LITERATURE REVIEW

Implementation of Home-based Cardiac Rehabilitation Program in Patients with Coronary Artery Disease: A Literature Review

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ABSTRACT

Introduction: Coronary artery disease (CAD) is the major cause of disability and death worldwide. An integral aspect of the management strategy for CAD patients is cardiac rehabilitation (CR) program, where exercise assumes a central role in enhancing functional capacity. This program reduces healthcare burden and improves quality of life due to its benefits in reducing mortality and morbidity. Even though the benefits of CR are widely proven, participation and adherence of CAD patients are low. Home-based CR (HBCR) program is the strategy developed to increase the coverage of CR services. This is equally effective as center-based CR (CBCR) and considered safe. Therefore, this study aimed to conduct a comprehensive exploration of HBCR program, with a specific emphasis on the implementation among CAD patients.

Methods: Original articles and systematic or narrative reviews were searched using PubMed, Google Scholar, and Research Gate databases. Further exploration of literature citations was also conducted to meet the inclusion criteria needed to explain the topic.

Results: HBCR started with pre-participation screening. Patient assessment was done to identify physical function or personal impairment. Generally, all prescription in HBCR is similar to CBCR. Risk factor management in HBCR provided by home monitoring through home visit or telemonitoring and evaluation is carried out to assess outcome achievement which focuses on behaviour target so this prescription can be used as secondary prevention program.

Conclusion: The implementation of the HBCR program in CAD patients is quite similar with CBCR, and begin with pre-participation screening, patient assessment, exercise prescription, management of risk factors, monitoring, and evaluation.

Keywords: Cardiac rehabilitation, coronary artery disease, exercise, morbidity, quality of life
ABSTRAK

Pendahuluan: Penyakit arteri koroner (PAK) merupakan penyebab utama kecacatan dan kematian di seluruh dunia. Aspek integral dari strategi penatalaksanaan pasien PAK adalah program rehabilitasi jantung (RJ), dengan latihan sebagai faktor utama yang berperan penting dalam meningkatkan kapasitas fungsional. Program ini mengurangi beban layanan kesehatan dan meningkatkan kualitas hidup karena manfaatnya dalam mengurangi angka kematian dan kesakitan. Meskipun manfaat RJ telah terbukti secara luas, partisipasi dan kepatuhan pasien PAK terhadap program RJ masih rendah. Program home-based cardiac rehabilitation (HBCR) merupakan strategi yang dikembangkan untuk meningkatkan cakupan layanan RJ. Program ini sama efektifnya dengan center-based cardiac rehabilitation (CBCR) dan dianggap aman. Oleh karena itu, kajian ini bertujuan untuk melakukan eksplorasi komprehensif terhadap program HBCR, dengan penekanan khusus terhadap penerapannya pada pasien PAK.

Metode: Artikel asli dan kajian sistematis atau naratif dicari menggunakan database PubMed, Google Scholar dan Research Gate. Eksplorasi lebih lanjut terhadap kutipan literatur juga dilakukan untuk memenuhi kriteria inklusi yang diperlukan untuk menjelaskan topik.

Hasil: HBCR dimulai dengan pre-participation screening. Penilaian pasien dilakukan untuk mengidentifikasi fungsi fisik atau gangguan personal. Secara umum, peresepan latihan pada HBCR mirip dengan CBCR. Pengelolaan faktor risiko pada HBCR dilakukan dengan cara pengawasan ke rumah melalui kunjungan rumah atau pengawasan jarak jauh (telemonitoring) dan evaluasi dilakukan untuk menilai pencapaian hasil yang bersinergi pada sasaran perilaku sehingga peresepan ini dapat digunakan sebagai program pencegahan sekunder.

Kesimpulan: Penerapan program HBCR pada pasien PAK mirip dengan CBCR, dan dimulai dengan pre-participation screening, penilaian pasien, peresepan latihan, pengelolaan faktor risiko, pengawasan dan evaluasi.

Kata kunci: Kualitas hidup, latihan, morbiditas, penyakit arteri koroner, rehabilitasi jantung

INTRODUCTION

Cardiovascular disease (CVD), including coronary artery disease (CAD), is a non-communicable disease whose number of patients continues to increase as the major cause of disability and death worldwide.¹ In 2019, around 17.9 million people died from CVD, which is 32% of global deaths.² The deaths caused by CAD and stroke are approximately 7.4 million and 6.7 million, respectively.³ Indonesian Basic Health Research data in 2013 showed that around 17.3 million deaths in Indonesia were caused by CAD. Based on prediction, there will be an
increase to 23.3 million deaths in 2030. The incidence of CAD increases with age, namely 0.7%, 1.3%, and 2% at the age of 45-54 years, 55-64 years, and > 64 years.  

Cardiac rehabilitation (CR) program is a non-pharmacological treatment given to CAD patients. This program can be given since patients are hospitalized before returning to activities in the community. Physical exercise is the main component to increase functional capacity allowing the returning of patients to activities before the illness. CR has proven to be useful in reducing mortality due to CAD, preventing recurrent myocardial infarction in 12 months, reducing the number of hospitalizations, increasing the cost-effectiveness of using healthcare resources, and improving health-related quality of life (QoL).  

The level of participation and adherence of CVD patients to CR in both developed and developing countries is low, even though the benefits have been widely proven. The low adherence is caused by several burdens such as transportation problems, health service costs, program availability at the hospital, time problems, job demands, lack of motivation, and lack of acceptance to CR model offered.  

In this context, home based cardiac rehabilitation (HBCR) is one of the strategies used to increase the coverage of CR services. This program has been proven to overcome several burdens in conducting center based cardiac rehabilitation (CBCR). Several previous studies related to the effectiveness and safety of HBCR have shown evidence that the program is as effective as CBCR and considered safe. Based on the previous explanation, it is necessary to determine the activities of HBCR. This review aimed to describe HBCR in CAD patients focused on its implementation. The result of this review hopefully can describe the steps of HBCR implementation.

**METHODS**

Related articles were searched using PubMed, Google Scholar, and ResearchGate databases. The inclusion criteria were original articles from any methods of research and systematic or narrative reviews without limitation of publication year. Further exploration of literature citations was also done to meet the inclusion criteria needed to explain the topic. The keywords used were “home-based cardiac rehabilitation”, “cardiac rehabilitation”, “cardiovascular diseases”, “center-based cardiac rehabilitation”, “home-based exercise”, and “coronary artery disease”. Articles not written in English or available in the full text were excluded. Results were presented in the form of text, tables, and figure.

**RESULTS**

We reviewed eight articles to explore the implementation of HBCR in CAD patients. We used three, four, two, three, and two articles to explain patient assessment, exercise prescription, risk factors management, HBCR monitoring, and HBCR evaluation, respectively.
DISCUSSION

Cardiac Rehabilitation (CR) Program
CR is defined as a structured set of activities aimed at addressing the causes of disease, including both mental and physical facets, with the overarching objectives of enhancing QoL and social well-being. The primary objectives are to prevent deterioration and mortality and improve physical, mental, and social conditions. The comprehensive nature aims to empower patients to autonomously manage the well-being, promoting sustained functionality in the community. Additionally, CR decelerates the progression of the disease through the cultivation of improved health behaviors. The aim is to reduce disability, improve and restore cardiac function, as well as reduce and identify cardiovascular risk factors.  

Cardiovascular risk factors can be classified into reversible and irreversible. Reversible or modifiable risk factors include sedentary lifestyle, smoking habits, hypertension, hypercholesterolemia (>200 mg/dL), low high-density lipoprotein level (<35 mg/dL), high lipoprotein A level, hypertriglyceridemia (>250 mg/dL), obesity, diabetes mellitus, and hyperinsulinemia. Irreversible or non-modifiable risk factors are male sex, age, history of CAD, family history of premature CAD, cerebrovascular disease, or peripheral vascular disease.

Some of the disease conditions that are a priority for CR program are heart failure, coronary revascularization, and acute coronary syndrome (ACS). Furthermore, CR may also be recommended for patients with peripheral arterial disease, stable angina pectoris, post-heart valve repair, post-coronary artery bypass graft (CABG), hypertension, arrhythmia, ventricular assist devices, post-heart transplantation, post-stroke, adult congenital heart disease, and post cardiac defibrillator implantation and synchronization devices. Asymptomatic individuals identified as having a high cardiovascular risk can benefit from the same professional lifestyle interventions and risk factor management. In addition, the risk factors are largely the same as those of a wider spectrum of non-communicable diseases such as chronic obstructive pulmonary disease, atrial fibrillation, and cancer. In this context, CR is known to be beneficial. In the elderly, the program is carried out to continue normal life activities without significant cardiac symptoms.

There are several phases of CR, specifically in ACS including: 1) Phase 1 lasting about 5 days while in hospital; 2) Phase 2 lasting for 4-8 weeks on an outpatient basis; and 3) Phase 3, or maintenance for 3-6 months. The expected target after these three phases is to return to activities as before the attack.

Many of the advantages of CR derived from exercise to enhance maximal oxygen uptake (VO2 max) and augment endurance for prolonged physical activity. Exercise manifests various additional favorable impacts, such as myocardial flow reserve and endothelial function, while reducing body weight, tobacco use, blood pressure, and blood lipid levels. Additionally, exercise has shown its efficacy in decelerating the advancement of coronary atherosclerosis in CAD patients. CR programs also plays an important role in aiding individuals with heart disease in alleviating anxiety and depression.
Approximately half of the mortality reduction achieved with exercise-based CR (28%) can be attributed to decreases in major risk factors, specifically smoking. Other mechanisms such as ischemia preconditioning, reduced inflammation, better fibrinolytic balance, and increased endothelial function may contribute to the benefits. The benefits of CR also include an increase in VO2 max of 16% and metabolic equivalent (MET) of 33%. This improvement in exercise performance is associated with beneficial effects on cardiovascular events and QoL. Furthermore, patient QoL improved as a result of symptom relief (reduced chest pain, shortness of breath, and fatigue), reduced stress, and increased sense of psychosocial well-being.  

Participation in CR program is associated with reduced cardiac mortality rates. An observational study of 601,099 United States Medicare recipients enrolled in CR found a 21% to 34% reduction in all-cause mortality over 5 years. A Cochrane review comparing usual care with the addition of CR program found a significant reduction in hospital readmission of low-risk patients after percutaneous intervention or myocardial infarction. A meta-analysis also showed that participation in CR program was associated with a reduction in blood pressure. The comprehensive program reduced systolic blood pressure significantly by 3 mmHg to 7 mmHg, while diastolic decreased by 2 mmHg.  

Based on American Heart Association (AHA) guidelines, CR consists of several components, namely nutritional management, basic patient assessment, psychosocial interventions, risk factor management, and exercise and physical activity. The entire series is a long process, resulting in risk factor modification and maintaining a good lifestyle.

Despite the proven benefits, referral and participation rates remain low. Previous studies from various countries found average referral rates of around 30%-50% in the United States, Europe, and Canada. The main barrier to CR reported in middle and low-income countries is a lack of personnel and resources. The main barrier that causes patients not to register is the lack of awareness and encouragement from the physicians. Barriers to the program implementation are comorbidities, costs, distance, and family responsibilities.

Strategies to increase participation and referrals include the following: 1) Patient education by physicians and other healthcare providers regarding the benefits of CR and automated referral systems. The strongest predictor of CR participation was found to be physician support; 2) HBCR as an alternative to CBCR. A meta-analysis showed that the effect of HBCR is similar to CBCR; 3) The inclusion of primary care physicians to improve long-term access and retention; and 4) The use of modern technology (cardiac telerehabilitation) such as the internet, telephone, and other communication tools offers interesting prospects for the distribution and expansion of the program. This increases the number of registrants, reduces risk factors, and improves cost-benefit ratios.

Home-based Cardiac Rehabilitation

1. Rationale in Giving HBCR
CR program is the main intervention in the management of CVD due to the significant benefits, but most patients do not participate. Data shows that in the United States, more than 80% of
CAD patients do not participate in the program after being hospitalized. HBCR was developed to overcome this problem and could be delivered at home, in the community, and parks. This program can overcome geographical and logistical barriers and other burdens in CR implementation.\(^6,11,23\)

Several studies showed that the effectiveness of HBCR is the same as CBCR. The cost of HBCR is 70% lower than CBCR and advances in technology have also increased the use of monitoring tools. There are difficulties in implementing HBCR program in developing countries, specifically for elderly patients because of burdens in using technology.\(^11,24-26\) The program is associated with increased physical activity behaviour, functional capacity, medication adherence, quality of life, physiological risk factors, smoking behaviour, depression, and hospitalization related to heart disease with the same effectiveness as CBCR.\(^12,26\) Compared to CBCR, HBCR has disadvantages and advantages as listed in Table 1.\(^11\)

<table>
<thead>
<tr>
<th>Table 1. HBCR Advantages and Disadvantages Compared to CBCR</th>
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<tr>
<td><strong>Advantages</strong></td>
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<tr>
<td>Expanded capacity/access</td>
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<tr>
<td>Reducing enrolment delays</td>
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<tr>
<td>Flexible and convenient scheduling</td>
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<tr>
<td>Individually customized program</td>
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<tr>
<td>Integration with regular home routines</td>
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<tr>
<td>More privacy when receiving cardiac rehabilitation services</td>
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<tr>
<td>Minimal travel/transportation barriers</td>
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<tr>
<td><strong>Disadvantages</strong></td>
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<tr>
<td>Less intense exercise</td>
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<tr>
<td>Lack of replacement</td>
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<tr>
<td>Lack of patient accountability</td>
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<tr>
<td>Lack of social support</td>
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<tr>
<td>Safety issues for patients with higher risk</td>
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<tr>
<td>Lack of face-to-face monitoring and communication</td>
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<tr>
<td>Lack of published standards for home-based cardiac rehabilitation</td>
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</table>

In CAD patients who are referred for HBCR, the program is feasible and safe with good adherence.\(^11,27\) A study by Schopfer et al., during a follow-up period of 3 months after enrolment found that there were no elective hospitalizations, cardiovascular hospitalizations, or deaths for cardiac procedures among participants.\(^13\) Another study found that HBCR program in patients aged 65 years or more proved to be safe and beneficial in improving cardiorespiratory fitness.\(^28\)

Severe cardiovascular events are rare in CR program because high-risk patients are excluded from HBCR.\(^11\) A combined supervised HBCR was effective and safe in CAD patients who had moderate cardiovascular risk.\(^29\)
2. Components of HBCR

The main components of HBCR were developed to reduce cardiovascular mortality and morbidity, promote healthy behaviors, and optimize cardiovascular risk reduction. These main components are commonly the same as CBCR as shown in Figure 1.  

The American Association of Cardiovascular and Pulmonary Rehabilitation, the American Heart Association, and the American College of Cardiology made slight adjustments to the five components of HBCR by adding medication adherence to control risk factors. Health-modifying behaviours such as physical activity, eating habits, health, stress management, smoking, and medication adherence are important as part of HBCR.

3. HBCR Program Challenges and Strategies

The home-based CR program also has its limitations and challenges, including patient concerns regarding safety and security, costs not covered by health insurance, and various problems related to motivation, knowledge, and standardized interventions, as described in Table 2.  

<table>
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<tr>
<th>Challenges</th>
<th>Strategies to Overcome the Challenges</th>
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<tbody>
<tr>
<td>Concerns about safety issues due to lack of supervision</td>
<td>Pre-participation screening and appropriate supervision procedures in high-risk patients</td>
</tr>
<tr>
<td>Costs incurred during the implementation of the program which is not covered by health insurance</td>
<td>Providing HBCR program through telerehabilitation which in some countries is covered by health insurance</td>
</tr>
<tr>
<td>Some patients may lack motivation or interest in participating in HBCR program or may not understand the importance or benefits</td>
<td>Re-education about the benefits of HBCR and providing easier access to the program</td>
</tr>
<tr>
<td>Communication, education, and counseling as well as social support are felt less compared to CBCR</td>
<td>Optimizing education and counseling as well as communication through the use of the telephone or other communication tools and providing easier access to conduct the HBCR program and consult</td>
</tr>
<tr>
<td>There are no specific guidelines for implementing HBCR program</td>
<td>Implement CBCR principles and protocols for HBCR program after conducting individual assessments</td>
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HBCR: home-based cardiac rehabilitation, CBCR: center-based cardiac rehabilitation.
Another challenge in HBCR program is determining exercise intensity. Patients often have difficulty determining heart rate during exercise. The calculation requires pausing and some cannot determine their heart rate accurately or find abnormalities in heart rhythm. This can be overcome by teaching patients an alternative method of determining exercise intensity, namely the dyspnoea scale and talk test. The physical activity is executed until experiencing a sensation of breathlessness, and subsequent exercise is prescribed at an intensity slightly below the threshold triggering shortness of breath. Talk test has been recognized for eliciting a response comparable to the determination of intensity based on heart rate. As part of this protocol, the individual subjected to the exercise is requested to engage in speaking and singing. Moderate intensity exercise is characterized by the ability of patients to articulate comfortably while participating in the activity. 23, 30-32

**Implementation of HBCR in CAD Patients**

1. **Pre-Participation Screening**
   In instances where CR center is not available, and there are limited resources for symptom exercise testing, specific criteria were applied to identify patients at higher risk. This includes individuals with heart failure and New York Heart Association functional class III to IV symptoms, significant dysrhythmia, reduced ejection fraction (<40%), pronounced angina pectoris or Canadian Cardiovascular Class 3, advanced age (>75 years), markedly reduced peak functional capacity (<2 metabolic equivalent tasks), or significant physical limitations. Furthermore, patients meeting these criteria were contraindicated for HBCR. 23

2. **Patient Assessment**
   The initial assessment comprised anamnesis, physical examination, and test. Anamnesis was performed to obtain data regarding cardiovascular events, cardiovascular surgical procedures, left comorbid conditions (drug abuse and mental health), ventricular function, lifestyle habits (physical activity, diet, alcohol habits, and smoking), and current symptoms (lower extremity edema, shortness of breath, and chest pain). Physical examination including vital signs and a complete cardiovascular examination. In addition, test comprised assessment of cardiorespiratory fitness (measured by walking the distance on a 6-minute walk test or maximal exercise capacity), cardiovascular health assessments such as blood pressure, 12-lead electrocardiography, lipid levels, resting heart rate, waist circumference, body mass index, blood glucose and glycosylated haemoglobin, hip-to-hip ratio waist, assessment of psychosocial factors (social support, marital status, depressive symptoms, and anxiety), assessment of weakness (cognitive function, balance, and neuromuscular status) as well as assessment of health-related to sleep and QoL. 17, 33, 34

3. **Exercise Prescription**
   HBCR program with monitoring improves rehabilitation adherence and the physical capacity of patients. A physical exercise program includes a warm-up, aerobic exercise (such as cycling or walking) followed by a cool down and stretching. 27 Most exercise protocols are provided with some support through home visits or phone calls from a therapist or nurse. Other forms are monitored program with heart rate monitoring and remote telemetry monitoring or combination of CBCR and HBCR (hybrid) programs. 11, 23 Exercise prescriptions are given based on the results of previous studies as shown in Table 3. 11, 17
### Table 3. Exercise Prescription in HBCR Program

<table>
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<tr>
<th>Prescription Components</th>
<th>Dosage</th>
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<tr>
<td><strong>Frequency</strong></td>
<td>3-5 exercise sessions/week</td>
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<tr>
<td><strong>Intensity</strong></td>
<td>50-95% of exercise capacity, peak heart rate, or heart rate reserve</td>
</tr>
<tr>
<td><strong>Exercise Time</strong></td>
<td>20-80 minutes (with cool-down and warm-up)</td>
</tr>
<tr>
<td><strong>Type (Equipment)</strong></td>
<td>Treadmill, cycle ergometer, cross-country skiing, hall games, circuit training</td>
</tr>
<tr>
<td><strong>Length of Program</strong></td>
<td>12 sessions (4 weeks) for supervised program continued with 12 sessions of home exercise program. For 8-12 weeks: home exercise program</td>
</tr>
<tr>
<td><strong>Progression</strong></td>
<td>Patients should walk at a brisk pace without undue fatigue. Daily exercise duration is increased weekly in 2 to 5 minutes increments until patients can walk briskly for at least 30 minutes daily.</td>
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The use of long-term program for >36 weeks (maintenance phase) improves long-term compliance to therapy initiated in the early phase of HBCR. The intensity of exercise for an individual program can be determined using heart rate when no cardiopulmonary testing facility is available. Exercise should be conducted with moderate to vigorous intensity (60% – 75% maximum heart rate). Formula \([220 - \text{age}]\) can be used to predict maximum heart rate. \(^{17,23}\)

Jogging or brisk walking has been known as a type of exercise conducted by most patients to achieve physical activity levels as recommended by the guidelines. However, this type of exercise cannot be carried out by some patients with comorbid conditions and facility barriers such as the availability of a gymnasium or level surface. The use of other exercise modalities such as the treadmill or stationary bike may yield additional benefits. For outdoor walking activities, it is advisable to promote patients to engage in circular laps to facilitate prompt assistance in the present of an adverse events. Individuals with lower extremity disorders resulting from orthopedic conditions, often encounter challenges in performing walking exercises. In this context, alternative exercise modalities, such as stationary cycling, elliptical training, water aerobics, and swimming can be recommended. However, some patients may face difficulties in accessing these exercise options due to a lack of suitable facilities. \(^{11}\)

### 4. Risk Factor Management

Risk factor management programs include the administration and monitoring of medication therapy in collaboration with primary healthcare providers. Additionally, these programs offer education on lifestyle modifications, incorporating guidance on weight management, regular physical exercise or activity, increased consumption of low-fat dairy products and vegetables, promotion of fresh fruit intake, adherence to sodium restrictions and cessation of smoking and alcohol consumption. \(^{33}\)

Most of the diet counseling programs are given through diet education and counseling from a
nutritionist. In HBCR program, this education and counseling are provided through telephone, weekly education, or home visits. Education can also be in the form of diet counseling with cooking sessions, or the use of educational materials on website portals or smartphones. Regarding to the educational materials the system offers guidance in the form of prescribing a specialized diet designed to meet specified limits for cholesterol and saturated fat content. This includes recommendations for lifestyle changes, and designed diet plans in line with the specific targets such as weight loss, management of hypertension, and diabetes.

Psychosocial interventions are administered through counseling sessions that focus on adapting to heart disease. These sessions comprise small group and individual education, addressing health-related lifestyle changes and stress management techniques. In the context of the feasibility, it is recommended to include housemates, significant others, and family members. Establishing a nurturing rehabilitation environment and facilitating access to community resources can enhance the levels of social support for patients and the family. In instances where significant psychosocial distress is experienced, the referral process should be initiated to a qualified mental health specialist for assessment and treatment.

5. HBCR Monitoring

Exercise monitoring in HBCR can be achieved through home visits or remote monitoring (telemonitoring). Several studies applied technology systems to CR such as the use of 1-lead electrocardiography, and heart rate monitoring with global positioning system (GPS). This can be transmitted to the network in health care centers for real-time monitoring. Other monitoring modalities could be WhatsApp or video calling and conferencing to allow sufficient specialist feedback, coaching, and consultation. Exercise diaries, cell phones, and smartphones that enable the use of internet-based health fitness applications can be used. Integration between wearable sensors and mobile telecommunication technologies has not been explored precisely in HBCR.

In elderly patients, a study was conducted monitoring CR with a heart rate meter and a smartphone. Interviews were conducted weekly, every 2 weeks, and monthly in the 1st, 2nd, and 6th months, respectively. The physical exercise program is given for a minimum of 30 minutes, 5 days a week, with moderate intensity. This study found that the program was safe and participation in this program improved physical fitness better than no participation.

CR innovation with the help of technology is more effective in terms of communication between doctors and patients compared to CBCR. Communication can be achieved through telephone, web-based video telephone, or social networking platforms.

6. HBCR Evaluation

HBCR evaluation is carried out after the completion of the exercise or 3 months later. The components evaluated include behavioral targets, medium-term outcomes, and secondary prevention objectives. Behavioral targets comprise physical activity, body mass index and waist circumference, smoking cessation, stress management, and medication adherence. Medium-term outcomes consist of exercise capacity and cardiovascular symptoms,
blood pressure, glycemic control, lipid level, tobacco use, as well as anxiety and depression. Meanwhile, secondary prevention objectives include improving physical fitness, cardiorespiratory fitness, and quality of life. These objectives aim to reduce cardiovascular events, hospitalizations, mortality rates, and adverse events, as well as enhance cost-effectiveness and resource use.\textsuperscript{11,13}

**CONCLUSIONS**

Implementation of HBCR is quite similar with CBCR. Implementation of HBCR in CAD patients is begin with pre-participation screening, patient assessment, exercise prescription, management of risk factors, monitoring, and evaluation. This review only describes the steps of HBCR implementation based on article review and doesn’t describe any further implementation such as programs, outcome measurement of HBCR, and also application of the outcome from HBCR in any study.

**Acknowledgment**
The authors have none to declare.

**Conflict of Interest**
No conflict of interest is to be stated.

**Funding**
This study received no grant from funding agencies in the public, commercial, or non-profit sectors.

**Author Contribution**
AN has contributed to all processes in this review, including preparation data gathering and analysis, drafting, and approval for publication of this manuscript. GA contributed to drafting and approval for publication of this manuscript.

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