

## Cardiac syndrome X from a psychosomatic point of view

Magdalena Piegza, Robert Pudlo, Karina Badura-Brzoza, Robert T. Hese

### Summary

The aim of this paper was to explain the idea of cardiac syndrome X, particularly the association between emotional disturbances, somatoform disorder and syndrome X.

Cardiac syndrome X is defined by the presence of angina-like chest pain, a positive response to stress testing and a angiographically normal coronary arteriogram. It has been shown to occur in approximately 20 - 30 percent of angina patients undergoing cardiac catheterization. Most of the patients with normal angiograms are women especially in the perimenopausal age. Syndrome X patients reported more depression, anxiety and somatic concerns than positive angiographic patients. They have high scores on psychological inventories that measure anxiety and depression, and are very prone to somatization. They have better prognosis with death from cardiac causes than patients with coronary heart disease. With regard to female chest pain patients, somatoform disorder can be assumed. At the present time, there is no common agreement on the exact cause of the symptoms associated with syndrome X.

**cardiac syndrome X / somatoform disorder / women**

### INTRODUCTION

Cardiac syndrome X is regarded as a form of ischemic heart disease. Patients complain of chest pain, most of them demonstrate emotional disorders and a disproportion between the reported complaints and objective findings of coronary investigations can be observed. It seems to be very probable, that like in somatoform disorders, patients with cardiac syndrome X do not take into consideration the psychological aspect of their condition and consequently do not seek adequate psychological help.

---

**Magdalena Piegza, Robert Pudlo, Karina Badura-Brzoza, Robert T. Hese** : Chair and Hospital Department of Psychiatry, Tarnowskie Góry, Medical University of Silesia, Poland ; Correspondence address: Magdalena Piegza, Chair and Hospital Department of Psychiatry, Medical University of Silesia in Katowice, 49 Pyskowicka Str., 42-600 Tarnowskie Góry, Poland ; E-mail : magdalena.piegza@op.pl

This research has not been aided by any grant.

### CONCEPT AND PATHOGENESIS OF THE CARDIAC SYNDROM X

The concept of “cardiac syndrome X” was introduced by Kemp in 1973 in order to distinguish a population of patients with coronary chest pain, in which there are no coronarographic pathological changes [1]. Despite the fact that over 30 years have passed since the first resorts on cardiac syndrome X appeared, the syndrome still remains a riddle. There are many controversies over the classification of patients, its pathogenesis and prognosis as well as therapeutic management [2].

Just like depressive and anxiety disorders, syndrome X tends to occur considerably more often in women [3, 4, 5]. Its incidence in patients undergoing invasive diagnostics for coronary heart disease was estimated at approximately 20–30% [2, 6, 7]. About 60–70% of patients with syndrome X are female, often in menopausal age [2,

3]. The syndrome is diagnosed in a patient with chest pain of probable coronary aetiology, positive ECG changes during exercise testing and no significant changes in epicardial coronary arteries in coronarography. The pain can be typical or atypical – prolonged chest pain at rest, no response to nitrates administration. First symptoms usually occur between 45 and 50 years of age. Aetiology of discussed syndrome remains unknown [8, 9, 10, 11]. It seems that the syndrome has a heterogeneous nature and views on its pathogenesis are very divergent. It is also unknown, whether there is the only one or several underlying pathophysiological mechanisms. Potential causes of the syndrome are as follows: coronary microcirculation impairment, endothelial dysfunction [12, 13], oestrogen deficiency [3], sympathetic-parasympathetic balance disturbance, abnormal adenosine secretion, vasospasm of small coronary arteries, as well as psychosomatic disorders accompanied by changes in pain perception [2, 3, 11, 14].

Supporters of the coronary microcirculation impairment conception as a basic anomaly responsible for syndrome X enumerate among other things the following factors as causes of the suggested coronary microcirculation disturbances: increased adrenergic system reactivity, abnormal adenosine secretion, peripheral tissue insulin resistance as well as oestrogen deficiency in women. In all the patients we can observe reduced coronary reserve. A hypothesis has been proposed that in these patients, coronary chest pain is caused by abnormal coronary adenosine secretion or adenosine receptor hypersensitivity. Accuracy of a given hypothesis may be proved by the fact that anginal symptoms regress following aminophylline administration, which blocks adenosine receptors [15].

The question whether symptoms of cardiac syndrome X are really caused by cardiac ischaemia still remains unanswered. There are doubts whether ischaemia is an underlying process of cardiac chest pain, which is reported by patients with syndrome X [11]. During the exercise test in women, ST-segment depression was accompanied by chest pain in as much as 50%, whereas in the case of a typical course of coronary heart disease, this percentage was only 30%.

ST-segment depression may be caused by different factors and in and of itself does not con-

stitute sufficient evidence for ischaemia. Many authors suggest that in these patients, stimulation of the adrenergic system is a predominant factor responsible for ECG changes [13, 16]. Other researchers pay attention to the stimulation of the sympathetic system and a simultaneous reduced parasympathetic system activity, while others emphasize an importance of impaired parasympathetic activity as a main cause of the observed symptoms [17].

On the basis of information coming from an extensive review study on the described syndrome, we can have the impression that many authors regard the so called microvascular angina to be the most often pathogenetic mechanism of cardiac syndrome X [3]. It is a functional disorder of small intramuscular vessels, which is connected with an excessive dilatation of small arteries at rest, reduced vasodilatation in response to relaxants or particularly strong vasoconstriction in response to vasospastic stimuli. It is unknown whether these disorders are connected with smooth muscle dysfunction or abnormal endothelial activity.

#### **RELATIONSHIP BETWEEN SYNDROM X, EMOTIONAL AND SOMATOFORM DISORDERS**

Some intriguing relations have been observed between syndrome X and emotional disturbances. Pathogenetic importance of psychosomatic disorders accompanied by changes in pain perception seems to be more distinctly emphasized, although precise processes responsible for this phenomenon still remain unknown [11, 14, 18].

Most authors confirm in their studies that especially women with syndrome X demonstrate disturbed pain perception, which may be a consequence of hypersensitivity to physiological variation in catecholamine levels [11]. Assessing cerebral blood flow with the use of positron emission tomography (PET) Rosen et al. have reached a conclusion that in women with syndrome X, both a degree and an area of cerebral activation during a pain sensation was greater (including thalamus and frontal lobes of cerebral cortex) than in patients with typical form of coronary heart disease [19]. Results of this study seem to confirm the hypothesis that in syndrome X, the pain threshold is being reduced at the tha-

lamus level. Normal pain stimuli reach the thalamus where they are intensified and in this form are transmitted to the cerebral cortex [20].

Academic literature includes several scientific studies which compare a group of patients with pain located in the cardiac region and normal coronarography result with a group of patients with confirmed atheromatus changes in coronary vessels [21, 22, 23, 24]. In 20% of people with normal coronary angiography results, seizure-like anxiety disorders have been reported, while over 60% of women and 50% of men met criteria of generalized anxiety disorders [22]. In another study, the authors noticed a difference in fear perception during the sensation of chest pain between a group of patients with coronary heart disease confirmed coronarographically and persons with normal coronarography results as well as patients with generalized anxiety. Fear was a dominant sensation in 83% of patients with seizure-like anxiety, in 48% of patients with no significant coronary atheromatus changes and in only 4% of people with angiographic evidence for coronary heart disease [6]. For this reason, the authors called for a psychiatric examination in each case of chest pain so that a seizure-like anxiety disorder could be excluded. Chernen et al. [21] observed that in a group of patients with normal coronarography, women reported anxiety, depressive symptoms as well as sleep disorders more often than men, whereas in this group, a duration of chest pain episodes was shorter. They were also more prone to somatization. Similar problems have been noticed by Rosen et al. [11] simultaneously, they claim that an increased tendency to somatization may be connected with sympathetic system stimulation, which is responsible for an excessive inadequate sensitivity to inner stimuli. However, there are no differences between women and men in the severity of depression and anxiety.

Ruggeri et al. [25] have found a positive correlation between anxiety degree and severity of cardiac ischaemia in cardiologic syndrome X. For this reason, they suggested that an increased susceptibility to an anxiety reaction may induce coronary microvascular disorders. A similar stand on this matter is taken also by other authors [26].

Another research, which aimed to compare women with cardiologic syndrome X and con-

firmed coronary heart disease, with a control group of healthy women in terms of influence of different factors on symptoms of anxiety and depression, showed a higher level of depression among all women with myocardial ischaemia and a higher level of anxiety in women with syndrome X as compared to the whole population of the examined women [27]. In another study, it has been pointed out that an incidence of depression and anxiety disorders in patients with cardiologic syndrome X is similar to this observed in patients with non-cardiac aetiology of chest pain [28].

At present, it is a commonly accepted belief that patients with normal coronarography belong to a group which seems to be at the lower risk of an unfavourable course of ischemic heart disease. This favourable clinical course of the disease is observed despite recurrent chest pain episodes [14]. There is an assumption that in these patients, in most cases, coronary arteriospasm as well as coagulation system disorders are responsible for cardiac infarction [5]. Episodes of persistent pain have become frequent reasons for cardiologic hospitalizations and consequent next hemodynamic investigations, which in most cases confirm no relevant atheromatus changes within coronary arteries. Despite the fact that doctors assure them of a mild course of disease, many patients strongly believe that their cardiac condition is severe and continually seek medical help. This line of thought and perception as well as the way of acting is close to somatoform disorders.

A diametrically opposed opinion is presented by Bugiardini et al. [13] who regard results of their studies as strong evidence for the hypothesis on endothelial dysfunction as a predictive factor responsible for development of atheromatus changes within initially normal coronary vessels. During a 10-year observation, they noted that one-third of women with syndrome X developed different stages of coronary atheromathosis and one woman died because of cardiac infarction. They point out the abnormal response of endothelium to acetylcholine (vasodilatation) as a determinant of its dysfunction. Based on the arguments quoted above, they suggest that special healthcare should be provided to the subgroup of women with syndrome X who demonstrate an abnormal response to acetylcholine due

to an increased risk of both atheromatous changes and severe cardiac episodes [13].

### THERAPEUTIC MANAGEMENT

Due to unknown aetiology of the syndrome and scientific knowledge being as it is, there is as yet no reliable and widely accepted therapeutic scheme of cardiac syndrome X. Pharmacological treatment includes: nitrates, beta-adrenolytic agents, slow calcium-channel blockers, alpha-adrenolytic agents, oestrogens, Angiotensin-Converting Enzyme (ACE) Inhibitors, aminophylline and others. The vast majority of researches claim that beta-adrenolytic agents seem to be the most effective drugs since they reduce the frequency of chest pain incidents as well as improve the life quality of patients [2]. Moreover, therapeutic management may include antidepressants such as imipramine, which repeatedly offer satisfactory outcome for the patient [14, 29]. Adequate evidence confirming this application has been provided by Cannon et al. [29], in their study, which have proved that a two-year administration of imipramine at a dose of 50 mg daily, in patients with chest pain and normal angiography reduces the frequency of chest pain by more than 50%. In addition, they have observed that administration of imipramine at a given dose and period of time does not induce irregularity of rhythm and improvement in the patient's condition may be a consequence of probable analgesic properties of the drug. Some authors recommend that therapeutic management should be initiated by introducing psychotherapy and changes in lifestyle habits [2, 14, 30].

### CONCLUSION

The presentation of this paper aimed at introducing the reader the idea of cardiac syndrome X, particularly its pathogenesis and association between emotional and somatoform disorders. Most patients are female, especially in the perimenopausal age. The syndrome itself has a heterogeneous nature; views on its pathogenesis seem to be very divergent. The condition is diagnosed in a patient with the following symp-

toms: chest pain of probable coronary aetiology accompanied by positive ECG changes during exercise testing and no significant coronarographic changes within epicardial coronary arteries. The condition is regarded as a form of ischemic heart disease. Regardless of clearly defined diagnostic criteria as well as the fact that the definition also includes cases of atypical chest pain, cardiologists charily diagnose this condition. Cardiologic pharmacology is predominantly based on beta-adrenolytic agents. Some authors recommend application of antidepressants and psychotherapy as well.

### REFERENCES

1. Kemp Jr. HG. Left ventricular function in patients with anginal syndrome and normal coronary arteriograms. *Am J Cardiol.* 1973; 32: 375–376.
2. Świątecka G. Choroby serca u kobiet. Gdańsk: Via Media; 2000. p. 188-201.
3. Kaski JK. Overview of gender aspects of cardiac syndrome X. *Cardiovasc Res.* 2002; 53(3): 620–6.
4. Ketter MW, Denollet J, Chapp J, Thayer B, Keteyian S, Clark V, John S, Farha AJ, Deveshwar S. Men deny and women cry, but who dies? Do the wages of "denial" include early ischemic coronary heart disease? *J Psychosom Res.* 2004; 56(1): 119–23.
5. Westin L, Carlsson R, Erhardt L, Cantor-Graae E, McNeil T. Differences in quality of life in men and women with ischemic heart disease. A prospective controlled study. *Scand Cardiovasc J.* 1999; 33(3): 160–5.
6. Fraenkel YM, Kindler S, Melmed RN. Differences in cognitions during chest pain of patients with panic disorder and ischemic heart disease. *Depress Anxiety* 1996-7; 4(5): 217–22.
7. Ladwig KH, Hoberg E, Busch R. Psychological comorbidity in patients with alarming chest pain symptoms. *Psychother Psychosom Med Psychol.* 1998; 48(2): 46–54.
8. Chodorowski Z, Majkovicz M, Waldman W, Cieciewicz D, Sein Anand J, Wnuk K, Ciechanowicz R. Badania psychologiczne osobowości chorych z zespołem kardiologicznym X. *Przeg Lek.* 2002; 59(4-5): 281–285.
9. Kane FJ, Harper RG, Wittels E. Angina as a symptom of psychiatric illness. *South Med J.* 1988; 81: 1412–1416.
10. Rogacka D, Guzik P, Kaźmierczak M, Minczykowski A, Baliński M, Wykrętowicz A, Rzeźniczak J, Dziarmaga M, Michalski M, Wierchowicki M, Sowiński J, Wysocki H. Kardiologiczny zespół X. *Kardiologia Pol.* 1999; 51: 300–304.
11. Rosen SD, Uren NG, Kaski JC, Tousoulis D, Davies GJ, Camici PG. Coronary vasodilator reserve, pain perception and

- sex in patients with Syndrome X. *Circulation*. 1994; 90(1): 50–60.
12. Lanza GA. Cardiac syndrome X: a critical overview and future perspectives. *Heart* 2007; 93 (2): 159–166.
  13. Bugiardini R, Manfrini O, Pizzi C, Fontana F, Morgagni G. Endothelial function predicts future development of coronary artery disease: a study of women with chest pain and normal coronary angiograms. *Circulation*. 2004; 109(21): 2518–23.
  14. Kaski JC, Aldama G, Cosin – Sales J. Cardiac syndrome X. Diagnosis, pathogenesis and management. *Am J Cardiovasc Drugs*. 2004; 4(3): 179–94.
  15. Radice M, Giudici V, Pusineri E, Breggi L, Nicoli T, Peci P, Giani P, De Ambroggi L. Different effects of acute administration of aminophylline and nitroglycerin on exercise capacity in patients with syndrome X. *Am J Cardiol*. 1996; 78: 88–92.
  16. Okraska – Bylica A, Piwowarska W, Paradowski A, Gajos G, Gackowski A, Matysek J. Obraz kliniczny choroby niedokrwiennej serca u kobiet. *Przegl Lek*. 2003; 60(12): 797–801.
  17. Gulli G, Cemin R, Pancera P, Menegatti G, Vassanelli C, Cevese A. Evidence of parasympathetic impairment in some patients with cardiac syndrome X. *Cardiovasc Res*. 2001; 52(2): 208–16.
  18. Valeriani M, Sestito A, Le-Pera D, De-Armas L, Infusino F, Maiese T, Sgueglia GA, Tonalì PA. Abnormal cortical pain processing in patients with cardiac syndrome X. *Eur Heart J*. 2005; 26 (10): 975–982.
  19. Rosen SD, Paulesu E, Tousoulis D, Frąckowiak RSJ, Camici PG. Is altered central processing of afferent signals from the heart the cause of chest pain in syndrome X? *Eur Heart J*. 1997; 18 (supl): 627.
  20. Rosen SD, Paulesu E, Wise RJS, Camici PG. Central neural contribution to the perception of chest pain in cardiac syndrome X. *Heart*. 2002; 87: 513–519.
  21. Chernen L, Friedman S, Goldberg N, Feit A, Kwan T, Stein R. Cardiac disease and nonorganic chest pain: factors leading to disability. *Cardiology*. 1995; 86(1): 15–21.
  22. Flugelman MY, Weisstub E, Galun E, Weiss AT, Fischer D, Kaplan De-Nour A, Gotsman MS, Eliakim M. Clinical, psychological and thallium stress studium in patients with chest pain and normal coronary arteries. *Int J Cardiol*. 1991; 33: 401–408.
  23. Kawachi I, Sparrow D, Vokonas PS, Weiss ST. Symptoms of Anxiety and Risk of Coronary Heart Disease. The Normative Aging Study. *Circulation*. 1994; 90: 2225–2229.
  24. Ketter MW, Brymer J, Rhoads K. Emotional distress among males with syndrome X. *J Behav Med*. 1996; 19; 455.
  25. Ruggeri A, Taruschio G, Loricchio ML, Samory G, Borghi A, Bugiardini R. The correlation between the clinical characteristics and psychological status in syndrome X patients. *Cardiologia Rome Italy*. 1996; 41(6): 551–7.
  26. Cunningham C, Brown S, Kaski JC. Effects of transcendental meditation on symptoms and electrocardiographic changes in patients with cardiac syndrome X. *Am. J. Cardiol*. 2000; 85 (5): 653–655.
  27. Asbury EA, Creed F, Collins P. Distinct psychosocial differences between women with coronary heart disease and cardiac syndrome X. *Eur. Heart J*. 2004; 25 (19): 1695–701.
  28. Asbury EA, Collins P. Psychosocial factors associated with noncardiac chest pain and cardiac syndrome X. *Herz* 2005; 30 (1): 55–60.
  29. Cannon RO, Quyyumi AA, Mincemoyer R, Stine AM, Grace-ly RH, Smith WB, Geraci MF, Black BC, Uhde TW, Wac-lawiw MA, Maher K, Benjamin SB. Imipramine in patients with chest pain despite normal coronary angiograms. *N Engl J Med*. 1994; 330 (20): 1411–17.
  30. Hurst T, Olson TH, Olson LE, Appleton CP. Cardiac syndrome X and endothelial dysfunction: new concepts in prognosis and treatment. *Am. J. Med*. 2006; 119 (7): 560–566.

