Kardiovaskularni bolesnik u fokusu u doba pandemije COVID-a 19

Staying Focused on Cardiovascular Patients During the COVID-19 Pandemic

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SAŽETAK: Tijekom pandemije COVID-a 19 smanjio se broja pregleda te dijagnostičkih i terapijskih zahvata u bolesnika s kardiovaskularnim bolestima. U nekoliko zemalja zabilježen je porast mortaliteta u iste skupine bolesnika, kako od COVID-a 19, tako i od samih kardiovaskularnih bolesti. Važno je nastaviti liječiti takve bolesnike i spriječiti nedostupnost zdravstvene zaštite zbog subjektivnih ili objektivnih razloga. U tome nam može pomoći i telemedicina, no velik dio odgovornosti ostaje na samim bolesnicima da samokontrolom i redovitim uzimanjem terapije spriječe pogoršanje bolesti. Mi im možemo pomoći olakšavanjem te zadaće (telefonski kontakt, fiksne kombinacije lijekova). Također je važno zdravstvenu zaštitu prilagoditi pandemiji kako bi ta zaštita bila učinkovita i sigurna i za bolesnike i za pružatelje zaštite.

SUMMARY: During the COVID-19 pandemic, there fewer examinations and diagnostic and therapeutic procedures were performed in patients with cardiovascular diseases. In several countries, an increase in mortality has been reported in this group of patients, both from COVID-19 and from cardiovascular diseases. It is important to continue to treat these patients and to prevent the unavailability of health care for subjective or objective reasons. Telemedicine can also help us in this, but much of the responsibility remains with the patients themselves to prevent the disease from getting worse through self-monitoring and regular therapy. We can help them by facilitating this task (telephone contacts, fixed drug combinations). It is also important to adapt healthcare to the pandemic in order to make it effective and safe for both patients and caregivers.

KLJUČNE RIJEČI: COVID-19, kardiovaskularne bolesti, mortalitet, zdravstvena zaštita.

KEYWORDS: COVID-19, cardiovascular diseases, mortality, healthcare.

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Otkad je prvi put prijavljena u Wuhanu u Kini potkraj prosinca 2019., respiratorna infekcija uzrokovana virusom SARS-CoV-2 (COVID-19) brzo se proširila diljem svijeta i postala globalna pandemija koja pogađa više od 200 zemalja. Ta pandemija uzrokovala je dramatične javnozdravstvene intervencije i izazvala duboke globalne socioekonomske poremećaje (koji uključuju i najdublju recesiju u posljednjih stotinu godina). Dramatičan porast broja bolesnika s COVID-om 19 u posljednjih 6 mjeseci preplavio je zdravstvene sustave u brojnim zemljama širom svijeta.[1] Pandemija je također stvorila nove značajne izazove sustavima javnoga zdravstva razvijenih zemalja jer su oni bili fokusirani na mahom kronične neprenosive bolesti. S obzirom na to da trenutačno ne postoji učinkovito kauzalno liječenje kao ni cjepivo, mnoge su se zemlje odlučile na određeni stupanj odgraničenja kretanja i izolacije svojih stanovnika, a neri-

Since it was first reported in Wuhan, China in late December 2019, the respiratory infection caused by the SARS-CoV-2 virus (COVID-19) has spread rapidly around the world and become a global pandemic affecting over 200 countries. This pandemic has caused dramatic public health interventions and profound global socio-economic disruptions (which include the deepest recession in a hundred years). The dramatic increase in the number of patients with COVID-19 in the last 6 months has flooded health systems in many countries around the world.[1] The pandemic also created new significant challenges to the public health systems of developed countries, as they had been mostly focused on chronic non-communicable diseases. Given that there is currently no effective causal treatment or vaccine, many countries have opted for a certain degree of movement restriction and isolation of their residents, and there has often

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jetko je postojalo i razdoblje potpunog zatvaranja većeg dijela gospodarskih aktivnosti.[2] Iste sudbine nije bila pošteđena ni Republika Hrvatska, gdje je sredinom ožujka proglašena pandemija pa je bilo preporučeno maksimalno moguće smanjenje dolazaka bolesnika u ordinacije te dopušteno obavljanje samo hitnih i neodgodivih pregleda i postupaka dok traje epidemija.[3] Zbog svega navedenog te dodatnog straha od zaraze, smanjio se i broj pregleda i dijagnostičkih postupaka u bolesnika s kardiovaskularnim (KV) bolestima. Uspoređujući broj pregleda u primarnoj zdravstvenoj zaštiti RH u travnju 2019. i travnju 2020. (prema objavljenim podatcima HZJZ-a[3]), vidi se signifikantan pad (P <0,001, Whiteheadov test za Poissonovu distribuciju) djelatnosti, što je uvijek loše za KV bolesti pri kojima je ključna prevencija. Nadalje, prema velikom upitniku namijenjenom kliničkim kardiolozima provedenom u 141 zemlji sa 6 kontinenata, 78,8 % odgovorilo je da je broj bolesnika koji su bolnički liječeni zbog infarkta miokarda s elevacijom ST-spojnice (STEMI) smanjen od izbijanja pandemije, a 65,2 % ispitanih naznačilo je da je to smanjenje veće 40 %. Otprilike 60 % svih ispitanika izvijestilo je da su se bolesnici sa STEMI-jem dolazili kasnije nego obično, a 58,5% da je više od njih 40 % bolesnika koji su primljeni u bolnicu došlo izvan optimalnog prozora za primarnu perkutanu koronarnu intervenciju (PCI) ili trombolizu.[2]

Prema dostupnim podatcima smanjen je dakle broj pregleda u primarnoj zaštiti, kao i broj postupaka u sekundarnoj zdravstvenoj zaštiti. Pogledajmo sada reperkusije svih navedenih čimbenika na mortalitet. Europska skupina za monitoriranje prekomjernog mortaliteta (EuroMOMO) objavila je podatke o tjednom mortalitetu u 2020. u nekoliko europskih zemalja te ih je usporedila s prijašnjim višegodišnjim prosjekom (na taj se način svake godine izračunava „prekomjerni", odnosno mortalitet veći od očekivanog za to razdoblje). Iz tih je podataka vidljivo znatno povećanje mortaliteta u 15. tjednu 2020. u većini promatranih zemalja, i to u svim dobnim skupinama, osim 0 – 14 godina.[4] Slično povećanje ukupnog mortaliteta tijekom pandemije zabilježeno je i izvan Europe, no je li za taj porast odgovoran SARS-CoV-2 izravno ili neizravno? U odgovoru na to pitanje mogli bi nam pomoći elektronički nacionalni registri mortaliteta. Prema jednom istraživanju provedenom među bolesnicima sa šećernom bolesti u Ujedinjenom Kraljevstvu, tijekom pandemije zabilježen je porast broja umrlih slučajeva u kojih COVID-19 nije bio uzrok smrti (**slika 1**).[5] Isto istraživanje također ilustrira i povećani rizik od smrti zbog COVID-19 u ljudi s višim kardiovaskularnim rizikom (mnogo je zajedničkih rizičnih čimbenika).

Iz svega navedenog vidljivo je da se tijekom pandemije COVID-a 19 smanjila dostupnost zdravstvene zaštite (i primarne i sekundarne) i porastao mortalitet čiji uzrok nije izravno COVID-19. Na taj su način stvoreni novi izazovi u svakodnevnom radu kardiologa i u životu bolesnika s KV bolestima. Kako se onda nositi s tim izazovom i povećati dostupnost i kvalitetu zdravstvene zaštite za bolesnike? Svakako je važno zadržati fokus na KV bolestima (koje i dalje imaju znatan udio u morbiditetu i mortalitetu opće populacije) te ne dopustiti da se zbog straha od zaraze ne provode ili odgađaju pravodobna dijagnostika i liječenje KV bolesti. S obzirom na zajedničke čimbenike rizika s COVID-om 19, a radi zaštite od zaraze, u bolesnika s KV bolestima trebalo bi u što većoj mjeri primjenjivati telemedicinske mogućnosti liječenja, npr. korekcija farmakološke terapije putem A5 uputnice ili očitavanje digitalno snimljenog EKG-a. Također je važan i telefonski kontakt s bolesnicima,

been a period of complete closure of most economic activities (lockdown).[2] The Republic of Croatia was not spared this fate: a pandemic was declared in mid-March and the maximum possible reduction of patients' visits to outpatient clinics was recommended, with only urgent examinations and procedures being allowed during the epidemic.[3] Because of the aforementioned reasons and fear of infection, the number of examinations and diagnostic procedures in patients with cardiovascular (CV) diseases has also decreased. Comparison of the number of primary health care examinations in the Republic of Croatia in April 2019 and April 2020 (according to data published by the Croatian National Institute for Public Health[3]) shows a significant decline (P<0.001, Whitehead test for Poisson distribution) of activity, which always has negative consequences for CV diseases, in which prevention is key. Furthermore, according to a large questionnaire intended for clinical cardiologists conducted in 141 countries on 6 continents, 78.8% respondents answered that the number of patients hospitalized for ST-segment elevation myocardial infarction (STEMI) decreased since the outbreak of the pandemic and 65.2% indicated that it was a reduction greater than 40%. Approximately 60% of all subjects reported that patients with STEMI arrived to hospital later than usual, and 58.5% answered that more than 40% of patients with STEMI admitted to the hospital arrived outside the optimal timeframe for primary percutaneous intervention (PCI) or thrombolysis.[2]

According to available data, the number of examinations in primary health care as well as the number of procedures in secondary health care have been reduced. Let us now examine the repercussions of all of these factors on mortality. The European Group for Monitoring Excessive Mortality (EuroMOMO) published data on weekly mortality in 2020 in several European countries and compared them with the previous multi-year average (thus calculating "excessive" or higher-than-expected mortality each year). These data show a significant increase in mortality in the 15th week of 2020 in most of the observed countries in all age groups except the 0-14 years group.[4] A similar increase in total mortality during the pandemic has been recorded outside Europe, but is SARS-CoV-2 directly or indirectly responsible for this increase? Electronic national mortality registries could help us answer that question. According to a study conducted among patients with diabetes in the United Kingdom, an increase in the number of deaths in which COVID-19 was not the cause of death was recorded during the pandemic (**Figure 1**).[5] The same study also illustrates the increased risk of death from COVID-19 in people at higher cardiovascular risk (there are many common risk factors).

From all the above, it is evident that pandemic there has been a decrease in the availability of health care (both primary and secondary) during the COVID-19 and an increase in mortality not directly caused by COVID-19. This has created new challenges in the daily work of cardiologists and the lives of patients with CV diseases. How then to deal with this challenge and increase the availability and quality of health care for patients? It is certainly important to keep the focus on CV diseases (which still have a significant share in the morbidity and mortality of the general population) and not to allow delays or cancelations of timely diagnosis and treatment of CV diseases due to fear of infection. Given the common risk factors with COVID-19, and in order to protect against infection, telemedicine treatment options should be used as much as

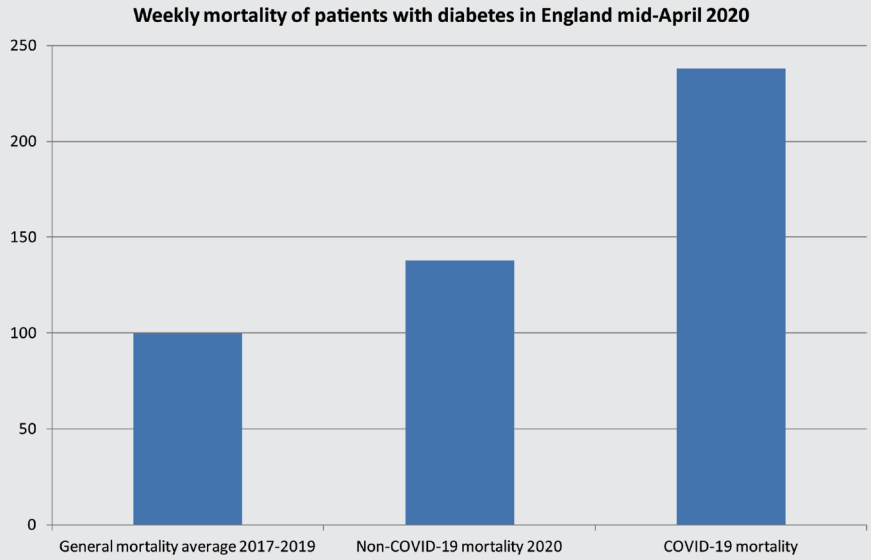

FIGURE 1. The increase in mortality of diabetics in England during the COVID-19 pandemic.[5]

putem kojeg ih se može poticati na samokontrolu čimbenika rizika (npr. arterijskog tlaka) te ih ohrabriti u ustrajanju uzimanja terapije.

Redovito uzimanje antihipertenzivne i hipolipemičke terapije važno je ne samo zbog redukcije komplikacija tih bolesti (npr. infarkt miokarda) nego i zbog dokazane redukcije mortaliteta.[6] Pri tome valja imati na umu da će ustrajnosti pridonijeti i fiksne (dvojne i trojne) kombinacije lijekova, zbog čega su one i preporučene u smjernicama Europskog kardiološkog društva.[7] Pri liječenju arterijske hipertenzije u doba pandemije COVID-a 19 važno je istaknuti i sada već poznatu zabludu o ACE inhibitorima. Naime, na početku pandemije (vrhuncu epidemije u Kini) pojavilo se opservacijsko istraživanje koja je povezivala uporabu ACE inhibitora s većim rizikom od mortaliteta u COVID-u 19.[8] SARS-CoV-2 posjeduje peptomer (glikoproteinski šiljak) s pomoću kojeg se virion veže za enzimatsku domenu transmembranskoga proteina ACE2 (angiotenzin konvertirajućeg enzima) koji je najprisutniji na endotelnim stanicama (tipa 2) plućnih alveola, enterocitima, endotelu, srcu te u glatkim mišićima arterija. Smatralo se da bi bolesnici pod terapijom ACE inhibitorima bili nekako vulnerabilniji prema virusu. Nedugo nakon toga uslijedio je globalni strah pa čak i zaziranje od navedenih lijekova (bilo je to doba kad su neki vjerovali da je klorokin učinkovit protiv SARS-CoV-2, a on je u toj indikaciji privremeno odobren i u Hrvatskoj). Priča je tek recentno dobila svoj znanstveno utemeljeni epilog (još neobjavljeno randomizirano istraživanje BRACE CORONA) uz podršku velikih stručnih društava nastavku liječenja arterijske hipertenzije ACE inhibitorima.[9] To je još jedan primjer zašto se iz malih opservacijskih istraživanja ne bi trebali izvlačiti zaključci o uzročno-posljedičnim vezama pa makar je rad objavljen u časopisu s visokim čimbenikom odjeka.

Za kraj možemo rezimirati da pojavom pandemije COVID-a 19 KV bolesti nisu iščeznule, dapače, moramo uložiti dodatni napor kako bismo očuvali pretpandemijsku kvalitetu liječe-

possible in patients with CVD, such as correction of pharmacological therapy via A5 referral or digital ECG interpretation. Telephone contact with patients is also important, through which they can be encouraged to self-monitor risk factors (e.g. blood pressure) and be encouraged to persevere in adhering to therapy.

Regular use of antihypertensive and hypolipemic therapy is important not only for the reduction of complications of these diseases (e.g. myocardial infarction) but has also been proven to reduce mortality.[6] It should be kept in mind that fixed (double and triple) combinations of drugs also contribute to therapy adherence, which is why they are recommended in the guidelines of the European Society of Cardiology.[7] Regarding hypertension treatment during the COVID 19 pandemic, it is important to point out the now well-known misconception about ACE inhibitors. Namely, at the beginning of the pandemic (the peak of the epidemic in China), an observational study was published linking the use of ACE inhibitors with a higher risk of mortality in COVID-19.[8] SARS-CoV-2 has a peplomer (glycoprotein spike) by which the virion binds to the enzymatic domain of the transmembrane protein ACE2 (angiotensin converting enzyme) which is most present on lung endothelial cells (type 2), enterocytes, endothelium, the heart, and the arterial smooth muscle. Patients under ACE inhibitor therapy were thought to be somehow more vulnerable to the virus. This resulted in a global fear and even aversion towards these drugs (there was a time when some believed that chloroquine was effective against SARS-CoV-2, which was temporarily approved for this indication in Croatia). The story has only recently received its scientifically-based epilogue (the yet unpublished randomized BRACE CORONA study), with large professional societies supporting the continuation of hypertension treatment with ACE inhibitors.[9] This is another fine example of why small observational studies should not be used to draw conclusions on causal links even if the paper was published in a journal with a high impact factor.

nja. U tome nam mogu pomoći razna telemedicinska pomagala, ali je jednako tako važno zadržati kontakt sa samim bolesnicima. Treba ih ohrabriti, podržati i educirati u što većoj samokontroli i ustrajnosti u uzimanju terapije. Ako za tim ima potrebe, dijagnostička obrada i liječenje trebaju se provesti bez odgode, a dužnost je svih pružatelja zdravstvene zaštite organizirati rad i prilagoditi ustanove kako bi se zdravstvena zaštita mogla provoditi učinkovito i sigurno i za bolesnike i za osoblje.

Finally, we can summarize that CV diseases have not disappeared with the onset of the COVID-19 pandemic, and we must in fact engage in additional efforts to preserve the pre-epidemic quality of treatment. Various telemedicine aids can help us with this, but it is equally important to maintain contact with the patients themselves. As much as possible, patients should be encouraged, supported, and educated in achieving self-control and adhering to therapy. If necessary, diagnostic processing and treatment should be carried out without delay, and it is the duty of all healthcare providers to organize work and adjust facilities so that healthcare can be carried out efficiently and safely for both patients and staff.

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