

Posttraumatski stresni poremećaj nakon akutnoga koronarnog sindroma ili kardiokirurške operacije; podcijenjena realnost

Posttraumatic Stress Disorder after Acute Coronary Syndrome or Cardiac Surgery; Underestimated Reality

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RECEIVED:

August 1, 2019

UPDATED:

November 15, 2019

ACCEPTED:

December 1, 2019



SAŽETAK: Osim somatskih posljedica akutnoga koronarnog sindroma u obliku različitoga stupnja intolerancije napora, radne nesposobnosti, simptoma kroničnog srčanog zatajavanja, angine pectoris, pojave različitih aritmija i sl., moguć je već u ranoj subakutnoj te u kroničnoj fazi u oboljelih osoba razvoj niza psihosomatskih i psihičkih poremećaja, koji, ako se ne prepoznaju navrijeme i aktivno ne liječe, mogu pridonijeti nepovoljnom ishodu i povećanoj smrtnosti takve skupine bolesnika. Osim povezanosti akutnoga koronarnog sindroma i kroničnog stresa, anksioznosti i depresije, on može biti „okidač“ za razvoj kasnijega posttraumatskoga stresnog poremećaja (PTSP) sa stopom prevalencije od prosječno 15-ak posto među oboljelim osobama. Više je istraživanja pokazalo da bolesnici sa simptomima PTSP-a povezanog s prethodnim akutnim koronarnim sindromom, napose oni neliječeni, imaju povećanu smrtnost i veću stopu reinfarkta miokarda. Budući da PTSP povezan s akutnim koronarnim sindromom ili kardiokirurškom operacijom zna biti zanemaren i podcijenjen, svrha je ovog rada podizanje svijesti o ovom problemu u svakodnevnoj kliničkoj praksi.

SUMMARY: In addition to the somatic consequences of acute coronary syndrome (ACS) that include different levels of intolerance to exertion, incapacity for work, symptoms of chronic heart failure, angina pectoris, the manifestation of various arrhythmias, etc., the development of a whole range of psychosomatic and mental disorders is also possible already in the early subacute and chronic phases of the disease, and if these mental disorders are not actively treated in a timely fashion they can contribute to unwanted outcomes and increased mortality in this group of patients. ACS is associated with chronic stress, anxiety, and depression and can be a trigger for later development of posttraumatic stress disorder (PTSD) with an average prevalence rate of 15% in patients with ACS. Several studies have shown that patients with symptoms of PTSD associated with ACS, especially if untreated, have increased mortality and higher rates of myocardial reinfarction. Since PTSD associated with ACS or cardiac surgery can be neglected or underestimated, the aim of this review was to raise awareness about this issue that is present in everyday clinical practice.

KLJUČNE RIJEČI: posttraumatski stresni poremećaj, akutni koronarni sindrom, kardijalna kirurgija.

KEYWORDS: posttraumatic stress disorder, acute coronary syndrome, cardiac surgery.

CITATION: *Cardiol Croat.* 2020;15(1-2):3-8. | <https://doi.org/10.15836/ccar2020.3>

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TO CITE THIS ARTICLE: Lakušić N, Kamenečki G, Sopek Merkaš I, Cerovec D, Fučkar K, Gabrić ID, et al. Posttraumatic Stress Disorder after Acute Coronary Syndrome or Cardiac Surgery; Underestimated Reality. *Cardiol Croat.* 2020;15(1-2):3-8. | <https://doi.org/10.15836/ccar2020.3>

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Koronarna bolest srca (KBS) glavni je uzrok smrti i invaliditeta u razvijenim zemljama. Iako se stopa smrtnosti od KBS-a u svijetu stalno smanjuje tijekom posljednja četiri desetljeća, ona je i dalje odgovorna za otprilike trećinu svih smrtnih slučajeva u osoba starijih od 35 godina¹. Procjenjuje se da će se broj umrlih od srčanožilnih bolesti u svijetu do 2030. godine povećati sa sadašnjih 17,5 milijuna na oko 23 milijuna^{2,3}.

Coronary heart disease (CHD) is the main cause of mortality in developed countries. Although the global mortality rate from CHD has been in a downward trend over the last four decades, CHD is still responsible for approximately one third of all deaths in persons above the age of 35¹. It is estimated that the global number of deaths from cardiovascular diseases will increase from the current 17.5 million to about 23 million by 2030^{2,3}.

Iako je posljednjih 15-ak godina prisutan pozitivan kontinuirani trend smanjenja smrtnosti od srčanožilnih bolesti (SŽB) u Hrvatskoj, što je izraženije za cerebrovaskularne bolesti nego za KBS, one su ipak i dalje na vrhu ljestvice smrtnosti. Tako je 2016. godine u Hrvatskoj od SŽB-a umrlo 23 190 osoba, što je 45 % ukupno umrlih. Hrvatska se sa standardiziranom stopom smrtnosti od 314/100 000 ubraja među europske zemlje koje imaju srednje visoke stope smrtnosti⁴.

Povezanost koronarne bolesti srca i kroničnoga stresa te anksioznosti

Osim somatskih posljedica akutnoga koronarnog sindroma (AKS) u obliku različitog stupnja intolerancije napora, radne nesposobnosti, simptoma kroničnoga srčanog zatajavanja, angine pectoris, pojave različitih aritmija i sl., moguć je već u ranoj subakutnoj te u kroničnoj fazi razvoj niza psihosomatskih i psihičkih poremećaja oboljelih osoba što, ako se ne prepozna navrijeme i aktivno ne liječi, može pridonijeti nepovoljnom ishodu i povećanoj smrtnosti te skupine bolesnika⁵.

Akutni i kronični stres te anksioznost odavno su prepoznati te danas jasno etablirani rizični čimbenici za razvoj akutnog infarkta miokarda (AIM)⁶. Primjerice, u istraživanju INTERHEART izvori kroničnoga stresa bili su podijeljeni na stres na poslu, u obiteljskom domu te na stres vezan za financije i egzistencijalne probleme. Bolesnici s prvim AIM-om prijavili su mnogo više stresa u svakoj od tih kategorija u usporedbi s kontrolnom skupinom⁷.

Nadalje, tijekom dvogodišnjega praćenja gotovo trideset četiri tisuće muških zdravstvenih djelatnika u Sjedinjenim Američkim Državama u dobi od 42 do 77 godina, koji su u početku bili bez dijagnosticirane bolesti, relativni rizik od pojave fatalne SŽB bio je trostruko veći za one s najvišim razinama anksioznosti u usporedbi s ispitanicima s najnižim razinama⁸.

Povezanost koronarne bolesti srca i depresije

Širok spektar dokaza podupire depresiju kao snažan čimbenik rizika od SŽB-a, bilo da je riječ o osobama bez manifestne ili o onima s već dokazanom KBS. Pregledom 53 istraživanja i četiriju metaanaliza koji je provela *American Heart Association* (AHA) utvrđeno je da je depresija nakon akutnoga koronarnog sindroma čimbenik rizika za nepovoljne ishode, uključujući povećanu smrtnost bilo kojeg uzroka, kao i kardiovaskularnu smrtnost⁹.

Predloženo je nekoliko potencijalnih patofizioloških mehanizama povezanosti depresije i AIM-a koji uključuju disfunkciju hipotalamično-hipofizno-adrenalne osi, upalne i protrombotičke promjene, niske razine omega-3 masnih kiselina, sniženu varijabilnost sinusne frekvencije i dr. uz nesudjeljivost bolesnika u liječenju¹⁰. Najveća analiza povezanosti depresije i AIM-a vezana je za istraživanje provedeno u više od 93 000 žena u postmenopauzi u dobi od 50 do 79 godina koje su sudjelovale u studiji Inicijative za zdravlje žena. Na početku istraživanja utvrđeno je da je 16 % ispitanica trenutačno bilo depresivno, a u njih 12 % postojao je anamnestički podatak o prethodnoj depresiji. U četiri godine praćenja bolesnice s trenutačnom ili prijašnjom depresijom imale su mnogo veće stope kardiovaskularne smrti i ukupne smrtnosti neovisno o uzroku u usporedbi s onima bez depresije¹¹.

Although a continuous positive trend of reduced mortality from cardiovascular diseases (CVD) has been observed in Croatia over the last 15 years, with an even greater improvement for cerebrovascular diseases, they are still the top cause of mortality. There were 23,190 deaths from CVD in Croatia in 2016, which is 45% of total deaths. With a standardized mortality rate of 314/100,000, Croatia is among the European countries that have a moderately high mortality rate⁴.

The association between coronary heart disease and chronic stress and anxiety

In addition to the somatic consequences of acute coronary syndrome (ACS) that include different levels of intolerance to exertion, incapacity for work, symptoms of chronic heart failure, angina pectoris, the manifestation of various arrhythmias, etc., the development of a whole range of psychosomatic and mental disorders is also already possible in the early subacute and chronic phases of the disease, and if these mental disorders are not actively treated in a timely fashion they can contribute to unwanted outcomes and increased mortality in this group of patients⁵.

Acute and chronic stress and anxiety have long been recognized and are now clearly established as risk factors for the development of acute myocardial infarction (AMI)⁶. For instance, the INTERHEART study divided sources of chronic stress into stress at work, stress at home, and stress related to financial and existential issues. Patients with first AMI reported significantly more stress in all of these categories in comparison with the control group⁷.

Furthermore, two-year follow-up of almost 34 thousand male healthcare workers in the USA aged between 42 and 77 that initially had no disease diagnosis found that relative risk for fatal CVD was three times higher for those with the highest levels of anxiety in comparison with participants with the lowest levels of anxiety⁸.

The association between heart disease and depression

A wide spectrum of evidence indicates depression as a strong risk factor for CVD, both in persons without manifested CHD or with previously established CHD. A review of 53 studies and 4 meta-analyses by the American Heart Association (AHA) found that depression after acute coronary syndrome constitutes a risk factor for adverse outcomes, including increased all-cause mortality and cardiovascular mortality⁹.

Several potential pathophysiological mechanisms of association between depression and AMI have been suggested, including dysfunction of the hypothalamic-pituitary-adrenal axis, inflammatory and prothrombotic changes, low levels of omega-3 fatty acids, low sinus frequency variability, etc., as well as lack of treatment compliance¹⁰. The largest analysis of the association between depression and AMI is related to a study conducted on more than 93,000 postmenopausal women aged 50 to 79 that participated in the Women's Health Initiative study. At baseline, 16% of participants reported depression and 12% had previous depression in their medical history. In four years of follow-up, patients with current or previous depression had significantly higher rates of cardiovascular mortality and total mortality from all causes compared with participants without depression¹¹.

Unatoč nedostatku uvjerljivih i nedvojbenih dokaza da liječenje depresije poboljšava preživljavanje nakon AKS-a, AHA je ipak zaključila i preporučila da je potrebno razmotriti sveobuhvatnu procjenu koronarnih bolesnika i liječenje klinički značajnije ili trajne depresije⁹.

Posttraumatski stresni poremećaj i njegova povezanost s akutnim koronarnim sindromom i kardiokirurškom operacijom

Posttraumatski stresni poremećaj (PTSP) relativno je čest entitet u psihijatrijskoj praksi koji je definiran kao složeni somatski, kognitivni i afektivni poremećaj uzrokovan različitim oblicima psihološke traume. PTSP karakteriziraju nametljive misli, noćne more i uspomene na prošle traumatske događaje, izbjegavanje podsjetnika na traumu i poremećaji spavanja, što sve uzrokuje znatnu socijalnu, profesionalnu i interpersonalnu disfunkciju¹².

Dijagnoza PTSP-a može biti izazovna zbog heterogenosti prezentacije i otpora oboljelog da raspravlja o prošloj traumi. Različiti oblici traume mogu uzrokovati pojavu PTSP-a, poput najrazličitijih oblika seksualnog zlostavljanja, rastave braka, smrti bliske osobe, aktivnog sudjelovanja u ratnim operacijama itd., a često se pojavljuje i među civilima u ratnim zonama, u izbjeglicama, tijekom prirodnih katastrofa i sl.¹².

Ukupna prevalencija PTSP-a bilo kojeg uzroka kreće se od 6 do 9 % u nacionalnim uzorcima opće populacije odraslih u Sjedinjenim Američkim Državama i u Kanadi¹³. Prema istraživanjima Svjetske zdravstvene organizacije, nešto niža stopa prevalencije ustanovljena je izvan Amerike i u ekonomski srednje razvijenim zemljama ona iznosi oko 2 %¹⁴.

Iako veći dio patofiziologije PTSP-a nije jasan, pregledom literature nalaze se intrigantni izvještaji. Tako je u bolesnika s PTSP-om snimanjem moždanih struktura magnetnom rezonancijom nađen smanjen volumen hipokampusa, lijeve amigdale i prednjega cingularnog korteksa u odnosu prema kontrolnoj skupini bez PTSP-a^{15,16}. Druga su izvješća pokazala povećanu razinu norepinefrina u središnjem živčanom sustavu s „down“ regulacijom adrenergičkih receptora, kronično snižene razine glukokortikoida itd.^{17,18} Također se smatra se da određena genska predispozicija može pridonijeti osjetljivosti pojedinca na razvoj PTSP-a kroz interakciju s okolišnim čimbenicima¹⁹.

Osim opisane povezanosti AKS-a i kroničnoga stresa, anksioznosti i depresije, on, baš kao i različite druge navedene akutne traume, može biti „okidač“ za razvoj kasnijeg PTSP-a sa stopom prevalencije od 4 do čak 25 % među oboljelim osobama (prosječno 10 – 15 %)²⁰⁻²². Iako su podatci o PTSP-u nakon moždanog udara manje opsežni od literature o PTSP-u i AKS-u, postoje izvještaji da jedan od četiriju slučajeva moždanog udara ili tranzitornog ishemijskog napadaja može biti povezan s kasnijim razvojem PTSP-a^{23,24}. Također je i nakon kardiokirurškog zahvata²⁵, poglavito nakon produljenog boravka u jedinici intenzivnog liječenja te kompliciranoga poslijepoperativnog tijeka²⁶, velika mogućnost razvoja kasnijeg PTSP-a. Simptomi koji upućuju na PTSP u bolesnika koji su bili prolongirano liječeni u jedinici intenzivnog liječenja uključuju afektivne i bihevioralne reakcije na podražaje koji izazivaju „flashbackove“, tešku tjeskobu i hiperekscitaciju, kao i intruzivno sjećanje i izbjegavanje iskustava koja uzrokuju simptome²⁷.

Despite the lack of convincing and indubitable evidence that treating depression improves survival after ACS, AHA has nevertheless concluded and recommended consideration of a holistic assessment of coronary patients and treatment of clinically significant or long-lasting depression⁹.

Posttraumatic stress disorder and its association with acute coronary syndrome and cardiac surgery procedures

Posttraumatic stress disorder (PTSD) is a relatively common entity in psychiatric practice that is defined as a complex somatic, cognitive, and affective disorder caused by different forms of psychological trauma. PTSD is characterized by intrusive thoughts, nightmares, and memories of past traumatic events, avoidance of reminders of trauma, and sleep disorders, all of which leads to significant social, professional, and interpersonal dysfunction¹².

Diagnosing PTSD can be challenging due to the heterogeneity of presentation and resistance from the patient in discussing past traumas. Different forms of trauma can cause PTSD, including all kinds of sexual abuse, divorce, death of a loved one, active participation in military operations, etc., and it is also common amongst civilians in warzones, refugees, during natural disasters, etc.¹².

The total prevalence of all-cause PTSD is between 6-9% in national samples of the general population of the United States and Canada¹³. According to research from the World Health Organization, a somewhat lower prevalence was found outside America and is approximately 2% in economically moderately developed nations¹⁴.

Although the greater part of the pathophysiology of PTSD is still unclear, a review of the literature yields intriguing reports. Magnetic resonance imaging of brain structures in patients with PTSD found reduced volumes of the hippocampus, left amygdala, and the frontal cingulate cortex in comparison with the control group without PTSD^{15,16}. Other reports found elevated norepinephrine levels in the central nervous system with downregulation of adrenergic receptors, chronic reduction of glucocorticoid levels, etc.^{17,18} Furthermore, it is thought that certain genetic predispositions can contribute to individual sensitivity to PTSD through interaction with external factors¹⁹.

Other than the previously described association between ACS and chronic stress, anxiety, and depression, ACS can also be a trigger for subsequent development of PTSD just like other traumas, with a prevalence of PTSD between 4% to as much as 25% among persons suffering from ACS (average prevalence of 10-15%)²⁰⁻²². Although data on PTSD after stroke are less extensive than the literature on PTSD and ACS, there are some reports that one out of every four cases of stroke or transitory ischemic attacks can be associated with subsequent development of PTSD^{23,24}. Additionally, cardiac surgery procedures²⁵ and especially long hospital stays in the intensive care unit and complicated postoperative progression²⁶ have a high chance of leading to subsequent development of PTSD. Symptoms that indicate PTSD in patients who underwent prolonged treatment in an intensive care unit include affective and behavioral reactions to stimuli that cause “flashbacks”, severe anxiety and hyperexcitation, and intrusive memories and avoidance of experiences that cause the symptoms²⁷.

Metaanaliza 24 opservacijska istraživanja koja je uključivala 2383 koronarna bolesnika dokazala je stopu prevalencije PTSP-a povezanog s AKS-om od 12 %²¹. Nadalje, podatci iz triju istraživanja provedenih u 609 pacijenata koji su zadovoljili kriterije kvalitete za metaanalizu pokazali su da su pacijenti s PTSP-om nakon akutnog koronarnog sindroma imali dvostruki rizik od recidiva infarkta miokarda ili nagle smrti u usporedbi s onima koji nisu imali simptome PTSP-a²¹. Također je više drugih istraživanja pokazalo da bolesnici sa simptomima PTSP-a povezanog s prethodnim AKS-om, posebice oni neliječeni, imaju povećanu smrtnost i veću stopu reinfarkta miokarda^{28,29}.

Iskustva s bolesnicima uključenima u program kardiovaskularne rehabilitacije

Iskustvo u liječenju i rehabilitaciji bolesnika koji su imali AIM ili su bili podvrgnuti kardiokirurškom zahvatu pokazuje da, unatoč gore navedenim činjenicama i podatcima iz literature, barem dio bolesnika sa simptomima PTSP-a povezanima s AKS-om ili kardiokirurškom operacijom ostaju neprepoznati³⁰ i neliječeni u subakutnoj i kroničnoj fazi bolesti koja vodi do kaskade daljnjih prethodno opisanih nepovoljnih događaja i ishoda.

U kliničkoj se praksi često događa da se AKS razvije u do tada „zdrave“ osobe koja nije imala doticaja s bolničkim liječenjem. Nagli nastanak simptoma bolesti, hitna hospitalizacija, urgentno interventno, a pokatkad i kardiokirurško liječenje, boravak u jedinicima intenzivnog liječenja, rane komplikacije u obliku zloćudnih aritmija i resuscitacijski postupci („blizina smrti“), obilno novouvedeno medikamentno liječenje, naglo nastala (privremena) radna nesposobnost te briga za buduću egzistenciju itd. naravno da vode do različita spektra psihogenih manifestacija poput akutne anksioznosti i depresivnog raspoloženja. Ovisno o različitim čimbenicima i predispozicijama, osobnosti, prethodnim bolestima, kompenzacijskim mehanizmima, potpori obitelji i sl. u dijela oboljelih postupno će doći do privikavanja na novonastalo stanje, ali će se u dijela bolesnika razviti simptomi PTSP-a vezanog uz AKS. Takva je skupina bolesnika u daljnjem liječenju manje suradljiva i motivirana za redovito i dugoročno uzimanje lijekova te provođenje kardioloških kontrola³¹, ima lošiju kvalitetu života³², a, osim oboljelog, nerijetko i cijela obitelj trpi određene posljedice takvoga stanja oboljelog člana.

U rehabilitacijskom centru u Krapinskim Toplicama (kao i u drugim dvama hrvatskim rehabilitacijskim centrima^{33,34}) psiholog je važan i integrativni dio tima, tako da relativno često uspješno otkrivamo elemente PTSP-a nakon AKS-a ili operacije srca³⁰. Nažalost, u bolnici u Krapinskim Toplicama nije dostupna redovita konzilijarna psihijatrijska služba. Zbog toga nakon završetka kardiološke rehabilitacije takve bolesnike upućujemo na ambulantni psihijatrijski pregled i daljnje liječenje te psihološku potporu.

Zaključak

Svrha je ovog rada bila podizanje svijesti kardiologa o spomenutom problemu u svakodnevnoj kliničkoj praksi. Integrativni i nezaobilazni dio svakog ozbiljnog šireg „Heart Team“, osim kardiologa, anesteziologa i kardijalnog kirurga, trebaju biti psiholog i psihijatar. Takav, sveobuhvatni pristup postigao bi željeni učinak ne samo na somatsku nego i na punu

A meta-analysis of 24 observational studies that included 2383 coronary patients found that the prevalence of PTSD associated with ACS was 12%²¹. Furthermore, data from three studies on 609 patients who fulfilled the quality criteria for meta-analysis show that risk of repeated myocardial infarctions or sudden death was twice as high in patients with PTSD after ACS in comparison with those without PTSD symptoms²¹. Additionally, multiple studies have demonstrated that patients with PTSD symptoms associated with previous ACS, especially if untreated, have increased mortality and higher rates of myocardial reinfarction^{28,29}.

Experience with patients included in the cardiovascular rehabilitation program

Experience in the treatment and rehabilitation of patients who had AMI or underwent a cardiac surgery procedure shows that despite the abovementioned facts and data from the literature, at least a portion of patients with symptoms of PTSD associated with ACS or cardiac surgery is not recognized³⁰ and remain untreated in the subacute and chronic phase of the disease, which leads to a cascade of the previously described adverse events and outcomes.

It is a common occurrence in clinical practice for a previously “healthy” person who has not had any experience of hospital treatment to develop ACS. Rapid onset of the symptoms, emergency hospitalization, urgent interventional and sometimes surgical treatment, staying in an intensive care unit, early complications that can include malignant arrhythmias and resuscitation procedures (“proximity to death”), copious amounts of newly-introduced medications, sudden (temporary) incapacity for work, worrying about future existential needs, etc., can of course lead to a varied spectrum of psychogenic manifestations such as acute anxiety and depression. Depending on various factors and predispositions, personality traits, previous illnesses, compensation mechanisms, family support, etc., some of these patients will gradually adjust to their new state, but some of them will develop symptoms of PTSD associated with ACS. This group of patients is less cooperative in further treatment and less motivated for regular, long-term medication treatment and cardiological controls³¹, has a lower quality of life³², and the whole family of the patient often suffers from some of the consequences of the patient's condition.

In the Krapinske Toplice rehabilitation center (and in two other Croatian rehabilitation centers^{33,34}) the psychologist is an important and integral part of the team, so we fairly often successfully discover elements of PTSP after ACS or heart surgery³⁰. Unfortunately, the hospital in Krapinske Toplice does not have regular psychiatric consultations available. After completion of their rehabilitation program we therefore refer these patients to a clinical psychiatric evaluation and further treatment as well as psychosocial support.

Conclusion

The aim of this review was to raise the awareness of cardiologists regarding this issue in everyday clinical practice. In addition to a cardiologist, anesthesiologist, and cardiac surgeon, a psychologist and psychiatrist should be an integral part of every serious wider “Heart Team”. Such a holistic approach would achieve the desired effect not just on the somatic, but

psihološku stabilnost ovakvih ozbiljnih bolesnika³⁵, što bi u konačnici poboljšalo kvalitetu života, smanjilo nove neželjene kardiovaskularne događaje i smrtnost.

S obzirom na to da je, prema dosadašnjim istraživanjima i dostupnim podatcima, prevalencija PTSP-a povezanog s AKS-om relativno širokog raspona od 4 do čak 25%²², idealno bi bilo na reprezentativnom uzorku istražiti njegovu prevalenciju u Hrvatskoj, kao i dugoročni ishod takvih bolesnika.

also on the total psychological stability of these seriously ill patients³⁵, which would ultimately improve quality of life and reduce the incidence of new unwanted cardiovascular events and mortality.

Given that current studies and available data indicate the prevalence of PTSD associated with ACS has a fairly wide range of 4% to as much as 25%²², a study would ideally be conducted with a representative sample to determine its prevalence in Croatia and long-term outcomes for these patients.

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