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Review

The contribution of cardiac rehabilitation program in management of diabetes mellitus: A systematic review

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ABSTRACT

Aims: to determine the effectiveness of cardiac rehabilitation (CR) programs in management of DM.
Methods: Pubmed database was researched from June 2018 to July 2018 for randomized control trials and cohort studies between 2013 and 2018. Data were extracted, and validity was assessed by 2 reviewers and graded using the Cochrane Collaboration tool for assessing risk of bias.
Results: A total of 208 articles were screened for relevance. Only 8 articles were deemed eligible for this review, 4 retrospective and 4 prospective studies. Totally 23.415 people with DM participated in CR, whereas the mean duration of CR programs was 12 weeks. The findings indicated a reduction in total mortality, length of hospitalization and risk for cardiac surgery. Also, it was observed a decrease in body weight, blood glycose, glycated hemoglobin, insulin resistance and blood lipids.
Conclusion: It is imperative the increase of CR programs and people' participation with DM with the aim of effective management of their disease and reduction of health care cost. In addition, it is observed a gap in knowledge and more research is needed.

1. Introduction

Diabetes mellitus (DM) is one of the most common chronic diseases, since 382 million people globally face DM in 2013. It is estimated that this number will be raised at 592 million by 2035 (Forouhi and Wareham, 2014). According to World Health Organization, the incidence of DM among people over 18 years old increased from 4.7% in 1980 to 8.5% in 2014. In addition, 1.6 million deaths were attributed to DM in 2015, whereas in 2012 2.2 million deaths believed to be caused by high blood sugar (World Health Organization, 2017).

Diabetes mellitus triggers the scientific interest not only because of its increasing incidence but also since its side effects and especially damages in major organs like kidney, cerebrum and heart. More specific, it is estimated that persons with DM have the double risk of having a cardiovascular event than people without DM (American Diabetes Association, 2018). In addition, it is observed a higher number of deaths due to any cardiovascular disease among people with DM by 1.7 times than in persons without DM (Leon and Maddox, 2015).

The management of DM demands a comprehensive approach in order not only to handle the level of blood glycose but to prevent possible damages in heart and vascular system. Cardiac rehabilitation (CR) programs offer a great opportunity to people with DM to handle their health condition since provides services both for the management of blood glycose and for strengthening the muscles concluding heart muscle and vessels (Scottish Intercollegiate Guidelines Network, 2002).

The aim of the present systematic review is to determine the outcome of cardiac rehabilitation programs in management of DM in terms of prevention of side effects in cardiovascular system and other major organs. Moreover, it is examined the impact on elimination of cardiovascular risk factors.

2. Material and methods

The authors searched the electronic databases PubMed between June 2018 and July 2018. They evaluated articles published between 1 January 2013 and 1 June 2018. The key-words: 'cardiac rehabilitation', 'diabetes mellitus', 'management and 'outcomes' were searched as text word in abstract or title or mesh subject heading. Data were extracted,

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and validity was assessed by 2 reviewers and graded using the Cochrane Collaboration tool for assessing risk of bias.

In the review the following types of studies were included:

- Randomized control trials examining the effects of cardiac rehabilitation on diabetes mellitus
- Longitudinal studies testing the effects of CR among people with diabetes mellitus
- Cohort studies examining outcomes of CR
- Cross-sectional studies testing outcomes of CR.

Studies were considered eligible if they included adult patients with diabetes mellitus, involved any form of supervised or unsupervised structured CR programme undertaken in a patient-, outpatient-, community- or home-based setting and were in English.

From the initial search, 208 studies were found, the title and abstracts of these were screened and 177 were excluded according to selection criteria. Twenty-five studies were later excluded because of confounding intervention or confounded data and raw data could not be obtained. Therefore, only 6 studies included in the present systematic review. We also searched the references list and identified 20 eligible studies. Out of these 20 studies, 14 were excluded at first inspection as duplicates, 4 were excluded because of confounding factors, leaving 2 included studies for analysis. In Diagram 1 presented the flow chart of studies.

3. Results

Data from totally 8 studies with 23.415 patients randomized were used in the analyses. Of these 8 trials, 2 studies are prospective, 2 are randomized trials and 4 are retrospective trials. Four studies evaluate a comprehensive intervention and four only exercise training programs. Mean follow up was 12 weeks (range 7–52 weeks). Details of the studies included in the review are shown in Table 1 and Table 2.

A randomized control trial was conducted by Karstoft et al., in 2013 to assess the effect of interval and continuous walking training in physical fitness, body composition and glycose control both in people with DM and without DM (Karstoft et al., 2013). More specific, 32 individuals enrolled in the study who subdivided into three groups, interval walking training group (IWT), continuous walking training (CWT) and control group (CG). The training in IWT and CWT carried out 5 days per week for 4 months and each session lasted 1 h. The intense of exercise in IWT was at 70% of HRmax and at 50% of HRmax in CWT. People in CG received the usual care. According to the findings, participants in IWT achieved an increase of VO_2max by 4.4 ± 1.2 mL/kg/min (16.1 ± 3.7%, $p < 0.001$) and their absolute VO_2max by 249 ± 85 mL/min (10.9 ± 3.2%, $p < 0.01$). On the contrary, it was not observed any change in the CG or CWT groups. Regarding body composition, IWT group experienced a mean reduction in their body weight by 4.3 ± 1.2 kg ($p < 0.001$) and body fat mass by 3.1 ± 0.7 kg ($p < 0.001$). Also, waist-to-hip ration was reduced ($p < 0.01$), as well their abdominal visceral fat (0.54 ± 0.15 L, $p < 0.001$). No improvement occurred in CG and CWT groups.

The interval walking training seems to be effective in management of dyslipidemia, since subjects in IWT achieved a decrease in LDL cholesterol by 0.4 ± 0.2 mmol/L ($p < 0.05$). On the other hand, total cholesterol increased by 0.5 ± 0.2 mmol/L in the CG group ($p < 0.05$). It is important to mention that none of the interventions affected systolic or diastolic blood pressure. Finally, the study showed that individuals in CG were characterized by an increase of fasting insulin ($p < 0.05$), whereas subjects in IWT group achieved a reduction in continuous monitoring glycose.

In 2014, Clair et al. examined the impact of CR on presence of cardiovascular risk factors among people with DM and nondiabetic persons (Clair et al., 2014). In the study included 370 individuals with DM and 942 without diagnosis of DM. The sample participated in CR sessions 3 times per week for totally 12 weeks. Each session lasted 30–40 min and included both exercise session (aerobic and resistance training) and education about nutrition and health status. The intense of exercise was at 11 to 14 on Borg scale of perceived exhaustion. The study indicated that both groups experienced an improvement of quality of life, exercise capacity and a reduction in systolic blood pressure (SBP), diastolic blood pressure (DBP), body weight, lipid profile and resting heart rate (HR) after CR. However, people with DM marked higher improvement in triglyceride concentration and glycated hemoglobin levels in comparison with nondiabetic group. More specific, the reduction for triglycerides estimated at 37.3 mg/dl for diabetic group and 12.3 mg/dl for nondiabetic group ($p < 0.001$), whereas regarding glycated hemoglobin the decrease was at 0.5 and 0.1, respectively ($p = 0.002$). In addition, participants with DM achieved greater improvement in exercise capacity by 1.7 METs than nondiabetic group ($p < 0.001$), but this was lower than nondiabetic individuals.

During the same period, Armstrong et al. (2014) conducted a retrospective cohort study to determine how the presence of DM affects cardiorespiratory response to exercise sessions (Armstrong et al., 2014). In the study participated 1546 persons with DM and 7036 nondiabetic individuals. All of them attended exercise sessions 2 days per week for totally 12 weeks. Each session lasted 1 h and included aerobic, resistance and stretching exercises, as well nutrition education and stress management. The results ended that CR leads to an improvement of exercise capacity both for diabetic and nondiabetic group. More specific, exercise capacity enhanced by +1.0 METS in nondiabetic men, +0.9 METs in diabetic men, +0.9 METs in nondiabetic women and +0.7 METs in diabetic women ($p = 0.0009$) at 12 weeks. It is important that this increase remains after 1 year of program completion, since it was observed an improvement of +0.9 in nondiabetic men, +0.6 in diabetic men, +0.9 in nondiabetic women and +0.5 in diabetic women ($p = 0.0001$). These METs correspond to 11%, 8%, 13% and 7% increase in exercise capacity from the baseline assessment, respectively. Also, people who did not complete the CR sessions were characterized by worse exercise capacity at 1-year assessment than those who completed the program.

One year later, Armstrong et al. (2015) examined the effect of CR on mortality, rate of overall hospitalization and cardiovascular hospitalization among people with and without DM (Armstrong et al., 2015). The CR program lasted 12 weeks and its session included exercise (aerobic and resistance), nutrition education, smoking cessation and stress management. The intense of exercise was at 45–85% of resting HR. Totally, 13,158 people participated in the study of whom only 2956 had DM. The study demonstrated that CR resulted in a reduction of total mortality both in diabetic and nondiabetic group especially compared to individuals who did not complete the 12-week CR program. Also, it is observed a decrease in risk for total hospitalization by 0.91 and for cardiac hospitalization by 0.78.

Motahari-Tabari et al. (2015) assesses the effect of aerobic exercise in insulin resistance in people with DM type II (Motahari-Tabari et al., 2015). The sample included 53 people who subdivided into two groups, the exercise and the control group. Subjects in control group received the usual care, whereas in the exercise group practiced an aerobic exercise 3 days per week for 8 weeks. Each session lasted 50 min and the intense was moderate to high (60% HRmax). The findings showed that aerobic training leaded to a reduction in body weight ($p = 0.01$), waist circumference ($p = 0.004$), hip circumference ($p < 0.001$), body mass index ($p = 0.01$), plasma insulin ($p = 0.002$), and insulin resistance ($p = 0.004$) both within and between the groups over time. However, it was not achieved any improvement in the number of pills which persons received, since the number of pills in exercise group on the baseline assessment was 4.33 ± 1.64, 4.55 ± 2.02 and 4.66 ± 2.14 after one month and after two months, respectively. The respective number for control group was 4.57 ± 2.21, 4.61 ± 2.45 and 5.08 ± 2.32.

In 2016, Wald et al. conducted cohort retrospective study to assess any change in quality of life among individuals with DM who

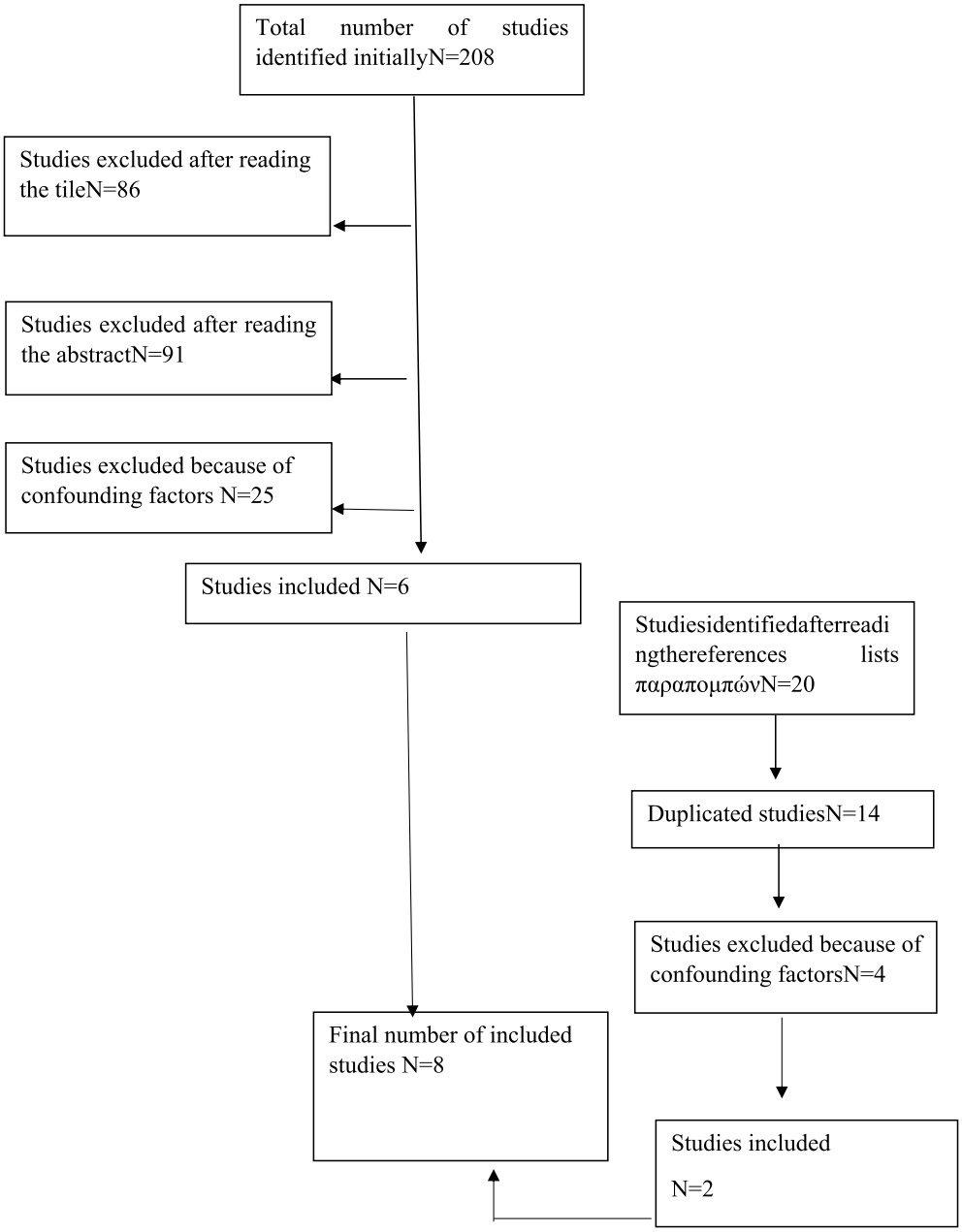

Diagram 1. Flow chart of studies.

participate in CR in comparison with patients who do not (Wald and Crecelius, 2016). Ninety-five persons fulfilled at least 22 sessions of aerobic exercise and nutrition and cardiovascular risk factors education. The intense of aerobic exercise was at 40–70% of HRmax and at level 11–13 on Borg scale of perceived exhaustion. Participants in both groups (diabetic and nondiabetic) experienced an improvement in quality of life after CR, however the difference between groups was not statistically significant. Also, diabetic group achieved greater improvement in terms of physical status and health change, whereas nondiabetic group in physical fitness, daily and social activities and overall health.

Pandey et al., in 2017 compared the results of moderate intensity exercise training (MICT) and burst exercise training (BET) in people with DM (Pandey et al., 2017). In the study included thirty people with DM who divided into two groups. In the MICT group subjects exercised 30 min of continuous moderate intensity training (60% HRmax) 5 days per week, whereas in the BET group the level of intense was high (85% HRmax) and lasted 10 min three times each day for 5 days/week. The analysis showed a decrease in body mass index (BMI) in the BET group at 3 months follow-up period compared to the MICT group (-2.2 ± 1.3 vs. $-0.7 \pm 0.7\ kg/m^2$, $p < 0.001$). More specific, BMI was $30.1 \pm 1.5\ kg/m^2$ in the BET group and 31.7 ± 1.8 in the MICT ($p < 0.001$). Also, subjects in the BET group exercised more than the MICT group as figured out of their improvement in aerobic fitness according to the Bruce treadmill exercise stress test (6.87 ± 1.44 vs. 5.40 ± 1.96 min, $p < 0.001$).

Regarding glycemic control, the BET group achieved a reduction in glycated hemoglobin by $10 \pm 4\%$ in comparison with the other group where the decrease was only $3 \pm 3\%$. Similarly, the BET group was characterized by significant reduction in glycated hemoglobin per minute of exercise by 0.0376%, whereas the percentage in the other group was only 0.0197%. Apart from the contribution of burst exercise in glycemic control, its effectiveness was proved regarding the management of dyslipidemia, since it was observed lower level of LDL and

Table 1
Main characteristics of studies included in the present systematic review.

Author (year)	Country	Type of study	Sample size	Scientific interest
Karstoft et al. (2013)	Denmark	Randomized control trial	N = 32	The change of interval and continuous walking training in physical fitness, body composition and glycemic control in people with and without DM.
Clair et al. (2014)	USA	Cohort prospective	N = 1312	The effect of cardiac rehabilitation in cardiovascular risk factors in individuals with and without DM.
Armstrong et al. (2014)	Canada	Cohort retrospective	N = 8582	The effect of DM in cardiorespiratory response.
Armstrong et al. (2015)	Canada	Cohort retrospective	N = 13,158	The impact of CR on total mortality, rate of total hospitalization and rate of cardiac hospitalization in patients with and without DM.
Motahari-Tabari et al. (2015)	Iran	Randomized clinical trial	N = 53	The effect of aerobic exercise in insulin resistant among people with DM.
Wald et al. (2016)	USA	Cohort retrospective	N = 95	The change in quality of life among individuals with DM after participating in CR.
Pandey et al. (2017)	Great Britain	Cohort prospective	N = 40	The effect of short duration high intensity burst exercise in cardiometabolic response in people with DM.
Jiménez-Navarro et al. (2017)	USA	Cohort retrospective	N = 143	The effect of CR in cardiovascular outcome in people with DM who have undergone percutaneous coronary intervention.

DM: Diabetes Mellitus, CR: Cardiac Rehabilitation.

triglycerides in the BET group than the MICT group. The level of triglycerides was reduced by 25 ± 14% in the BET group and by 5 ± 9% in MICT ($p < 0.05$). Simultaneously, the levels of HDL were increased in BET by 23 ± 14% and only by 3 ± 5% in MICT ($p < 0.05$).

Finally, Jiménez-Navarro et al. (2017) tried to determine the effect of CR in cardiovascular outcomes among individuals with DM who have undergone percutaneous coronary intervention (Jimenez-Navarro et al., 2017). In the study took part in 700 people who fulfilled 3 h sessions each week for 3 months. The results indicated that CR decreased all-cause mortality (HR, 0.77; 95% CI, 0.60–0.98; $p = 0.037$); however, it was not observed any difference regarding cardiac mortality and incidence of myocardial infraction. Also, it was not found any association among CR, risk of mortality and cardiac event ($p = 0.62$).

4. Discussion

Our work aimed to determine the effect of CR programs in the management of DM. We identified only 8 studies, 2 randomized trials and 6 cohort studies. Our review shows that people with DM participating in CR experience lower level of glycated hemoglobin (Karstoft et al., 2013; Motahari-Tabari et al., 2015; Pandey et al., 2017). Also, they achieve better management of their body weight and dyslipidemia since it is observed a reduction in their body weight, waist and hip ratio, LDL cholesterol and triglycerides (Karstoft et al., 2013; Clair et al., 2014). Apart from the cardiometabolic outcomes, CR programs tend to reduce total mortality and rate of hospitalization and revascularization among subjects with DM (Armstrong et al., 2015; Jiménez-Navarro et al., 2017). Finally, they experience an enhancement in their quality of life in terms of physical status (Wald and Crecelius, 2016).

The findings of the present systematic review are in concordance with the results of other studies which demonstrated that people with DM achieve the preferable levels of glycated hemoglobin and a reduction in insulin resistance via CR (Umpierre et al., 2011; Figueira et al., 2014; Grace et al., 2017). The contribution of exercise in glycemic control is attributed to the increase of insulin in skeletal muscles during physical activity (Guyton and Hall, 2010). As a result, it is increased the loss of body fat and the reduction of lipids' production (Turcotte and Fisher, 2008).

The effectiveness of CR programs in the management of DM is associated with plenty of factors. For instance, Karstoft et al. (2013) found that the intense of exercise is related to reduction of blood lipids, glycated hemoglobin and body weight (Karstoft et al., 2013). More specific, as high the intensity is as greater the improvement. Also, the component of CR sessions seems to be a significant element to handle cardiovascular risk factor. Clair et al. (2014) proved that comprehensive CR, included both exercise training and nutrition education, results in reducing blood lipids, glycated hemoglobin and blood pressure, whereas the study of Karstoft et al. (2013) which based on exercise training only figured out that CR does not affect blood pressure (Karstoft et al., 2013; Clair et al., 2014).

We would like to mention here that health care providers and especially cardiac rehabilitation nurses are responsible for identifying patients who are eligible to participate to cardiac rehabilitation programs. Nurses should be in contact with the staff of diabetes mellitus units and other setting both in primary care services and in hospitals in order to be informed about eligible patients. Cardiac rehabilitation team inform patients about the aim, the duration and the objectives of the program. Following the above procedure, individuals with DM could be benefit by participating in CR programs.

Another significant finding of the present systematic review is the low rate of participation in CR in people with DM. Armstrong et al. (2014) mentioned that individuals' attendance with DM to CR is significantly lower than among people without DM, 79.6% vs 84.9% respectively ($p < 0.0001$) (Armstrong et al., 2014). In addition, people with DM are more likely to discontinue the program (41.3% vs 56.2%,

Table 2
Main findings of studies included in the present systematic review.

Author (year)	Mean age (years)	Intervention	Results
Karstoft et al. (2013)	58	Control group (CG): usual care. Interval walking training (IWT): 5 sessions per week for 4 months, each session lasted 60min, intense at 70% of HRmax. Continuous walking training (CWT): 5 sessions per week for 4 months, each session lasted 60min, intense at 55% of HRmax.	• Increase of VO_2max in IWT •Decrease of body weight, body fat mass, waist-to-hip ratio and abdominal visceral fat in IWT • Reduction of LDL cholesterol in IWT • Increase of total cholesterol in CG • Decrease of blood glycose in IWT
Clair et al. (2014)	62	3 exercise and health education sessions per week for 12 weeks.	•Reduction of systolic blood pressure (SBP), diastolic blood pressure (DBP), resting heart rate (HR), body weight •Greater improvement in exercise capacity by 1.7 METs ($p < 0.001$) •Significant decrease in triglyceride concentration and glycated hemoglobin ($p < 0.002$)
Armstrong et al. (2014)	59	2 exercise, nutrition education and stress management sessions per week for 12 weeks.	• Improvement of exercise capacity at 12 weeks and 1-year assessment after CR completion
Armstrong et al. (2015)	59	2 exercise, nutrition education, smoking cessation and stress management sessions per week for 12 weeks.	• Decrease of total mortality •Decrease of total hospitalization and cardiac hospitalization
Motahari-Tabari et al. (2015)	53	Control Group: Received usual care. Exercise group: 50 min moderate to intense (60%HRmax) 3 days/week for 8 weeks.	•Reduction in body weight, body mass index (BMI), insulin resistance, waist and hip circumference • No change in the number of pills
Wald et al. (2016)	95	Aerobic sessions, nutrition and cardiovascular risk factors education 3 times per week at least for 7 weeks.	• Improvement of quality of life both in diabetic and nondiabetic group • No difference between groups
Pandey et al. (2017)	67	Moderate intensity continuous training (MICT): 30min continuous exercise, moderate intense at 60% HRmax. Burst exercise group (BEG): 10 min exercise 3 times per day 5 days per week, high intense at 85% HRmax.	• Reduction of BMI Reduction in the levels of LDL cholesterol, triglycerides and glycated hemoglobin • Increase in the levels of HDL cholesterol • Improvement in aerobic fitness
Jiménez-Navarro et al. (2017)	65	3 h per week for 3 months.	• Reduction of all-cause mortality

$p < 0.001$) (Armstrong et al., 2015). The main reason for this is that patients with DM sometimes face variations in blood glycose and especially hypoglycemia during and after exercise. Thus, they believe that exercise exacerbates their health condition, however the main cause is that patients are not adherent to instructions regarding diet and medication taking before exercise.

Therefore, it is imperative the education and information of health care providers regarding the effect of CR in the management of DM to refer patients to CR. However, the most significant is people with DM to understand the importance to take part in CR not only these with any cardiovascular disease but also and those without history of cardiac event.

A limitation of the studies identified in that they do not refer whether people have DM type I or II. Therefore, it is needed more research to demonstrate any different between different types of DM. More research is demanded, also, since we identified only 8 studies examining the effect of CR in the management of DM, thus it is observed a gap in knowledge.

5. Application to practice

The knowledge of outcomes of CR in management of DM will contribute significantly to the prevention of DM complications like kidney failure, heart failure and myocardial infraction. Therefore, people will experience an improvement in their quality of life without losing their social roles. Apart from that, the economic effect is an important factor for governments and health care systems to structure CR programs and education interventions both for patients and health care providers regarding effects of CR in DM management.

6. Summary

People with DM experienced a significant reduction in glycated hemoglobin, blood lipids and body weight through their participation in CR. Also, they are characterized by lower rate of all-cause mortality, rate of hospitalization and rate of revascularization leading in an improvement in their quality of life in terms of physical status.

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Conflicts of interest

None to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.obmed.2019.100103.

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