Original Article
The impact of psychiatric disorders with cardiac syndrome X on quality of life: 3 months prospective study

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Abstract: The aim of the study is to investigate the impact of psychiatric disorders with cardiac syndrome X (CSX) on the patients’ quality of life, as well as the efficacy of psychiatric support. Fifty-six CSX and fifty-three Coronary Heart Disease patients were included in the study after coronary angiography. Patients were evaluated right after the angiography and 3 months thereafter. The socio-demographic characteristics, comorbid disorders, Beck Anxiety (BAI), Depression (BDI) Inventory, and Health Related Quality of Life (SF-36) were compared between groups. The most common mental disorders was depression which account for 41%, the next were anxiety disorders (64%, n = 36) and somatoform (24%, n = 14). Initially, BAI, BDI in the CSX group were significantly higher when compared to the control group. There was significant difference in all subgroups of SF-36 at the end of the second evaluation versus the first evaluation in the CSX patients. The present study revealed that patients with CSX have higher prevalence of psychiatric comorbidities and lower quality of life. Psychiatric approaches are benefit for CSX patients to improvement their quality of life.

Keywords: Cardiac syndrome X, psychiatric comorbidity, quality of life

Introduction
Cardiac syndrome X (CSX) is a disease with indefinite etiopathogenesis and treatment and was first defined in 1973 by Kemp [1]. This syndrome is characterized by chest pain, positive treadmill test and normal coronary arteries. In addition, this syndrome must not include coronary artery spasm, systemic hypertension, left ventricle hypertrophy or valvular heart disease.

It has been reported that chest pain results from extra-cardiac reasons in 50% of the patients that present to emergency room with chest pain and the fear of having heart attack [2]. Reasons for extra-cardiac chest pain include gastroesophageal diseases, pulmonary embolus, pneumonia, pneumothorax, nerve entrapment syndrome, and psychiatric disorders such as panic disorder and depression. Although its prevalence in the population is not clear, approximately 20-30% of patients that underwent coronary angiography were diagnosed with CSX [3].

Psychiatric disorder was detected in 15-60% of the patients that presented with chest pain and had normal angiography [4, 5]. These patients most frequently had panic disorder followed by depression, hypochondriasis, somatization disorder, and generalized anxiety disorder. Researches corroborate that at least one third of the cases with unexplained chest pain and normal coronary artery on angiography has panic disorder [6]. It was demonstrated that severity of anxiety and depression is higher in females with CSX as compared to the healthy group and to the patients with coronary artery disease [3]. In addition, it was determined that social support and traumatic life events are more common and quality of life is poorer in such patients [7].

Cognitive behavioral therapy, meditation and relaxation, and enhancing social support were tried for the treatment of psychiatric diseases associated with CSX, but a definite protocol could have not been established. Low-dose imipramine was used in the patients with chest pain but with normal coronary arteries; despite
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alleviation in chest pain, no significant improvement was observed in the quality of life [8, 9].

The aim of the present study is to investigate the psychiatric disorders that accompany CSX, on the etiology of which various hypotheses have been suggested and which was encountered frequently in cardiology polyclinics, and to determine in what way the quality of life is influenced in these patients, as well as to determine the efficacy of psychiatric support in the patients with psychiatric disorder.

Methods

Study population

The study was approved by Baskent University Ethical Committee (project no: KA 12/255) and supported by Baskent University Research Fund.

The study comprised 56 patients with CSX, who presented to Baskent University Medical Faculty, Adana Practice and Research Center, Cardiology Polyclinic between July 2012 and January 2014 with chest pain and had positive treadmill test and normal coronary arteries on angiography. Control group consisted of 53 patients, who presented with chest pain and diagnosed with coronary artery disease (CAD) based on coronary angiography (stenosis > 50% in one or more coronary arteries). After informing all patients about the aim and method of the study, their written consents were obtained. Patients with psychotic disorder, mental retardation, severe neurological diseases, baseline ECG abnormality, inability to perform treadmill test, and angiography needed to be postponed due to deep anemia, renal function disorder, hepatic enzyme abnormalities and thyroid function disorder, as well as 14 patients that were reluctant to participate in the study, were excluded from the study.

Patients were evaluated by the same psychiatrist both right after the angiography and 3 months thereafter. The psychiatrist evaluated the patients on the 1st and 3rd months without knowing the results of coronary angiography. On the initial evaluation, socio-demographic data form, Turkish Version of Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Short Form-36 Quality of Life Scale (SF-36) were performed.

Stress management methods, techniques for interpreting the symptoms, breathing and relaxation exercises were performed in the patients that were diagnosed with psychiatric disease on the first evaluation after angiography. On the first and 3-month interviews, the patients were asked to evaluate how severe they feel the chest pain by scoring between 0 and 10 on a Likert-type scale. On the second interview, BDI, BAI and SF-36 scales were performed. Tests were performed via phone call in three patients that were unable to come to the hospital.

Measurements

Socio-demographic data form: Age, gender, occupation, marital status, stressful life events in the last 6 months, and family history for psychological and cardiologic diseases were inquired via socio-demographic data form, which was performed by the psychiatrist.

Structured clinical interview for DSM-IV Axis I disorders (SCID-I), is a structured clinical interview scale applied by the interviewer to explore the diagnosis of Axis I psychiatric disorder. It consists of six modules investigating diagnostic criteria of a total of 38 axis I disorders. Two modules are used for mood episodes and mood disorders, two modules are used for psychotic symptoms and psychotic disorders, and each of remaining two modules is used for anxiety disorders, and substance abuse and other disorders. It was developed in 1997 by First et al [10]. Validity and reliability study of Turkish version was done by Ozkaurkugil under the name of Structural Clinical Interview for DSM-IV Axis-I disorder [11].

Beck depression inventory (BDI), is a self-report scale developed by Beck [12]. This scale consists of 21 questions each of which includes 4 situations. Each answer is scored between 0 and 3 with a total score changing between 0 and 63. Total score is interpreted as follows: 0-4 no/minimal depression, 10-16 mild depression, 17-29 moderate depression and 30-63 severe depression. Validity and reliability of Turkish version of the scale was done by Hisli et al. A score of 17 or higher is considered as major depression for Turkish population [13].

Beck anxiety inventory (BAI), is a 21-item scale developed by Beck et al. and widely used to
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Table 1. Sociodemographic variables

<table>
<thead>
<tr>
<th></th>
<th>CSX (n = 56)</th>
<th>CHD (n = 53)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.7 ± 7.8</td>
<td>55.2 ± 9.8</td>
<td>0.245</td>
</tr>
<tr>
<td>Educational levels (years)</td>
<td>6.4 ± 2.3</td>
<td>7.3 ± 3.0</td>
<td>0.062</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>41 (73.2%)</td>
<td>31 (58.5%)</td>
<td>0.105</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>13 (23.2%)</td>
<td>22 (41.5%)</td>
<td>0.175</td>
</tr>
<tr>
<td>Employed</td>
<td>6 (10.7%)</td>
<td>4 (7.5%)</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>1 (1.8%)</td>
<td>2 (3.8%)</td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td>36 (64.3%)</td>
<td>25 (47.2%)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>9 (16.1%)</td>
<td>4 (7.5%)</td>
<td>0.364</td>
</tr>
<tr>
<td>Married</td>
<td>39 (69.6%)</td>
<td>42 (79.2%)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>8 (14.3%)</td>
<td>7 (13.2%)</td>
<td></td>
</tr>
<tr>
<td>Physical disease</td>
<td>44 (78.6%)</td>
<td>40 (75.5%)</td>
<td>0.820</td>
</tr>
<tr>
<td>History to death due to CVD</td>
<td>25 (51.0%)</td>
<td>33 (62.3%)</td>
<td>0.318</td>
</tr>
<tr>
<td>Family history for CVD</td>
<td>39 (69.6%)</td>
<td>38 (71.7%)</td>
<td>0.836</td>
</tr>
<tr>
<td>History for psychiatric disorder</td>
<td>21 (37.5%)</td>
<td>14 (26.4%)</td>
<td>0.227</td>
</tr>
<tr>
<td>Family history for psychiatric disorder</td>
<td>16 (28.6%)</td>
<td>2 (3.8%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Stressful life events</td>
<td>39 (69.6%)</td>
<td>23 (43.4%)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Conclusions

The level of statistical significance was considered to be p = 0.05.

Results

Socio-demographic characteristics are summarized in Table 1. Of the 56 patients with CSX, 73.2% was female, whereas 58.5% of the control group was female. There was no statistically significant difference between the groups in terms of age, gender, marital status, occupation, family history for psychiatric and cardiac diseases, and concomitant physical diseases. Family history for psychiatric disease was present in 26.6% of CSX patients and in 3.8% of the control group and the difference was statistically significant (p = 0.001). Stressful life events are statistically higher in CSX group (69.6%) than in the control group (43.4%) (p = 0.007) (Table 1).

During the first interview, chest pain scoring by Likert type scale revealed a pain score of 6.1 (4-8) in the CSX group and 5.8 (3-10) in the CAD group. On the second interview, severity of chest pain decreased in both groups, but no statistically significant difference was found between the two groups (1.23 (0-4) in the CSX group and 1.56 (0-6) in the CAD group).

Depression was detected in 41% (n = 23) of the patients with CSX and in 64% (n = 21) of the control group. Anxiety disorder was present in 64% (n = 36) of CSX group, of which 29% (n = 16) was diagnosed with panic disorder, 21% (n = 12) was diagnosed with phobic anxiety disorder and 14% (n = 5) was diagnosed with generalized anxiety disorder. In the control group, prevalence of anxiety disorder was 19% (n = 10), and 6% (n = 3) of these was diagnosed with panic disorder and 13% (n = 7) was diag-
nosed with phobic anxiety disorder. Somatoform disorder was determined in 24% (n = 14) of CSX group and 4% (n = 2) of the control group. No psychiatric disorder was found in 13% (n = 7) of the CSX group and 47% (n = 25) of the control group.

Scales used in the study were evaluated according to the CSX and CAD groups comparing the 1st and 2nd interviews separately, and the results are summarized in Table 2.

Baseline BDI score was significantly higher in the patients with CSX as compared to the control group (18.9 ± 8.4 (4-40) vs. 15.7 ± 7.8 (5-38); p = 0.025). At the end of the 3rd month, statistically significant decrease was determined in the mean BDI scores of both groups (p = 0.0001 for CSX and p = 0.004 for CAD). However, with regard to the changes in the groups in time, it was observed that improvement in the CSX group was more significant as compared to the control group (pgroup = 0.0001) (Table 2).

Baseline BAI score of the CSX group (26.9 ± 11.0) was significantly higher than that of the control group (21.5 ± 10.8) (p = 0.003). Post-treatment BAI score was found to be 16.2 ± 10.5 in the CSX group and 15.5 ± 8.9 in the control group (p = 0.959). Although decrease in BAI score on the second interview was higher in the CSX group, difference between the groups was not significant (Table 2).

With regard to the assessment of quality of life on the first interview, mean physical functionality was 22.5 (11-30) in the CSX group and 23.5 (14-30) in the control group. On the second interview, these rates were 26 (14-30) and 23.5 (14-30) respectively. Improvement at the end of three months was statistically significant in the CSX patients (p = 0.003). Results of the evaluation in two groups by short form-36 scale are summarized in Table 2.

Whilst there was significant difference in all subgroups of SF-36 at the end of the second evaluation versus the first evaluation in the CSX patients, significant improvement was determined in only pain, energy, and mental health subgroups of quality of life scale in the CAD group.

Patients with CSX were divided into two groups as with and without psychiatric disease. Pretreatment BDI and BAI scores were significantly higher but energy, difficulty in role-emo-
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Beck Depression Inventory score was statistically higher in the patients with baseline depression, and BAI score was statistically higher in those with baseline anxiety and somatoform disorder as compared to the other groups. No significant difference was found in paired comparisons at the end of 3-month period. Post-hoc paired comparison revealed that scores of the scales were not statistically different between the patient groups with anxiety disorder and somatoform disorder (Table 3).

Discussion

The present study is one of the first studies that evaluated the relation between quality of life and psychiatric co-morbidities in CSX patients. Although psychiatric co-morbidity has been investigated in CSX patients in the literature, the number of studies investigating the relation between psychiatric diseases and quality of life is limited. Husser et al. evaluated psychiatric co-morbidity based on DSM-IV-TR diagnostic criteria in 37 patients with normal coronary arteries and compared with the results of SF-36 quality of life scale. This study found that quality of life was impaired in those with psychiatric co-morbidity and they experienced chest pain more frequently and less benefited from treatment [18]. In contrast, comparing the results of psychiatric diseases and SF-36 scale in CSX patients, the present study revealed that impairment in quality of life was higher in difficulty in role-emotional, energy and mental health subgroups.

In the literature, results of the studies conducted on the quality of life in the patients with CSX were different from each other. Some studies found that impairment in quality of life was higher in these patients as compared to the control group [7, 19], whereas some studies found that quality of life is similar in both groups.

**Table 3.** The distribution of the scales according to comorbidity before and after treatment in CSX patients

<table>
<thead>
<tr>
<th></th>
<th>No Anxiety Disorders</th>
<th>Somatoform Disorders</th>
<th>Depressive Disorder</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (Min-Max)</td>
<td>Median (Min-Max)</td>
<td>Median (Min-Max)</td>
<td></td>
</tr>
<tr>
<td>BDI-1</td>
<td>8 (4-16)</td>
<td>18 (4-40)</td>
<td>17 (9-27)</td>
<td>26 (10-35)</td>
</tr>
<tr>
<td>BDI-2</td>
<td>6 (3-15)</td>
<td>8 (2-33)</td>
<td>8 (3-19)</td>
<td>12 (4-30)</td>
</tr>
<tr>
<td>BAI-1</td>
<td>10 (5-29)</td>
<td>30 (5-45)</td>
<td>32 (22-42)</td>
<td>23 (15-50)</td>
</tr>
<tr>
<td>BAI-2</td>
<td>6 (4-16)</td>
<td>14 (3-41)</td>
<td>12 (4-29)</td>
<td>18 (5-42)</td>
</tr>
<tr>
<td>SF-36 (1)-physical functioning</td>
<td>28 (18-30)</td>
<td>25 (14-30)</td>
<td>21 (11-28)</td>
<td>21 (13-28)</td>
</tr>
<tr>
<td>SF-36 (2)-Physical functioning</td>
<td>29 (18-30)</td>
<td>28 (14-30)</td>
<td>27 (19-29)</td>
<td>28 (18-30)</td>
</tr>
<tr>
<td>SF-36 (1)-Bodily pain</td>
<td>8 (4-10)</td>
<td>6 (3-11)</td>
<td>5 (4-7)</td>
<td>5 (3-7)</td>
</tr>
<tr>
<td>SF-36 (2)-Bodily pain</td>
<td>7 (4-11)</td>
<td>9 (3-11)</td>
<td>9 (7-11)</td>
<td>8 (3-11)</td>
</tr>
<tr>
<td>SF-36 (1)-General health</td>
<td>15 (7-21)</td>
<td>12 (5-21)</td>
<td>11 (7-22)</td>
<td>11 (5-21)</td>
</tr>
<tr>
<td>SF-36 (2)-General health</td>
<td>16 (7-20)</td>
<td>15 (8-23)</td>
<td>18 (7-22)</td>
<td>17 (7-23)</td>
</tr>
<tr>
<td>SF-36 (1)-Vitality</td>
<td>14 (9-17)</td>
<td>10 (5-23)</td>
<td>9 (7-14)</td>
<td>9 (6-12)</td>
</tr>
<tr>
<td>SF-36 (2)-Vitality</td>
<td>14 (9-17)</td>
<td>16 (5-22)</td>
<td>16 (8-20)</td>
<td>14 (0-20)</td>
</tr>
<tr>
<td>SF-36 (1)-Social functioning</td>
<td>8 (6-10)</td>
<td>7 (3-9)</td>
<td>6 (4-9)</td>
<td>5 (3-7)</td>
</tr>
<tr>
<td>SF-36 (2)-Social functioning</td>
<td>8 (6-10)</td>
<td>8 (3-10)</td>
<td>9 (5-10)</td>
<td>8 (3-9)</td>
</tr>
<tr>
<td>SF-36 (1)-Emotional role functioning</td>
<td>6 (4-6)</td>
<td>4 (3-6)</td>
<td>4 (3-6)</td>
<td>3 (3-6)</td>
</tr>
<tr>
<td>SF-36 (2)-Emotional role functioning</td>
<td>6 (3-6)</td>
<td>6 (3-8)</td>
<td>6 (3-6)</td>
<td>6 (3-6)</td>
</tr>
<tr>
<td>SF-36 (1)-Mental health</td>
<td>21 (11-25)</td>
<td>14 (7-26)</td>
<td>15 (9-21)</td>
<td>11 (8-16)</td>
</tr>
<tr>
<td>SF-36 (2)-Mental health</td>
<td>21 (11-25)</td>
<td>20 (7-27)</td>
<td>21 (14-25)</td>
<td>19 (5-24)</td>
</tr>
</tbody>
</table>

BDI-1: Baseline Beck Depression Inventory score; BDI-2: post-treatment Beck depression Inventory score; BAI-1: Baseline Beck Anxiety Inventory score; BAI-2: post-treatment Beck Anxiety Inventory score; SF-36 (1): Baseline SF-36 score; SF-36 (2): post-treatment SF-36 score.
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[20]. Atienza et al. evaluated 90 patients with CSX in terms of quality of life using a questionnaire and the standardized chest pain diary. In this study, they found that quality of life was significantly impaired in the patients with CSX and that impairment in quality of life was associated with severity and frequency of chest pain attacks [7].

Studies revealed that the majority of patients with CSX are females of postmenopausal period [21-24]. In the present study, difference between CSX and CAD groups in terms of age, education status, marital status and occupation was consistent with the literature. More than half of the CSX patients were females of peri/postmenopausal period, but there was no difference with the control group in terms of gender, which was not consistent with the literature. This might have resulted from small sample size.

Corlando et al. found a positive correlation between development of chest pain and presence of problems in the family and social lives of CSX patients [22]. Asbury et al. found that life events and degree of social communication are associated with high anxiety and depression scores in the females with CSX [21]. Prevalence of loss of a beloved person or emotional trauma was found to be higher in the patients with CSX as compared to the patients with CAD and to the healthy control group [25]. In the present study, higher prevalence of traumatic life events and family history for psychiatric disorder in the CSX group versus CAD group was consistent with the literature.

In the present study, prevalence of history for cardiac disease or death due to cardiac disease in the first degree relatives of CSX patients was not different from the control group, but there are different results in the literature. Asbury et al. evaluated 100 CSX patients, 100 CAD patients and 100 healthy subjects in terms of family history for cardiac disease [25]. This study stated that family history for cardiac disease may be associated with development of psychiatric disorder in CSX patients. Interestingly, it was demonstrated that females with CSX had higher awareness about their family histories for cardiac diseases as compared to the females of the same age with CAD. It was also demonstrated that presence of cardiac disease in parents has an effect on cardiac anxiety.

Consistent with the literature, the present study found that the most frequent psychiatric comorbidity in CSX patients were depression, anxiety disorder and somatoform disorder with panic disorder being the most common anxiety disorder [4, 6, 19, 26, 27]. Potts et al. conducted a study in the patients with normal coronary arteries and determined psychiatric comorbidity in 61% of the patients during angiography and in 49% of the patients after 11.4-year follow-up period, which was significantly higher as compared to the CAD group. During angiography, 49% of the patients had anxiety disorder (15% panic disorder), 22% had somatoform disorder and 27% had depressive disorder [28]. Different from the present study, Valkamo et al. found the prevalence of psychiatric comorbidity to be 28% and stated that there was no difference with the patients having CAD [4]. Different study methods may partially explain the difference between the results of present study and the study conducted by Valkamo et al. They performed psychiatric diagnostic interview on the day before angiography and both the patients and researchers were uninformed about the results of angiography. In the present study, since the psychiatric evaluation was done after angiography, both patient- and researcher-related factors might have led to over diagnosis in the patients without CAD.

In the present study, patients that have been diagnosed with psychiatric disease were trained about methods of coping with stress, techniques for interpreting the symptoms, and breathing and relaxation exercises, and significant decrease was observed in quality of life scores, depression and anxiety scales on the interview performed at the end of three months. This indicates that improvement in quality of life can be achieved as the result of stress control by psychiatric support. Many patient groups with chronic pain have described increase in the frequency and severity of pain during stress, which suggests that stress recognition, management and reducing program may play an important role in the treatment of CSX [22]. A number of treatment methods have been implemented to reduce chest pain in CSX patients, but any effective treatment model could not be identified. The number of studies on the efficacy of psychiatric therapies is limited although it is one of the agreed reasons in the etiology. Studies with imipramine demonstrated that chest pain was decreased due to visceral analgesic effect of imipramine but
there was no improvement in the quality of life due to the side effects of drug [8, 9]. Benzodiazepines as well have been used in the treatment owing to their analgesic, neuralgic, anti-inflammatory and muscle relaxant effects. Small, randomized studies demonstrated that cognitive behavioral therapy and group therapy reduce frequency of chest pain attacks in 3 to 6-month period [29-31]. It has been reported that treatment would be more effective in case psychological therapy is started in early period before the onset of chronic pain [32]. Relaxation techniques such as transandental meditation have been successfully used in small studies and were demonstrated to improve not only the chest pain but also exercise-induced ST segment depression, and it was reported that these techniques improve quality of life [32].

Cross-sectional design of the study is one of the limitations. Since the sample was selected from a single center, it may not give accurate information about general population and self-report scales used in the study may be limiting factors. The facts that family history for cardiac disease was not obtained from family members, stressful life events were not evaluated using a standardized scale, questions of survey could be evaluated according to the subjects because of different education status, and some of CSX and CAD patients were included in the study based on the answers that require voluntariness might have led to the biases in patient selection.

Conclusions

Although prognosis is good in the patients with Cardiac Syndrome X, resistant chest pain and functional failure is common in such patients. Therefore, patients may continue to admit to the emergency room, may be admitted to the coronary intensive care units, and even undergo repeated angiography. Thus, a situation that might have a good prognosis may lead to impairment in quality of life, labor loss, and unnecessary utilization of health care services. It must be kept in mind that identification of psychological factors that might impair quality of life in such patients and that psychiatric support would significantly improve quality of life. The present study revealed that prevalence of psychiatric co morbidity is high and impairment in quality of life is notable in the patients with CSX. Therefore, by means of this study, we have highlighted the importance of following the patients, who present to cardiology polyclinic with chest pain and have normal angiography, together with psychiatry clinic because of resistant nature of chest pain.

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Disclosure of conflict of interest

None.

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