

DIGITAL HEALTH FOR IMPROVING MANAGEMENT OF ACUTE CORONARY SYNDROME

DIGITALNO ZDRAVLJE ZA POBOLJŠANJE MENADŽMENTA AKUTNOG KORONARNOG SINDROMA

Ana Vasić¹, Ivan Soldatović², Stefan Mandić-Rajčević¹

¹ Univerzitet u Beogradu, Medicinski fakultet, Beograd, Srbija

² Univerzitet u Beogradu, Medicinski fakultet, Institut za medicinsku statistiku i informatiku, Beograd, Srbija

Correspondence: anikadasc@gmail.com

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Abstract

In the management of acute coronary syndrome (ACS), providing the best and most equitable care to all patients is a major challenge. Clinical studies pinpoint the areas of pre-hospital and hospital care that need improvement. In Serbia, problems relate to timely ACS symptoms recognition, time to first medical contact, diagnostic accuracy, and rehabilitation. “Digital Health” (DH) can aid in resolving these issues. In this mini-review, several digital health interventions are suggested as ways to improve ACS patient care.

Ključne reči:

digitalno zdravlje,
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akutni koronarni
sindrom,
AI-ECG,
digitalne zdravstvene
tehnologije,
mHealth

Sažetak

U menadžmentu akutnog koronarnog sindroma (AKS) veliki je izazov pružiti optimalnu i jednaku zdravstvenu zaštitu svim pacijentima. Kliničke studije ukazuju na probleme u prehospitarnom i hospitalnom zbrinjavanju. U Srbiji se ti problemi tiču blagovremenog prepoznavanja AKS simptoma, vremena do prvog medicinskog kontakta, preciznosti dijagnostičkih testova i rehabilitacije. Digitalno zdravlje (DH) može pomoći u njihovom rešavanju. U ovom mini-pregledu razmotreno je nekoliko digitalnih zdravstvenih intervencija za poboljšanje zdravstvene zaštite AKS pacijenata.

Introduction

Essential and proven part of ischaemic heart disease (IHD) patient management is secondary prevention and cardiac rehabilitation (CR). Those include optimal medical therapy, risk factor modification and permanent lifestyle changes (specific diet, physical activity, physical therapy, supplementation, sleep), with regular evaluation of adherence to recommended measures (1-3). Traditionally, the term “therapeutic patient education” (TPE) is used for the part of the non-pharmacological management of cardiovascular diseases (CVD), aimed to empower patients to self-manage a chronic disease after an acute event. The use of TPE strongly depends on physician availability.

Studies showed that patients rather comply with pharmacotherapy than with a healthy lifestyle (4-6). It is also found that even adherence to medication therapy after myocardial infarction (MI) is suboptimal (7,8), with one study showing around 25% only (9). Studies in post-MI patients revealed poor control of cardiovascular risk factors (CVRF), and that much better results are achieved when TPE is applied (2). Additionally, studies of TPE in ACS showed lifestyle improvements, better adherence to medication, lower mortality from CVD, and lower risk of MI and stroke, with some finding a positive impact on smoking cessation (10-12).

From traditional health care to digital health care

With growing medical knowledge and innovations that follow, a need for personalized patient care and equal care has arisen. “Medicine has built on a long history of innovation, from the stethoscope and roentgenogram to magnetic resonance imaging and robotics. Doctors have embraced each new technology to advance patient care.” Presently, the world is rapidly digitalized and connected, transforming many industries. Healthcare is next to be redesigned, traditional healthcare models are to be reformed and innovation, technology, and digital devices actively embraced (13, 14).

For the novel healthcare model – called digital health (DH) – there are two main definitions (15).

World Health Organization (WHO) defines DH according to the health system challenges it seeks to address (16). The digital health interventions (DHI) are grouped based on the targeted primary user: interventions for clients, interventions for healthcare providers, interventions for health system, and interventions for data services.

Corresponding health system challenges are listed in **figure 1**.

The U.S. Food and Drug Administration (FDA) defines DH based on the product or service to guide legal regulations for each product. Categories include mobile health (mHealth), health information technology (IT), wearable devices, telehealth and telemedicine, and personalized medicine (17). These technologies are intended for use as a medical product, in a medical product, as companion diagnostics, as addition to other medical products or they are used to develop or study medical products (17).

In ACS patient management, clear motivation to use CR, TPE, or DH is: for patients to achieve a quality of life they had before the disease, to reduce the onset of certain complications or incidents and to prevent new acute events. Healthcare providers aim to reduce readmissions (readmission in 24 hours, after a month, 6 months or a year period). Treatment and readmission reduction, leading to reduced direct or indirect costs on the healthcare system side and reduced patient out of pocket expenses, is the major outcome to estimate in numerous CR, TPE and DH studies.

1	INFORMATION	3	QUALITY	6	EFFICIENCY
1.1	Lack of population denominator	3.1	Poor patient experience	6.1	Inadequate workflow management
1.2	Delayed reporting of events	3.2	Insufficient health worker competence	6.2	Lack of or inappropriate referrals
1.3	Lack of quality/reliable data	3.3	Low quality health commodities	6.3	Poor planning and coordination
1.4	Communication roadblocks	3.4	Low health worker motivation	6.4	Delayed provision of care
1.5	Lack of access to information or data	3.5	Insufficient continuity of care	6.5	Inadequate access to transportation
1.6	Insufficient utilization of data and information	3.6	Inadequate supportive supervision		
1.7	Lack of unique identifier	3.7	Poor adherence to guidelines		
2	AVAILABILITY	4	ACCEPTABILITY	7	COST
2.1	Insufficient supply of commodities	4.1	Lack of alignment with local norms	7.1	High cost of manual processes
2.2	Insufficient supply of services	4.2	Programs which do not address individual beliefs and practices	7.2	Lack of effective resource allocation
2.3	Insufficient supply of equipment			7.3	Client-side expenses
2.4	Insufficient supply of qualified health workers	5	UTILIZATION	7.4	Lack of coordinated payer mechanism
		5.1	Low demand for services		
		5.2	Geographic inaccessibility	8	ACCOUNTABILITY
		5.3	Low adherence to treatments	8.1	Insufficient patient engagement
		5.4	Loss to follow up	8.2	Unaware of service entitlement
				8.3	Absence of community feedback mechanisms
				8.4	Lack of transparency in commodity transactions
				8.5	Poor accountability between the levels of the health sector
				8.6	Inadequate understanding of beneficiary populations

Figure 1. Health System Challenges (HSC), World Health Organization (16).

Management and challenges of ACS in Serbia

In an ideal situation, *after the onset of chest pain, the patient calls the emergency medical service (EMS)*. The EMS operator sends a modern equipped vehicle to the location with an educated team that performs and *interprets the 12-lead ECG recording*. If the ECG recording shows ST segment elevation or a new left bundle branch block, the nearest PCI center is notified. The catheterization room is already being prepared during the transport of the patient, the team is ready and waiting for the patient, who bypasses the emergency room and the coronary unit. If the ECG was performed elsewhere (e.g. in a non-PCI hospital, or a doctor's office, etc.), the EMS is called and the procedure is the same as above (18).

The time from the onset of symptoms to the start of the treatment is the main moderator of therapy (primary percutaneous coronary intervention-pPCI or fibrinolytic therapy-FT), and the type of therapy affects the outcome of the disease, including readmissions and survival. The DANAMI study (DANish trial in Acute Myocardial Infarction) showed the advantage of pPCI in AMI patients compared to FT (19). When pPCI is timely and expertly performed, it is more effective than FT, reduces mortality, reinfarction, re-occlusion of the infarcted artery, and recurrence of ischemia, and leads to fewer complications (intracranial bleeding). The advantage of FT is that it can be started at the first medical contact, but complete flow through the coronary artery is achieved only in 50 - 60% of cases, while in the case of pPCI it is even up to 90% (18).

The most comprehensive clinical ACS study in Serbia showed that the "weak link in the chain" in ACS patient management is the prehospital health care of ACS patients. Due to the insufficient *number of specialized personnel* and the insufficient *number of adequately equipped EMS vehicles*, pre-hospital FT is rarely performed, and an additional problem is for patients who need to be transported from hospitals without a PCI room to a hospital with a PCI room in an appropriate manner, which in Serbia is not always possible to provide (18).

It is published that there are 6 districts with *no PCI hospital in 90-minutes range* (North Banat, West Backa, North Backa, Bor, Pcinj, Zlatibor), and 8 districts that are partly covered (Middle Banat, Branicevo, Pirot, Toplica, Raska, Morava, Kolubara, Macva) (18).

A study in Sombor conducted during one year period included patient data from EMS working protocol, internal medicine department, coronary care unit in Sombor and medical records, and found only 67.1% of patients diagnosed with ACS on admission were true positive ACS cases (20). Similar study in North Backa district showed true positive predictive value (PPV) to be 77.9% for ACS diagnosis on admission. The reason was found to be in ECG interpretation – low specificity and low positive predictive value, where paramedics were not so well trained for *ECG interpretation*. Another reason for low PPV study stated to be history of chronic heart disease, with *persistent or chronic ECG changes*. These types of studies showed that

in Australia only 14.7% of patients admitted for ACS had confirmed ACS diagnosis, and in Austria 46.8% (20). A study in the city of Nis EMS that looked at calls due to suspected ACS found PPV of ACS triage to be 28.6%, negative predictive value of 99.8%, a false negative value 3.0%, and false positive value 15.8%. The study concluded that there is a need to conduct *continual education of physicians working at EMS*, in addition *extensive education of entire population on chest pain* and MI symptoms and *establish up-to-date call centers* (21).

Recent publication reported that ACS mortality in Serbia decreased in last 15 years as a result of improved treatment and secondary prevention. Population health surveys in this period showed *no reduction in cardiovascular risk factors* - hypertension, dyslipidemia, diabetes mellitus, smoking and obesity prevalence were higher in 2019 compared to 2006 (22,23). It was cited that *primary CVD prevention in Serbia is not organized*, it is carried out in primary health centers, by providing individual advices on lifestyle modification and by identifying high-risk patients using SCORE charts (24).

Digital Health solutions

Smartphone-Based Secondary Preventive Strategies

Smartphone technologies like AliveCor, Apple and Verily watches use hardware and software to capture data such as exercise metrics, respiratory rate, body mass, bioimpedance, medication, blood pressure, glycemia. In patients with coronary artery disease (CAD) or (previous) ACS, data can be combined with chronically measured ST segment dynamics over time. This innovative approach in follow-up and prevention can improve the management of atherosclerosis or anticipate further events before the onset of clinical symptoms (25).

Multicenter randomized controlled trial CONNECT recruited from primary care 934 patients with or at risk of cardiovascular disease (CVD). There were two groups of patients – one received traditional CR, and the other group received DHI. In the intervention group participants received an interactive application supplied with electronic health records (EHR), risk factor data, diagnoses and medications, together with interactive risk calculators, motivational messages and tracking of lifestyle goals. As a primary outcome in this trial, it was looked at patient adherence to medication ($\geq 80\%$ of days covered for blood pressure (BP) and statin medications). Secondary outcomes included achieving desired risk factors and eHealth literacy (26). Improvements in the intervention group were seen for physical activity, but in terms of BP and LDL targets, there was no significant difference. This is similar to findings in a systematic review of smartphone technologies use in CAD patients, where greater exercise capacity in the intervention group showed to be single improvement (no difference in BMI reduction, systolic blood pressure, or LDL cholesterol levels was seen) (27). Adherence to medication after 12 months was low and there was no

difference between DHI and control group. A similar study in Australia did find improved medication adherence, and in addition, improved CR completion and reduction in six-month readmissions (28).

A study that evaluated the development, acceptability, and user acceptance of mobile text messages meant to provide advice, motivation and support to decrease CVRF, highlighted the importance of behavior change techniques in creating (semi-personalized) content. Those include providing information on consequences, identifying obstacles to desired behavior and a plan to overcome them, rewards for the right effort or performance, advices on how to perform a desired behavior and how to prepare for it, helping the person in time management, setting easy task and increase difficulty, message delivery according to a predefined schedule, etc. (29).

A nonrandomized controlled trial in 4 US hospitals included 1064 patients with acute myocardial infarction (AMI) for 4 years. The DHI was a smartphone app, smartwatch, and blood pressure monitor designed to help with patient care both during their time in the hospital and 30 days after they were released. Included were also outpatient care coordination, education, monitoring of vital signs and activity, and medication reminders. Patient knowledge, skills, and confidence in managing their health care as well as all-cause 30-day readmissions were measured outcomes. The 30-day readmission for all causes was 52% lower in the DHI group. Additionally, this group had the highest levels of patient activation for self-managing healthcare (30).

One of the most promising DHI used in AMI recovery is “Corrie”, part of The Johns Hopkins Myocardial infarction, COMbined device Recovery Enhancement (MiCORE) study, which aims to investigate and reduce 30-day readmissions. In “Corrie” DHI, downloaded smartphone applications, Apple smartwatch, and iHealth wireless blood pressure monitor are used for medication tracking, education, vital signs monitoring and care coordination. Participants are able to manage their medications (track daily adherence, indication, and side effects), monitor vital signs (heart rate, blood pressure, weight, mood, and steps), learn about the risk factors for CVD, and lifestyle modification through educational articles and videos, schedule and track follow-up appointments, connect with their clinicians and store health information. It was found that this DHI reduced costs from the hospital side through the reduction of risk for all-cause readmission following AMI. While DHI costs \$2750 per patient, the use of the DHI leads to a cost-savings of \$7274 per patient compared with standard care (30).

Devices to detect acute coronary syndrome

Devices for ASC detection require severe assessment of technical and clinical validity, so as practical utility. The population at risk that can benefit from the device has to be defined, together with an estimation of the net risk–benefit ratio (25).

The most notable devices to detect ACS are handheld

devices with specifically developed algorithms - RELF algorithm for early detection of acute coronary 60 s occlusion, and implantable device - the AngelMed Guardian System for early STEMI detection. The RELF algorithm and device (which has an embedded 3-lead detection system) are connected to smartphone for the purpose of self-recording and 60 s occlusion detection. A study published in *The Lancet Digital* reported that the algorithm can be used in 91% of patients. A detection of acute coronary occlusion showed to be 87%, if there were ECG changes it showed to be 95% and 100% for acute coronary artery occlusion with ECG changes and ST-segment elevation (31).

The ALERT trial investigated the use of the AngelMed Guardian System for early STEMI detection; it included 907 high-risk ACS patients who all had implanted devices, whereas in the control group alarm was deactivated. Trial showed device reduces the time from ACS detection to patient arrival to medical facility in a 90-days window (51 min vs. 30.6 h). Importantly, patient is alerted for asymptomatic cardiac ischemia. When it was looked at detecting an event within 7 days, there was no difference between groups. Additional analysis using data after the study period found a higher positive predictive value (25.8% vs. 18.2%) and a significantly lower false positive rate in the group with alarms on. This device has been approved by FDA for “patients who have had prior ACS events and who remain at high risk for recurrent ACS events” (32).

The ECG devices

There are two main novelties in the ECG use in DH era. One is related to mobile ECG (mECG) devices, and another is use of AI algorithms for ECG interpretations.

Mobile ECG monitors are being increasingly used by patients for self-rhythm monitoring and detection of ST-segment deviations which may unveil coronary ischemia (before the patient has actual symptoms). It can result in a reduction of premature deaths or years lost due to disability/disease. Compared to traditional ambulatory ECG devices, novel devices have improved design in terms of size and weight, and they record more data. One commercially available mECG device, relatively inexpensive, is KardiaMobile (from AliveCor). Using electrode sensors for the right and left fingers, the device provides a 30-second or longer tracing corresponding to lead I of a standard 12-lead electrocardiogram (ECG) (33).

Company AliveCore has developed mECG as an iPhone application that uses phone-embedded sensors to provide single-channel ECG. The FDA approved this device as an ambulatory cardiac rhythm monitor. When used by a trained medical professional, the device was shown to distinguish between normal sinus rhythm and atrial fibrillation. Moreover, the device accurately assesses QTC intervals, when compared to standard 12-lead ECG. When the most recent AliveCor cardiac rhythm monitors Kardia 12L (records 12-lead ECG sequentially) and Kardia 6L (records 6-lead ECG sequentially) were compared to standard 12-lead ECG, they showed high correlation (34).

Use of AI algorithms in ECG interpretation has bright future as this data format is simple for data mining (compared to data used in radiology AI), unlike other electronic medical records ECGs are standardized, always obtained in the same format, and always reported in the same way. The ECGs can be readily stored in a cloud-based or centralized database in large quantities (35). Data can be further combined with other modalities such as EMR, data from disease registries (troponin, age, gender, chest pain, comorbidities, etc.), echocardiogram, cardiac CT or MRI, etc., and reveal patterns, suggest therapy or predict outcomes (36-38). Faster ECG interpretations could reduce the time from symptom onset to medical facility, potentially increasing chances for pPCI, which means better survival and quality of life for the patient. Placing AI ECG in every EMS vehicle would provide more equal treatment for all patients. Improved accuracy of ECG and more data from ECG interpretations save money from unnecessary admissions, and with proper staff training, this software could be part of triage.

Telemedicine

In patients with ACS, telemedicine can be used for virtual visits (VV), as an alternative to in-person (IV) follow-up office visits (40). Another application is virtual instead of in-person cardiac rehabilitation (41). Despite being seen as the most cost-effective intervention to ensure favorable outcomes after ACS, CR is not offered to most of the patients and uptake is very low, even before the Covid-19 pandemic (41). In Serbia, one study reported CR completion during pandemic in 1% of patients only (42). In Cochrane review clinical benefits from virtual CR, including the hybrid model (combined virtual and in-person CR) in ACS were shown to be similar and with equivalent costs (41). Meta-analysis of 11 trials, found that telehealth interventions were as effective as center-based programs in the reduction of modifiable cardiovascular risk factors and exercise capacity. In terms of adherence to cardiac rehabilitation, home-based programs were comparable with that in center-based programs, with some studies showing better adherence to home than center-based CR (41, 43). European guidelines recommend home based rehabilitation, as evidence showed those increase participation and support behavior changes (44).

Telemedicine platforms can be used to provide training content to healthcare providers (45, 46). One field where this would be beneficial is interventional cardiology/radiology; recent studies in Serbia reported a limited number of trained interventional cardiologists to be an obstacle for pPCI (47, 48).

Conclusion

The DHI shows to improve certain segments of ACS patient management, as adduced challenges and related to DHI solutions. In addition to benefits for patients and for the healthcare system, there is a motivation to keep learning from the data. Algorithms and devices built on

evidence-based data should be an asset to present workflow, and strongly supported by the country's rules and regulations, unified standards, and integrated infrastructure.

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