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Wpływ użytkowania aplikacji mobilnej afterAMI na kontrolę czynników ryzyka chorób sercowo-naczyniowych u pacjentów po zawale serca

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu w dyscyplinie nauki medyczne

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1. Krzowski B, Peller M, Boszko M, et al. Mobile app and digital system for patients after myocardial infarction (afterAMI): study protocol for a randomized controlled trial. Trials. 2022;23(1):522. Published 2022 Jun 21. doi:10.1186/s13063-022-06463-x

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Spis treści

1 Wykaz zastosowanych skrótów

AI - artificial intelligence (sztuczna inteligencka)

AMI - acute myocardial infarction (ostry zawał serca)

BMI - body mass index (wskaźnik masy ciała)

CAD - coronary artery disease (choroba wieńcowa)

CG - control group (grupa kontrolna)

CR - cardiac rehabilitation (rehabilitacja kardiologiczna)

CVD - cardiovascular disease (choroby sercowo-naczyniowe)

HF - heart failure (niewydolność serca)

IG - interventional group (grupa poddana intervencji)

LDL - low-density lipoprotein (lipoproteina o niskiej gęstości)

MI – myocardial infarction (zawał serca)

NT-proBNP – N-terminal pro-brain natriuretic peptide (Peptyd natriuretyczny typu B)

PCI - percutaneous coronary interventions (przezskórne interwencje wieńcowe)

SD - standard deviations (odchylenie standardowe)

SMS - short message service (krótkie wiadomości tekstowe)

2 Streszczenie w języku polskim

Leczenie zawału serca było przedmiotem licznych badań na przestrzeni ostatnich lat. Kluczowe z punktu widzenia rokowania pacjenta są pierwsze miesiące po zawale mięśnia sercowego. Niezwykle ważne jest, aby zadbać o kontrolę wszystkich czynników ryzyka sercowo-naczyniowego i przejść pełny program rehabilitacji. Rehabilitacja kardiologiczna to kompleksowe działanie, którego celem jest poprawa kontroli czynników ryzyka sercowo-naczyniowego oraz zmiana w zakresie nawyków dotyczących aktywności fizycznej. Proces ten może być wspierany przez aplikacje mobilne, a rozwiązania telemedyczne mają coraz większe znaczenie w codziennej praktyce. Opisywana praca zawiera szczegółowy protokół, jak również wyniki przeprowadzonego badania, w którym oceniono wykorzystanie aplikacji mobilnej afterAMI u pacjentów po przebytym zawale mięśnia sercowego. Aplikacja oferuje tryb edukacyjny, kalendarz, dzienniczek parametrów życiowych, przypomnienia o przyjmowanych lekach, kartę historii medycznej oraz panel kontaktowy do personelu medycznego. Stworzenie systemu afterAMI umożliwiło połączenie rozwiązań, które pojedynczo okazały się skuteczne i dowiodły poprawy rokowania pacjentów w opublikowanych wcześniej pracach naukowych. Pomimo ogólnie obiecujących wyników z poprzednich badań dotyczących rozwiązań telemedycznych, ilość dowodów naukowych jest niewystarczająca, szczególnie w zakresie prospektywnych badań randomizowanych. Moim celem była kompleksowa ocena nowo opracowanej aplikacji mobilnej w warunkach klinicznych ze szczególnym uwzględnieniem częstości rehospitalizacji, pilnych wizyt ambulatoryjnych oraz kontroli czynników ryzyka sercowo-naczyniowego.

Do badania włączono 100 pacjentów hospitalizowanych w I Katedrze i Klinice Kardiologii Warszawskiego Uniwersytetu Medycznego z powodu ostrego zawału serca. Pacjenci zostali losowo przydzieleni do grupy z dostępem do aplikacji afterAMI oraz standardowej rehabilitacji lub jedynie do standardowej rehabilitacji kardiologicznej. Analizie poddano czynniki ryzyka sercowo-naczyniowego, liczbę rehospitalizacji oraz wiedzę pacjentów na temat czynników ryzyka sercowo-naczyniowego. Pierwszorzędowym punktem końcowym badania były ponowne hospitalizacje i/lub pilne wizyty ambulatoryjne oceniane łącznie po 6 miesiącach od randomizacji. W tym prospektywnym, otwartym, randomizowanym, jednoośrodkowym badaniu wszystkich 100 pacjentów obserwowano przez 6 miesięcy po wypisie ze szpitala. Punkty końcowe oceniano podczas wizyt kontrolnych po 1 i 6 miesiącach od włączenia do badania.

Mediana wieku pacjentów wynosiła 61 lat, a 65% badanych stanowili mężczyźni. Różnice w wyjściowej charakterystyce badanej populacji opisano szczegółowo niżej. Po 30 dniach nie stwierdzono różnic w kontroli czynników ryzyka sercowo-naczyniowego między badanymi grupami poza stężeniem cholesterolu LDL, które było istotnie niższe w grupie stosujących aplikację afterAMI ($p<0,001$), mimo braku różnic na początku badania. Podobnie w przypadku stężenia NT-proBNP pacjenci w grupie z aplikacją mieli istotnie niższe wartości w porównaniu z grupą kontrolną ($p=0,02$), pomimo braku istotnych różnic przy randomizacji.

Pomimo niższej częstości liczby zdarzeń opisanych jako pierwszorzędowy punkt końcowy (8% w grupie „afterAMI" vs. 27% w grupie kontrolnej; $p=0,064$) nie osiągnięto różnicy istotnej statystycznie. Po 6 miesiącach obserwacji pacjenci w grupie interwencyjnej nadal mieli niższe stężenie NT-proBNP ($p=0,02$) i wyższy wynik w teście oceniającym wiedzę na temat czynników ryzyka chorób sercowo-naczyniowych ($p<0,001$), pomimo braku różnic na początku badania.

W celu oceny rokowania pacjentów wymagana jest jednak dłuższa obserwacja. Poprawa rokowania pacjentów wymaga usprawnienia procesu rehabilitacji kardiologicznej. Dowody dotyczące wykorzystania aplikacji mobilnej w opisywanej grupie pacjentów są ograniczone i zwykle obejmują niewielką liczbę uczestników. Ten projekt jest przykładem zastosowania rozwiązania telemedycznego w codziennej praktyce klinicznej, co jest zgodne z wytycznymi międzynarodowych towarzystw kardiologicznych.

3 Streszczenie w języku angielskim

Treatment of acute myocardial infarction has been the subject of studies over the past years. However, the initial months after myocardial infarction are crucial from the perspective of the patient's prognosis. It is extremely important to take care of all cardiovascular risk factors and undergo full rehabilitation program. Cardiac rehabilitation is a complex program which aims to better control a patient's cardiovascular risk factors. It can be supported by mobile applications. Telemedical solutions are becoming more and more relevant in everyday practice. We described a protocol and conducted a study evaluating the use of mobile application 'afterAMI' in patients after myocardial infarction. The app offers educational mode, calendar, vital signs diary, medication reminders, medical history card and healthcare professional contact panel. It offers several solutions, which individually proved to be effective and improve patient's prognosis. Despite general promising results from previous studies regarding telemedical tools, there is paucity of evidence when it comes to prospective randomized trials. Our aim was to perform a comprehensive evaluation of a newly developed mobile application in the clinical setting with special regards to rehospitalisations, urgent outpatient visits and cardiovascular risk factors control.

100 patients with myocardial infarction were recruited on admission to the Department of Cardiology at Medical University of Warsaw. Patients were randomized into group with an access to afterAMI app or to standard cardiac rehabilitation. Cardiovascular risk factors were analyzed along with the number of rehospitalizations and patients' knowledge regarding cardiovascular risk factors. The primary study endpoint were rehospitalisations and/or urgent outpatient visits combined assessed after 6 months from randomization. In this prospective, open-label, randomized, single-center study, all 100 patients were observed for 6 months after discharge from the hospital. Endpoints were assessed during control visits 1- and 6-months after inclusion into the study.

The patients' median age was 61 years and 65% of the subjects were male. The differences in the baseline population characteristics were described in detail below. After 30-days there were no differences in cardiovascular risk factor control between the study groups apart from LDL cholesterol levels, which were lower in the "afterAMI" group ($p<0.001$), despite no differences being found at the beginning of the study. Similarly, regarding NT-

proBNP level patients in the mobile app group had significantly lower values when compared to control group (p=0.02), despite a lack of significant differences at randomization.

This study failed to limit the number of primary endpoint events (8% with app vs. 27% without app; p=0.064). However, patients in the interventional group had lower NT-proBNP levels (p=0.02) and better knowledge regarding cardiovascular disease risk factors (p<0.001), despite no differences at baseline.

However, longer follow-up is required to establish prognosis in this population. Cardiac rehabilitation process enhancements are required to improve patients' prognosis. The evidence regarding the use of the mobile application in the described group of patients is limited and usually covers a small number of participants. This project is an example of a telemedical solution application embracing everyday clinical practices, conforming with multiple international cardiac societies' guidelines.

4 Wstęp uzasadniający połączenie wskazanych publikacji w jeden cykl, jak i komentujący osiągniecie naukowe kandydata na tle dotychczasowego stanu wiedzy.

Choroby sercowo-naczyniowe pozostają wiodącą przyczyną zgonów na świecie i skutkują pogorszeniem jakości życia, utratą aktywności zawodowej i wiążą się z wysokimi kosztami dla systemów opieki zdrowotnej. Do głównych wyzwań współczesnej kardiologii należy leczenie zawałów serca, niewydolności serca, a także zaburzeń rytmu serca. Zawał serca definiuje się patofizjologicznie jako śmierć komórek mięśnia sercowego z powodu długotrwałego niedokrwienia. Zgodnie z czwartą uniwersalną definicją zawału serca termin „ostry (świeży) zawał serca" powinno się stosować w warunkach klinicznych w przypadku ostrego uszkodzenia mięśnia sercowego z klinicznymi cechami ostrego niedokrwienia mięśnia sercowego, jeżeli stwierdzono wzrost i/lub spadek stężenia cTn we krwi z co najmniej jedną wartością powyżej górnej granicy zakresu wartości referencyjnych na poziomie 99. centyla oraz spełnione jest co najmniej jedno z następujących kryteriów:

- występowanie objawów niedokrwienia mięśnia sercowego;
- obecność nowych niedokrwiennych zmian w elektrokardiogramie (EKG);
- pojawienie się patologicznych załamków Q w EKG;
- uwidocznienie w badaniach obrazowych nowego ubytku żywotnego mięśnia sercowego lub nowych regionalnych zaburzeń czynności skurczowej, których umiejscowienie odpowiada etiologii niedokrwiennej;
- wykrycie skrzepliny w tętnicy wieńcowej podczas koronarografii lub badania sekcyjnego (nie dotyczy zawału serca typu 2 i 3) [1].

Wśród głównych przyczyn zawału serca wyróżnia się zaburzenie przepływu krwi w tętnicach wieńcowych, co prowadzi do niedokrwienia i martwicy kardiomiocytów. Możliwe jest również niedokrwienie wtórne do niewystarczającej podaży składników odżywczych w odniesieniu do zapotrzebowania poszczególnych komórek mięśnia sercowego. Za najczęstszą przyczynę zawałów serca uznaje się zmiany miażdżycowe, które utrudniają przepływ krwi przez tętnice wieńcowe. Czynniki ryzyka rozwoju miażdżycy dzieli się na niemodyfikowalne i modyfikowalne. Do tych pierwszych zalicza się wiek, płeć męską i

czynniki genetyczne. Wśród modyfikowalnych czynników ryzyka wymienia się nikotynizm, nadciśnienie tętnicze, dyslipidemię, zaburzenia gospodarki węglowodanowej, otyłość i nadwagę, brak aktywności fizycznej oraz nieprawidłową dietę [2].

Zawał serca to zdarzenie, które pomimo opracowanych metod leczenia wiąże się z ryzykiem groźnych powikłań. W ostrej fazie zawału serca istnieje ryzyko wystąpienia groźnych dla życia zaburzeń rytmu serca – zarówno tachy-, jak i bradyarytmii, udaru mózgu, powikłań mechanicznych, a nawet zgonu. W długoterminowej perspektywie zawał serca zwiększa ryzyko rozwoju niewydolności serca, pogarsza jakość życia pacjentów, a także wiąże się ze zwiększonym ryzykiem kolejnego zawału serca w przyszłości [3].

Leczenie zawału serca obejmuje farmakoterapię oraz leczenie zabiegowe. Bardzo ważne jest możliwie najszybsze przywrócenie przepływu przez niedrożną tętnicę wieńcową, ponieważ w ten sposób można zmniejszyć obszar komórek, których funkcja zostanie upośledzona poprzez niedokrwienie. Leczenie ostrej fazy zawału serca uległo istotnej poprawie na przestrzeni ostatnich lat, zarówno ze względu na rozwój technik zabiegowych, jak i na postępy w farmakoterapii. Celem leczenia jest udrożnienie tętnicy odpowiedzialnej za zawał, a także zwykle zastosowanie stentu, co ma za zadanie zmniejszenie ryzyka ponownego zwężenia naczynia w tym samym miejscu. Według danych z Narodowego Funduszu Zdrowia w 2019 r. w Polsce wystąpiło ok. 103 tys. Ostrych Zespołów Wieńcowych, w tym 78,6 tys. Zawałów serca (27 tys. z uniesieniem odcinka ST + 51,6 tys. bez uniesienia odcinak ST) [4]. W Polsce jest około 160 pracowni hemodynamicznych, które świadczą całodobowe usługi dla chorych z podejrzeniem zawału serca. Leczenie ostrej fazy zawału serca w Polsce nie odbiega od standardów europejskich, co znajduje potwierdzenie w podobnej do innych krajów śmiertelności okołozawałowej [5].

Śmiertelność z powodu zawału serca różni się pomiędzy krajami, ale obserwuje się trend spadkowy [6]. Niemniej jednak, szacuje się, że około 12% pacjentów po zawale serca umiera w ciągu kolejnych 12 miesięcy [7], a niemal co piąty pacjent umiera w trakcie 3 lat po incydencie niedokrwiennym [8]. Wśród głównych przyczyn wymienia się brak odpowiednich interwencji dotyczących stylu życia, niezadawalające stosowanie się do zaleceń lekarskich przez pacjentów, jak również brak indywidualnie dostosowanej aktywności fizycznej podczas programów rehabilitacji kardiologicznej. Te dane pozwalają wnioskować, że wskazane jest podjęcie działań mających na celu optymalizację procesu rehabilitacji kardiologicznej pacjentów po zawale serca. Kluczowa jest odpowiednia kontrola czynników ryzyka chorób

sercowo-naczyniowych, ponieważ dzięki niej ogranicza się ryzyko kolejnych, groźnych incydentów niedokrwiennych [9].

Celem prewencji wtórnej jest kontrola wszystkich czynników ryzyka chorób sercowo-naczyniowych, co stanowi duże wyzwanie w kontekście codziennej praktyki klinicznej. Według danych z dostępnej literatury wszystkie znane czynniki ryzyka są kontrolowane optymalnie, czyli w odniesieniu do wartości sugerowanych przez odpowiednie wytyczne towarzystw kardiologicznych, jedynie u 2,9% pacjentów z chorobą wieńcową w polskiej populacji [10]. Wyniki te świadczą o potrzebie optymalizacji opieki nad pacjentami, jak również ich edukacji, która przekłada się na stosowanie zaleceń lekarskich. Biorąc pod uwagę wydolność polskiego systemu opieki zdrowotnej, jak również nakłady przeznaczane na prewencję i leczenie chorób kardiologicznych zastosowanie narzędzi uniwersalnych, łatwo skalowalnych i korzystnych finansowo wydaje się uzasadnione. Należy podkreślić, że obecnie społeczeństwo polskie jest na etapie „spłacania długu zdrowotnego" zaciągniętego podczas pandemii COVID-19. Ze względu na konieczność przeorganizowania opieki szpitalnej i ambulatoryjnej wiele chorób przewlekłych nie było optymalnie kontrolowanych. Ten okres gorszej kontroli czynników ryzyka chorób sercowo-naczyniowych może wiązać się z większym ryzykiem groźnych incydentów niedokrwiennych w przyszłości [11]. Podkreśla się konieczność intensyfikacji opieki nad chorymi z chorobami przewlekłymi, w celu minimalizacji ryzyka poważnych powikłań kardiologicznych. Udział w rehabilitacji kardiologicznej w Polsce jeszcze przed pandemią, w 2018 roku, wynosił 11% w pierwszych 14 dniach, 19% po 30 dniach i 35% po 365 dniach po wypisie ze szpitala [12], co było wartościami odbiegającymi od pożądanych.

Do tej pory opisano szereg podejść i prób poprawy opieki nad pacjentami po zawale serca. Jednym z rozwiązań mających za zadanie sprostać potrzebom pacjentów jest program skoordynowanej opieki nad pacjentami po zawale serca – KOS-Zawał, czyli nowatorska koncepcja organizacji opieki nad pacjentami po zawale serca. Program został opracowany przez zespół ekspertów Polskiego Towarzystwa Kardiologicznego oraz Agencji Oceny Technologii Medycznych i Taryfikacji i jest stopniowo wprowadzany do kolejnych ośrodków w kraju. Program opiera się przede wszystkim na ułatwionym dostępie do rehabilitacji kardiologicznej oraz kardiologów przez pierwsze 12 miesięcy po zawale serca. Główne cele programu KOS-Zawał to skrócenie czasu od wypisu ze szpitala do osiągnięcia pełnej rewaskularyzacji, poprawa dostępu do zabiegów elektroterapii, skrócenie czasu oczekiwania

na konsultację kardiologiczną w okresie poszpitalnym, znaczne skrócenie czasu oczekiwania na rehabilitację kardiologiczną.

Dotychczasowe analizy wskazują na duży sukces i wymierne korzyści dla pacjentów. W jednej z analiz pochodzącej z katowickiego ośrodka wykazano, że udział w programie KOS-Zawał wiązał się aż z 40% redukcją występowania istotnych powikłań sercowo-naczyniowych w porównaniu do analogicznej grupy kontrolnej po zastosowaniu metody ‘propensity score matching’ w trakcie 12-miesięcznej obserwacji [5]. W kolejnej pracy, w której oceniono wyniki po 24-miesiącach dowiedziono, że udział w programie KOS-Zawał wiązał się z 30% redukcją śmiertelności niezależnie od przyczyny oraz z 14% redukcją niepożądanych zdarzeń sercowo-naczyniowych [13]. Niestety, pomimo opisanych powyżej zachęcających wyników nie wszyscy pacjenci po zawale serca korzystają z tego programu. Obecnie program KOS-Zawał jest realizowany w około 70% ośrodków, w których leczy się pacjentów z powodu zawału serca. Podnosi się argumenty, że być może powodem, dla którego niektóre ośrodki nie przystąpiły jeszcze do realizacji tego programu są braki kadrowe. Kolejnym wyzwaniem może też być, np. brak działającej przy szpitalu przychodni kardiologicznej. Co więcej, część ośrodków kardiologii inwazyjnej funkcjonuje poza tzw. siecią szpitali, dlatego nie uczestniczą w postępowaniach konkursowych NFZ, m.in. na realizację świadczeń w ramach KOS-Zawał. Warto także podkreślić, że KOS-Zawał to program niezwykle wymagający, w obszarze administracji i wiąże się z dużym nakładem dodatkowej pracy. Z tego względu procentowy udział pacjentów w programie KOS-Zawał nadal jest niezadowalający. W niektórych ośrodkach, pomimo dostępnego programu jedynie kilka procent pacjentów po zawale serca jest do niego włączanych. A zatem, istnieje potrzeba dalszej optymalizacji i poszukiwania kolejnych form wsparcia pacjentów po zawale serca.

Niewątpliwie elementem leczenia i edukacji, który zyskuje na popularności są rozwiązania z zakresu telemedycyny. Obecnie na świecie jest aż 3,8 miliarda użytkowników smartphonów, a do 2024 roku liczba ta ma wzrosnąć do 4,2 miliarda osób [14]. Naturalnym wydaje się być przenikanie świata technologii i zdrowia wobec potencjału dostępnego na wyciągnięcie ręki. Wydaje się więc, że wsparcie procesu rehabilitacji kardiologicznej poprzez zastosowanie dedykowanej aplikacji mobilnej może być obiecującym rozwiązaniem, tym bardziej, że poszczególne produkty zostały poddane ewaluacji klinicznej, a wyniki należy uznać co najmniej za obiecujące. Rynek dostępnych rozwiązań telemedycznych rośnie w bardzo szybkim tempie i proponuje różne interesujące rozwiązania dla pacjentów i dla lekarzy, od systemów opartych na przeglądarkach internetowych, przez moduły domowej

rehabilitacji, aż do dedykowanych aplikacji mobilnych. Niemniej jednak, jedynie pojedyncze z nich zostały zwalidowane w badaniach klinicznych, których wyniki zostały opublikowane w recenzowanych czasopismach. W obowiązujących wytycznych Europejskiego Towarzystwa Kardiologicznego dotyczących prewencji sercowo-naczyniowej autorzy podkreślili, że rozwiązania z zakresu telemedycyny powinny być uważane za przyjazne dla użytkownika i jako atrakcyjne ekonomicznie narzędzie wspierać kontrolę czynników ryzyka oraz promować nie tylko lepsze przestrzeganie zaleceń, ale także wspierać modyfikację stylu życia w długotrwałej perspektywie [15].

Zastosowania z zakresu telemedycyny okazały się być skuteczne w określonych sytuacjach klinicznych. Jedną z przełomowych prac było badanie przeprowadzone w Mayo Clinic (Rochester, MN, USA), gdzie dowiedziono, że uzupełnienie standardowego procesu rehabilitacji kardiologicznej poprzez zastosowanie aplikacji mobilnej przełożyło się na poprawę kontroli czynników ryzyka chorób sercowo-naczyniowych. Co więcej, w grupie pacjentów, którzy mieli dostęp do dedykowanego programu zaobserwowano aż 40% redukcję rehospitalizacji i pilnych wizyt ambulatoryjnych ($p<0,05$) [16]. Niemniej jednak, naturalnie aplikacje mobilne nie są optymalnym rozwiązaniem dla wszystkich pacjentów ze względu na umiejętność obsługi smartphone'a. W jednej z opublikowanych prac Gallagher wraz ze współautorami opisał, że 54,6% pacjentów kwalifikujących się do rehabilitacji kardiologicznej używa nowoczesnych technologii w celach zdrowotnych. Pacjenci korzystają z nich głównie w celu uzyskania informacji o schorzeniach oraz o lekach [17]. Wydaje się, że odsetek pacjentów, którzy posiadają i wykorzystają smartphone'y będzie rósł, dzięki czemu na istotności będą także zyskiwać rozwiązania takie jak aplikacje mobilne.

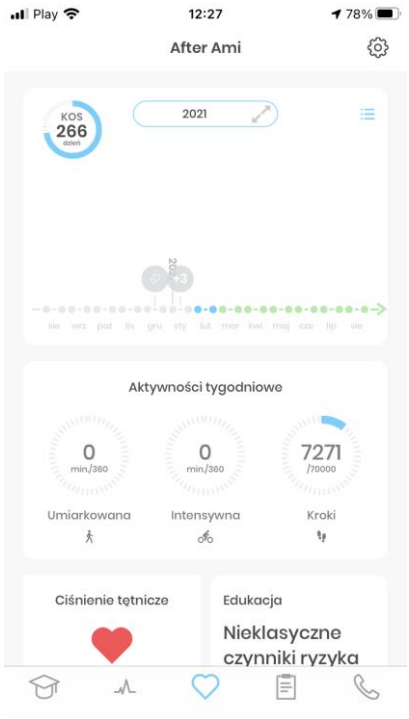
Ważne, aby osoby poszukujące wiadomości zdrowotnych uzyskiwały je z wiarygodnego źródła. Niestety, obecnie każdy ma możliwość publikacji wszelkich zdrowotnych treści w internecie. Tym bardziej na istotności zyskują aplikacje mobilne, które są opracowane przez ekspertów i dedykowane do konkretnej grupy pacjentów. Ilość mniejszych badań, które zostały do tej pory opublikowane pozwoliła na przeprowadzenie meta-analizy, na podstawie której Coorey wraz ze współautorami wywnioskował, że aplikacje mobilne mają korzystny wpływ na kontrolę czynników ryzyka chorób sercowo-naczyniowych, ale wskazane jest uzyskanie większej ilości dowodów naukowych w celu określenia miejsca poszczególnych rozwiązań w praktyce klinicznej [18].

Wdrażanie do codziennej praktyki rozwiązań z zakresu telemedycyny było już rekomendowane przez wytyczne towarzystw naukowych [19, 20]. Niemniej jednak, uzyskanie dowodów naukowych na skuteczność określonego rozwiązania pozwala uzasadnić stosowanie konkretnego rozwiązania w określonej grupie pacjentów. Wpływ dedykowanych aplikacji mobilnych na kontrolę czynników ryzyka pacjentów po zawale serca w ramach randomizowanego badania w warunkach polskiego systemu opieki zdrowotnej nie został do tej pory przebadany. Co więcej, tego typu przedsięwzięcie jest także jednym z pierwszych tego typu w Europie.

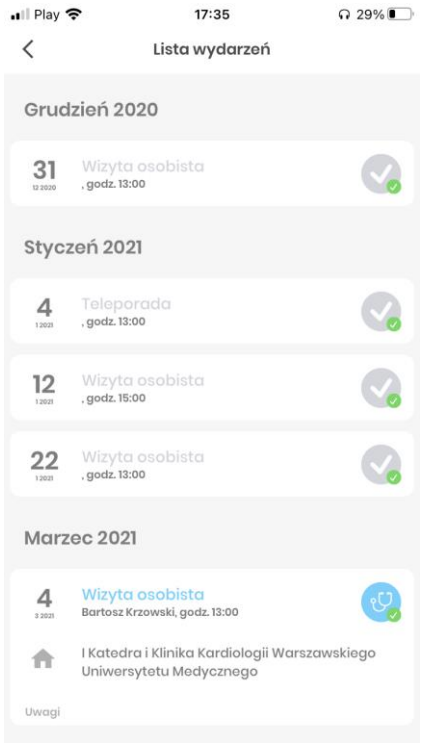
Aplikacja afterAMI powstała z inicjatywy lekarzy (dr hab. n. med. Paweł Balsam, prof. dr hab. n. med. Marcin Grabowski, dr hab. n. med. Łukasz Kołtowski) I Katedry i Kliniki Kardiologii, którzy widzieli potrzeby uzupełnienia opieki nad pacjentami hospitalizowanymi w Klinice. Program był rozwijany przez kolejne lata i modyfikowany na podstawie obserwacji własnych oraz pacjentów. Ostateczne prace nad aplikacją zostały zakończone przed rozpoczęciem opisywanego badania. System składa się z dwóch części: aplikacji mobilnej dla pacjenta oraz panelu w postaci strony internetowej dla przedstawicieli systemu opieki zdrowotnej. Aplikacja składa się z modułu edukacyjnego, modułu kontroli czynników ryzyka chorób sercowo-naczyniowych, kalendarza, informacji o jakości powietrza, funkcji przypominania leków oraz czatu do kontaktu z lekarzem prowadzącym. W ramach modułu edukacyjnego zostało przygotowane kompendium wiedzy, które było indywidualnie dopasowywane do każdego pacjenta na podstawie zdiagnozowanych jednostek chorobowych. Ponadto wszyscy pacjenci dostawali dwa razy w tygodniu powiadomienia z krótkimi notatkami z ogólnymi poradami dotyczącymi stylu życia, z których możliwe było przekierowanie do kompendium. Wszystkie treści były przygotowane przez specjalistów kardiologii na podstawie obowiązujących wytycznych Europejskiego Towarzystwa Kardiologicznego. W ramach panelu kontroli czynników ryzyka mogły być monitorowane poszczególne parametry życiowe, które mogły być wprowadzane do systemu manualnie lub synchronizowane automatycznie poprzez integrację z oprogramowaniem smartphone'a. Przykładowo: dane o aktywności, tzn. ilość kroków była automatycznie przekazywana do aplikacji, podobnie informacje o tętnie pacjentów w przypadku posiadania zsynchronizowanego smartwatcha. Jeżeli pacjent nie posiadał jednak dedykowanego urządzenia, które łączyłoby się z jego telefonem, to dane te mogły być również wprowadzone ręcznie – np. po codziennym pomiarze ciśnienia. Pacjent miał dostęp do swoich parametrów, dzięki czemu podczas wizyty kontrolnej eliminowany był problem braku dzienniczka z wartościami ciśnienia, tętna, masy ciała itd. Na podstawie lokalizacji pacjenci

mieli przedstawiane dane o jakości powietrza na podstawie danych z Głównego Inspektoratu Ochrony Środowiska wraz z komentarzem, czy warunki są odpowiedni do aktywności fizycznej na zewnątrz. Lekarz przy wypisie ze szpitala wprowadzał informacje o zleconych lekach dla danego pacjenta, dzięki czemu chory otrzymywał powiadomienia z przypomnieniem o przyjęciu konkretnych leków. Ponadto przedstawiono historię choroby pacjenta, która miała być wsparciem pacjenta w trakcie nieplanowanej hospitalizacji i braku dostępności do tradycyjnej dokumentacji medycznej. Finalnie aplikacja oferowała również możliwość czatu z lekarzem, który miał charakter informacyjno-koordynacyjny. Pacjenci byli poinstruowani, że wszystkie nagłe stany zdrowotne wymagały pilnego, osobistego kontaktu z przedstawicielem systemu opieki zdrowotnej. Lekarz miał dostęp do danych pacjenta, które były analizowane podczas wizyty kontrolnej. Możliwość zgromadzenia poszczególnych składowych w jednym miejscu pomagała usprawnić i lepiej zorganizować wizytę kontrolną poszczególnych pacjentów. Na rycinach 1-11 przedstawiono aplikację mobilną oraz panel lekarza.

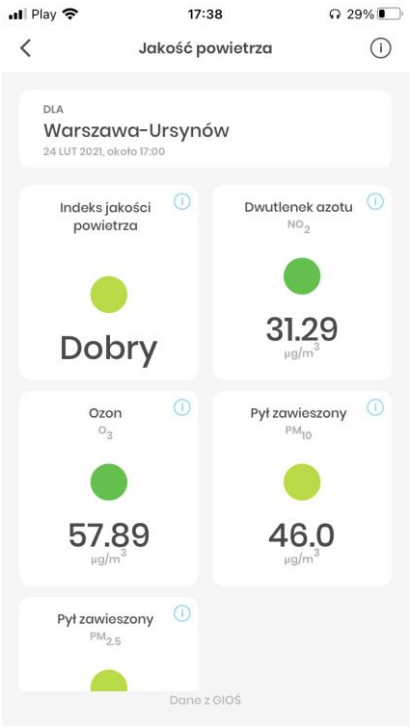
Do niniejszej rozprawy zostały włączone trzy publikacje naukowe, które stanowią cykl prac dotyczący projektu „Wpływ użytkowania aplikacji mobilnej afterAMI na kontrolę czynników ryzyka chorób sercowo-naczyniowych u pacjentów po zawale serca”. W ramach publikacji został szczegółowo opisany protokół badania, a w kolejnych dwóch manuskryptach przedstawiono wyniki oceniane odpowiednio po 30 dniach i po 6 miesiącach od wypisu ze szpitala. Przedstawienie tych trzech prac razem stanowi integralne podsumowanie całego przedsięwzięcia i jest swojego rodzaju syntezą uzyskanych dowodów naukowych, które zostały opublikowane w międzynarodowych czasopismach z wysokim wskaźnikiem cytowań.



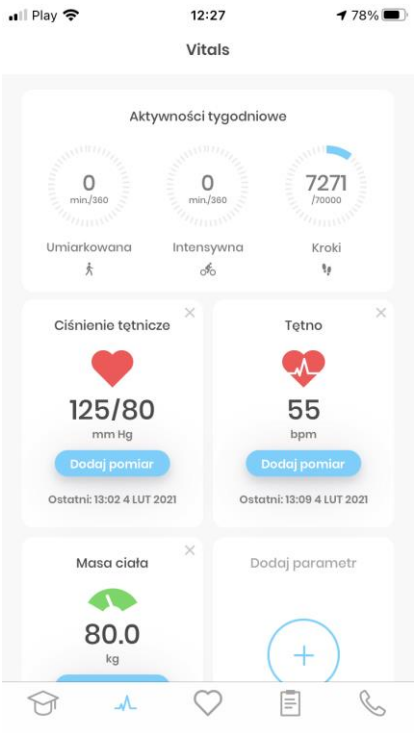
Ryc. 1 Ekran startowy aplikacji



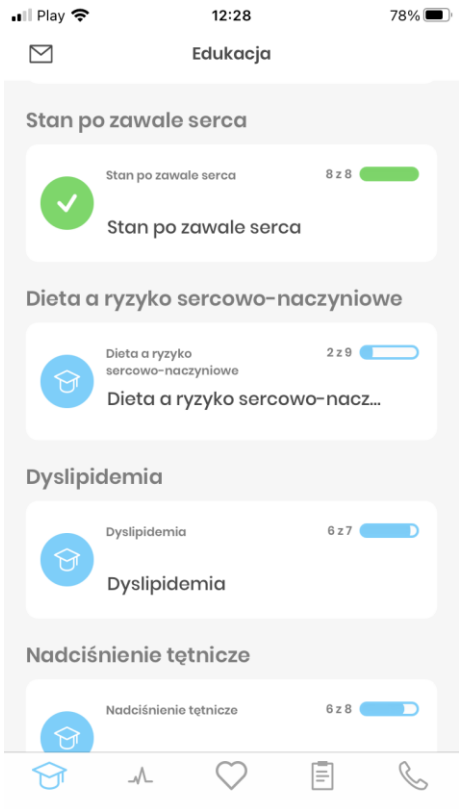
Ryc 2. Widok kalendarza



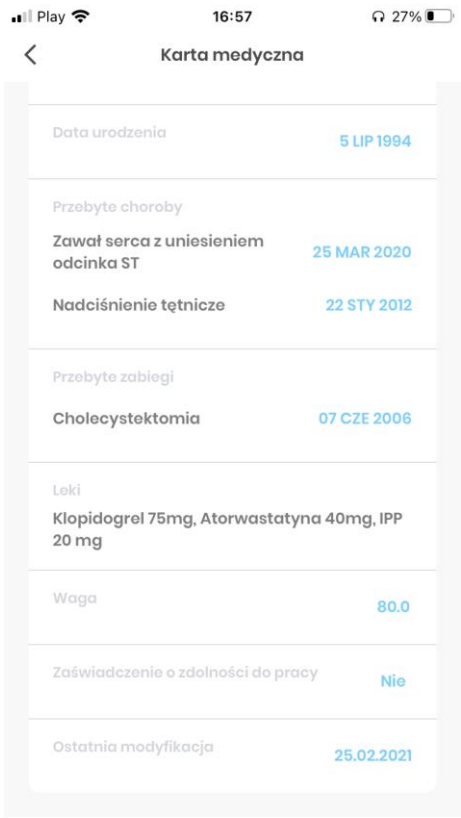
Ryc 3. Panel jakości powietrza



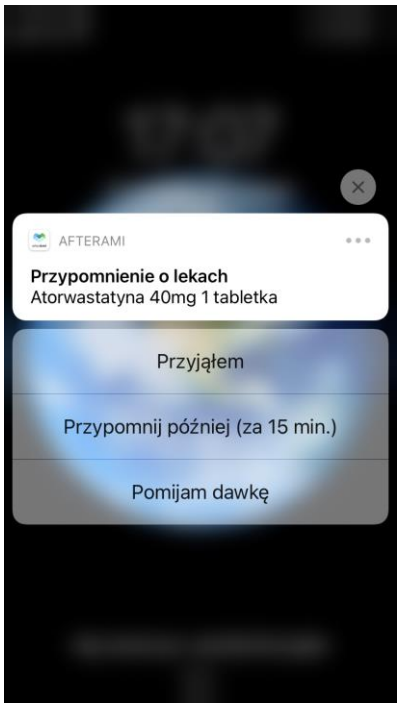
Ryc. 4 Panel kontroli czynników ryzyka chorób sercowo-naczyniowych



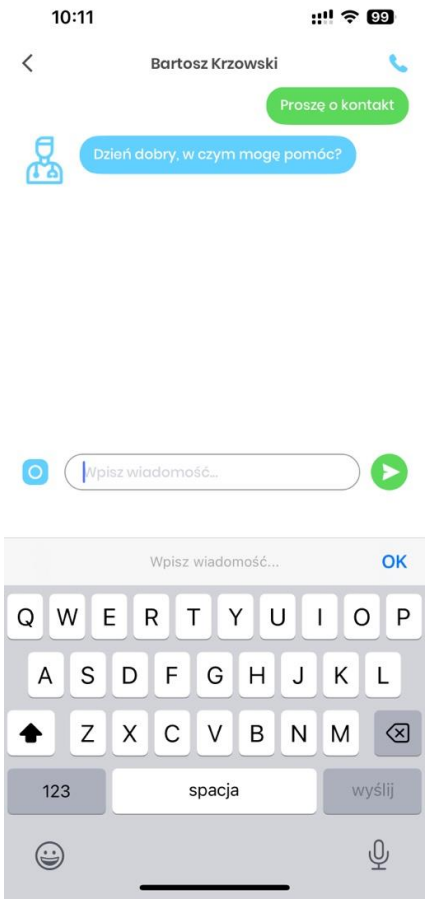
Ryc. 5 Panel edukacyjny



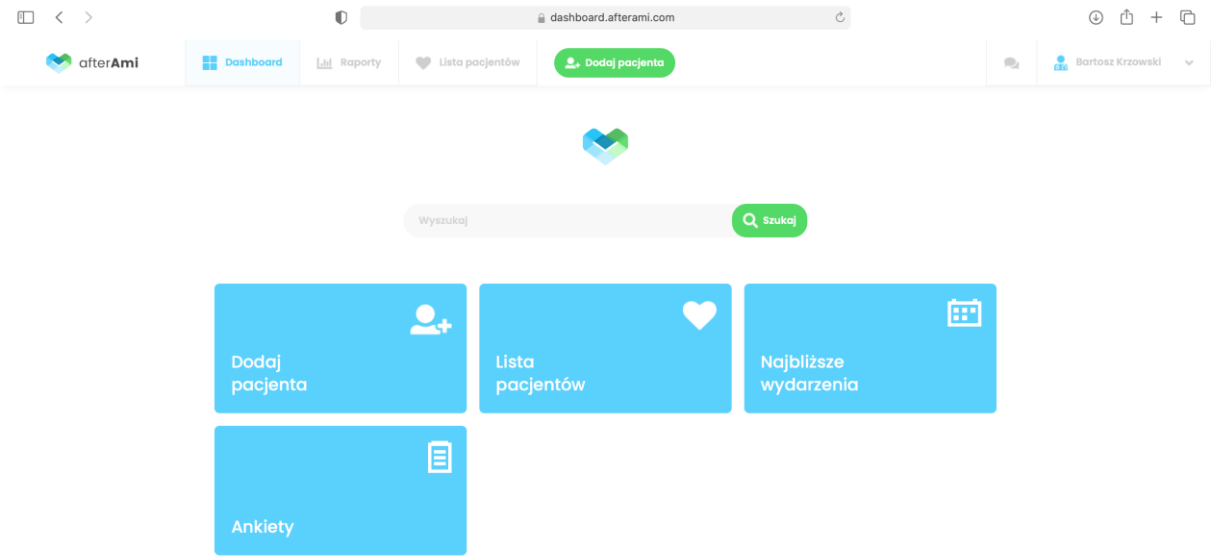
Ryc 6. Karta medyczna pacjenta



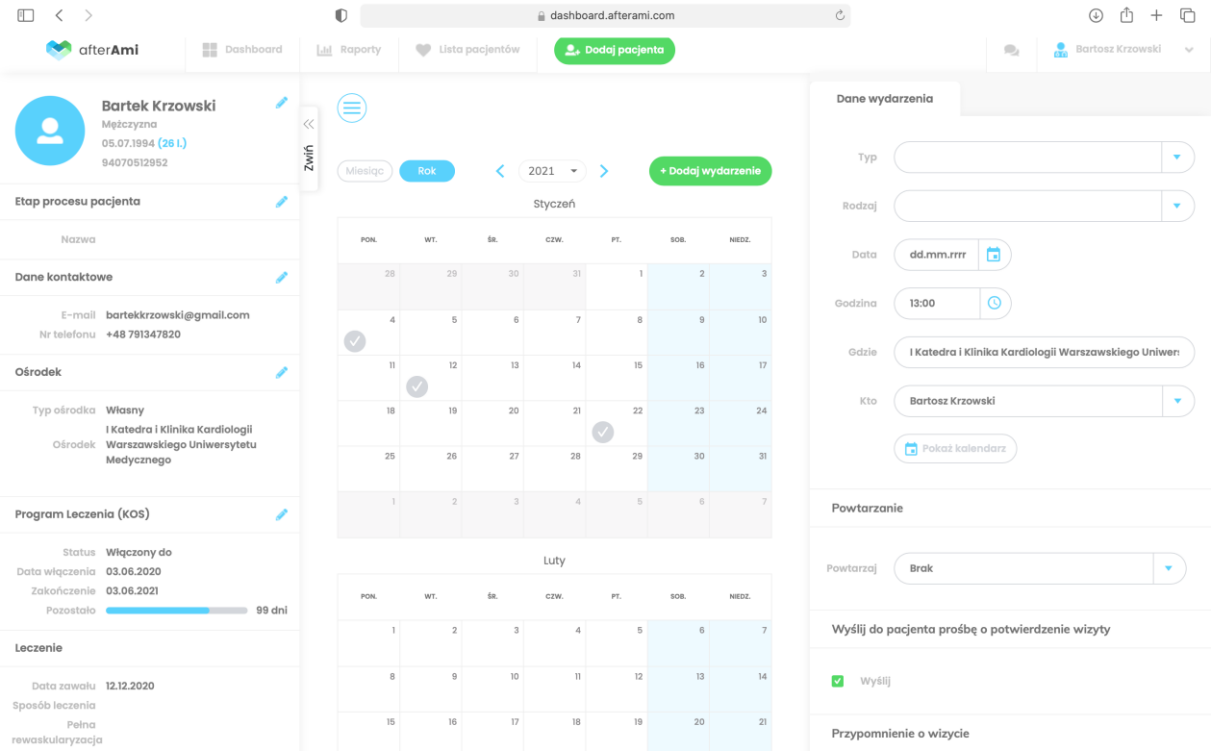
Ryc. 7 Przypomnienia o przyjmowaniu leków



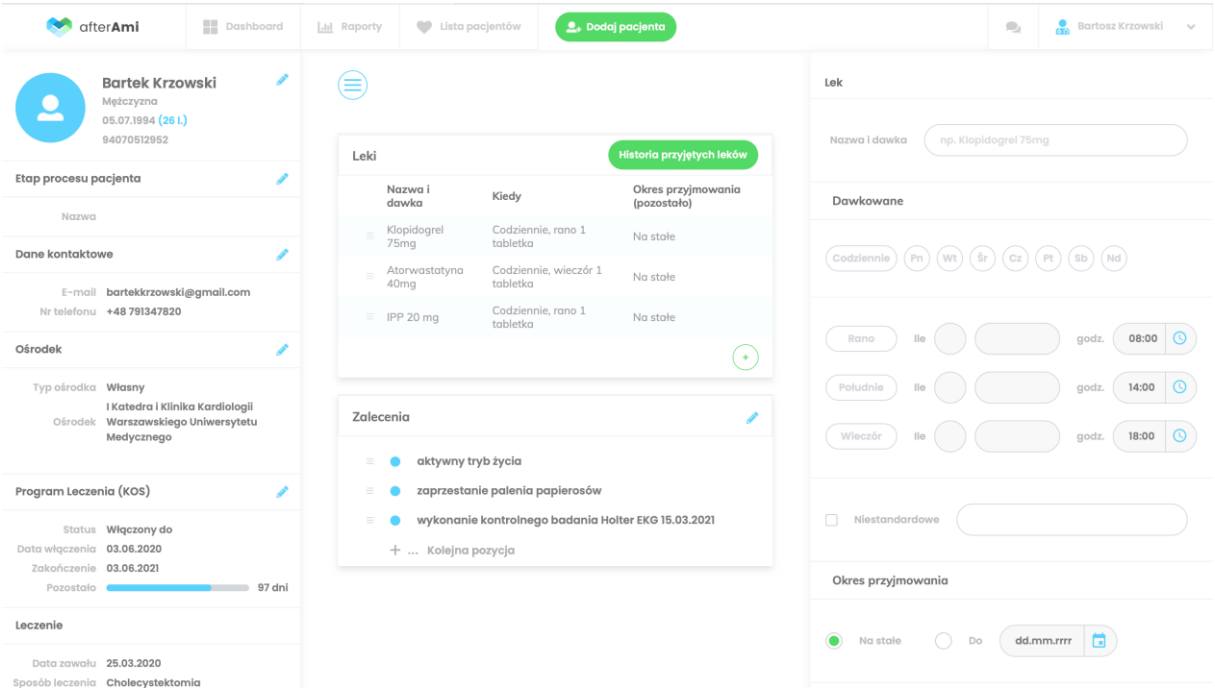
Ryc. 8 Chat z lekarzem



Ryc. 9 Widok panelu lekarza



Ryc. 10 Widok karty pacjenta



Ryc. 11. Widok zaleceń pacjenta

5 Założenia i cele

Ogólnym celem projektu była ocena możliwości nowoczesnego zastosowania telemedycznego w warunkach polskiego systemu opieki zdrowotnej.

Szczegółowe punkty końcowe wyznaczone w ramach badania obejmowały:

Pierwszorzędowy punkt końcowy:

- ocena częstości występowania rehospitalizacji i/lub pilnych wizyt ambulatoryjnych oceniana po 6 miesiącach od randomizacji;

Drugorzędowe punkty końcowe:

- ocena częstości występowania rehospitalizacji i/lub pilnych wizyt ambulatoryjnych oceniana po 30 dniach od randomizacji;

- ocena kontroli wartości ciśnienia tętniczego oceniana po 30 dniach i po 6 miesiącach od randomizacji;

- ocena masy ciała oceniana po 30 dniach i po 6 miesiącach od randomizacji;

- ocena statusu palenia papierosów oceniane po 30 dniach i po 6 miesiącach od randomizacji;

- ocena statusu gospodarki lipidowej oceniane po 30 dniach i po 6 miesiącach od randomizacji;

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7 Kopie opublikowanych prac

Krzowski *et al. Trials* (2022) 23:522
https://doi.org/10.1186/s13063-022-06463-x

Trials

STUDY PROTOCOL Open Access

Mobile app and digital system for patients after myocardial infarction (afterAMI): study protocol for a randomized controlled trial

Bartosz Krzowski, Michał Peller*, Maria Boszko, Paulina Hoffman, Natalia Żurawska, Karolina Jaruga, Kamila Skoczylas, Gabriela Osak, Łukasz Kołtowski, Marcin Grabowski, Grzegorz Opolski and Paweł Balsam

Abstract

Background: Treatment of acute myocardial infarction has been the subject of studies over the past years. However, the initial months after myocardial infarction are crucial from the perspective of the patient's prognosis. It is extremely important to take care of all cardiovascular risk factors and undergo a full rehabilitation program. Telemedical solutions are becoming more and more relevant in everyday practice. We describe a protocol of a study evaluating the use of the mobile application "afterAMI" in patients after myocardial infarction. The app offers an educational mode, calendar, vital signs diary, medication reminders, medical history card, and healthcare professional contact panel. It offers several solutions, which individually proved to be effective and improve a patient's prognosis. Despite general promising results from previous studies regarding telemedical tools, there is a paucity of evidence when it comes to prospective randomized trials. Our aim was to perform a comprehensive evaluation of a newly developed mobile application in the clinical setting.

Methods: A group of 100 patients with myocardial infarction on admission at the 1st Chair and Department of Cardiology, Medical University of Warsaw, will be recruited into the study. The project aims to assess the impact of the application-supported model of care in comparison with standard rehabilitation. At the end of the study, cardiovascular risk factors will be analyzed, along with rehospitalizations, the patients' knowledge regarding cardiovascular risk factors, returning to work, and quality of life. In this prospective, open-label, randomized, single-center study, all 100 patients will be observed for 6 months after discharge from the hospital. Endpoints will be assessed during control visits 1 and 6 months after inclusion into the study.

Discussion: This project is an example of a telemedical solution application embracing everyday clinical practices, conforming with multiple international cardiac societies' guidelines. Cardiac rehabilitation process enhancements are required to improve patients' prognosis. The evidence regarding the use of the mobile application in the described group of patients is limited and usually covers a small number of participants. The described study aims to discuss whether telemedicine use in this context is beneficial for the patients.

Trial registration: ClinicalTrials.gov NCT04793425. Registered on 11 March 2021.

Keywords: Acute myocardial infarction, Telemedicine, Telehealth, Mobile application, Cardiac rehabilitation

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Administrative information

Note: the numbers in curly brackets in this protocol refer to SPIRIT checklist item numbers. The order of the items has been modified to group similar items (see http://www.equator-network.org/reporting-guidelines/spirit-2727-statement-defining-standard-protocol-items-for-clinical-trials/).

Title {1}	Mobile app and digital system for patients after myocardial infarction (afterAMI)
Trial registration {2a and 2b}.	ClinicalTrials.gov, NCT04793425, registered 11 March 2022.
Protocol version {3}	Version 4.0, 04.05.2022
Funding {4}	The work is carried out in the years 2020 to 2022, financed by the subsidy allocated to science, obtained by the Medical University of Warsaw
Author details {5a}	1) 1st Department of Cardiology, Medical University of Warsaw, Warsaw, Poland
Name and contact information for the trial sponsor {5b}	Not applicable; this trial does not have a sponsor.
Role of sponsor {5c}	Not applicable; this trial does not have a sponsor.

Background and rationale {6a}

Cardiovascular diseases are the leading cause of death and a focal contributor to disability. Managing acute myocardial infarction (AMI) has improved significantly over the past years due to progress in both pharmacotherapy and invasive procedures. The mortality rate following AMI varies between countries, but an overall decrease has been observed [1]. Nevertheless, 12% of the patients die within one year after AMI [2]. Therefore, efforts should be made to optimize the cardiac rehabilitation process. It is crucial to focus on preventing future ischemic events by providing optimal care for patients at-risk [3]. Secondary prevention aims to control all cardiovascular disease (CVD) risk factors, which may be challenging in everyday practice. Jankowski et al. reported that only 2.9% of patients with coronary artery disease (CAD) have all CVD risk factors adequately controlled corresponding to values recommended in the guidelines [4]. Proper CVD risk factor control remains a challenge in the real-world setting.

Several efforts are being made to improve patients' prognosis. The latest approach to improve cardiac rehabilitation is the use of novel telehealth-based solutions. Over 3.2 billion smartphones are used globally, and the mobile applications market is expected to grow by 18.4% between 2018 and 2026. Therefore, enhancing cardiac rehabilitation by mobile application support may be a promising tool. Telemedicine has proved to be an effective solution in clinical scenarios. Widmer et al. demonstrated that augmentation of usual cardiac rehabilitation with an online and smartphone-based program improved CVD risk factor management and reduced rehospitalizations or emergency department visits by 40% ($p<0.05$) [5]. Naturally, not all cardiac patients are capable of using smartphones. Gallagher et al. reported that 54.6% of cardiac patients eligible for attending cardiac rehabilitation used technology for health purposes. Patients used it to access information on health conditions and medications mainly [6]. Coorey et al. concluded in the meta-analysis that mobile applications have a beneficial influence on CVD risk factors control, but more scientific evidence is required to enhance the implementation of telemedicine into clinical practice [7].

Although several international cardiac societies recommend telemedicine use [8, 9], evidence-based conclusions are required to adjust specific telemedical tools individually to the patient and improve the prognosis. The influence of mobile application support on cardiac rehabilitation in a European setting is yet to be studied.

Objectives {7}

This study will aim to determine the effect of mobile application-supported cardiac rehabilitation on CVD risk factors control, rehospitalization, emergency department visits, quality of life, and the ability to return to work. We hypothesized that cardiac rehabilitation enhancement with the mobile application would improve the prognosis expressed by CVD risk factors management and the patient's quality of life.

Methods

Study setting {9}, Eligibity criteria {10}, Who will take informed consent? {26a}, Additional consent provisions for collection and use of participant data and biological specimens {26b}, Explanation for the choice of comparators {6b}, Trial design {8}, Provisions for post-trial care {30}

This protocol is a randomized, open-label, superiority, interventional study with two arms. Participants will be randomized to (1) a control group (CG) with standard cardiological care or (2) a mobile application-supported interventional group (IG). The participants will continue with traditional care after the trial is finished.

This single-center study will be carried out at the 1st Department of Cardiology at the Medical University of Warsaw, an academic, public hospital in the capital of Poland. Cardiologists and fellows of cardiology will conduct all study-related procedures. The Department ensures all treatment options for patients with AMI and

during their cardiac rehabilitation process. It is regarded as the leading Department of Cardiology in Poland. The anticipated number of eligible participants is 100.

Inclusion criteria:

- Signing the informed consent to participate in the study
- Hospitalization due to myocardial infarction, based on the Guidelines on Fourth Universal Definition of Myocardial Infarction [10]
- Owning a mobile device with Internet access and the Android/iOS operating system
- Age ≥18 years old
- Positive results of a test verifying the basic skills of using mobile applications (Supplementary material 1)

Exclusion criteria:

- Life expectancy shorter than 6 months due to non-cardiac illness (Those with malignant tumors, severe mental illness, and/or uncontrolled systemic diseases were excluded from the present study)
- Negative test results, regarding everyday mobile application use
- Lack of signed informed consent
- Age <18 years old
- Pregnancy or breastfeeding
- Lack of a mobile device with Internet access and the Android/iOS operating system

Participant recruitment will occur daily from Monday to Friday. A study team member will approach every patient presenting with AMI, and the inclusion criteria will be assessed. The study design will be thoroughly described to the patient, including all potential benefits, harms, and ethical implications. Each eligible patient will be proposed to enter the study. Patients will be given time to ask questions and all doubts will be clarified before inclusion into the study. If the patient agrees to participate in the research, the informed consent will be signed in 2 copies: one for the participant and one for the research archives. The informed consent will explain how participant data and blood samples will be handled and where they will be sent. This trial does not involve collecting biological specimens for storage. Every participant will receive a note with a summary of the study design.

Every year approximately 400 patients are hospitalized due to acute myocardial infarction. However, a significant part of those patients are unable to use a mobile application and therefore they do not meet one of the main inclusion criteria. Going further, only some of the patients who meet inclusion criteria are willing to take part in a trial. The recruitment began in December 2020. Approximately 7 patients per month are included in the trial. Last patient recruitment is expected in Q1 2022.

Assignment of interventions: allocation, blinding

Sequence generation {16a}, Concealment mechanism {16b}, Implementation {16c}, Who will be blinded {17a}, Procedure for unblinding if needed {17b}

This is an open-label study. Randomization will be performed with an online tool by an independent statistician available at (www.randomizer.org). A hundred sets will be generated, each with a number (1 for CG and 2 for IG). All allocations to CG and IG will be executed before the study begins. The list of subsequent allocations will not be visible for the recruiting physician until the initial eligibility assessment of the patient and obtaining the patient's consent for study participation. After collecting the initial documentation, the physician will be unblinded and will receive the group allocation information from the principal investigator. It should be underlined that the person who checks for inclusion criteria and introduces the patient into the trial protocol is blinded until patient agreement. Figure 1 shows the study design flow chart, describing all the steps of the study (Fig. 1). The investigator performing statistical analysis will be blinded, as well as nurses collecting blood samples on the follow-up visits. Taking into consideration the use of the mobile application in everyday practice, it is impossible to blind physicians performing follow-up visits. It could be regarded as ethically doubtful, because based on the data provided via mobile application, clinical decisions can be made (i.e., blood pressure treatment augmentation).

Intervention description {11a}, Criteria for discontinuing or modifying allocated interventions {11b}, Strategies to improve adherence to interventions {11c}, Relevant concomitant care permitted or prohibited during the trial {11d}

Patients in the intervention group will be granted access to the mobile application (afterAMI) during the rehabilitation process. Access to the app is what differentiates the groups. afterAMI app offers several features described below. What is more, a dedicated web page will be used by medical professionals to improve everyday clinical work organization and enable better contact with the patients.

Patients in the intervention group will also be given access to educational data about their diseases. Every educational chapter was prepared by a cardiologist experienced in managing patients after MI.

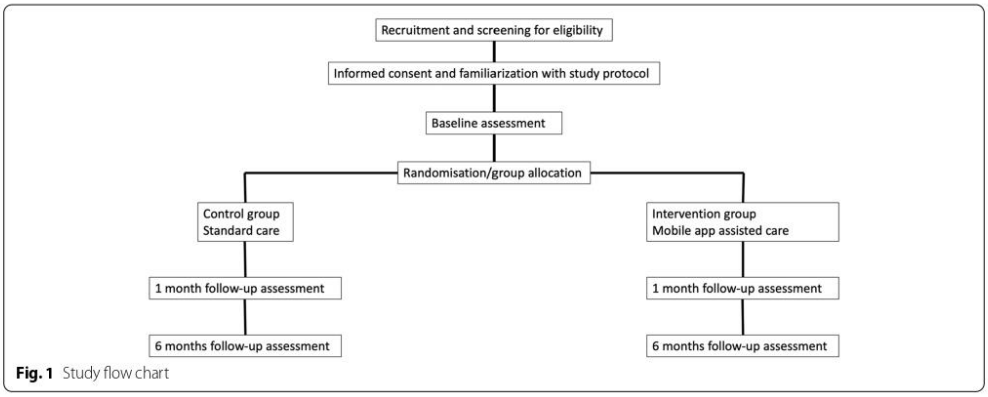

Fig. 1 Study flow chart

Additionally, every patient will regularly receive messages with notifications about the recommended lifestyle interventions and promoting adherence to the therapy. The notes focus mainly on cardiovascular risk factors and ways of controlling them. We made na effort to emphasize the importance of everyday lifestyle changes in terms of minimizing the risk of potential ischemic events in the future. The role of physical activity and drug adherence was frequently emphasized. All notes were prepared based on recommendations provided by the European Society of Cardiology [11]. An optimal scheme for message quantity and structure has not been described yet in the case of cardiac patients. In a recent meta-analysis, Bashi et al. concluded that the results of mobile application-assisted patient education generally show a positive, promising result. However, due to poor reporting quality and considerable heterogeneity of applied interventions, further studies are required in order to develop a comprehensive, optimal educational scheme [12]. In another paper, a cardiac telerehabilitation program augmented by a short message service (SMS) delivered to patients once a week, resulted in both physical fitness and quality of life improvements [13]. Based on those reports, the authors of this trial decided to send 2 messages weekly. The notifications are also considered as a strategy to improve adherence to the recommendations.

Another essential feature of the application is a panel dedicated to reporting patients' vital signs (blood pressure, heart rate, weight, saturation, and glycemia), which will be daily analyzed, and if necessary, a short message will be sent to the patient, advising to present to the primary healthcare clinic or emergency department. Patients will be instructed to report their parameters daily, in case of manually entered data. If the patient has a wrist-worn wearable device, compatible with 'health; application on iOS or Android, then this data will also be presented in the afterAMI app. For instance, in the case of patients with smartwatches allowing for heart rate measurement with photopletyspography or ECG, these parameters (heart rate, blood pressure, body weight, saturation, and physical activity) will automatically be transferred into the app, directly after measurement. Patients with a pressure gauge without a connection to the mobile phone will have to enter the data manually. Naturally, there is room for error associated with adding the value of a particular parameter, but it can also happen during traditional "notebook" notes. A possible clinical scenario is the detection of an alarming rapid increase in bodyweight, which might foreshadow incoming heart failure exacerbation. Another potential use of the application is reporting rapid pulse. Then, new-onset atrial fibrillation might be suspected. In every case requiring medical confirmation, the patient will be referred to the nearest emergency room. However, all patients will be informed, that they should immediately present to the nearest emergency unit or contact the emergency services, in case of recurring angina or any other acute complaints.

Additionally, the application will send notifications with reminders to take drugs. This solution has been previously evaluated in many studies and proved to be a successful tool in increasing adherence to therapy [14].

Moreover, the application includes a module with air pollution parameters measured amidst the localization set up. If they exceed the alarming levels, the patients will be notified, and it will be suggested to minimize outdoor physical activities

Additionally, a medical history card will be created for each patient, based on the discharge documents from the hospital. This solution aims for the patient always to have brief information about undergoing coronary

interventions. This knowledge might be crucial for the physicians performing subsequent percutaneous coronary interventions (PCI) in the future and could potentially decrease time-to-balloon.

Finally, the application offers a contact panel to text message and call the cardiologists at the hospital. We believe that this will translate into better work organization, better time management (as fewer consultations are likely to be missed by patients), and increased patient safety. All patients randomized to IG will be thoroughly trained in application features and capabilities before discharge.

On the contrary, patients randomized to the CG will be provided with the best available care, based on current guidelines and standards of care [15]. What is more, all patients will be provided with intense medical care supervision, as every patient included in the study will have two additional cardiological consultations.

Rehabilitation programs are recommended for every patient hospitalized due to MI. It has been underlined, that it improves a patient's prognosis. However, the final decision on the participation is up to the patient. It should be noted, that the study is carried out during the COVID-19 pandemic. Some patients are refusing to participate in the rehabilitation program in fear of infection. However, owing to the randomization, the number of patients who refused to attend rehabilitation is expected to be similar between the groups. Rehabilitation programs include regular cardiac consultations with an experienced physician, psychological sessions, exercise training, stress management programs, and dietary recommendations. The patient is offered versatile support for one year after MI. Patients who refuse to take part in the rehabilitation program are managed by a general practitioner. Owing to the randomization, patients' distribution is expected to be similar in both groups.

All data implemented into the application was prepared by experienced cardiologists with considerable experience in both, clinical practice as well as eHealth use.

The market currently offers a wide variety of mobile applications offering simple features to the general population (i.e., blood pressure diaries). However, as far as the authors know, this is one of the very first digital solutions to combine several previously tested features. Moreover, the number of mobile applications dedicated to MI patients is limited. What is more, the first few weeks and months after discharge can be a considerable challenge in everyday activities, therefore it is crucial to recognize the need to support the patient in this period. The described digital tool should be regarded as an opportunity to improve patients' prognosis, augmenting the traditional approach with standard practice. The only criterion for discontinuing is the participants' request. What is more, concomitant care is neither permitted nor prohibited in the trial. At the end of the study, the participants will receive a full report with the results of their assessments after the data is analyzed. At the end of the study, the principal investigator will contact the participants to provide them with final educational materials and information regarding secondary cardiovascular prevention.

Outcomes {12}, Participant timeline {13}, Plans to promote participant retention and complete follow-up {18b}

All 100 patients will be observed for 6 months after discharge. The endpoints will be assessed twice, during two control visits, in 1- and 6-months, after enrollment. Patients will be called to schedule the control visit's date after discharge. Additionally, patients in the IG will receive a notification in their mobile app reminding them about the upcoming ambulatory visits.

Figure 2 shows the recommended SPIRIT figure with the participant timeline. Primary outcome includes both need for rehospitalization and/or urgent outpatient visit and assessed between baseline and 6-month control visit. There are five secondary outcomes related to cardiovascular risk factors control: blood pressure, body mass, nicotinism, dyslipidemia and need for rehospitalization and/or urgent outpatient visit assessed between baseline and 1-month control visit. Detailed target values regarding risk factors control have been presented in Table 1 based on ESC Chronic Coronary Syndrome guidelines [16]. Each value will be categorized as met or not. Secondary outcomes will also include quality of life and depression severity assessment (MacNew, EQ-5D-5L, and DASS-21 questionnaires), cardiovascular risk factors knowledge (CVD risk factors identification recommended BP values, desired lifestyle intervention identification). and return to work in case of professionally active patients.

Further data collection will cover demographic parameters (like sex, age), as well as laboratory test results, and types of prescribed pharmacotherapy.

Secondary outcome measures

Cardiovascular risk factors Blood pressure

All patients at discharge are asked to measure and note blood pressure values daily. The mobile application-derived mean blood pressure values covering 5 days prior to their visits will be averaged for the IG patients. The mean blood pressure values of CG-comprised patients will also be averaged, but based only on the presented written notes. Additionally, meeting guidelines-based recommended values will be checked in both groups. Hypertension is one of the main cardiovascular risk factors, with a significant prevalence of 1.13 billion

	STUDY PERIOD			
	Enrolment	Allocation	Post-allocation	
TIMEPOINT	$-t_1$	0 *(during hospitalization due to MI)*	t_1 *(30 days after discharge from hospital)*	t_2 *(6 months after discharge from hospital)*
ENROLMENT:				
Eligibility screen	X			
Informed consent	X			
Allocation		X		
INTERVENTIONS:				
AfterAMI group			←	→
Control Group				
ASSESSMENTS:				
Laboratory test		X		
Rehospitalization or urgent outpatients visits			X	X
Cardiovascular risk factors control			X	X
Quality of life - MacNew		X	X	X
Quality of life – EQ-5D-5L		X	X	X
Depression – DASS21		X	X	X
Cardiovascular risk factors knowledge		X	X	X
Return to work			X	X

Fig. 2 Recommended SPIRIT figure with participant timeline

Table 1 Risk factors targets for endpoint assessment

Risk factor		Target level
LDL-c level	No history of MI within 2 years prior	LDL-C lowered by at least 50% from baseline and to <1.4 mmol/L (<55 mg/dL)
	History of MI within 2 years prior	LDL-C of <1.0 mmol/L (<40 mg/dL) in patients who have experienced a second vascular event within 2 years
Body mass index		18.5–24.9 (kg/m^2)
Systolic blood pressure	General	120–130 mmHg
	Older (aged >65 years)	130–140 mmHg
Nicotinism		Currently non-smoker

Abbreviations: MI myocardial infarction, *LDL* low-density lipoprotein cholesterol

worldwide [17]. Hypertension control in patients after MI is crucial and correlates with patients' prognosis [18].

Body mass

All patients will be weighed on admission tl and during control visits 1 and 6 months after discharge. Weight change will be measured. Maintaining a healthy body weight is one of the fundamental aspects of preventing cardiovascular diseases and an essential treatment element after an MI.

Nicotinism

All patients will be asked about smoking on admission and during control visits 1- and 6-months after discharge. Smoking cessation is one of the main goals of patients after MI. Quitting smoking is necessary to reduce the risk of another ischemic incident. It has been documented that smoking cessation results in 50% reduction in the risk of experiencing another MI [19].

Dyslipidemia

All patients after MI will have their cholesterol levels measured during hospitalization. Subsequent cholesterol level measurements will be performed during control visits. According to ESC guidelines, different groups of patients have different LDL cholesterol target values, which should be met during the rehabilitation process [20]. Lowering LDL cholesterol levels correlates with a better prognosis after MI [21].

Quality of life

Quality of life will be assessed with four questionnaires. The MacNew questionnaire contains 27 questions [22]. The scoring of the MacNew is as follows, the maximum score in every domain is 7 [high quality], and the minimum is 1 [poor quality]. The quality of life is assessed in the context of physical, emotional, and social aspects. The the EQ-5D-5L questionnaire refers to 5 aspects: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression [23]. Every segment is assessed based on a 5 level scale-LEVEL 1: indicating no problem; LEVEL 2: indicating slight problems; LEVEL 3: indicating moderate problems; LEVEL 4: indicating severe problems; LEVEL 5: indicating an inability to/extreme problems. DASS 21 scale will be used to assess depression, anxiety, and stress [24]. The DASS is a quantitative measure of distress along the 3 axes of depression, anxiety, and stress. Seven questions are assigned to every aspect: depression, anxiety, and stress. Each question has 4 possible answers:

0- Did not apply to me at all - Never
1- Applied to me to some degree, or some of the time - Sometimes
2- Applied to me to a considerable degree, or a good part of the time - Often
3- Applied to me very much, or most of the time - Almost always

Seven questions are assigned to every aspect: depression, anxiety, and stress.

Higher result in each section contributes to higher severity in depression, anxiety, and stress.

Cardiovascular risk factors knowledge

Cardiovascular risk factors knowledge will be assessed with a previously prepared questionnaire (Supplementary material 2).

Return to work

In the case of previously working patients, the likelihood of returning to work will be assessed, as well as the timing of returning to work will be counseled.

Sample size {14}

Currently, data regarding the achieved reduction of rehospitalizations or prelevance of urgent visits associated with mobile application use remains limited. Most previous studies were conducted on smaller populations. The sample calculation was based on Widmer and colleagues' [5] study, considering rehospitalization and urgent ambulatory visits—comparing the effects of an online and smartphone-based program with standard rehabilitation on the mentioned endpoint. A 40% decrease in the primary endpoint was observed. Fifty percent of patients in the control group and 20% in the interventional arm were rehospitalized or visited the emergency department.

An online calculator (https://clincalc.com/) was used to determine the sample size, assuming the power of 80% and significance of 5%. A total of 76 patients (38 per group) were required. However, considering a possible lost-to-follow-up group and possible dropouts, a decision to recruit 100 patients was made. The reason for the dropout is lack of consent or inability to attend control visits or consent withdrawal.

Data collection and management and confidentiality

Plans for assessment and collection of outcomes {18a}, Data management {19}, Confidentiality {27}, Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

The assessment of outcomes will be carried out at the 1st Department of Cardiology, Medical University of Warsaw, while the rehabilitation will be conducted according to a scheduled program. An experienced cardiologist familiar with the study protocol will conduct all the control visits, which will take place in the cardiac ambulatory clinic. Blood samples will be sent to the local laboratory. All blood samples will be tested in the laboratory according to the locally implemented standards and subsequently utilized. There are no plans for future blood use. No other biological specimen will be tested during this trial. Patients will be asked to fulfill the MacNew, EQ-5D-5L, and DASS21 questionnaires. The highest data quality is one of the authors' primary goals while conducting a trial. Every information will be entered into a database and subsequently checked by another investigator. Every investigator will have a valid good clinical practice certificate.

All data collected during the study and medical documents will be protected and stored in a room dedicated to clinical trial records. All electronic materials will be duly stored in the principal researcher's computer protected with a password known only to the principal researcher. Additionally, a backup in the cloud will be performed after new data collection.

The highest level of confidentiality will be applied. The participants' data will be kept separately from any identifying information. According to good clinical practice, all investigators will make every effort to keep the sensitive data confidential.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}, Methods for additional analyses (e.g. subgroup analyses) {20b}, Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}, Interim analyses {21b}

In terms of the endpoints, we will look at the frequency of the events 6 months after the discharge, since we believe that due to randomization the groups will be similar at the beginning. No other (including no interim) analyses will be performed in the present study. Regarding secondary endpoints, the change from baseline will be assessed and the frequency of the events in case of rehospitalizations and/or urgent ambulatory visits after 1 month. The distribution of continuous variables will be estimated using the Shapiro-Wilk test. Continuous variables presented with normal distribution will be presented as mean values and standard deviations (SD). All continuous variables presented non-normal distribution will be demonstrated as median values and interquartile ranges. In the case of variables with a normal and non-normal distribution, the groups will be compared using the Student's t-test and the non-parametric Mann-Whitney U test. The comparison of qualitative variables between the groups will be performed using the Fisher exact test. In order to compare changes in the values of continuous variables over time, the analysis of variance will be performed. To compare the outcome of the patients, the Kaplan-Meier estimators will be utilized. For quantitative variables, the change from baseline will be assessed. Additionally, in order to diminish differences in sex and age related to group size, propensity score matching analysis will be performed as well. We also plan to conduct a subanalysis in the group of patients who attended rehabilitation, as well as in those who did not attend.

A per-protocol analysis will be performed after completing all of the follow-up visits. In the analysis, we will include all patients who meet inclusion criteria and sign informed consent regardless of the follow-up completion. Statistical calculations will be performed twice; after obtaining data from the first follow-up visit from all patients and after the final follow-up, 6 months after discharge. In case of missing data, patients will be excluded from the particular analysis.

Plans to give access to the full protocol, participant-level data and statistical code {31c}

Access to the data sets and statistical code is not planned for this study. However, this material might be available upon an adequately justified request to the corresponding author while maintaining participants' anonymity.

Oversight and monitoring

Composition of the coordinating center and trial steering committee {5d}, Composition of the data monitoring committee, its role and reporting structure {21a}, Adverse event reporting and harms {22}, Frequency and plans for auditing trial conduct {23}, Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

The research center is coordinated and managed by GO and the researcher MG. The principal investigator-BK will direct and continuously monitor trial conduct.

No additional external monitoring committee is considered for this study. The principal investigator will meet monthly with all the researchers involved in this study via an online platform (Zoom) to discuss the research

progress and solve possible issues. Researchers are instructed to immediately report any issues to the principal investigator, who will subsequently organize an additional committee meeting and inform the board review committee from the Medical University of Warsaw and the Ethics Committee of the Medical University of Warsaw, Warsaw, Poland, when appropriate. Additional auditing will be conducted on request from the Ethics Committee of the Medical University of Warsaw.

As serious adverse events of mobile application usage have not been described so far, we do not expect the need for adverse event reporting However, any adverse events will be reported and thoroughly documented and presented in the study summary. Furthermore, monthly reports regarding any potential adverse events and protocol violations will be prepared

Any protocol amendments will be reported to and approved by the Ethics Committee of the Medical University of Warsaw. All modifications will be updated at clinicaltrials.gov by the principal investigator (BK). Any important protocol modifications will be communicated to the investigators and patients verbally.

Dissemination plans {31a}

Study outcomes will be reported at both local and international cardiological conferences. The final study results will be submitted to a peer-reviewed indexed scientific journal within the 3 years after the last patient's enrollment.

Discussion

This study aims to investigate the effects of mobile application-assisted cardiac rehabilitation after MI on rehospitalization rate, cardiovascular risk factors control, and patients' quality of life. Considering the alarmingly high 12-month mortality rate after MI, there is a considerable need for improving the rehabilitation process by intensifying and optimizing cardiovascular risk factors' control. Standard approaches consisting of pharmacotherapy and recommended lifestyle modification have been thoroughly studied and included in the current guidelines [3]. Novel methods supporting the patient's involvement and adherence are of the highest importance.

Telemedicine is a rapidly growing branch of heatlhcare, with numerous novel technologies proposed for improving the diagnostic, therapeutic, and rehabilitation process. Cardiology is one of the primary beneficiaries of the newly implemented tools. Several cardiac guidelines recommend enhancing everyday clinical practice with mHealth solutions [9, 25, 26]. Even though there is a varirty of mobile applications dedicated to patients, only a few were validated in clinical settings, with regard to the mentioned endpoints. Additionally, many of them were not developed by clinicians. It is crucial to establish whether such an approach, based on digitally supported rehabilitation, may translate into a better prognosis through facilitating more adequate cardiovascular risk factors control. In previous studies, the use of mobile applications has been associated with a reduction of the rehospitalization rate after MI, but the data were collected only in a smaller sample of patients and in different healthcare systems [5]. Johnston et al. reported that using a simple, mobile application results in better self-reported drug adherence and may correlate with lifestyle changes and quality of life [27]. However, the discussion regarding the use of mobile applications in cardiac patients is still ongoing.

Despite several strengths, certain limitations of this study should be considered. Firstly, we will be unable to assess the mortality rate due to a short observation period and small sample size (both due to organizational issues). However, we do not expect this parameter to differ between groups. Additionally, this single-center analysis might be biased due to internal protocols, which might differ in other clinics.

Nonetheless, our project stands as a practical example of implementing modern solutions to improve patients' prognoses. If our assumptions regarding the potential beneficial effects of using the afterAMI application appear trustworthy, this study will provide a stronger voice in discussing broader telemedicine usage in everyday clinical practice.

Trial status

Recruiting.

Version 3. February 21st, 2022.

Date recruitment began: December 1, 2020. Approximate date when recruitment will be completed: March 31, 2022.

Abbreviations

AMI: Acute myocardial infarction; CVD: Cardiovascular disease; CAD: Coronary artery disease; CG: Control croup; IG: Interventional group; PCI: Percutaneous coronary intervention.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-022-06463-x.

Additional file 1: Supplementary material 1. Test verifying the basic skills of using mobile applications.

Additional file 2: Supplementary material 2. Cardiovascular risk factors' knowledge test.

Acknowledgements

We thank all the participants for their involvement in the study.

Authors' contributions {31b}
B.K. is the principal investigator. B.K., M.P., P.B., Ł.K., and G.Op. were responsible for the concept and the design of the study. M.B. P.H., K.J., K.S., N. Ż., and G. Os. were involved in data collection. B.K. and M. P, are responsible for statistical analysis. B.K., M. P, and P.B. wrote the first version of the manuscript. All authors edited and approved the final version of the manuscript.

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Availability of data and materials {29}
After the final study is published, the materials and data will be available upon a reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate {24}
The study has been developed in accordance with the declaration of Helsinki guidelines and was approved by the Scientific Ethics Committee of the Medical University of Warsaw (KB 150/2020). All participants will be asked to provide written informed consent before inclusion. Please see the annexing "Ethical Approval."

Consent for publication {32}
Please see the annexing "Informed Consent."

Competing interests {28}
The authors declare that they have no competing interests.

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Mobile app and digital system for patients after Myocardial Infarction (afterAMI): early results from a randomized trial

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Mobile app and digital system for patients after Myocardial Infarction (afterAMI): early results from a randomized trial

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What's new

For patients who have suffered from acute myocardial infarction (AMI), it is important to prevent further heart attacks, by controlling risk factors, for instance. Our study demonstrated that everyday care in such patients may be improved with a novel telemedicine solution. Supporting standard rehabilitation through the use of a dedicated mobile app – a simple and harmless tool – resulted in better control of cardiovascular disease risk factors such as LDL-cholesterol level and blood pressure. Moreover, it was noted that a majority of the patients were able to use the mobile app and were eager to benefit from it. These results may contribute to telemedicine being introduced into standard medical practice and to improved care for post-AMI patients.

Abstract

Introduction: Cardiac rehabilitation is a complex program which aims to better control a patient's cardiovascular risk factors. It can be supported by mobile applications. Despite promising results from previous studies with telemedicine tools, there is a paucity of evidence when it comes to prospective randomized trials.

Objectives: The aim was to perform a comprehensive evaluation of a newly developed mobile application – called afterAMI – in the clinical setting and to assess the impact of the application-supported model of care in comparison with standard rehabilitation.

Patients and methods: 100 patients with myocardial infarction were recruited on admission to the Department of Cardiology at Medical University of Warsaw. Patients were randomized into group with an access to afterAMI app or to standard cardiac rehabilitation. Cardiovascular risk factors were analyzed along with the number of rehospitalizations and patients' knowledge regarding cardiovascular risk factors. This analysis focused on the results 30 days after discharge.

Results: The patients' median age was 61 years and 65% of the subjects were male. There were no differences in cardiovascular risk factor control between the study groups apart from LDL cholesterol levels, which were lower in the "afterAMI" group ($P<0.001$), despite no differences being found at the beginning of the study. Similarly, a significant difference in NT-proBNP levels was observed ($P=0.02$), despite a lack of significant differences at randomization.

Conclusions: This study serves as an example of a telemedicine tool being implemented into everyday practice. The augmented rehabilitation program resulted in better control of cholesterol level. Longer follow-up is required to establish prognosis in this population.

Key words:

acute myocardial infarction, cardiac rehabilitation, mobile application, telemedicine, telehealth

Introduction

Cardiovascular disease (CVD) remains a huge challenge for both societies and individuals, carrying a substantial burden in terms of mortality and disability. Significant progress has been made in the treatment of acute myocardial infarction (AMI) in recent decades due to novel invasive procedures and tailored pharmacotherapy schemes. There are still major differences between countries regarding treatment outcomes, but in general, lower mortality has been observed recently [1]. Nevertheless, approximately one in ten AMI patients dies within a year of hospital discharge [2]. It has been emphasized several times how important it is to control CVD risk factors in patients within secondary prevention [3]. According to data published by Jankowski et al., only 2.9% of patients with coronary artery disease (CAD) control all CVD risk factors according to recommended values [4], with even worse control in woman when compared with men [5]. Moreover, one study found that more than one fourth of patients died within 5 years of discharge after hospitalization for AMI in Poland [6]. Only one third of patients underwent cardiac rehabilitation (CR) during the 12 months following AMI. It seems that there is huge potential for a further decrease in mortality in patients suffering from myocardial infarction in Poland. [7] Up to 45% of the mortality from recurrent myocardial infarction is preventable [3]. It is crucial to constantly look for potential optimization, which could result in improved prognosis.

A number of approaches have been tested in several clinical trials aimed at improving patients' prognosis. One of the newest solutions is based on the use of novel telemedicine devices and systems. There are approximately 6 billion smartphones in use globally and the

market is estimated to continue to grow [8]. Therefore, implementing mobile apps into everyday clinical practice seems a natural step forward. Protocols and results of studies including mobile app use in patients after myocardial infarction have been published [9-11]. Moreover, some of them have shown promising results and improved blood pressure control [12]. In one preliminary study published a few years ago, Widmer et al. demonstrated that augmenting a regular cardiac rehabilitation program with an online and smartphone-based program improved CVD risk factor management and reduced rehospitalizations and emergency department visits by 40% ($p<0.05$) [13].

According to the available literature, cardiac patients are using mobile apps mainly to access information about illnesses and drugs [14]. However, the potential of dedicated mobile apps is much greater and it seems that this solution is under-utilized in the clinical setting. Still, in the metanalysis published by Coorey et al., mobile apps were found to have a positive effect on CVD risk factor control [15], which is crucial in secondary prevention.

It should also be pointed out that both national and international societies recommended broader use of tele-health solutions [16, 17]. On the other hand, adding them to everyday clinical practice remains a challenge, perhaps partially due to the unsatisfactory amount and quality of evidence. In this study, we aimed to test the impact of a novel telemedicine solution on rehospitalizations and/or urgent outpatient visits and on CVD risk factor control in patients after myocardial infarction.

Patients and methods

Study design

This study consisted of data from the ongoing single-center, randomized, open afterAMI trial (Mobile App and Digital System for Patients After Myocardial Infarction), registered in ClinicalTrials.gov under the number NCT04793425. The study was approved by

a local ethical review board (KB/150/2020) and informed consent was obtained from each patient. The detailed methods and description of the study design have been described in another paper [18]. In brief, the study includes patients who were hospitalized due to AMI in a leading cardiac university department between 2019 and 2021. Following current guidelines, the diagnosis was made based on symptoms, troponin concentration, and ECG results [19]. Patients were randomized (1:1) into either the control group (CG), which underwent regular cardiac rehabilitation, or the intervention group (IG or afterAMI), whose rehabilitation was supported by the use of a dedicated mobile app. Briefly, app provides patients with an access to educational data about their diseases. Every educational chapter was prepared by a cardiologist experienced in managing patients after MI. Additionally, every patient regularly received messages with notifications about the recommended lifestyle interventions and promoting adherence to the therapy. All notes were prepared based on recommendations provided by European Society of Cardiology [3] Another essential feature of the application is a panel dedicated to reporting patients' vital signs (blood pressure, heart rate, weight, saturation and glycaemia), which was daily analyzed and if necessary, a short message has been sent to the patient, advising to present to the primary healthcare clinic or emergency department. Patients were instructed to report their parameters daily. Moreover, the application sent notifications with reminders to take drugs.

On top of that, the application includes a module with air pollution parameters measured amidst the localization setup. Additionally, a medical history card will be created for each patient, based on the discharge card from the hospital. This solution aimed for the patient always to have brief information about underwent coronary interventions. This knowledge might be crucial for the physicians performing subsequent percutaneous coronary interventions (PCI) in the future and could potentially decrease time-to-balloon. Finally, the application offers a contact panel to text message and call the cardiologists at the hospital.

All demographic, clinical, and laboratory data, quality of life questionnaires, and information regarding etiology of AMI and medication at discharge were collected. All endpoints are set to be assessed twice: at 30 days and 6 months after randomization. A flowchart of the study is presented in Figure 1.

Study endpoints

The primary outcome includes the need for rehospitalization and/or urgent outpatient visit, assessed between baseline and a 6-month follow-up visit. Moreover, there are five secondary outcomes related to cardiovascular risk factor control: blood pressure, body mass, nicotinism, dyslipidemia, and the need for rehospitalization and/or urgent outpatient care between baseline and a 1-month follow-up visit. Detailed target values regarding risk factor control have been presented previously [18]. Each value will be categorized as being met or not. Secondary outcomes will also include quality of life and depression severity assessment (MacNew, EQ-5D-5L, and DASS-21 questionnaires), knowledge about cardiovascular risk factors (CVD risk factors, recommended blood pressure values, and desired lifestyle intervention identification), and return to work in the case of employed patients. Further data collection will cover demographic parameters (sex and age) and laboratory test results.

Statistical analysis

In terms of the endpoints, we looked at the frequency of the events. Regarding secondary endpoints, the change from baseline and the frequency of rehospitalizations and/or urgent outpatient visits after 1 month were assessed. The distribution of continuous variables was estimated using the Shapiro–Wilk test. Continuous variables with a normal distribution are presented as mean values and standard deviations (SD). All continuous variables with a non-normal distribution are presented as median values and interquartile ranges. In the case of

variables with normal and non-normal distributions, the groups were compared using Student's t-test and the non-parametric Mann–Whitney U test. The comparison of qualitative variables between the groups was performed using Fisher's exact test. For quantitative variables, the change from baseline was assessed. A per-protocol analysis was performed after all of the follow-up visits were completed. We included in the analysis all patients who met the inclusion criteria and signed an informed consent form, regardless of whether the follow-up was completed. In the case of missing data, the patients were excluded from the particular analysis.

Results

The current analysis of the afterAMI study included 100 patients. During hospitalization, 50% (n=50) of them were randomized to the IG and 50% (n=50) to the CG. Unfortunately, 11 individuals were lost to follow-up (5 from the intervention group and 6 from the control group), representing an 11% attrition rate. One patient did not receive the allocated intervention due to his death during the initial hospitalization. The patient characteristics at baseline are presented in Table 1. The two groups did not differ significantly at baseline in terms of sociodemographic characteristics (sex, body weight, and general cardiovascular risk factors, CR). The median age of the study group was 61 years and 65% of them were male. The individuals assigned to the CG were older (63.42 years old vs. 56.8) in the intervention group, P=0.002). Both heart failure and atrial fibrillation were more prevalent in the CG. Over the 30-day period, more patients in the intervention group achieved target LDL concentrations than members of the control group (27 [58.06%] vs. 9 [21.88%], P=0.005). Similarly, significant difference in NT-proBNP level was observed (257 (127.5-502.5) vs. 626 (254-1043); p=0.02), despite lack of significant differences at the moment of randomization (422 (133-1256) vs. 886.5 (230- 2250); p=0.07).

There was no significant difference in the need for rehospitalization and/or urgent outpatient care (4 [8%] vs. 5 [10%], *P*=1.0). Fewer patients in the afterAMI group had a BMI within the normal range (5 [11.1%] vs. 10 [21.73%], *P*=0.14). Fewer patients in the intervention group smoked at follow-up (39 [86.67%] vs. 35 [81.39%], *P*=0.57). At the beginning of the study there was no difference in smoking status between both groups (33 [66%] vs. 32 [64%], *P*=1.0*)*. More patients using the afterAMI app met the blood pressure target value; but the difference not statistically significant (44 [98.78%] vs. 39 [88.63%], *P*=0.11). A summary of the results is presented in Figure 2. An overall trend towards better CVD risk factor control was demonstrated.

Discussion

In the afterAMI trial we evaluated the impact of a CR augmentation with mobile app. Despite some differences in the compared groups, which could have been related to relatively small sample size, IG had significantly lower LDL and NT-proBNP level with no significant differences at the moment of randomization.

Providing CAD patients with continuity of care remains challenging, as over time many patients return to previous habits, including a sedentary lifestyle, poor diet, and nicotinism. As a result, their cardiovascular health deteriorates, potentially leading to further adverse cardiac events. Therefore, investigating novel solutions to support risk factor control, educate patients, and sustain their motivation is crucial to improving long-term prognosis.

According to the latest ESC guidelines, participation in CR programs is highly recommended after AMI and/or revascularization in chronic coronary syndrome (Class I, Level A) [3]. The definition of CR extends far beyond physical exercise. It should be considered a multidisciplinary intervention involving psychosocial support, patient education, diet counselling, and risk factor modification. As indicated by several systematic reviews, CR

programs effectively contribute to improved blood pressure, heart rate, body mass, and lipid profile [20]. Moreover, many studies have demonstrated the beneficial effects of CR programs on clinical outcomes through reduced rates of recurrent myocardial infarction, cardiovascular hospitalization and mortality, and all-cause mortality [21, 22]. Patient's motivation in terms of lifestyle improvement is the highest at right after the discharge from the hospital. The aim of supporting patients with an app was to maintain possibly the highest level of motivation as long as possible. Similar conclusions were made by Sinnadurai et al., who stated that a long-term strategy to sustain the beneficial CR effects should be applied [23].

The market of digital health solutions is growing exponentially and is considered a promising approach. There are a variety of potential applications of telemedicine in CR, ranging from web-based nationwide systems and online counselling platforms, through home-based exercise programs, to mobile apps. However, only a few mobile apps have been adequately validated by demonstrating their evidence-based effectiveness. Current ESC guidelines on CVD prevention state that mHealth solutions should be considered a user-friendly, economically attractive tool in risk factor control for promoting not only better therapy adherence, but also lifestyle modifications in long-term patient management [3].

The principal finding of this analysis is that augmenting CR with a mobile app resulted in a significant reduction in LDL-cholesterol concentrations and facilitated meeting guideline-recommended target values in AMI patients during a 30-day follow-up. However, one should consider differences in the randomized groups at the beginning of the study when analyzing the results. Nevertheless, the significant cholesterol level reduction might have been greater in the IG due to some app features, among which both expanded educational panel and reminder of the drugs option, seem to be the most crucial in this regard. The use of mHealth technologies in improving cardiovascular risk factor control in CAD patients has

already been widely explored. Although early feasibility studies showed promising results [13, 24], more contemporary findings seem to be slightly conflicting. Some mobile apps have been aimed at improving one particular risk factor, for example, physical activity [25] or blood pressure [26]. However, authors currently tend to apply a more holistic approach, targeting most of the modifiable risk factors simultaneously, which is a strategy that we also decided to adapt [12]. Patients in the IG had significantly lower NT-proBNP level. Since this molecule has been found to be an independent prognostic factor for HF development and future coronary events [27], we believe IG has therefore better prognosis.

In some cases, improvement was observed for only a singular risk factor. In a study by Lunde et al., the only significant differences were demonstrated in improved the VO_{2peak}, exercise performance, and exercise habits of the app-equipped patients [28]. Another app contributed to significantly improved blood pressure and dietary habits in the first months after myocardial infarction, with a nonsignificant trend toward better exercise capacity and higher smoking cessation rates [12]. However, due to difficulties with objective diet changes assessment we decided to focus on other endpoints, which might be indirectly or sometimes directly influenced by dietary habits. Studies conducted by Michelsen et al. and by Lunde et al. focused on the outcomes after 25 weeks and one year respectively, therefore comparison to our findings would be misleading. While Johnston et al. found no differences between their groups in BMI, physical activity, or smoking, a significant reduction in LDL-cholesterol concentrations in the intervention group was achieved during a 6-month follow-up. Patients also had a visit 6-10 weeks after the discharge, but no lab oratory reports were presented in the paper making it impossible to directly compare [29]. Nevertheless, the trend towards lower LDL level was similar results to this observed in our study. Commonly, an overall trend for improved control of other risk factors can be observed, but without statistically significant values. However, considering the significant heterogeneity of the proposed interventions in

terms of technology and duration, as well as the studies' sample sizes and clinical outcomes, drawing clear conclusions remains a challenge.

One feature of the app is the patient education module. Poor health literacy among patients has been associated with increased hospitalization rates and greater emergency care use, resulting in higher costs for the healthcare system [30]. This phenomenon further advocates the vital role of patient education in their long-term management. The mobile-based educational materials can be provided in various forms, including podcasts, videos, written articles, daily checklists, chatrooms for professional counselling, etc. The afterAMI app features an option to send notifications in the form of short, motivational text messages about healthy lifestyle habits, transferring the user to the corresponding educational module when they click on it. Personalized, patient-tailored lifestyle advice supported by mobile phone texts has been proven to be a clinically effective and cost-effective solution in smoking cessation [31], hypertension management [32], and glycemic control in diabetic patients [33]. Interestingly, the results of the TEXTMEDS trial suggest that after acute coronary syndrome, cardiac education and support delivered via text message did not impact medical adherence, but small effects on lifestyle risk factors were noted. Patients in the IG of this trial more often met BMI goals, which we didn't observe in our study, and reported to have healthier dietary habits. The endpoints were assessed at 6 and 12 months [34]. These findings may suggest the need for a more complex and comprehensive approach involving multiple interventions instead of only text-message-based management.

As with most novel solutions, to successfully implement mHeath in long-term management of CAD patients, one must overcome the barrier of the initial learning curve. With growing evidence on the clinical effectiveness and feasibility of mobile app use in this population, the most efficient strategies are expected to be established soon.

Improving the patient's prognosis remains the main goal of optimizing risk factor control. In a recently published study by Indraratna et al., an app-based model of care (TeleClinical Care) dedicated for patients who have suffered acute coronary syndrome or heart failure has led to a significant reduction in unplanned hospital readmissions, higher rates of completing CR, better medication adherence, and proven cost-effectiveness [35]. Interestingly, such observations were not made in the short-term follow-up period, which is in line with our results.

It should be noted that the rate of patients taking part in CR within comprehensive coordinated care after myocardial infarction (KOS-Zawał) and outside of it was relatively low, but similar across studied groups. Every patient, if only assessed eligible was given a referral for CR, but the response rate seemed to be low. It might have been due to fact that the study was conducted right in the middle of pandemic and some patients refused to participate in any form of stationary CR due to fear of COVID-19 infection. Future studies, out of pandemic, will show the influence of this mobile app on mentioned above endpoints.

Several studies were aimed at comparing the clinical effectiveness of digital and traditional models of CR. Hybrid CR is the combination of stationary and telemedical rehabilitation. Participation in CR programs often requires multiple visits to a clinic, which can limit attendance, especially for patients living in rural areas. Therefore, telehealth interventions can successfully complement traditional CR. Moreover, mobile app interventions have been shown to increase traditional CR attendance, completion rates, and outcomes [36, 37]. Future digital interventions in CR may include smartphones or wearable devices for monitoring patients' vital parameters during remote CR structured exercise, providing them with detailed instructions, allowing them to design their own activity schedules or create personalized exercise programs using AI-based algorithms, or interacting with chatbots for educational purposes [37].

The median age of patients suffering from AMI in Poland is 66.8 years [6]. There is general concern regarding the feasibility of mHealth interventions in older patients. However, the recently published AHA statement on mobile health technologies in preventing cardiovascular disease among older adults points out that mobile technology can be effective in improving healthy behavior and medication adherence [38]. It stresses that in the context of an aging society, it is crucial to implement mHealth solutions to improve health outcomes in older adults suffering from CAD. Similarly, the results from Fibricheck indicate that older age correlates with better motivation and adherence [39].

Telemedicine is undoubtedly a field of extensive research. Recently, more and more studies are exploring other potential applications of the mHealth-based model of care. Our study seems to bring a piece of new evidence regarding mobile app use in AMI patients.

Limitations

Despite several strengths, certain limitations of our study should be discussed when interpreting the results. Firstly, the participants in the control group were younger, had less heart failure and less atrial fibrillation, which may be due to an insufficient number of randomized patients. It should be also considered that possibly younger and healthier patients from IG are more eager to cooperate with the doctor, which translates into better adherence and finally cholesterol level reduction. Larger studies with afterAMI are planned to overcome this issue. Also, a single-center study should be regarded as a feasibility project and an introduction to a larger, multicenter study. Secondly, not all cardiac patients are capable of using smartphones. Gallagher et al. reported that 54.6% of cardiac patients eligible for CR used technology for health purposes [14], which is similar to our findings. In the screened population, 62.23% of the patients were able to use mobile app. Thus, the solution is not currently for everyone. However, since technology use increases, we believe that this

percentage will grow in the future. It should be emphasized that this was not a blinded study, but it is impossible to blind patients in mobile app interventions, as also stated in other similar studies. Moreover, it was not possible to objectively compare physical activity between the groups, as the patients in the control group were not equipped with any form of wearable activity trackers, due to the financial limitations of our study.

This was a pilot study with a 30-day duration and, as such, it was not yet feasible to assess the effects of the afterAMI app on long-term outcomes in CAD patients. However, the authors are planning to publish more findings on this subject.

Conclusions

Telemedicine solutions are widely discussed and are gaining momentum when it comes to augmenting standard care. Our study proves the feasibility of mobile app support in myocardial infarction patients. The benefits regarding cholesterol level may contribute to improved prognosis. Nevertheless, a longer observation period should be used and larger, multicenter studies should be planned.

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Table 1. General population characteristics

Variable		afterAMI	Control	*P*-value
Clinical data				
Age, years (SD)		56.8 (9.23)	63.42 (11.4)	**0.002**
BMI, kg/m^2 (SD)		28.5 (4.06)	28.11 (5.38)	0.72
Body weight, kg (SD)		88.95 (13.86)	85.47 (24.33)	0.46
Height, cm (SD)		176.3 (7.2328)	171.6 (8.9729)	**0.02**
Sex, male		34 (68%)	31 (61%)	0.67
Comprehensive coordinated care after myocardial infarction (KOS-Zawał)		17 (34%)	9 (18%)	0.11
CR (KOS-Zawał and outside of KOS-Zawał combined)		27 (54%)	22 (44%)	0.42
Hospitalization, days		6 (4-8)	7 (5-11)	0.21
STEMI		25 (50%)	20 (40%)	0.42
NSTEMI		25 (50%)	30 (60%)	0.42
Infarction artery	LAD	26 (52%)	24 (48%)	1
	LCA	15 (30%)	17 (34%)	0.52
	RCA	16 (32%)	24 (48%)	0.14
PCI		39 (78%)	39 (78%)	0.62
Bypass surgery		5 (10%)	6 (12%)	0.76
Nicotinism		33 (66%)	32 (64%)	1
Packet years		20 (0-30)	14 (0-32.5)	0.79
Diabetes, type I		2 (4%)	0 (0%)	0.49
Diabetes, type II		11 (22%)	11 (22%)	1
Hypertension		30 (60%)	34 (68%)	0.38
Dyslipidemia		36 (72%)	39 (78%)	0.31
Atrial fibrillation/atrial flutter		1 (2%)	7 (14%)	**0.03**
Heart failure		6 (12%)	15 (30%)	**0.03**
Implanted pacemaker or ICD		1 (2%)	5 (10%)	0.11
Chronic kidney disease		1 (2%)	1 (2%)	1
Peripheral artery disease		1 (2%)	1 (2%)	1
EF in hospital, % (SD)		51.78 (8.42)	48.0 (9.22)	**0.04**
CVD risk factors knowledge		8 (6-9)	8 (4-9)	0.41
Employed		27 (54%)	17 (34%)	0.13
Lab tests at hospital				
Troponin I, µg/L		0.7930 (0.2250-5.5710)	0.694 (0.111-4.350)	0.72

Troponin II, µg/L	2.2550 (0.7145-8.7340)	5.640 (0.437-34.635)	0.17
Creatinine, mg/dl (SD)	0.98 (0.21)	1.05 (0.34)	0.20
eGFR, ml/(min×1.72 m²) (SD)	79.16 (17.22)	73.28 (20.93)	0.14
Na, mmol/L (SD)	139.1 (3.05)	139.6 (4.36)	0.54
K, mmol/L (SD)	4.17 (0.45)	4.38 (0.51)	**0.04**
WBC, x 10^9/L (SD)	10.27 (3.04)	10.19 (2.94)	0.91
HbA1C, %	5.8 (5.4-7.1)	5.6 (5.4-6.0)	0.46
NTproBNP, pg/ml	422 (133-1256)	886.5 (230-2250)	0.07
HgB, g/dl (SD)	14.58 (1.49)	14.14 (1.83)	0.20
Total cholesterol, mg/dl (SD)	191.3 (71. 57)	192.1 (52.29)	0.95
HDL, mg/dl (SD)	39.55 (10.02)	46.78 (10.65)	**0.001**
LDL, mg/dl (SD)	117.5 (68.59)	111.7 (61.56)	0.66
Tg, mg/dl	146 (92-233)	136.5 (87-201)	0.24
Drugs at discharge			
ACEi	42 (84%)	40 (80%)	0.52
ARB	4 (8%)	2 (4%)	0.23
ARNI	0 (0%)	0 (0%)	
MRA	9 (18%)	15 (30%)	0.23
B-blocker	42 (84%)	41 (82%)	0.74
CCB	20 (40%)	10 (20%)	**0.03**
Statin	46 (92%)	45 (90%)	1
Ezetimibe	5 (10%)	2 (4%)	0.27
VKA	0 (0%)	0 (0%)	
NOAC	1 (2%)	2 (4%)	1
ASA	45 (90%)	43 (86%)	1
Clopidogrel	12 (24%)	13 (26%)	1
Prasugrel	2 (4%)	0 (0%)	0.24
Ticagrelor	28 (56%)	28 (56%)	1
Digoxin	0 (0%)	0 (0%)	

ACEi - angiotensin-converting-enzyme inhibitors, ARB – angiotensin receptor blockers, ARNI – angiontensin receptor neprilysin inhibitor, ASA – acetylsalicylic acid, BMI – body mass index, CR – cardiac rehabilitation, CVD – cardiovascular disease, EF – ejection fraction, eGFR – estimated glomerular filtration rate, HbA1C – hemoglobin A1c, HDL – high-density lipoprotein, ICD – implantable cardioverter-defibrillator, LAD – left anterior descending artery, LCA – left circumflex artery, LDL – low-density lipoprotein, MRA – aldosterone receptor antagonists, CCB – calcium channel blockers, NOAC – novel oral anticoagulants, NSTEMI – Non-ST–elevation myocardial infarction, NTproBNP – N-terminal pro–B-type natriuretic peptide, PCI – percutaneous coronary intervention, RCA – right coronary artery, STEMI – ST-elevation myocardial infarction, Tg – triglycerides, VKA – vitamin K antagonist, WBC – white blood cells

Table 2. Laboratory results after 30 days

Endpoint	afterAMI	Control group	*P*-value
Creatinine, mg/dl (SD)	1.02 (0.18)	1.01 (0.29)	0.78
eGFR, ml/(min×1.72 m²) (SD)	78.73 (16.23)	74.5 (19.70)	0.34
HbA1C, %	5.8 (5.6-6.6)	5.75 (5.5-6.0)	0.35
NTproBNP, pg/ml	257.0 (127.5-502.5)	626.0 (254-1043)	**0.02**
HgB, g/dl (SD)	14.38 (1.46)	13.87 (1.15)	0.12
Total cholesterol, mg/dl (SD)	116.5 (30.43)	143.9 (36.93)	**0.002**
HDL, mg/dl (SD)	41.53 (8.64)	47.79 (12.70)	**0.023**
LDL, mg/dl (SD)	48.16 (25.97)	73.45 (28.91)	**<0.001**
Tg, mg/dl	106.0 (86.5-136.5)	99.5 (79.5-152.5)	0.96

eGFR – estimated glomerular filtration rate, HbA1C – hemoglobin A1c, HDL – high-density lipoprotein, LDL – low-density lipoprotein, NTproBNP – N-terminal pro–B-type natriuretic peptide, Tg – triglycerides

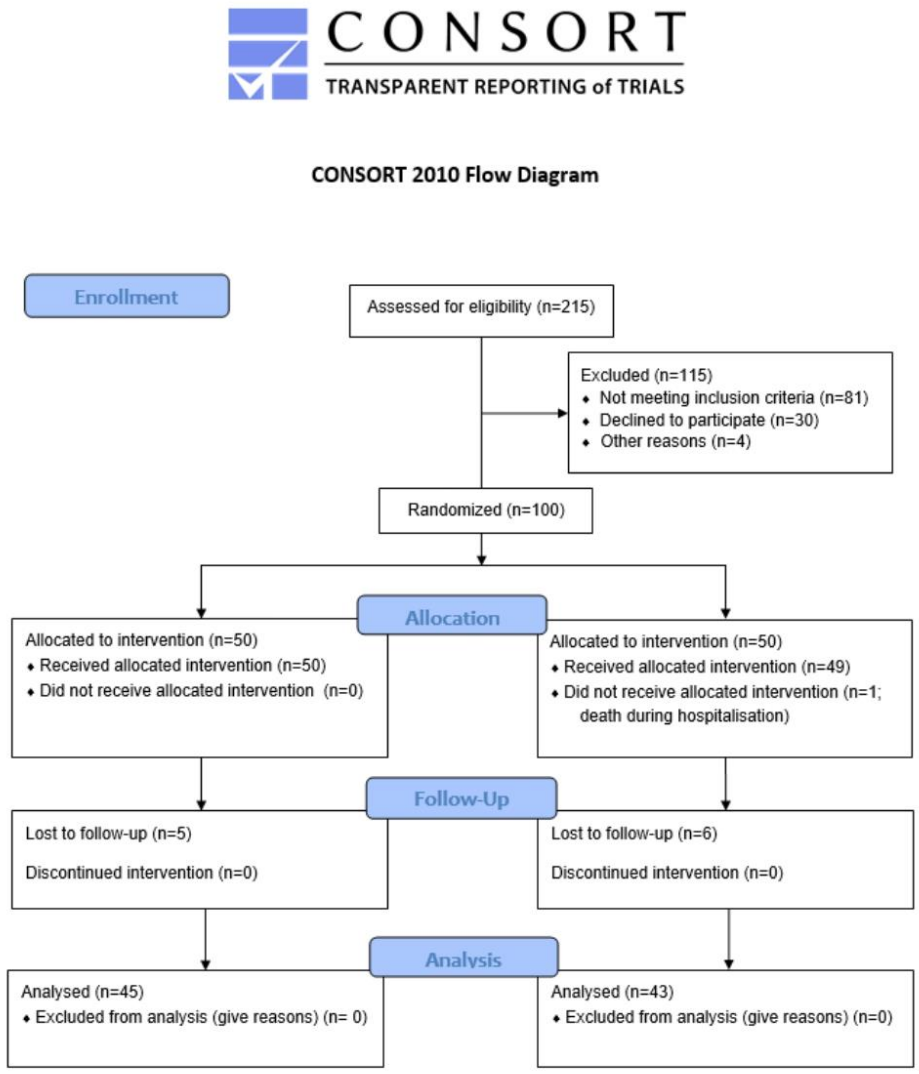

Figure 1. Enrollment and follow-up

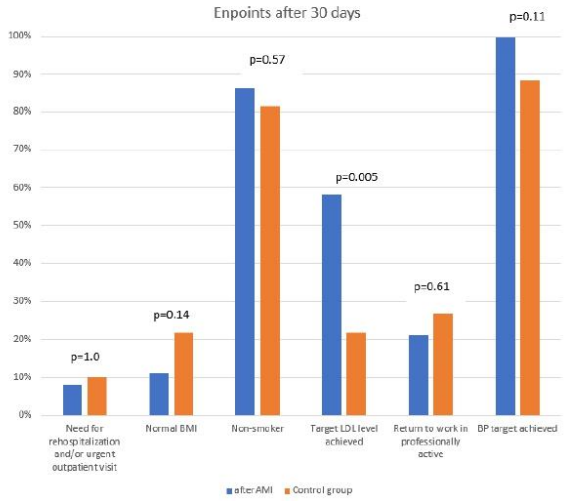

Figure 2. Endpoints 30 days after hospital discharge

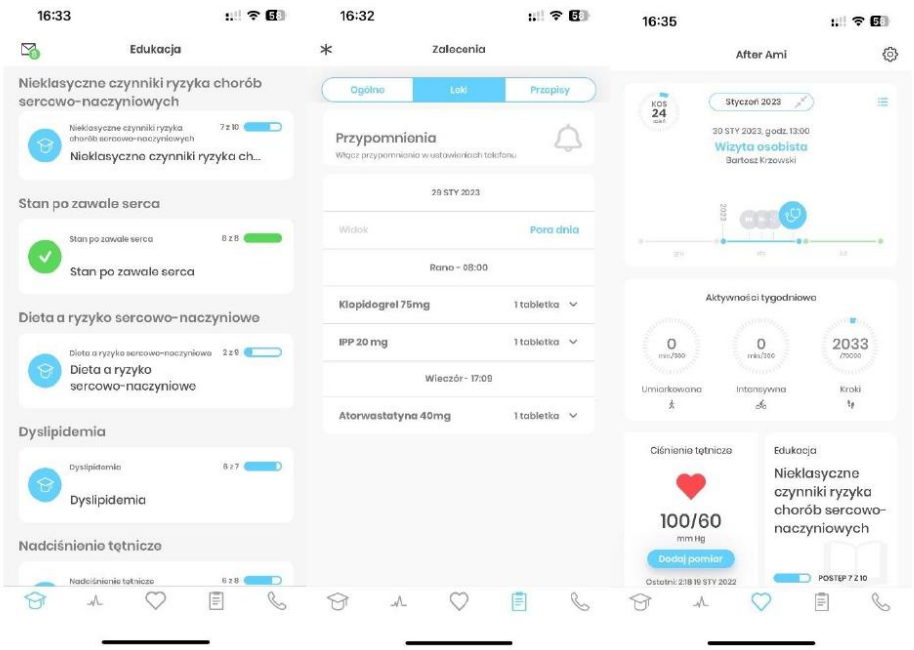

Figure 3. Example screenshots of the afterAMI app

Short title: Mobile app for patients after myocardial infarction

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MDPI

Article

Mobile App and Digital System for Patients after Myocardial Infarction (afterAMI): Results from a Randomized Trial

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Abstract: Cardiac rehabilitation after acute myocardial infarction is crucial and improves patients' prognosis. It aims to optimize cardiovascular risk factors' control. Providing additional support via mobile applications has been previously suggested. However, data from prospective, randomized trials evaluating digital solutions are scarce. In this study, we aimed to evaluate a mobile application—afterAMI—in the clinical setting and to investigate the impact of a digitally-supported model of care in comparison with standard rehabilitation. A total of 100 patients after myocardial infarction were enrolled. Patients were randomized into groups with either a rehabilitation program and access to afterAMI or standard rehabilitation alone. The primary endpoint was rehospitalizations and/or urgent outpatient visits after 6 months. Cardiovascular risk factors' control was also analyzed. Median age was 61 years; 65% of the participants were male. This study failed to limit the number of primary endpoint events (8% with app vs. 27% without app; $p = 0.064$). However, patients in the interventional group had lower NT-proBNP levels ($p = 0.0231$) and better knowledge regarding cardiovascular disease risk factors ($p = 0.0009$), despite no differences at baseline. This study showcases how a telemedical tool can be used in the clinical setting.

Keywords: acute myocardial infarction; cardiac rehabilitation; mobile application; telemedicine; telehealth

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1. Introduction

Cardiovascular diseases (CVD) are the leading cause of death worldwide and one of the biggest challenges of contemporary medicine [1]. Novel invasive procedures and tailored pharmacotherapeutic schemes contributed to significant progress in acute myocardial infarction (AMI) management, resulting in reduced mortality [2]. Still, approximately 10% of AMI patients die within a year after hospital discharge [3]. Optimal CVD risk factors' control is one of the most important components of secondary prevention, which has been highlighted many times [4]. According to the data reported by Jankowski et al., approximately only one in 30 patients after AMI had all CVD controlled according to recommended values [5]. Moreover, target cholesterol levels have been tightened up by now, so the actual percentage of patients who are optimally managed is likely to be even lower. What is more, at least a quarter of patients after AMI in Poland die within 5 years from the event [6]. Despite recent advances in cardiac rehabilitation (CR) programs in Poland [7], only one in three patients undergoes CR during the 12 months after AMI [8]. Therefore, there seems to be a significant field to act in order to improve patients' prognosis, especially since it is estimated that about half of the deaths from recurrent myocardial infarction are believed to be preventable [4]. Numerous efforts have been undertaken to boost CVD risk factors' control.

Several clinical trials assessed different approaches with the common goal of improving CVD risk factors' control in patients after AMI. Robust evidence points towards a noticeable growing interest in telemedical tools with mobile applications leading the field. The number of mobile smartphones is globally increasing [9]. Introducing mobile apps

into clinical practice seems inevitable and has been recommended by cardiac societies' guidelines [10]. Several protocols of studies testing the mobile app utility in cardiac patients have already been published [11–13]. Interestingly, many of them report promising results and provide evidence of, i.e., improved blood pressure value controls [14]. Widmer et al. carried out a study, which provided the momentum to further research the field of mobile apps' utility. It has been demonstrated that complementing a conventional CR program with a smartphone-based program improved CVD risk factor control. What is more, a 40% reduction ($p < 0.05$) in rehospitalizations and emergency visits has been observed [15]. Many studies were underpowered to show positive results, but according to a recent metanalysis, mobile apps positively impact CVD risk factor management [16]. Some of the previously published papers indicated that patients with CVD disease are using mobile apps to learn about the underlying disease and medicines [17].

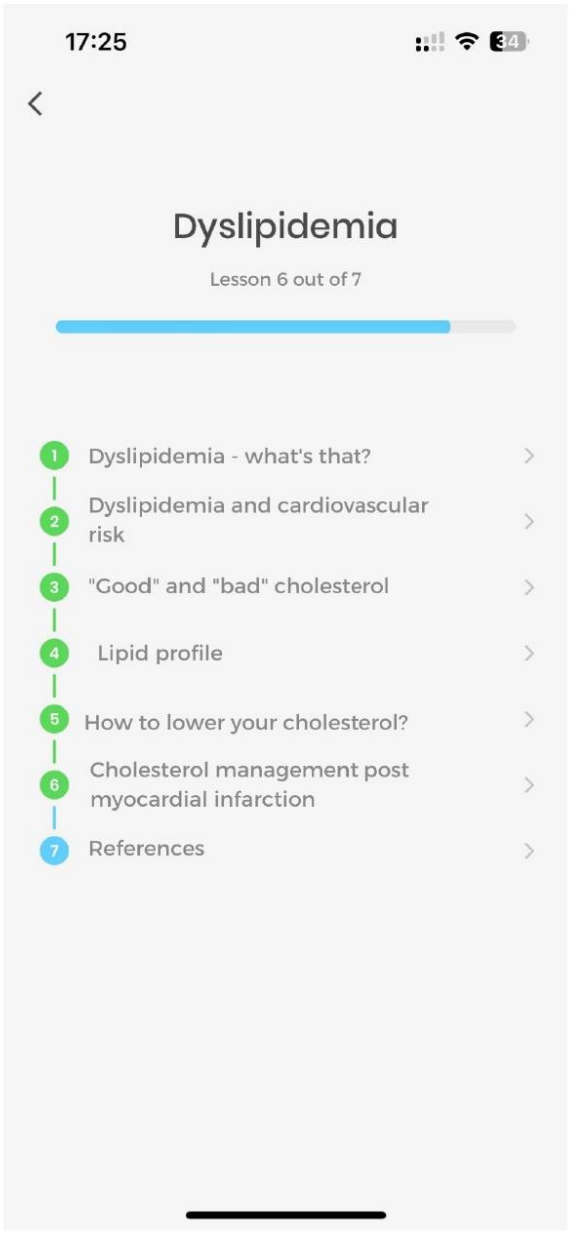
It should also be pointed out that recently many cardiac societies recommended broader use of telehealth solutions [10,18]. The afterAMI study aimed to assess the impact of a mobile app on the number of rehospitalizations and/or urgent outpatient visits, as well as its influence on CVD risk factor control in post-AMI patients. Early results were previously published. After the 30-day follow-up, patients had significantly lower LDL cholesterol ($p = 0.0007$) and NT-proBNP levels ($p = 0.0231$). No other differences were observed in CVD risk factors' control [19]. This analysis focuses on the final results after a 6month follow-up.

2. Materials and Methods

2.1. Study Design

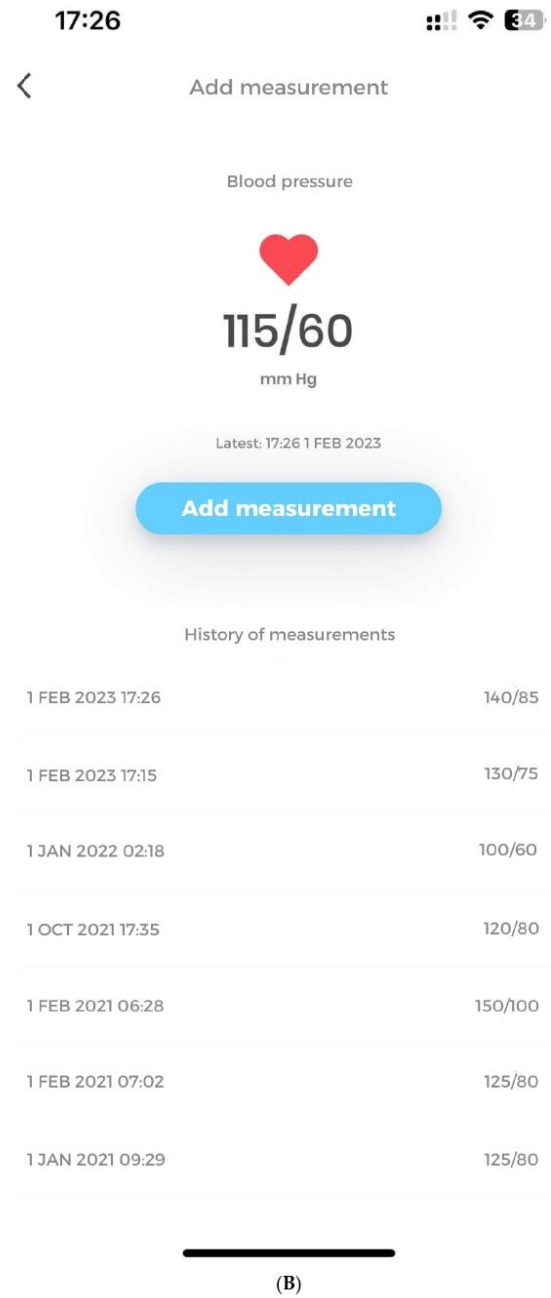
This was a single-center, randomized, open afterAMI trial (mobile app and digital system for patients after myocardial infarction), registered in ClinicalTrials.gov under the number NCT04793425. The study was approved by a local ethical review board (KB/150/2020). The inclusion criteria were as follows: signed informed consent, owning a mobile phone with Internet access and Android/iOS system, hospitalization due to myocardial infarction, age $\geq$ 18 years old, positive test results (basic mobile applications using skills). Exclusion criteria were: life expectancy < 6 months due to a non-cardiac disease, pregnancy or breastfeeding, negative test results (everyday mobile application use), age < 18 years old, lack of signed informed consent, lack of a mobile phone with Internet access and Android/iOS. Every patient signed informed consent before any study related procedure was conducted. Detailed methods and study design can be found in the study protocol [19]. Briefly, the study involved patients hospitalized due to AMI in a leading cardiac department between 2019–2021. The AMI diagnosis was made based on symptoms, troponin concentrations and ECG results, according to current guidelines [20]. Patients were randomly assigned (1:1) into the intervention group (IG or afterAMI), who received digital support (dedicated mobile app) to standard rehabilitation, or to the control group (CG), which underwent regular cardiac rehabilitation. An independent statistician performed the randomization using a dedicated online tool. The app consists of numerous modules. It provides short articles on a healthy lifestyle, as well as general knowledge on modifiable cardiovascular risk factors. Another feature is short educational messages sent as notifications. The patients can also report their vital signs (e.g., blood pressure, weight, glycemia) and set drug-taking reminders. There is a dedicated module for creating an electronic medical history card, where the patient can note and keep track of all past hospitalizations, underwent procedures, and medical recommendations. Exemplary screenshots from the afterAMI app are presented on Figure 1A–C. Each patient's account was individually tailored based on the diagnosed comorbidities. Standard rehabilitation consisted of a series of exercise trainings performed on a cycloergometer, as well as dietary and psychological education, and finally follow-up visits. Every patient was provided with extended medical supervision, as all study participants had two additional cardiological consultations. All demographic, clinical, laboratory data, etiology of AMI, as well as drugs

at discharge were collected. Endpoints were assessed twice: at 1 month and 6 months after discharge. Please see Figure 2, where a flowchart of the study is presented.



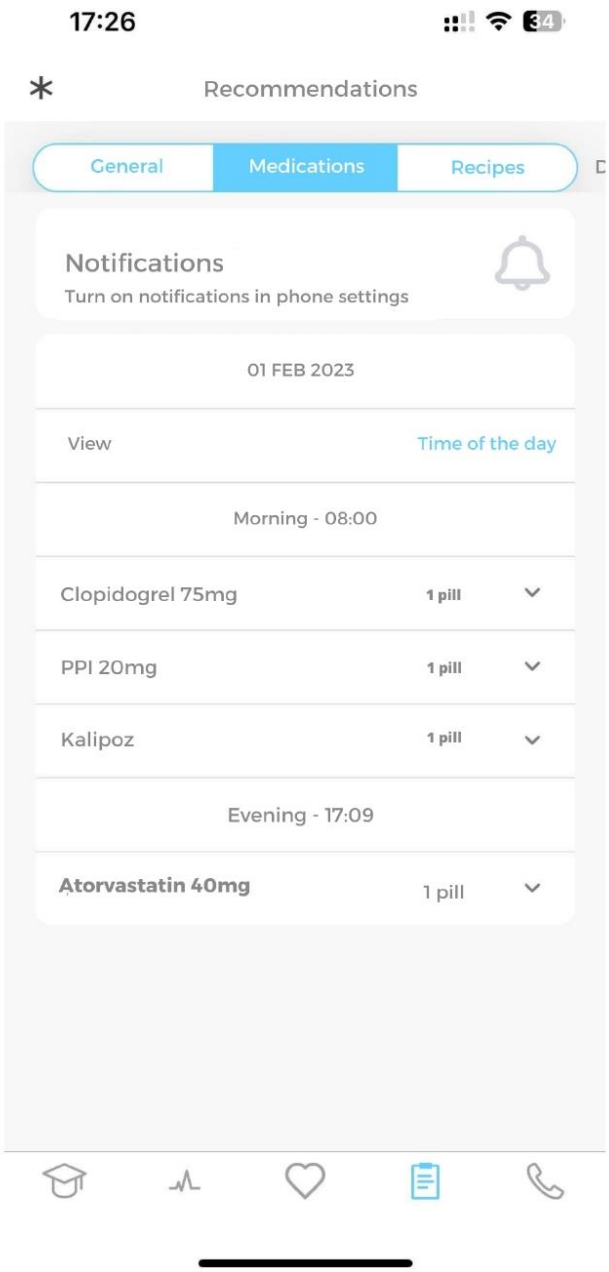
(**A**)

Figure 1. *Cont.*



(**B**)

Figure 1. *Cont.*



(C)

Figure 1. (**A**–**C**) Example screenshots of the afterAMI app.

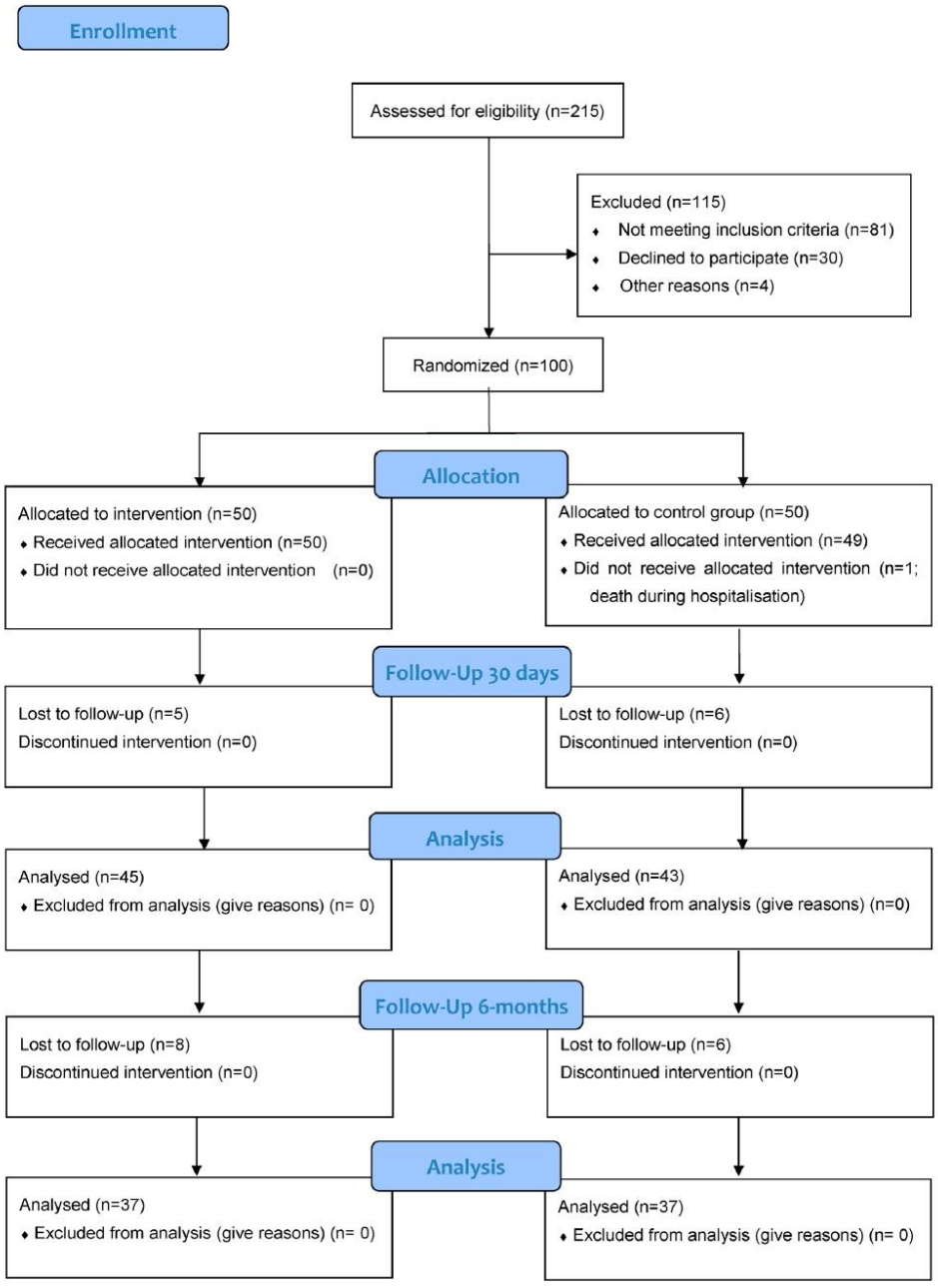


Figure 2. Enrollment and follow-up.

2.2. Study Endpoints

The primary outcome was rehospitalization and/or urgent outpatient visit, between baseline and at the 6-month follow-up visit. Secondary outcomes were related to cardiovascular risk factor management: body mass index, blood pressure, dyslipidemia, smoking. The study protocol contains detailed target values of mentioned risk factors [19]. Each value was categorized as being met or not. Other secondary outcomes included cardiovascular risk factor knowledge (CVD risk factors, normal blood pressure values, and recommended lifestyle modifications), as well as return to work. Further data collection covered laboratory test results (including HbA1c and lipid profile) and demographic parameters (sex and age).

2.3. Statistical Analysis

The investigator responsible for performing the statistical analysis was blinded. In terms of the endpoints, we looked at the frequency of the events. Regarding secondary endpoints, the change from baseline was assessed. The distribution of continuous variables was estimated using the Shapiro–Wilk test. All continuous variables with a non-normal distribution are presented as median values and interquartile ranges. Continuous variables with a normal distribution are presented as mean values and standard deviations (SD). In the case of variables with normal and non-normal distributions, the groups were compared using Student's t-test and the non-parametric Mann–Whitney U test. The comparison of qualitative variables between the groups was performed using Fisher's exact test. For quantitative variables, the change from baseline was assessed. A per-protocol analysis was performed after all of the follow-up visits were completed. We included in the baseline population analysis all patients who met the inclusion criteria and signed an informed consent form, regardless of whether the follow-up was completed. In the case of missing data, the patients were excluded from the particular analysis.

3. Results

One hundred patients were enrolled. During hospitalization, 50% (n = 50) of them were randomized to the IG and 50% (n = 50) to the CG. A total of 25 individuals were lost to follow-up (13 in IG and 11 in CG), and one patient died during the hospitalization, which translated into a 25% attrition rate. One patient did not receive the allocated intervention due to his death during the initial hospitalization, which happened after the consent signing and randomization. This patient was not included in the final results. Patient characteristics can be found in Table 1. The majority of the studied population were male (65%), and the median age of the study group was 61 years. There were some differences between the groups. The individuals assigned to the IG were younger (56.8 ± 9.23 years old vs. 63.42 ± 11.4 in the control group, p = 0.0019). Atrial fibrillation and heart failure were more prevalent in the CG.

Table 1. Patient characteristics.

Variable	afterAMI	Control	p-Value
Clinical data			
Age (years)	56.8 ± 9.23	63.42 ± 11.4	**0.0019**
BMI (kg/m^2)	28.5 ± 4.06	28.11 ±5.38	0.7247
Body weight (kg)	88.95 ± 13.86	85.47 ± 24.33	0.4625
Sex [1]	34 (68%)	31 (61%)	0.6753
KOS—rehabilitation	17 (34%)	9 (18%)	0.1095
Hospitalization (days)	6 (4–8)	7 (5–11)	0.2143
STEMI	25 (50%)	20 (40%)	0.4176
NSTEMI	25 (50%)	30 (60%)	0.4176

Table 1. *Cont.*

Variable		afterAMI	Control	*p*-Value
Clinical data				
Infarction artery	LAD	26 (52%)	24 (48%)	1
	LCA	15 (30%)	17 (34%)	0.5218
	RCA	16 (32%)	24 (48%)	0.1438
PTCA		39 (78%)	39 (78%)	0.6222
Bypass surgery		5 (10%)	6 (12%)	0.7589
Body weight (kg)		88.9459 ± 13.8663	85.4657 ± 24.3327	0.4625
Height (cm)		176.3 ± 7.2328	171.6 ± 8.9729	**0.0186**
Nicotinism		33 (66%)	32 (64%)	1
Packet years		20 (0–30)	14 (0–32.5)	0.7934
Diabetes, type I		2 (4%)	0 (0%)	0.4949
Diabetes, type II		11 (22%)	11 (22%)	1
Hypertension		30 (60%)	34 (68%)	0.3828
Dyslipidemia		36 (72%)	39 (78%)	0.3069
Atrial fibrillation/atrial flutter		1 (2%)	7 (14%)	**0.0288**
Heart failure		6 (12%)	15 (30%)	**0.0274**
Implanted pacemaker or ICD		1 (2%)	5 (10%)	0.1112
Chronic kidney disease		1 (2%)	1 (2%)	1
Peripheral artery disease		1 (2%)	1 (2%)	1
EF in hospital (%)		51.78 ± 8.42	48.0 ± 9.22	**0.0394**
CVD risk factors knowledge		8 (6–9)	8 (4–9)	0.4131
Employed		27 (54%)	17 (34%)	0.1261
Lab tests at hospital				
Troponin I (µg/L)		0.7930 (0.2250–5.5710)	0.694 (0.111–4.350)	0.7248
Troponin II (µg/L)		2.2550 (0.7145–8.7340)	5.640 (0.437–34.635)	0.1702
Creatinine (mg/dL)		0.98 ± 0.21	1.05 ± 0.34	0.1991
eGFR (mL/(min × 1.72 m^2)))		79.16 ± 17.22	73.28 ± 20.93	0.1351
Na (mmol/L)		139.1 ± 3.05	139.6 ± 4.36	0.5399
K (mmol/L)		4.17 ± 0.45	4.38 ± 0.51	**0.0363**
WBC ($\times 10^9$/L)		10.27 ± 3.04	10.19 ± 2.94	0.9052
HbA1C (%)		5.8 (5.4–7.1)	5.6 (5.4–6.0)	0.4593
NTproBNP (pg/mL)		422 (133–1256)	886.5 (230–2250)	0.0735
HgB (g/dL)		14.58 ± 1.49	14.14 ± 1.83	0.1989
Total cholesterol (mg/dL)		191.3 ± 71. 57	192.1 ± 52.29	0.9523
HDL (mg/dL)		39.55 ± 10.02	46.78 ± 10.65	0.0010
LDL (mg/dL)		117.5 ± 68.59	111.7 ± 61.56	0.6621
Tg (mg/dL)		146 (92–233)	136.5 (87–201)	0.2423

Table 1. *Cont.*

Variable	afterAMI	Control	*p*-Value
Drugs at discharge			
ACEi	42 (84%)	40 (80%)	0.5229
ARB	4 (8%)	2 (4%)	0.2314
ARNI	0 (0%)	0 (0%)	
MRA	9 (18%)	15 (30%)	0.2366
B-blocker	42 (84%)	41 (82%)	0.7398
CCB	20 (40%)	10 (20%)	**0.0257**
Statin	46 (92%)	45 (90%)	1
Ezetimibe	5 (10%)	2 (4%)	0.2673
VKA	0 (0%)	0 (0%)	
NOAC	1 (2%)	2 (4%)	1
ASA	45 (90%)	43 (86%)	1
Clopidogrel	12 (24%)	13 (26%)	1
Prasugrel	2 (4%)	0 (0%)	0.2419
Ticagrelor	28 (56%)	28 (56%)	1
Digoxin	0 (0%)	0 (0%)	

ACEi—angiotensin-converting-enzyme inhibitors, ARB—angiotensin receptor blockers, ARNI—angiotensin receptor neprilysin inhibitor, ASA—acetylsalicylic acid, BMI—body mass index, CVD—cardiovascular disease, EF—ejection fraction, eGFR—estimated glomerular filtration rate, HbA1C—hemoglobin A1c, HDL—high-density lipoprotein, ICD—implantable cardioverter-defibrillator, KOS—rehabilitation—coordinated care program for patients after myocardial infarction; LAD—left anterior descending artery, LCA—left circumflex artery, LDL—low-density lipoprotein, MRA—aldosterone receptor antagonists, CCB—calcium channel blockers, NOAC—novel oral anticoagulants, NSTEMI—non-ST–elevation myocardial infarction, NTproBNP—N-terminal pro–B-type natriuretic peptide, PTCA—percutaneous transluminal coronary angioplasty, RCA—right coronary artery, STEMI—ST-elevation myocardial infarction, Tg—triglycerides, VKA—vitamin K antagonist, WBC—white blood cells.

No difference in the rate of the primary endpoint of need for rehospitalization and/or urgent outpatient visit was observed (three [8%] in IG vs. 10 [27%] in CG, $p = 0.0640$). There were no statistically significant differences regarding nicotinism, BMI, meeting LDL target level, meeting target BP, as well as the rate of patients returning to work after AMI. A summary of the results is presented in Figure 3. There was a significant difference regarding knowledge about CVD risk factor observed in favor of the IG (11 points in the test (10–12) vs. nine (8–11) in CG, $p = 0.0009$).

Over the 6-month period, no differences in laboratory results were observed except for NT-proBNP, which was lower in the IG (119 (44–257) in IG vs. 244 (130–696) in CG, $p = 0.0286$), despite no differences observed at the randomization (422 (133–1256) in IG vs. 886.5 (230- 2250) in CG; $p = 0.0735$). The exact laboratory results are presented in Table 2.

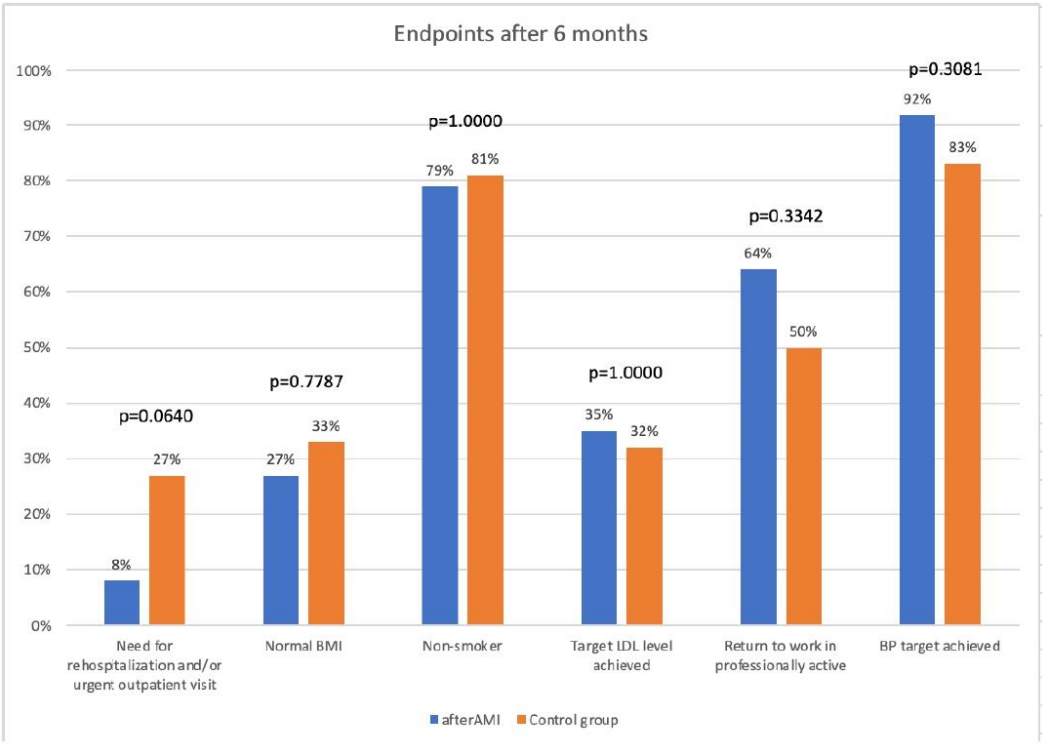


Figure 3. Endpoints 6 months after hospital discharge.

Table 2. Laboratory results after 6 months.

Endpoint	afterAMI	Control Group	*p*-Value
Creatinine (mg/dL)	0.945 (0.84–1.26)	0.95 (0.80–1.01)	0.4510
eGFR (mL/(min × 1.72 m^2))	78.18 ± 17.11	69.77 ± 20.10	0.0940
HbA1C (%)	5.8 (5.5–7.7)	5.7 (5.6–6.0)	0.7491
NTproBNP (pg/mL)	119 (44–257)	244 (130–696)	**0.0286**
HgB (g/dL)	14.4 (13.3–14.9)	13.85 (13.3–14.6)	0.3587
Total cholesterol (mg/dL)	130 (114–145)	134 (116–153)	0.5112
HDL (mg/dL)	44 (39–54)	46 (41–61)	0.1990
LDL (mg/dL)	58 (45–75)	64.5 (48.5–83.5)	0.3226
Tg (mg/dL)	98 (71–181)	100 (82.5–135)	0.8800
LDL difference vs. baseline	38.4 ± 50.75	49.44 ± 64.51	0.4721

eGFR—estimated glomerular filtration rate, HbA1C—hemoglobin A1c, HDL—high-density lipoprotein, LDL—low-density lipoprotein, NTproBNP—N-terminal pro–B-type natriuretic peptide, Tg—triglycerides.

4. Discussion

The primary finding of this study is that post-AMI patients who receive CR supported by a mobile app do not have significantly lower rates of rehospitalizations and/or urgent outpatient visits. Moreover, there were no differences observed in terms of CVD risk

factors' control. However, patients in the IG had significantly lower NT-proBNP levels when compared with CG, despite no differences at baseline. Additionally, a significant difference regarding CVD risk factor knowledge was observed in favor of patients using the afterAMI app.

AMI is often an important event in the patient's life, leading to high motivation to improve one's health status. However, the compliance and adherence decrease over time [21], which makes it difficult to provide CAD patients with continuous care due to common return to previous habits and unhealthy behaviors (sedentary lifestyle, poor diet, smoking). So far, several attempts were made to improve long-term CVD disease risk factors' management. However, as survival rates within a year after AMI range from 0.94 to 0.68 depending on the age group [6], one could conclude that further improvement is desired. Our study seems to provide valuable evidence into the ongoing search for care optimalization in postinfarction patients.

Participation in CR program is broadly recommended by ESC in patients after AMI [1]. CR extends far beyond just physical exercise and consists of several pillars, among which patient education, psychological support, diet counselling, and CVD risk factor control improvement should be named. Better CVD risk factors' control contributes to reduced risk of recurrent MI, rehospitalizations, and all-cause mortality, subsequently improving patients' prognosis [20,21].

Digital solutions have become a subject of extensive research in recent years. Telemedicine can be implemented in numerous forms including: home-based tele-rehabilitation programs, online counseling chatrooms, etc. In recent papers it has been suggested that telehealth CR is associated with similar training intensity and is as cost-effective as conventional outpatient CR [22,23]. What is more, mobile apps have been shown to increase traditional CR completion rates, outcomes, and attendance [24]. Of note, with regard to mobile apps, only a few of those dedicated to CR have been adequately validated. Despite still little evidence, current ESC guidelines on CVD prevention recommend considering mHealth solutions as economically attractive tools, which can contribute to better risk factor control by improving adherence and increasing encouragement in desirable lifestyle modifications [1].

Some of the previous studies on mobile app use in cardiac patients have demonstrated primarily positive effects on selected cardiovascular risk factors, e.g., physical activity [25–27]. Conteras et al. showed that hypertensive patients supported by a mobile app had better pharmacological therapeutic adherence resulting in improved BP control [28]. Similarly, in our study, more patients in the IG group met target BP values, but the difference was not statistically significant. Furthermore, lifestyle advice delivered by text messages has been shown to be a useful and cost-effective tool in smoking cessation [29], as well as glycemic control [30]. Mobile apps can also be used for educational purposes. In a recent paper, Min Jung Cho et al. described developing an mHealth solution to be used as a learning instrument dedicated to CAD patients [31]. In our study, patients in the IG who had access to the educational materials had significantly better knowledge of CVD risk factors. Improving health literacy may translate into better adherence and subsequent prognosis in the future.

Considering the results from previous research on mHealth solutions tailored for patients post-AMI, it seems that these novel technologies only contribute to an overall trend towards improved CVD risk factors but often without reaching statistical significance, which is consistent with our findings [14,32]. However, differences in the studied populations, but even more importantly the intervention (mobile app), should be considered. Since each digital intervention is slightly different, comparing obtained results across several trials and finally drawing clear conclusions remains challenging. What is more, lack of differences between studied groups might be a result of an underpowered size of conducted trials.

The reduction in cardiac rehospitalizations is highly desired, as it enables optimizing resource allocation in medical centers. In one of the recently published papers by

Indraratna et al., a novel, cost-effective model of care, including a mobile app for patients with heart failure or coronary syndrome, resulted in significant reduction in urgent rehospitalizations and higher rates of completed cardiac rehabilitation [33]. In our analysis, despite showing a trend towards reduction in the primary endpoint event rate, no significance has been shown. However, the population was somehow different, and we also took unplanned outpatient visits into account.

Digitally supported CR is expected to evolve along new, emerging technologies, e.g., wearables and artificial intelligence algorithms [34]. In addition, the barrier of age is highly debated in terms of mobile app implementation. The median age of patients suffering from acute myocardial infarction in Poland is 66.8 years [35], while the mean age of afterAMI study population was 61 years old. Interestingly, AHA recently published a statement on mHealth technologies for cardiovascular disease prevention among elderly patients, which suggests that mobile technology can be effectively used for improving healthy behaviors and medication adherence in this age group [36]. In the statement, it has been stressed that considering the aging of the society, implementing mHealth solutions to improve health outcomes in older adults with CAD is a crucial matter. Therefore, apps such as afterAMI can be regarded as an important move towards the future.

Limitations

Regardless of the strengths of the study, certain limitations should be considered when analyzing the results. Firstly, the participants in the intervention group were older and had more heart failure and atrial fibrillation, which may be a result of a relatively low number of randomized patients. Additionally, this was a single-center study, and larger studies would provide more information about broader implementation into clinical practice. Secondly, it is worth stressing that not all cardiac patients are capable of using smartphones. In the screened population, every third patient was not able to use a mobile app. Therefore, this solution is not for everyone at this moment. However, we believe that this percentage is expected to grow in the future. It should be stressed that this was not a blinded study because of its nature, which was also stated in other similar studies. Another important limitation that should be mentioned is the high number of patients lost to follow-up. However, one should consider that the study was conducted during the COVID-19 pandemic, which resulted in patients' fear of infection associated with additional hospital visits and led to their discontinuation of the study. Nevertheless, the investigators were able to collect some of the data via phone calls. As a result, the statistical power of the study has been limited.

5. Conclusions

Mobile apps are undoubtedly a field of interest for patients and medical practitioners. The growth of novel tools, programs, and emerging promising results from clinical trials is very encouraging. Telemedicine seems to be currently gaining its momentum. Our study provides new data on mobile app use in AMI patients. A trend towards reduction in rehospitalizations and/or unplanned outpatient visits in AMI patients has been shown. Furthermore, the feasibility of mobile app support in myocardial infarction patients has been proved. The benefits regarding NT-proBNP level may improve long-term prognosis. However, one should consider that mHealth solutions can potentially benefit only selected patients, as some of them are unable to use smartphones. Nevertheless, further research mediated by larger, multicenter studies should be conducted.

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8 Podsumowanie i wnioski (łączące wyniki zawarte w cyklu publikacji)

Cały projekt poza oceną wpływu zastosowania aplikacji mobilnej na poszczególne punkty końcowe, miał na celu ocenę możliwości zastosowania nowoczesnego rozwiązania telemedycznego podczas codziennej praktyki klinicznej. Objęcie opieką kilkudziesięciu pacjentów i dostarczenie im produktu wspierającego ich podczas rehabilitacji po zawale serca okazało się być nie tylko możliwe do wykonania, ale wręcz pomocne i przyjazne dla użytkowników systemu. Pacjenci niejednokrotnie podkreślali, że aplikacja stanowi dla nich użyteczne narzędzie, z którego korzystali na co dzień, a także mieli zapewnione poczucie bezpieczeństwa i możliwości kontaktu z przedstawicielem systemu opieki zdrowotnej.

W zakresie punktów końcowych opisanych w badaniu opisanym w załączonych publikacjach:

Pierwszorzędowy punkt końcowy:

- ocena częstości występowania rehospitalizacji i/lub pilnych wizyt ambulatoryjnych oceniana po 6 miesiącach od randomizacji;

- Pomimo niższej częstości liczby zdarzeń opisanych jako pierwszorzędowy punkt końcowy (8% w grupie „afterAMI" vs. 27% w grupie kontrolnej; p=0,064) nie osiągnięto różnicy istotnej statystycznie.

Drugorzędowe punkty końcowe:

- ocena częstości występowania rehospitalizacji i/lub pilnych wizyt ambulatoryjnych oceniana po 30 dniach od randomizacji;

- Nie wykazano istotnie statystycznych różnic w częstości występowania punktu końcowego (8% w grupie interwencyjnej vs. 10% w grupie kontrolnej, p=1,0).

- ocena kontroli wartości ciśnienia tętniczego oceniana po 30 dniach i po 6 miesiącach od randomizacji;

- Nie wykazano istotnie statystycznych różnic w ilości pacjentów, którzy osiągnęli docelowe wartości ciśnienia tętniczego po 30 dniach (99% w grupie interwencyjnej vs. 88% w grupie kontrolnej, p=0,11).

- Nie wykazano istotnie statystycznych różnic w ilości pacjentów, którzy osiągnęli docelowe wartości ciśnienia tętniczego po 6 miesiącach (92% w grupie interwencyjnej vs. 83% w grupie kontrolnej, p=0,31).

- ocena masy ciała oceniana po 30 dniach i po 6 miesiącach od randomizacji;

- Nie wykazano istotnych statystycznie różnic w ilości pacjentów, którzy osiągnęli docelową wartość wskaźnika BMI po 30 dniach (11% w grupie interwencyjnej vs. 22% w grupie kontrolnej, p=0,14)

- Nie wykazano istotnych statystycznie różnic w ilości pacjentów, którzy osiągnęli docelową wartość wskaźnika BMI po 6 miesiącach (27% w grupie interwencyjnej vs. 33% w grupie kontrolnej, p=0,78)

- ocena statusu palenia papierosów oceniana po 30 dniach i po 6 miesiącach od randomizacji;

- Nie wykazano istotnych statystycznie różnic w ilości pacjentów, którzy nie palili papierosów po 30 dniach (87% w grupie interwencyjnej vs. 81% w grupie kontrolnej, p=0,57)

- Nie wykazano istotnych statystycznie różnic w ilości pacjentów, którzy nie palili papierosów po 6 miesiącach (79% w grupie interwencyjnej vs. 81% w grupie kontrolnej, p=1,0)

- ocena statusu gospodarki lipidowej oceniana po 30 dniach i po 6 miesiącach od randomizacji;

- Wykazano istotnie statystycznie różnice w ilości pacjentów, którzy osiągnęli docelowe wartości stężenia cholesterol LDL po 30 dniach (58% w grupie interwencyjnej vs. 22% w grupie kontrolnej, p=0,005)

- Nie wykazano statystycznie istotnej różnicy w ilości pacjentów, którzy osiągnęli docelowe wartości stężenia cholesterol LDL po 6 miesiącach (35% w grupie interwencyjnej vs. 32% w grupie kontrolnej, p=1,0)

Ponadto, w ramach badania przeprowadzono badania laboratoryjne krwi, w wynikach których zwrócił uwagę fakt braku istotnych różnić w stężeniu NT-proBNP podczas randomizacji (422 (133-1256) w grupie interwencyjnej vs. 886.5 (230-2250) [pg/ml] w grupie kontrolnej; p=0,07), a następnie obserwowana istotna statystycznie różnica po 30 dniach (257.0 (127.5-502.5) w grupie interwencyjnej vs. 626.0 (254-1043) w grupie kontrolnej [pg/ml]; p=0,02), oraz po 6 miesiącach (119 (44–257) w grupie interwencyjnej vs. 244 (130–696) [pg/ml] w grupie kontrolnej; p=0,03). Wykazane różnice w stężeniu NT-proBNP mogą odzwierciedlać nasilenie niewydolności serca w obu grupach.

Warto również podkreślić, że pomimo wyjściowego braku różnic w wyniku testu oceniającego wiedzę o czynnikach ryzyka chorób sercowo naczyniowych (8 (6–9) w grupie interwencyjnej vs. 8 (4–9) w grupie kontrolnej; p=0,41) zaobserwowano istotną statystycznie różnicę podczas oceny po 6 miesiącach (11 (10–12) w grupie interwencyjnej vs. 9 (8–11) w grupie kontrolnej, p<0,001).

Podsumowując, w ramach projektu wykazano, że zastosowanie aplikacji mobilnej u pacjentów po zawale serca jest wykonalne. Wdrożenie aplikacji afterAMI w badanej populacji pacjentów po zawale serca nie przełożyło się na znaczącą redukcję częstości rehospitalizacji i/lub nieplanowanych wizyt ambulatoryjnych. Warto jednak zwrócić uwagę na wysoki odsetek pacjentów utraconych z obserwacji, który pomimo zaplanowanej utraty podczas obliczeń wielkości próby, okazał się większy niż zakładano, prawdopodobnie poprzez pandemię COVID-19. W związku z tym, możliwe że badanie nie miało odpowiedniej mocy statystycznej do wykazania różnicy pomiędzy obiema grupami. Osoby, którym udostępniono aplikację miały wyższy wynik w teście oceniającym wiedzę na temat czynników ryzyka chorób sercowo-naczyniowych, co może przełożyć się na lepsze nawyki prozdrowotne, lepsze stosowanie się do zaleceń lekarskich, a także potencjalnie na lepsze rokowanie pacjentów, pomimo braku zaobserwowanych różnic w kontroli poszczególnych czynników ryzyka chorób sercowo-naczyniowych po 6 miesiącach.

9 Opinia Komisji Bioetycznej

Komisja Bioetyczna
przy Warszawskim Uniwersytecie Medycznym

Tel.: 022/ 57 - 20 -303
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02-091 Warszawa

e-mail: komisja.bioetyczna@wum.edu.pl
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KB/159/2020

Komisja Bioetyczna przy Warszawskim Uniwersytecie Medycznym
w dniu 14 września 2020 r. po zapoznaniu się z wnioskiem:

Lek. Bartosz Krzowski
I Katedra i Klinika Kardiologii
ul. Banacha 1a, 02-097 Warszawa

dotyczącym: wyrażenia opinii w sprawie badania pt.: „Wpływ zastosowania cyfrowego systemu wsparcia na prewencję zdarzeń sercowo-naczyniowych u pacjentów po zawale serca".

wyraża następującą
o p i n i ę

- stwierdza, że jest ono dopuszczalne i zgodne z zasadami naukowo-etycznymi*.
- ~~stwierdza, że jest ono niedopuszczalne i niezgodne z zasadami naukowo-etycznymi.*~~

Uwagi Komisji – ***verte***

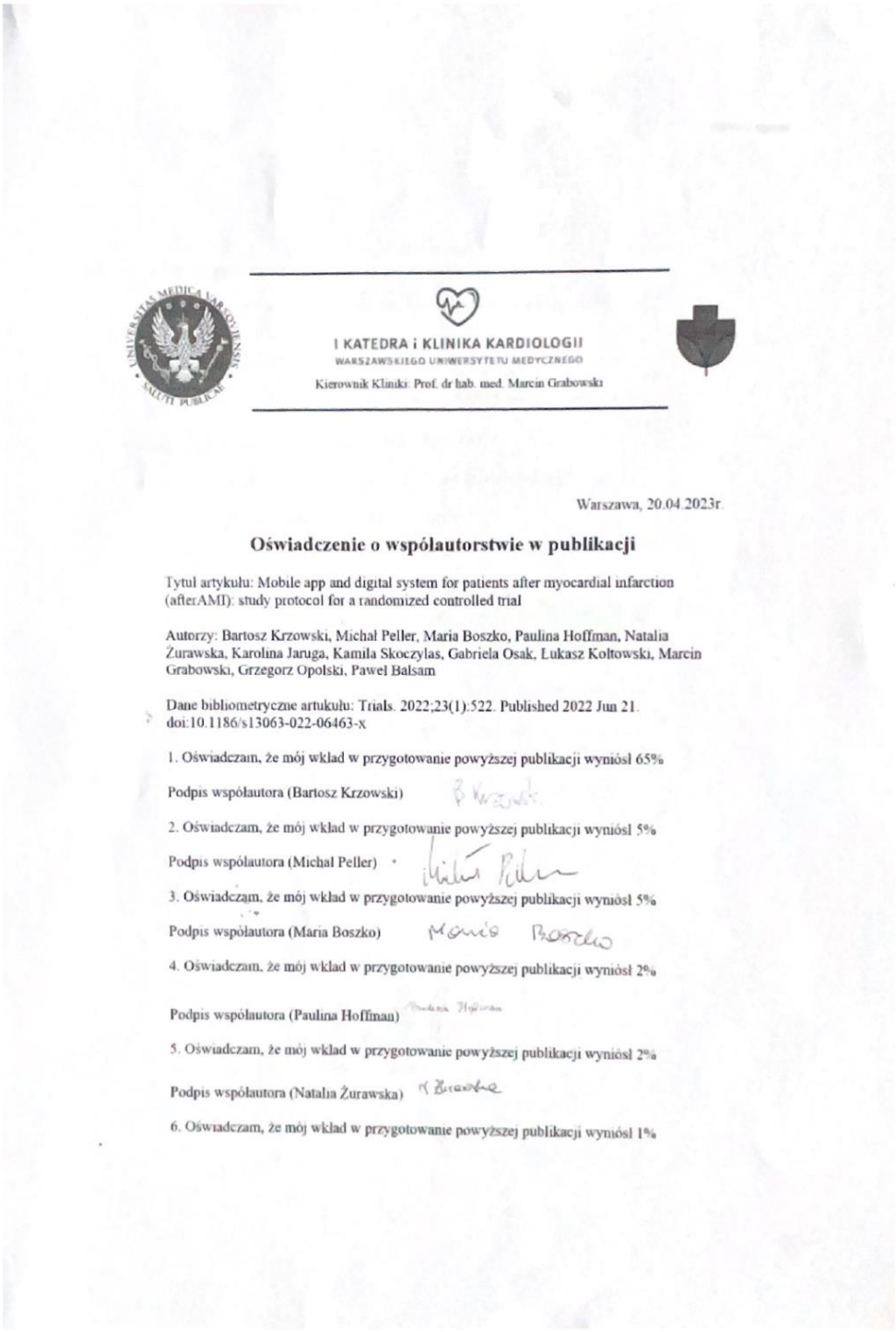
Komisja działa na podstawie art.29 ustawy z dnia 5.12.1996r. o zawodzie lekarza /Dz.U.nr 28/97 poz.152 wraz z późn.zm./, zarządzenia MZiOS z dn.11.05.1999r. w sprawie szczegółowych zasad powoływania i finansowania oraz trybu działania komisji bioetycznych /Dz.U.nr 47 poz.480/, Ustawy prawo farmaceutyczne z dnia 6 września 2001r. (Dz.U.Nr 126, poz. 1381 z późn. zm.) oraz Zarządzenie nr 56/2007 z dnia 15 października 2007r. w sprawie działania Komisji Bioetycznej przy Warszawskim Uniwersytecie Medycznym /Regulamin Komisji Bioetycznej przy Warszawskim Uniwersytecie Medycznym/.
Komisja działa zgodnie z zasadami GCP .

Przewodnicząca Komisji Bioetycznej

Prof. dr hab. n. med. Magdalena Kuźma-Kozakiewicz

*niepotrzebne skreślić

10 Oświadczenia współautorów publikacji



I KATEDRA i KLINIKA KARDIOLOGII
WARSZAWSKIEGO UNIWERSYTETU MEDYCZNEGO
Kierownik Kliniki: Prof. dr hab. med. Marcin Grabowski

Warszawa, 20.04.2023r.

Oświadczenie o współautorstwie w publikacji

Tytuł artykułu: Mobile app and digital system for patients after myocardial infarction (afterAMI): study protocol for a randomized controlled trial

Autorzy: Bartosz Krzowski, Michał Peller, Maria Boszko, Paulina Hoffman, Natalia Żurawska, Karolina Jaruga, Kamila Skoczylas, Gabriela Osak, Łukasz Kołtowski, Marcin Grabowski, Grzegorz Opolski, Paweł Balsam

Dane bibliometryczne artukułu: Trials. 2022;23(1):522. Published 2022 Jun 21. doi:10.1186/s13063-022-06463-x

1. Oświadczam, że mój wkład w przygotowanie powyższej publikacji wyniósł 65%

Podpis współautora (Bartosz Krzowski)

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Podpis współautora (Pawel Balsam)

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Kierownik Kliniki: Prof. dr hab. med. Marcin Grabowski

Warszawa, 20.04.2023r.

Oświadczenie o współautorstwie w publikacji

Tytuł artykułu: Mobile app and digital system for patients after Myocardial Infarction (afterAMI): early results from a randomized trial

Autorzy: Bartosz Krzowski, Maria Boszko, Michał Peller, Paulina Hoffman, Natalia Żurawska, Kamila Skoczylas, Gabriela Osak, Łukasz Kołtowski, Marcin Grabowski, Grzegorz Opolski, Paweł Balsam

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Kamila Skoczylas

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Podpis współautora (Paweł Balsam)

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Kierownik Kliniki: Prof. dr hab. med. Marcin Grabowski

Warszawa, 20.04.2023r.

Oświadczenie o współautorstwie w publikacji

Tytuł artykułu: Mobile App and Digital System for Patients after Myocardial Infarction (afterAMI): Results from a Randomized Trial.

Autorzy: Bartosz Krzowski, Maria Boszko, Michał Peller, Paulina Hoffman, Natalia Żurawska, Kamila Skoczylas, Gabriela Osak, Łukasz Kołtowski, Marcin Grabowski, Grzegorz Opolski, Paweł Balsam

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