<tr>
<td>p*</td>
<td>0.007</td>
<td>0.001</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-44.9 (n = 12)</td>
<td>6.5 (4.3)</td>
<td>4.8 (4.8)</td>
</tr>
<tr>
<td>45-54.9 (n = 18)</td>
<td>4.9 (2.6)</td>
<td>4.7 (5.0)</td>
</tr>
<tr>
<td>55-64.9 (n = 32)</td>
<td>7.0 (4.8)</td>
<td>3.7 (3.6)</td>
</tr>
<tr>
<td>65-74.9 (n = 14)</td>
<td>3.6 (3.1)</td>
<td>5.1 (4.2)</td>
</tr>
<tr>
<td>≥ 75 years (n = 08)</td>
<td>4.7 (5.7)</td>
<td>4.0 (3.0)</td>
</tr>
<tr>
<td>p**</td>
<td>0.104</td>
<td>0.832</td>
</tr>
</tbody>
</table>

SD: standard deviation; * Student’s t-test for independent samples; ** ANOVA.

provided a similar result to that from anxiety symptoms. Sex and age explained 0.098 (9.8%) of the variance of the measurement of depression symptoms. The variable sex remained statistically significant (p = 0.002) (Table 4). Similar to the previous interpretation, one male participant would present, on average, minus 2.933 in relation to a female participant of the same age in the measurement of depression symptoms. In the measurement of depression symptoms used in this study, higher scores in a 0-21 range indicate a greater presence of this symptom; thus, we concluded that men from the studied group presented on average 2.9 fewer symptoms than women.

**DISCUSSION**

In this study, women presented more anxiety and depression symptoms in the preoperative period of cardiac surgeries than men, with statistically significant differences. These results agree with those obtained by other studies found in the literature²,₁₆,₁₇. In a study conducted in Iran, women presented more anxiety symptoms in the preoperative period of cardiac surgeries than men (168 women and 132 men)⁵.
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A study conducted in Brazil showed that women presented more depression symptoms in the preoperative period of myocardial revascularization than men (24 women and 34 men)\textsuperscript{16}. Another study conducted with patients in the preoperative period of myocardial revascularization also showed women with more depression symptoms than men (65 women and 72 men)\textsuperscript{17}. The reasons that could explain a higher prevalence of anxiety and depression symptoms among women are still unknown and should be further investigated. However, some possible explanations have been discussed. Some authors suggested the factors that could contribute to these differences between men and women include biological factors, such as the influence of female sex hormones, and psychosocial factors, for instance, women’s multiple roles due to recent changes in society\textsuperscript{18}. Another study showed that women presented with more concern about their diseases, while men more often denied any stress associated with the surgery\textsuperscript{4}. Then, another possible reason for the higher prevalence of these symptoms among women would be their ability to express feelings. Women received psychotropic medication in the preoperative period more often than men, 25.8% and 7.5%, respectively, and this difference was statistically significant. These results agree with those of a study conducted with 3,692 patients submitted to cardiac surgeries, which shows a significantly higher number of women in the group of patients who received antidepressants\textsuperscript{19}. They also showed that 10.5% of women received antidepressants in the preoperative period versus only 5.1% of men\textsuperscript{19}. Considering that women presented with more anxiety and depression symptoms than men, and despite the greater consumption of psychotropic medication among women, some authors discuss probable differences in the absorption, bioavailability, and distribution of psychotropic medication in relation to sex\textsuperscript{19}. They also suggest these differences may play an important role in the development of treatment methods for women with anxiety disorders in the future\textsuperscript{19}. Regarding the presence of anxiety symptoms according to different age groups, patients between 55 to 64.9 years presented more symptoms, while patients between 65 to 74.9 years reported fewer symptoms. With regard to depression symptoms, patients between 65 to 74.9 years presented more symptoms, while patients between 55 to 64.9 years reported fewer symptoms; however, these differences were not statistically significant. Although these differences were not statistically significant, it is important to have this discussion, once it refers to the response of the study objective. A similar result was obtained by two other studies, which showed younger patients, between 36 and 60 years\textsuperscript{20} and below 65 years of age\textsuperscript{18} with higher levels of anxiety in the preoperative period. On the other hand, other studies observed a higher risk of depression among both younger patients\textsuperscript{21} and patients of less than 65 years\textsuperscript{17}, which was not observed in our results. The literature did not contain studies investigating the relation of anxiety and depression symptoms in the preoperative period with sex and age concomitantly, which does not allow to compare the linear regression results. In the regression model for anxiety symptoms, sex and age accounted for as low as 7.3% of the measurement variance, while in the regression model for depression symptoms these variables accounted for 9.8% of the measurement variance. These results should be taken into account when investigating other factors related to the presence of these symptoms in the preoperative period of cardiac surgeries. Anxiety and depression symptoms are known to aggravate heart diseases\textsuperscript{1}. Studies have shown the relation of preoperative anxiety and depression symptoms with increased postoperative complications\textsuperscript{21}, frequent rehospitalization\textsuperscript{21}, long postoperative length of stay\textsuperscript{3}, significant increases in pain and consumption

| Table 3. Multiple linear regression analysis using HADS-Anxiety as the response variable |
|-----------------|-----------|------------|--------|-------|-------|
| Explanatory variables | Coefficient | Standard error | $p$ value | $R^2$ | $P$  |
| Sex (reference: female) | -2.487 | 0.952 | 0.011 | 0.96 | 0.017 |
| Age (in years) | -0.035 | 0.038 | 0.352 | 0.073 | 0.12 |

* $p$ value for the $t$-test of null hypothesis of coefficient = 0; † $R^2$ (adjusted to the variables of the model) on a given line refers to the proportion of variance that is explained by the model that includes all variables and the line (sex and age) or above this line (sex); ‡ $p$ value from the $F$ test of null hypothesis that a change in $R^2$ between the prior model and the model containing all variables is 0.

| Table 4. Multiple linear regression analysis using HADS-Depression as the response variable |
|-----------------|-----------|------------|--------|-------|-------|
| Explanatory variables | Coefficient | Standard error | $p$ value | $R^2$ | $P$  |
| Sex (reference: female) | -2.933 | 0.900 | 0.002 | 0.120 | 0.006 |
| Age (in years) | -0.007 | 0.036 | 0.854 | 0.098 | 0.854 |

* $p$ value for the $t$-test of null hypothesis of coefficient = 0; † $R^2$ (adjusted to the variables of the model) on a given line refers to the proportion of variance that is explained by the model that includes all variables and the line (sex and age) or above this line (sex); ‡ $p$ value from the $F$ test of null hypothesis that a change in $R^2$ between the prior model and the model containing all variables is 0.
of analgesics in the postoperative period\textsuperscript{13}, poor cardiac rehabilitation results\textsuperscript{4}, and increased mortality\textsuperscript{7,21}.

Thus, the results of this study may contribute to the planning of medical care for patients submitted to cardiac surgeries.

Handling perioperative anxiety and depression symptoms may help reduce morbidity after cardiac surgeries\textsuperscript{22}.

The strategies used to cope with a cardiac surgery make it a less traumatic experience for patients. The provision of information is a consolidated strategy used by health professionals to discuss the patient’s fears and concerns\textsuperscript{3}.

In this context, nurses have a special role in the development and implementation of actions to minimize preoperative psychological tension. A simple tool such as HADS, which allows a fast assessment of anxiety and depression symptoms as part of a nursing evaluation, can help identify risks for which early interventions may be performed\textsuperscript{7}.

The data obtained in this study highlight the importance of the assessment of the preoperative emotional condition of patients to be submitted to cardiac surgeries. Qualitative studies can also be conducted to further explore preoperative anxiety and depression symptoms and their related factors.

One of the limitations of this study refers to the type of sample. As it was not possible to calculate the sample size, due to unavailable variance of measurements of anxiety and depression symptoms from the patients, we opted for a non-probability sample.

Another limitation was the cross-sectional approach, with no follow-up on the clinical progress of these patients in the postoperative period, in terms of physiological and psycho-emotional recovery.

CONCLUSION

In this study, women presented more anxiety and depression symptoms in the preoperative period of cardiac surgeries when compared to men, and the differences were statistically significant. Considering the age group, the differences found in terms of the presence of anxiety and depression symptoms were not statistically significant.

Data obtained in this study may help provide a better understanding of the behavior of anxiety and depression symptoms in patients waiting for cardiac surgery. Such data should be taken into account by nurses when developing an educational plan for surgical patients.

A detailed assessment and effective treatment of anxiety and depression symptoms, as part of the preoperative examination, may allow the identification of high-risk patients, with the aim of improving long-term medical and surgical prognosis and patient quality of life.

REFERENCES


