Symptoms of cardiovascular diseases in the course of mental disorders

Anna Ostachowska, Lech Popiołek, Jolanta Walczewska, Krzysztof Rutkowski

Summary:

Psychosomatic disorders are extremely common in patients in non-psychiatric departments. It is widely known that in these cases comorbid psychiatric disorders are highly prevalent and that the importance of psychosocial factors is relevant. However, it is still a challenge for both internal medicine and mental health professionals to diagnose and treat them effectively. The need of evidence-based treatment guidelines for clinicians is obvious. As far as it is concerned, DSM-5 has redefined the criteria of somatoform disorders, underlying the importance of incorrect thoughts about symptoms whether organic ethiology.

Methods/Design: The aim was to provide an insight into the barriers of diagnosing psychosomatic disorders in cardiology referring to possible psychiatric comorbidity. Over 150 actual abstracts and full text manuscripts were checked. The literature published in English and Polish, mostly in PubMED/MEDLINE, PsycINFO, EM-BASE, Cochrane Database of Systematic Reviews of past 10 years was studied and compared to the literature of psychoanalytic theory. Disscussion: It is worth to remember, that for high proportion of patients with mental disorders somatic syndrome is the only symptom they report to physicians. Emotion regulation theory, alexithymia theory and desomatization and resomatization theory find it as the effect of unsolved problems with emotions. Moreover, functional neuroimaging studies seem to reveal coherent findings. Based on it, the neurophysilogical model of emotion regulation and the mechanism of cognitive-emotional executive control were described. Accordingly, literature shows that in heart disease patients the incorporation of psychological interventions in healing process significantly reduces mortality and relapse.

INTRODUCTION

In medical practice we often meet patients with somatic symptoms without organic cause. This circumstance makes it necessary to think holistically, adding new areas of activity to the diagnostic and therapeutic pathways of internal medicine. In many cases problems reported by

Correspondence address: ostachowska.anna@gmail.com

patients are accompanied by undiagnosed mental health problems, which are often an important risk factor for serious somatic diseases. This paper aims to draw attention to the symptoms of cardiovascular system dysfunctions which, embedded in the context of psychopathology, will not only enable full diagnosis, but also an effective treatment [1]. It presents the current state of knowledge about psychosomatic symptoms.

Literature is full of vagueness and ambiguities of terms related to the definition of psychosomatic illnesses [2]. The very concept of *somatization*, according to Wilhelm Steckel a psychoanalyst who introduced this term, means a tendency to being more aware of physical than men-

Anna Ostachowska,¹ Lech Popiołek,² Jolanta Walczewska,³ Krysztof Rutkowski²: ¹Department of Adult, Child and Adolescent Psychiatry, Kraków, Poland. ²Department of Psychotherapy, Jagiel-Ionian University Medical College, Kraków, Poland. ³Department of Internal Medicine and Gerontology, Jagiellonian University Medical College, Kraków, Poland.

tal aspects of emotional states and expressing emotional suffering by means of somatic symptoms [3]. The ICD-10 lacks a separate diagnostic category related to psychosomatic illnesses. This term occurs primarily in relation to disorders in somatic form (ICD-10), and somatoform disorders (DSM-IV). Due to restrictive criteria, the categories capture only severe conditions. Rask et al. demonstrated in their study possible clinical benefits of the new category labelled ,multiple symptoms', which was addressing subthreshold categories of medically unexplained symptoms (MUS) classified as somatoform disorder [4]. In DSM-5 several modifications in this category have been done. In addition to the changes in nomenclature, one of the most important changes is the lack of need to exclude organic cause to diagnose the somatoform disorder. More important is that somatic symptoms are accompanied by inadequate thoughts, feelings and behaviors related to symptoms [5].

Because of the inadequacy of the classic psychiatric nosography for the concept of this kind of diseases, in 1995 The Diagnostic Criteria for Psychosomatic Research (DCPR) were introduced. This 12 "psychosomatic syndromes" provided operational tools for psychosocial variables and its' prognostic and therapeutic implications in clinical settings. Eight syndromes concern the main manifestations of abnormal illness behavior (persistent somatization, functional somatic symptoms secondary to a psychiatric disorder, conversion symptoms, anniversary reaction, disease phobia, thanatophobia, health anxiety, illness denial) and the other four syndromes refer to the domain of psychological factors affecting medical conditions (alexithymia, type A behavior, demoralization, irritable mood). Sirri and Fava made the comparison of the DCPR, DSM-IV and DSM-5 proposal. In their opinion the 12 DCPR syndromes, being more sensitive, may broaden the physician's perspective on patients' problems, capturing psychological variables which do not find room in the customary psychiatric classification [6].

It is worth noting that besides the diagnoses of psychosomatic disorders, symptoms localised in the body are characteristic for the diagnosis of many other mental disorders. In masked depression, the main complaint may be a problem with circulatory system that disappear after treatment with antidepressants. Faster heart rate and breathing, tremors, palpitations, shortness of breath, chest discomfort, dizziness, fear of death, are some of the functional symptoms of autonomic arousal and manifest themselves similarly to cardiovascular problems. They can occur in the course of social phobia, panic disorder, specific phobias, as a part of an acute stress reaction, in patients addicted to psychoactive substances, in conversion disorder or in alexithymic patients.

Psychosomatic syndromes in hospital emergency department, Primary Health Care and day hospital for neurotic disorders treatment

Patients reporting symptoms without organic cause of a disease are especially common in hospital emergency departments (HED) and primary health care (PHC). The most common complaint is pain in the chest. It may be a symptom of coronary artery disease or myocardial infarction, which is one of the most terrifying conditions for patients [7-8]. According to numerous studies, in emergency departments the diagnosis of organic cause of the ailment is excluded in 30% to 77% of patients [9-12]. A comparable proportion of patients in primary health care, i.e. between 22% and 58%, report somatic complaints that are not of organic nature [13]. Sobański et al. revealed that also 75% of patients admitted to the day hospital for neurotic disorders treatment submitted "pseudocardiac symptoms" of tachycardia/palpitations and chest pain [14]. In non-psychiatric units the diagnosis of the symptoms commonly ends at this point. Despite the good prognosis, the presence of chest pain with no evidence of organic heart disease frequently causes withdrawal from social activities at a level comparable to patients suffering from coronary artery disease [15]. It is known that mental health problems themselves may trigger, maintain, or even worsen pain in the chest [16]. Exclusion of organic cause of symptoms without explaining other possible causes, in many cases is not enough to reassure patients who are concerned about their health [17]. Even performing diagnostic tests to rule out heart disease can strengthen the patient's belief in struggling with a serious health problem [18]. In addition, anxiety may be accompanied by reduced level of quality of life (QoL), the incidence of consecutive episodes of chest pain, overuse of health care [19] and withdrawal from social roles. It has been observed that in primary care patients who reported more than five symptoms, increased impairment of social roles occurred more frequently when these symptoms had no medical explanation than when they were results of organic dysfunctions [20].

What is more, the study on the costs of somatization in English population shows that only mental health care service is the one that does not show significantly increased rates of utilization by somatizing patients [21]. We can assume that on the one hand this kind of patients tend to ignore their mental ailments and communicate their emotional states by somatic symptoms, usually being misunderstood by physicians. On the other hand, mental health care service seems to offer the most adequate treatment for them.

Here it is worth to present the results of a study evaluating medical care and treatment in the newly established Medically Unexplained Symptoms Clinic (MUS Clinic) in London [22]. The authors emphasize the fact that the vast majority of patients admitted to the diagnostics suffered primarily from previously undetected mental health disorders. Most often patients were diagnosed with depression and anxiety disorders, which implies two further issues. One of them is the need to improve the efficiency of recognition of these disorders at primary and secondary health care [23]. The second issue is related to diagnostic difficulties with clinical manifestations of depression and anxiety disorders, which could be restricted to somatic symptoms [24, 25].

Guidelines and treatment pathways

British guidelines for dealing with chest pain of 2010 [26] does not recommend further proceedings based on the assumption that the mere recognition of the absence of organic heart disease will improve the patient's condition [27]. The current German guidelines regarding the psychosocial factors in cardiology (2013) include the area of psychosocial functioning as an important etiologic factor in the development and prognosis of coronary artery disease (recommendations I A). Loneliness, lack of social support, death of a partner, similarly to depression, depressed mood, anxiety, hostility, or PTSD, are an independent etiological factors of coronary heart disease development. They have a negative impact on both the prognosis and the presence of complications during treatment [28]. These guidelines recommend to diagnose and treat psychiatric disorders as a part of the prevention of coronary heart disease (I B). Numerous reports support the aforementioned recommendations. Ashley M. Harris et al. observed that comorbidity of mental disorders in patients without diagnosed organic disease who report somatic symptoms is more than four times higher than in patients with organic diagnoses, and reaches 60% [29]. In another study, psychiatric diagnosis was present in 75% of patients reporting somatic symptoms with no evidence of organic disease. Panic disorder was diagnosed in a half of the studied patients (47.1%), and depression in 21.4% of patients. Generalized anxiety disorder and obsessive-compulsive disorders were diagnosed in 5.7% of patients, and less than 3% of patients were diagnosed with somatoform disorders. The most common complaint in patients with generalized anxiety disorder and panic disorders was the conviction of heart disease [30].

Moreover, anxiety disorders, depression, depressed mood or loneliness separately, are an important risk factors for cardiovascular diseases. Due to the frequent comorbidity of mental illness with cardiovascular diseases and worse prognosis for this coincidence, it is important to extract mentally disturbed person from the population of people suffering from cardiovascular diseases. In accordance with current knowledge, the assessment of mental functions is an important element in the diagnostic and therapeutic process in patients with cardiac symptoms, irrespective of diagnosis of organic heart disease.

Another study suggests that understanding the essence of reported complaints provides relief for patients and it may be an intervention with positive therapeutic outcomes [27]. Unfortunately, as reported in studies, psychosomatic disorders are diagnosed too rarely in primary care [31]. This situation has many causes [32],

among other things, it is doctor's fear of overlooking "serious illness" [7] and the lack of clear diagnostic pathways. In ICD-10 and DSM-IV somatization disorder is diagnosed after the exclusion of organic cause, which often is very difficult. The reports also highlight the lack of EBM (Evidence-based medicine) based guidelines for the management of patients reporting medical condition without organic explanation [33]. In 2012, in Germany, for the first time, an interdisciplinary team of specialists in medicine and psychosocial sciences, together with a representative of patients led to the drafting of guidelines for dealing with somatoform disorders. Innovations in this edition of the Guidelines include i.a. emphasis to features of the doctor-patient relationship important in the treatment of somatoform disorders, taking into account also iatrogenic areas [34].

Transient myocardial ischemia and stress-induced cardiomyopathy as psychosomatic syndromes

In 2012, carbon dioxide challenge test imitating panic attack triggering myocardial ischemia was described. The experiment was conducted in a man with a long history of occurrence of panic attacks in the course of agoraphobia. The study is important due to the fact that the impact of a panic attack on disturbances of myocardial perfusion in patients without structural heart disease has been experimentally demonstrated for the first time. During the study, the patient reported mild chest pain, palpitations and dizziness. There has been an increase in blood pressure to 190/100 mmHg and increased heart rate, oxygen saturation remained at 98%. No ischemic changes were observed in ECG, whereas single-photon emission tomography image demonstrated reversible myocardial ischemia [35]. Currently it is known that different mechanisms are responsible for triggering pain in the chest during a panic attack [36]. The one most often mentioned is hyperventilation which causes respiratory alkalosis. It is related to calcium influx into the cells, which induces spasm of coronary arteries resulting in myocardial ischemia [37]. In the described case, despite overactivity of the adrenergic system recorded during the test, the patient denied the occurrence

of a panic attack. The explanation may be found in a study by Bernard D. Beitman et al., where it has been noted that up to 32-41% of patients with anginal pain without coronary artery disease do not feel fear when experiencing a panic attack [38].

Takotsubo cardiomyopathy – in other words stress-induced cardiomyopathy (Transient left ventricular apical ballooning syndrome - TL-VABS) has the similarly transient nature of ischemia. It is manifested by pain in the chest, shortness of breath, hypotension and changes in ECG as in a myocardial infarction. The diagnosis is based on 1) the presence of transient dyskinesia of left ventricular apex and the centre of the ventricle, comprising an area of vascularisation of more than one coronary artery; 2) the lack of significant coronary artery disease and lack of angiographic characteristics of plaque rupture; 3) new changes in ECG; and 4) the exclusion of the presence of a pheochromocytoma or myocarditis. The described cardiomyopathy is associated with a good prognosis and with full recovery in up to 4 weeks. Mortality varies between 0% and 8% [39]. It is estimated to occur in 0.02% of the population of the United States, of which 89% are women, especially in postmenopausal period [40]. It is often comorbid with cerebrovascular diseases and psychiatric disorders, including anxiety disorders, mood disorders, as well as with liver failure, sepsis and cancer [41-42]. The exact mechanism of symptoms is still unknown. It is believed that the symptoms of cardiomyopathy are the result of severe stress, which occurs due to the release of catecholamines. The excess of catecholamines affects the modification of beta2-adrenergic receptors, leads to vasoconstriction, accumulation of toxic metabolites, and consequently blocks the contractility of certain areas of the heart muscle. This thesis is confirmed by reports on occurrence of cardiomyopathy, similar to that in Takotsubo cardiomyopathy, in patients with a diagnosis of pheochromocytoma. In this case, removal of the catecholamine-producing tumor results in left ventricular failure remission [43]. Some authors also believe that the described cardiomyopathy has a protective function, which allows a patient to survive a stressful situation without permanent damage to the myocardium [44]. The researchers suggest that the same

protective function is performed by dissociative amnesia for the psyche. In people who have experienced dissociative amnesia after traumatic events, the prevalence of posttraumatic stress disorder (PTSD) is lower [45] [46, 47]. In 2014, Amir Toussi et al. reported, for the first time, a case of a woman in whom Takotsubo cardiomyopathy was accompanied by the occurrence of dissociative amnesia in reaction to her sister's death [48]. The researchers suggest that dysregulation of glutamate levels in the blood and increased levels of catecholamines might be the mechanism responsible for the occurrence of dissociation in the course of transition cardiomyopathy [47, 49, 50]. Knowledge on the issue of these interdependencies is still incomplete and requires further studies.

Psychocardiology and the comorbidity

Bearing in mind the strong interdependencies between heart diseases and mental health, a new field of science - psychocardiology - has been created. Psychocardiology combines medical thinking and psychology. It is impossible not to mention that Poland is one of the first countries which recognized the role of psychological problems in patients with cardiovascular diseases. In 1961 prof. Zdzislaw Askanas opened psychological laboratory at the Institute of Cardiology, Medical University of Warsaw, one of the first of its kind in Europe [51]. The beneficial effects of cooperation of cardiologists and psychologists has been confirmed by the results of meta-analysis of 43 studies on psychological interventions in patients suffering from cardiovascular disorders. During the two year observation of patients with heart disease who simultaneously participated in psychological interventions, it has been shown that the mortality rate in this group decreased by 27% compared with patients who were monitored only by an internist. Moreover, in the long perspective frequency of disease reoccurrence was lower by 43%. Researchers explain the relationship between cardiology and psychology by common pathophysiologic and behavioral mechanisms. On the one hand psychologic factors may activate some negative pathophysiologic metabolic pathways, on the other, negative psychosocial conditions may promote unhealthy behavior [52].

The current review of studies [53] on the contribution of depression in the global prevalence of coronary artery disease (CAD) suggests that the risk of its development is increased in people with depression by 56%, and that depression is responsible for 2.95% of DALYs (Disability-adjusted life year - years of life lost due to premature death or bodily injury resulting from trauma or disease) associated with CAD. Bacon et al. (2014) showed that patients diagnosed with an anxiety disorder are four times more likely to develop hypertension during one year of observation. Contradictory information has been obtained in the study on the relationship between depression and hypertension. In the meta-analysis of prospective studies, results suggest that depression increases the incidence of hypertension by 42% [54]. On the other hand, the largest prospective study on this issue, including 36,000 people, that is about 50% more than the entire meta-analysis, does not confirm these results. In follow-up examinations after 11 and 22 years, the obtained results showed a combination of intensification of depressive symptoms with lower blood pressure [55, 56]. The explanation for these discrepancies could be other reports suggesting that only affective symptoms of depression impact the sympathetic nervous system dysfunction. Somatic component and the total score on a scale of depression have no significant influence [57].

Mechanisms of symptoms

Regulation of emotions

Trying to understand how psychology affects somatics, it is impossible not to mention the concepts of diseases stemming from psychoanalytic thinking. Some theorists believe that it is useless to distinguish psychosomatic illnesses from other diseases, as most somatic disorders have mental aspect, as well as mental illnesses have somatic aspect. They emphasize the fact of non-existence of simple cause and effect relation between the "'psyche" and "soma" [58]. Aleksandrowicz also says that neurosis and their psychotherapy are an integral

part of medicine and medical tasks and significantly exceed outside the scope of psychiatry [59]. Such thinking is supported by the theory of emotional regulation developed by Graeme J.Taylor [60], which does not distinguish organic and functional, physical or mental diseases, treating them as impaired regulation of various sub-systems of the body. In this approach, each illness is psychosomatic, as they can be accompanied by both physiological and mental changes. Sigmund Freud presented a similar way of thinking over 120 years ago. In addition to the symptoms of conversion neurosis, of symbolic significance, he mentioned actual neurosis whose bodily symptoms were the result of limited capacity to cope with tension [61]. This theory seems to be confirmed by Kyung Bong Koh. In his study, based on 47 patients, he showed that suppression of anger was a predictor of somatic symptoms [62]. Similarly, in patients after myocardial infarction, the intensification of somatization was associated with blocking the expression of unpleasant emotions [63]. Liang Liu et al. showed that, the tendency to react with anger, on the one hand, and excessive suppression, on the other, play an important role in the emergence of somatic symptoms in people with anxious-ambivalent attachment style. In this approach, the intervention directed to the ability to express and cope with feelings, could reduce, in some people, a tendency to present medically unexplained symptoms [13].

Alexithymia

The term alexithymia is defined as difficulty in identifying and expressing emotions, poverty of imagination and externally-oriented way of thinking [64]. Its relations with both mental illnesses and somatic diseases [65] including depression [66], anxiety disorders [67], eating disorders [68], hypertension [69], diabetes [70] and psoriasis [71] have been reported. Alexithymic features are relatively common in the general population, occurring in 10% of adults, slightly more frequently in men [72]. There are many concepts of its development. Genetic, neurobiological and environmental factors are considered to be essential. Referring to the etiology, Hellmuth Freiberger [73] introduced a distinction between primary alexithymia – a genetically determined personality traits and secondary alexithymia – which is a defense mechanism for experienced trauma [74, 75].

A study comparing the features of alexithymia in patients suffering from cardiovascular disorders and mood disorders showed an increased overall level of alexithymia in both groups. Higher score in terms of poverty of imagination and a lower emotional excitability have been observed among patients with cardiovascular diseases. In contrast, more intense characteristics - the difficulty in verbalizing emotional experience and poor insight into own emotional experience - have been observed in patients with mood disorders. Dysregulation of autonomic nervous system is considered to be the pathomechanism responsible for comorbidity of alexithymia and cardiovascular diseases [76]. The gap between the intensity of the emotional response and recorded reaction of the autonomic nervous system, described in other publications [77], has been also observed in the study [78]. According to Henry Krystal, lack of access to conscious experiencing the affective content in alexithymic patients leads to its disclosure in the body, i.e. somatization [2].

Theory of the desomatization - resomatization

The occurrence of somatic symptoms without organic cause related to illness is also explained by the psychoanalytic concept of early trauma. Krystal, explaining the genesis of psychosomatic disorders, drew attention to the difficulties in diagnosis of emotional states arising from blocking the processes of differentiation, verbalization and desomatization of child's affect on the basis of deprivation of the child's needs at an early stage of development. He believed that alexithymic people are the people who experienced trauma in early childhood. Consequently, in the face of overwhelming fear, it leads to the phenomenon of regression, resulting in secondary somatization (resomatization) of mental processes. People who have experienced long-term trauma in childhood, could fail in desomatization. As a result, the presentation of mental states is not transferred from the body into the realm of mind [2]. Currently, it seems reasonable to ask

about the diagnosis and treatment of difficulties associated with recognizing one's own emotional states in terms of prevention or potentiation of treatment of somatic diseases.

Functional imaging

The literature extensively describes changes in the nervous system of patients with mental disorders, including psychosomatic symptoms. The observation of these changes is possible by functional imaging techniques, such as functional nuclear magnetic resonance (fMRI), single photon emission tomography (SPECT), magnetoencephalography (MEG) and positron emission tomography (PET). As an example, there is a study in which the neurophysiological basis of alexithymia, indicating a malfunction of anterior cingulate gyrus has been evaluated [79-81]. Hasse Karlsson et al., have found that the reduced activation of the anterior cingulate gyrus is also correlated with the increase in the activation of the motor and somatosensory cortex, which could explain the mechanism of occurrence of somatic symptoms with the lack of recognition of experienced emotions. Julian F. Thayer et al. created a neurophysiological model of emotion regulation on the basis of functional examination [82]. According to him, during emotional stress increases the activity of the limbic system and certain prefrontal areas and there is a general decrease in activity of the prefrontal cortex, which triggers the automatic system of behavior control [83]. This concept corresponds with model of cognitive-emotional impulse control proposed by Sylvie J M van der Kruijs [84]. Explaining the phenomenon of dissociation, the model assumes that in the optimal emotional state the motor areas of the brain to a small extent are affected by emotions. However, in case of intensive emotional arousal, the centre responsible for the cognitive processing of excitation is omitted. In the imaging examination, the described model appears to be an increase in functional connection of the motor cortex with the limbic system with reduced prefrontal cortex impulsation. In another report, the researchers suggest that the phenomenon of somatization measured using a self-assessment questionnaire (SOMS-2) is associated with increased activity in the anterior ventral precuneus, posterior cingulate gyrus and anterior medial thalamus, and that the autonomic nervous system affects the occurrence and severity of symptom in the body. At the same time the researchers pay attention to the fact that their findings are consistent with the theory, according to which somatization is associated with cognitive style characterized by affective content rumination [85].

Diagnostics and treatment

In addition to the broad diagnostic capabilities, functional examination enables an assessment of the impact of pharmacological and psychotherapeutic treatment on nervous system metabolism modification, which in recent years has been repeatedly demonstrated [86]. It must be remembered that modern methods of brain imaging, although they are a milestone for the development of medical knowledge and make it possible to objectify the diagnosis and assessment of treatment effects, are burdened with the necessity of scientific reductionism in describing mental processes [87].

The clinical management still lacks clear guidelines for psychological and psychiatric diagnosis in patients with symptoms which suggest somatization. Due to the high comorbidity of somatic diseases with mental disorders, the implementation of diagnostic screening for mental health disorders, appears to be indispensable at some stage. Moreover, the conclusions of a meta-analysis of several studies clearly confirm that, in the treatment of somatoform disorders, psychotherapy is more effective than standard method (d=0.80 vs. d=0.31, p <0.05) [87]. Control studies show that the positive effect of the treatment occurs in case of psychotherapy and physical exercises, but it has not been observed for the administration of medicines [88-91]. Changes in DSM-5 come in the aid of diagnosticians, freeing them from the necessity to exclude organic cause in the case of unexplained somatic symptoms. Such an approach is also close to the psychoanalytic perspective. In psychotherapy, patients with somatic symptoms of mental disorders, the prospect of an organic explanation of complaints by the appropriate expert inhibits the progress of therapy.

The treatment of these diseases emphasizes the importance of awareness, disclosure and experiencing emotions, which is the core of psychodynamic psychotherapy [92]. In studies in the general population it has been shown that training in naming emotions and reading literary fiction [93] is beneficial for identifying one's own emotional states and affective regulation [94]. Psychotherapy also reduces the symptoms of alexithymia, although there is still a need to develop an individualized procedure in this respect [95]. In examining the impact of pharmacology, Anthony Lane et al. (2013) showed that oxytocin administered intranasally increase people's will to share their painful emotions [96]. Another therapeutic option is transcranial magnetic stimulation of the brain areas responsible for experiencing emotions and linguistic properties [97, 98]. Further studies in this regard, assessing various therapeutic interventions in randomized trials are needed.

Recapitulation

In medical practice we often meet patients with somatic symptoms without organic cause. In this case, usually reported symptoms are accompanied by undiagnosed mental health problems, which are often a significant factor in the risk of serious somatic illness. Despite the lack of a diagnosed organic cause, these symptoms are a cause of disability and withdrawal from normal social life. In addition, deepening and repeating diagnostic test for unexplained somatic symptoms increases patient's anxiety, which exacerbate symptoms, and generates considerable cost to the health care system. Unfortunately, there is still a lack of clear guidelines for diagnosis and treatment of psychosomatic disorders in primary care, and in many departments involved in the treatment of somatic illnesses.

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