ORIGINAL ARTICLE

Attendance at cardiac rehabilitation is associated with lower all-cause mortality after 14 years of follow-up

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ABSTRACT

Objective To investigate whether attendance at cardiac rehabilitation (CR) independently predicts all-cause mortality over 14 years and whether there is a dose–response relationship between the proportion of CR sessions attended and long-term mortality.

Design Retrospective cohort study.

Setting CR programmes in Victoria, Australia

Patients The sample comprised 544 men and women eligible for CR following myocardial infarction, coronary artery bypass surgery or percutaneous interventions. Participants were tracked 4 months after hospital discharge to ascertain CR attendance status.

Main outcome measures All-cause mortality at 14 years ascertained through linkage to the Australian National Death Index.

Results In total, 281 (52%) men and women attended at least one CR session. There were few significant differences between non-attenders and attenders. After adjustment for age, sex, diagnosis, employment, diabetes and family history, the mortality risk for non-attenders was 58% greater than for attenders (HR=1.58, 95% CI 1.16 to 2.15). Participants who attended <25% of sessions had a mortality risk more than twice that of participants attending ≥75% of sessions (OR=2.57, 95% CI 1.04 to 6.38). This association was attenuated after adjusting for current smoking (OR=2.06, 95% CI 0.80 to 5.29).

Conclusions This study provides further evidence for the long-term benefits of CR in a contemporary, heterogeneous population. While a dose–response relationship may exist between the number of sessions attended and long-term mortality, this relationship does not occur independently of smoking differences. CR practitioners should encourage smokers to attend CR and provide support for smoking cessation.

BACKGROUND

Coronary heart disease (CHD) remains the leading cause of death globally and it is essential that interventions shown to be effective in slowing progression of the disease are used where appropriate. Cardiac rehabilitation (CR) is one such intervention, with attendance at CR shown in many studies to be strongly associated with a reduction in all-cause mortality.1–4 However, few studies have investigated the longer-term benefits of CR and findings are mixed.5–11 One study from the USA found no difference in mortality at 19 years,12 while in Sweden, attendance at CR was associated with a reduction in mortality after 10 years, but not after 5 years.13 Further investigation of the long-term benefits of CR may provide valuable evidence to support the use of this intervention in slowing the progression of CHD. Moreover, most earlier studies reporting outcomes after CR included only younger male patients after acute myocardial infarction (AMI). No identified contemporary study has investigated the long-term effects of CR on mortality among the spectrum of patients most commonly referred to CR programmes today. These include older patients, women or other diagnostic groups, such as those who have undergone coronary artery bypass graft (CABG) surgery or percutaneous interventions (PCIs).

Adherence to CR programmes may also influence the survival benefits associated with CR. It is unclear whether there is a dose–response relationship between the proportion of CR sessions attended and all-cause mortality, particularly over the longer term.2 7 8 Evidence for such a relationship will support the development of strategies to encourage patients to remain in CR programmes. This study aims to investigate whether attendance at a CR programme independently predicts all-cause mortality over 14 years in 544 Australian men and women after AMI, CABG surgery or PCI, and whether there is a dose–response relationship between the proportion of CR programme sessions attended and long-term mortality.

METHODS

Study population

The sample for this study was drawn from 652 participants recruited for an earlier study investigating attendance patterns after referral to CR. Details and results of the study have been reported elsewhere.12 Subjects for the original attendance patterns study were patients with AMI, CABG or PCI who were consecutively admitted over an 11-month period during 1996 and 1997 to one of two major teaching hospitals in Melbourne. In accordance with the prevailing policy in Victoria of automatic referral to CR, all patients were encouraged to attend a CR programme at these and other hospitals in Victoria. Participants were tracked for 4 months after their acute event to determine their CR attendance. This subsequent follow-up study uses a retrospective cohort design to examine long-term mortality outcomes of the participants enrolled in the original attendance patterns study—
that is, the 573 patients whose CR attendance was successfully determined. To allow for disease severity and avoid survival bias, we excluded 12 participants who died within 1 year of their cardiac event. A further 17 had inadequate CR attendance records, leaving 544 subjects (83.4% of the 652 patients in the original attendance patterns study) available for this follow-up mortality study.

Description of CR programmes
Consistent with the usual model of CR programme delivery in Australia at that time, the outpatient CR programmes (n=43) attended by study participants consisted of 1 h of low-to-moderate-intensity exercise and 1 h of education per session, delivered by a multidisciplinary team of health professionals. Education topics included CHD, risk factor modification, psychosocial issues and return to usual activities. Programmes were group-based, but individual counselling was available if required. The programme duration was between six and 12 sessions, with most being between six and eight sessions. For this study, CR ‘attenders’ were defined as attending at least one session of group-based exercise and education. ‘Non-attenders’ at CR were those patients who attended no sessions. These definitions are consistent with those used in previous studies.

The original attendance patterns study (1996–7) was approved by the human research ethics committees of both hospitals. All subjects provided written informed consent for a brief baseline interview, access to hospital medical records and further contact. Ethics approval for this follow-up mortality study was received from the Australian Institute of Health and Welfare and the human research ethics committee representing both hospitals.

Baseline risk factors
Baseline interviews were conducted with patients to investigate sociodemographic, medical and behavioural characteristics. Sociodemographic factors included age, gender, marital status (married or de facto vs separated, divorced, widowed or never married) and living arrangements (living alone vs living with partner, relatives, friends or in a hostel). Questions were also asked about country of birth (Australia vs other), language spoken at home (English vs other language) and adequacy of spoken English (poor vs satisfactory), age of leaving school, occupation when in the workforce (non-manual vs manual according to the Australian Standard Classification of Occupations) and employment status (employed vs unemployed, retired, pensioner or home duties).

Medical variables included diagnosis (AMI, CABG or PCI), family history of heart disease (parent or sibling died of heart disease before age 65 years) and self-reported high blood pressure, high cholesterol or diabetes. Participants also reported their weight and height.

Behavioural characteristics included smoking status (currently smokes an occasional cigarette or more vs not currently smoking) and physical activity in the 3 months before admission (>6 h leisure-time activity per week vs ≤6 h). Assessment of behavioural, medical and sociodemographic factors was based on self-report using questions and protocols taken from previous national surveys of the prevalence of cardiovascular disease risk factors.

Ascertainment of mortality
Participant mortality was ascertained by linking to the Australian National Death Index (NDI), the national dataset of all deaths occurring in Australia since 1980. The NDI has been shown previously to have a sensitivity of 93.7% and specificity of 100% for the identification of deaths. The full name, date of birth and date of last known contact of study subjects were submitted to the NDI for automated record linkage. Results were also manually reviewed against our records to confirm matching.

Statistical analysis
Analyses were performed using Stata 10.1 (Stata Corp, College Station, Texas, USA). Baseline risk factors and sociodemographic data are reported as means or proportions. To identify covariates to be controlled for in predictive analyses, we assessed the significance of any difference in baseline variables between attenders and non-attenders using $\chi^2$ (for binary variables) and t-tests (for continuous variables). Survival was described using crude death rates. Cox proportional hazards models were constructed and HR and their 95% CIs were calculated to assess the association between CR attendance (vs non-attendance) and all-cause mortality. For these analyses, time at risk began at an event date and ended at the date of death, or 17 December 2010, whichever came first. This model was extended to adjust for age and sex, with the subsequent model adjusting for significant baseline risk factors. The proportional hazards assumption was tested and met for all variables used in analysis.

For attenders, a variable ‘proportion of CR sessions attended’ was derived from the number of sessions actually attended by the participant, divided by the number of sessions available for that CR programme. This variable did not follow a normal distribution and was therefore modelled in four categories, based on attendance as follows: (1) 0–24.9%; (2) 25–49.9%; (3) 50–74.9% and (4) 75–100% of sessions. Two-sided p values are presented, with p values <0.05 regarded as significant.

RESULTS
Non-attendance at CR
Baseline characteristics of attenders and non-attenders
Relevant baseline characteristics are presented in table 1. A total of 281 (52%) men and women attended at least one exercise session. Few statistically significant differences were seen between attenders and non-attenders. Compared with those who did not attend any sessions, attenders were more likely to be male (p=0.044), younger (p=0.001) and to have undergone CABG (p<0.001). Attendees were also more likely to be employed (p=0.019) and to have a family history of heart disease (p=0.008) and less likely to report having diabetes than non-attenders (p=0.012).

We also examined the characteristics of excluded participants. The 17 patients with inadequate CR records were more likely to have had an AMI (p=0.007), while the 12 participants who died within 12 months of their event were more likely to have had an AMI (p=0.048), not be employed (p=0.020), live alone (p=0.009), have left school earlier (p=0.015) and have diabetes (p=0.027).

Crude all-cause mortality rates and attendance at CR
There were 199 deaths during a median follow up time of 14.2 years (interquartile range 9.7–14.5). Crude (unadjusted) all-cause mortality rates of attenders and non-attenders are shown in table 2. Among the total study population, non-attenders had a mortality rate per 10 000 person years which was nearly double that of attenders. A similar trend was seen for both men and women, for those aged over 60 years at study baseline and for patients with AMI or CABG.
Mortality of non-attenders compared with attenders

HRs (unadjusted and adjusted) for all-cause mortality of CR non-attenders and attenders are shown in table 3. Non-attenders had a mortality risk that was more than twice that of programme attenders (p<0.001). This association was attenuated slightly after adjusting for age and sex (model 2), but remained significant (p=0.004). After further adjustment for diagnosis, employment status, diabetes, family history (model 3), the mortality risk for non-attenders was 58% greater than that of attenders (p=0.004).

Differences in diabetes status and age were noted in baseline characteristics between non-attenders and attenders that might have accounted for some of the difference seen in mortality. We repeated the analyses excluding patients who reported having diabetes at baseline, finding similar patterns (HR for all-cause mortality=1.69 (95% CI 1.20 to 2.39, p=0.003) adjusted for age, gender, diagnosis employment status, family history). Analysis was repeated excluding patients aged ≥70, again finding similar results (HR for all-cause mortality=1.65 (95% CI 1.04 to 2.61, p=0.034) adjusted for age, gender, diagnosis, employment status, family history).

Proportion of CR sessions and mortality

Baseline characteristics

Few statistically significant trends were seen across the four categories of CR sessions attended (10–24.9%, 25–49.9%, 50–74.9%, 75–100%) except for current smokers (data not shown). Low attenders were more likely to be current smokers (40%, n=12) than were high attenders (18%, n=33; p value for trend across categories=0.001).

Association between proportion of CR sessions attended and mortality

Participants who attended <25% of available sessions had an age- and sex-adjusted mortality risk that was more than twice that of participants attending ≥75% of sessions (p=0.041) (table 4). This association was attenuated after adjusting for current smoking (p=0.133). There were no statistically significant trends were seen across the four categories of CR sessions attended.
significant differences between those attending the two middle categories of sessions and those attending ≥75% of sessions. Across categories of attendance, there appears to be a dose-response relationship, whereby the lower the proportion of sessions that were attended, the greater the mortality risk, with the exception of the 50–74% attendance category.

**DISCUSSION**

The main findings from this study were that after a 14-year follow-up period, CR non-attenders had a higher all-cause mortality risk than did CR attenders, even after adjusting for baseline differences between groups. We also found a significant age- and sex-adjusted dose-response relationship between the proportion of sessions attended and all-cause mortality. This association became non-significant after further adjustment for baseline differences in smoking status.

**Overall benefits of CR**

The findings of this study are consistent with many meta-analyses and systematic reviews reporting significant reductions in all-cause mortality following attendance at comprehensive CR in patients with AMI. The magnitude of the reduction in our study was higher than that seen in these reviews, which generally found a reduction in all-cause mortality of between 20% and 32% for CR attenders. These meta-analyses and systematic reviews were predominantly based on smaller trials (dating from the 1970s) and were confined to younger men after AMI, thus excluding women, older patients and other diagnostic groups that are more reflective of the contemporary target group for CR. More recent studies, which have tended to include these patient subgroups, describe an effect of CR from around 50% reduction in all-cause mortality, more consistent with the 58% reduction reported by us. For example, a Canadian matched cohort study using registry-based data found a 50% lower mortality rate at 5 years after CR attendance, while a study of 2396 PCI patients found a 47% reduction in all-cause mortality at 12 months in attenders compared with non-attenders.

Not all contemporary studies have demonstrated a beneficial effect of CR, however. Two systematic reviews of CR attendance and all-cause mortality found no significant association in subgroup analyses of studies published after 1995, although in both subanalyses the number of included studies was low, the 95% CI boundaries crossed (reducing significance of results) and populations were limited to younger male patients with AMI. The recent Rehabilitation After Myocardial Infarction Trial (RAMIT) from the UK found no effect of CR attendance on all-cause mortality, although the study methodology has been criticised. Findings from RAMIT have led to suggestions that comprehensive CR may no longer be relevant in view of routinely used and highly effective treatments such as β blockers, statins and early revascularisation. However, others suggest that the RAMIT findings demonstrate not that CR itself is ineffective, but that CR as performed in the late 1990s in the UK was not ‘fit for purpose’. The UK model of CR is very similar to the Australian model described in our study. Although recent recommendations for CR in both countries encourage a more comprehensive approach, problems of funding, staffing, referral and attendance rates remain, all of which will continue to affect the optimal delivery of CR.

A further question remains about the continuing need for CR, given the population-level decline in CHD mortality over the past few decades. There is recent evidence that this decline is slowing among people aged <55 years. This pattern may be due to an increasing prevalence of diabetes and obesity in this age group, both of which are major risk factors for CHD. UK studies exploring the changing clinical profile of CR attenders between the 1990s and 2006 found that while there was a very large increase in statin use and a subsequent improvement in lipid parameters, participants were now more commonly diagnosed with diabetes and were more likely to be obese. This trend suggests that there will be a continuing need for interventions such as CR.

**Long-term benefits of CR**

The long-term association between CR attendance and mortality has been studied rarely. A randomised controlled trial of 651 men with AMI attending an exercise-only programme in the USA found no difference in all-cause or cardiac mortality at 19 years. Conversely, a Swedish observational study of 305 men and women after AMI found that attendance at CR was associated with a reduction in all-cause mortality (37% vs 48%) after 10 years, but not after 5 years. These were earlier studies (with the majority of patients enrolled in the 1970s) and outcomes might have been influenced by the changes in medical management that occurred during the 1980s and early 1990s, such as the introduction of β blockers in 1985 and of ACE inhibitors and statins in 1994–5. No contemporary studies have investigated the effects of CR on mortality in patients with combined AMI, CABG and PCI over a period of 10 years or more. Ours is the first study to do so and indicates that CR may have a sustained benefit on mortality.

Although the short-term benefits of CR on risk factors are clear (with risk factor reductions accounting for about half of the mortality reduction associated with CR), less research has been undertaken on the long-term impact of behavioural changes that begin in CR. CHD progresses over many years, and therefore long-term follow-up of patients with CHD will provide valuable evidence for strategies that may be effective in slowing progression of the disease. Findings such as ours lend support to the sustainability of the beneficial effects of CR.
although further research is required into the mechanisms by which this benefit occurs.

Dose–response and CR

It is unclear as to whether attending a greater proportion of CR sessions offers a greater benefit to patients (‘dose–response relationship’). A systematic review and meta-analysis of 48 randomised controlled trials (n=8940 patients) found no dose–response,\(^2\) while two recent registry-based studies\(^7\) \(^8\) of Medicare beneficiaries aged >65 years found that attending a higher number of CR sessions was associated with a significant reduction in mortality of between 19% and 47%. It is important to note that in these studies, ‘dose’ was modelled as a binary variable possibly reducing its sensitivity, whereas our analysis modelled ‘dose’ in four groups. Furthermore, in Australia, the majority of CR programmes offer low-to-moderate exercise intensity only and programme duration is generally between six and 12 sessions. This format differs from the CR programmes in the above studies (in which programme duration is as long as 36 sessions), making comparison with our study difficult. Nevertheless, our findings add support to the suggestion that attending a higher proportion of CR sessions confers greater long-term benefit than attending fewer sessions.

Our findings also showed that while a dose–response relationship may exist between the proportion of sessions attended and long-term mortality, this does not occur independently of smoking differences. When our analyses were adjusted for the fact that low attenders are more likely to be smokers, the dose–response relationship became non-significant, indicating that smoking may account for the mortality differences. This is not surprising given the important relationship between smoking and mortality, in which smoking has been shown to account for 35% of the risk of AMI.\(^27\) In this sample, current smoking is not a ‘confounder’ of the association between mortality and the proportion of sessions attended because smoking status was not independently associated with mortality. However, given there was a baseline difference in smoking prevalence between low and high attenders and given the established relationship between smoking and increased risk of death, it was considered important to adjust for this variable in analyses. The lack of association between current smoking and mortality may be due to a number of factors, including the cause of death not being smoking related for most participants, incorrect self-report of smoking, or a reduction in smoking prevalence among patients after their cardiac event. Thus, the results should be interpreted with caution.

As previously reported,\(^12\) smoking is a predictor of discontinuing CR and it may be that smokers feel isolated and stigmatised during programme attendance. CR practitioners must ensure that strategies are in place to encourage smokers to complete CR sessions by, for example, providing extra support and referral to smoking cessation services where required.

Strengths and limitations of the study

Our study has several strengths. By studying the mortality effect of CR attendance over a 14 year period, we were able to produce evidence suggestive of the long-term sustainability of patient benefits achieved through CR. Most previous studies have only tracked mortality status of patients for 6 months to 5 years after their acute cardiac event. Our study is also contemporary and includes patients consecutively admitted into a public hospital, thus providing a representative sample of cardiac patients in Australian metropolitan hospitals. Our patient sample included three different groups—namely, patients with AMI, PCI and CABG. This heterogeneity allows for a broader understanding of how CR independently predicts mortality after a range of coronary events.

Finally, in most previous observational studies, CR programme attendance was limited to those patients who were formally referred by their physicians. In this study, however, hospitals from which these patients were recruited practised a policy of routine CR referral. Hence, attendance patterns were investigated in a sample that was presumably not affected by physician selection bias. A recent review of CR referral methods\(^31\) found that automatic referral increased referral rates, with this strategy recommended for all inpatient units in order to increase CR enrolment and participation.\(^14\)

There were some limitations to this study. We were unable to adjust for all known covariates. For example, the baseline study from which this project was derived did not investigate psychosocial factors known to influence CR attendance or long-term health outcomes, including patient beliefs and perceptions and the presence of symptoms of anxiety and depression. In addition, most clinical characteristics reported were based on patient self-report with no external validation. Further, the original attendance patterns study was not designed to assess long-term mortality outcomes and there might have been insufficient power to detect a true association between CR attendance and mortality. Although our study did include women and a range of age groups, the sample predominantly comprised men (73%) of younger age (mean age 62.5±11.3 years). Additionally, it is acknowledged that changes might have occurred to CR programme delivery, although the model of CR practised in Australia has changed little since the late 1990s. Finally, no information about the severity of the cardiac event was obtained and controlled for in analysis, although we did exclude patients who died within 12 months of their cardiac admission date, thus reducing the risk of survivor bias.\(^5\) \(^13\)

Further research

Evidence for the benefits of comprehensive CR programmes is strong and research should now focus on the ‘gaps’. These include the development of interventions to encourage referral to, and participation in, CR and the testing of strategies to enhance patient retention, particularly among those population groups who do not attend CR such as smokers, women and younger patients. Investigators should also continue to produce evidence for alternative models of cardiac secondary prevention so that patients can choose from a range of options.

Observational studies need to be undertaken using larger samples from a variety of populations and countries. Such studies might identify predictors of ‘successful’ CR programmes and would also allow for subgroup analysis; for example, stratification of outcomes by socioeconomic status to assess the potential impact of CR on health inequalities. Collection of appropriate baseline data would also allow for exploration of the mechanisms by which CR confers long-term benefit.

CONCLUSION

Findings from this study provide further support for the long-term benefits of CR in a contemporary, heterogeneous population. We should continue to recognise that comprehensive models of CR have significant benefits for healthcare. Given the projected increase in obesity, diabetes and hence CHD, the need for effective interventions such as CR that are shown to reduce CHD mortality remains.
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