Cardiac Rehabilitation Attendance and Outcomes in Coronary Artery Disease Patients

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***Background*—**Cardiac rehabilitation (CR) is an efficacious yet underused treatment for patients with coronary artery disease. The objective of this study was to determine the association between CR completion and mortality and resource use.

***Methods and Results*—**We conducted a prospective cohort study of 5886 subjects (20.8% female; mean age, 60.6 years) who had undergone angiography and were referred for CR in Calgary, AB, Canada, between 1996 and 2009. Outcomes of interest included freedom from emergency room visits, hospitalization, and survival in CR completers versus noncompleters, adjusted for clinical covariates, treatment strategy, and coronary anatomy. Hazard ratios for events for CR completers versus noncompleters were also constructed. A propensity model was used to match completers to noncompleters on baseline characteristics, and each outcome was compared between propensity-matched groups. Of the subjects referred for CR, 2900 (49.3%) completed the program, and an additional 554 subjects started but did not complete CR. CR completion was associated with a lower risk of death, with an adjusted hazard ratio of 0.59 (95% confidence interval, 0.49–0.70). CR completion was also associated with a decreased risk of all-cause hospitalization (adjusted hazard ratio, 0.77; 95% confidence interval, 0.71–0.84) and cardiac hospitalization (adjusted hazard ratio, 0.68; 95% confidence interval, 0.55–0.83) but not with emergency room visits. Propensity-matched analysis demonstrated a persistent association between CR completion and reduced mortality.

***Conclusions*—**Among those coronary artery disease patients referred, CR completion is associated with improved survival and decreased hospitalization. There is a need to explore reasons for nonattendance and to test interventions to improve attendance after referral. **(*Circulation*. 2012;126:677-687.)**

Key Words: coronary artery disease ■ epidemiology ■ hospitalization ■ propensity score ■ rehabilitation ■ secondary prevention

Because survival from acute coronary syndromes has improved in recent decades, more attention is being paid to the people living with coronary artery disease (CAD) with a goal of decreasing their risk of recurrent events. The focus in secondary prevention for acute coronary syndromes in recent years has been the use of evidence-based pharmacological therapy, and significant success has been achieved.[1] Lost in this success, however, has been the importance of cardiac rehabilitation (CR). Despite the fact that this well-accepted treatment modality is advocated by multiple professional organizations,[2–4] it remains significantly underused.[2,4,5,6]

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In general, a CR program involves comprehensive health behavior interventions, including exercise therapy, dietary modification, lipid control, and smoking cessation therapy, in conjunction with psychological counseling and treatment target-driven pharmacological therapies, all delivered primarily in an outpatient setting.[2,7] The largest randomized trial of CR in myocardial infarction patients demonstrated significant reductions in the risk of nonfatal myocardial infarction and other cardiovascular outcomes among CR participants.[8] Meta-analyses of smaller trials have shown that CR results in a decrease in all-cause mortality of 15% to 28%.[9–11] However, these trials were limited in that they included relatively low-risk patients with very few women and elderly patients.

The discrepancies in the characteristics of patients participating in CR compared with those who do not have created profile differences that may influence the observed benefits of this intervention. To the best of our knowledge, a rigorous analysis of the benefits of CR, while tightly controlling for

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differences between participants and nonparticipants, is lacking. Specifically, are the anticipated benefits of CR still present when less highly selected groups of patients from a usual care context are assessed?

The objectives of this study were to examine the use of CR by assessing CR attendance after referral and to assess the relationship between completion of CR and outcomes of mortality and resource use in a large cohort of CAD patients who had undergone coronary angiography and were referred for CR. For all analyses, we applied propensity matching to control for differences in baseline characteristics between completers and noncompleters.

Methods

Study Population

In Calgary, AB, Canada, CR has been uniformly provided since 1996 through the Cardiac Wellness Institute of Calgary (CWIC), a single centralized program. All patients referred must have cardiovascular disease. An interventional 12-week CR program is offered. The reason for referral, provincial health number, and baseline demographics are recorded for all referrals received, regardless of attendance. Patients with a first referral for CR for CAD from the inception of the program who underwent coronary catheterization before February 28, 2009, made up the study population.

Data Sources

The Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) database was used to obtain further information on all patients. The APPROACH database has captured information on all patients undergoing cardiac catheterization in Alberta since 1995.[12] Two administrative databases were used to identify hospital readmissions and emergency room (ER) visits, along with visit timing and diagnoses: the Inpatient Discharge Abstract Database and the Emergency Abstract Database. The CWIC, APPROACH, and inpatient and emergency databases were linked through the use of provincial health numbers, which are unique identifiers. We used dissemination area median household income from Statistics Canada (2006) as a proxy for patient family income.[13]

Patient Selection

Patients were excluded if they were <18 years of age or did not have a valid provincial health number. Patients were also excluded if they did not survive for 6 months after catheterization because such patients could die before referral could occur and thus bias study findings in favor of CR. Patients identified in the CWIC database who were not found in the APPROACH database (and hence did not undergo catheterization) were excluded (n=1141, 11.49%).

Study Variables

The CWIC database was used to identify those who were referred for and attended CR. Three groups of subjects were considered: those who completed CR, those who did not complete CR, and those who never enrolled. Subjects were considered to have completed CR if they completed both their baseline and 12-week postrehabilitation assessment. Subjects who attended the baseline assessment but did not return for their 12-week assessment were considered noncompleters. Subjects who were referred but did not attend any assessment were considered nonenrollers. The APPROACH database linkage was used to obtain further clinical covariates. At the time of catheterization, data are collected in APPROACH on comorbidities, including age, sex, hypertension, hyperlipidemia, diabetes mellitus, lung disease, cerebrovascular disease, congestive heart failure, peripheral vascular disease, renal disease, and malignancy. Also recorded are results of coronary catheterization (including coronary anatomy, as summarized by the Duke jeopardy score),[14] procedures done at catheterization, and postcatheterization events. Because clinical covariates are captured only at the time of the initial catheterization, only those who were referred for CR within 1 year of their first catheterization were included to ensure that the covariate data reasonably reflected the state of the patient as he or she appeared at CR.

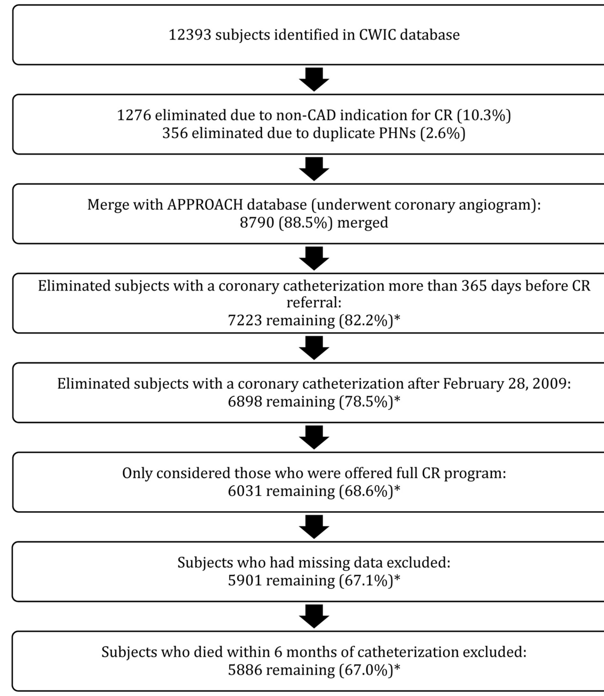

Figure 1. Study population flow diagram. CWIC indicates Cardiac Wellness Institute of Calgary; CAD, coronary artery disease; PHN, provincial health number; and CR, cardiac rehabilitation; *Percent reflects proportion of those who merged with the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) database.

Outcomes

Outcomes of interest included mortality, hospital readmissions, and ER visits. Outcomes were considered only after the date on which subjects attended their first CR session. For subjects who did not attend at least 1 session of CR, their outcomes were considered after the median time from catheterization to CR attendance, 84 days. Follow-up was complete to February 28, 2010. Deaths during the full follow-up period were considered. Hospitalizations and ER visits were considered only for those who entered the study on or after January 1, 1998, because beyond that date hospitalization and ER visit data were available.

In addition to considering all hospitalizations, we considered cardiac hospitalizations within 1 year after CR. Cardiac-specific readmissions were ascertained by the use of previously validated most-responsible *International Classification of Diseases*, ninth revision, clinical modification (ICD-9-CM), diagnosis codes for acute myocardial infarction (ICD-9: 410, 412, 4141; ICD-10: I21, I22, I2382) and congestive heart failure (ICD-9: 428, 415, 4254, 4298; ICD-10: I50, I255, I420, I429).[15]

Statistical Analysis

Differences in clinical characteristics across CR status (completed, did not complete, never enrolled) were compared by use of χ^2 tests for categorical variables and ANOVA for continuous variables. Pairwise comparisons with the never enrolled group were adjusted for multiple comparisons by use of the Bonferroni correction. Wilcoxon rank sum was used to compare ordinal data for pairwise comparisons. Cox proportional hazard models were used to determine the association between CR status and survival after catheterization, as well as the association between CR and freedom from rehospitalization (all cause and cardiac specific) and ER visits. These

Table 1. Baseline Population Characteristics by Cardiac Rehabilitation Attendance Status

	CR Status					
	Did Not Start (n=2432)	Started, Did Not Complete (n=554)	*P**	Completed CR (n=2900)	*P**	Overall *P*†
Male, %	75.4	71.8	0.085	83.8	<0.0001	<0.0001
Mean age, y	61.4	59.5	0.001	60.1	<0.0001	<0.0001
Elderly (age >75 y), %	13.6	10.3	0.036	7.6	<0.0001	<0.0001
Hypertension, %	61.8	59.8	0.361	57.1	<0.0001	0.002
Hyperlipidemia, %	70.1	67.5	n/a	67.1	n/a	0.060
Diabetes mellitus, %	23.6	24.7	0.588	17.8	<0.0001	<0.0001
Renal disease, %	2.6	2.5	0.976	1.3	0.001	0.002
On dialysis, %	0.5	0.5	n/a	0.2	n/a	0.257
Congestive heart failure, %	10.1	11.9	0.201	8.1	0.011	0.003
Peripheral vascular disease, %	6.8	8.5	0.160	4.5	<0.0001	<0.0001
Cerebrovascular disease, %	5.9	5.6	0.797	4.3	0.009	0.029
COPD, %	12.4	13.0	0.691	10.0	0.005	0.008
Current smoker, %	36.1	35.6	0.824	24.7	<0.0001	<0.0001
Previous smoker, %	32.4	38.3	0.008	40.0	<0.0001	<0.0001
Known malignancy, %	3.9	4.3	n/a	3.3	n/a	0.331
GI or liver disease, %	6.4	6.5	n/a	5.0	n/a	0.061
Previous MI, %	34.9	32.1	n/a	34.0	n/a	0.442
Prior PCI, %	6.0	4.9	0.288	4.3	0.005	0.019
Prior CABG, %	2.1	3.4	n/a	1.8	n/a	0.055
Treatment within 1 y after cardiac catheterization, %						
PCI	61.4	60.3	0.644	57.9	0.011	0.038
CABG	22.6	25.8	0.108	27.8	<0.0001	<0.0001
Duke jeopardy score, %			n/a		n/a	0.058
Normal	2.4	3.8		2.0		
<50%	3.5	4.2		3.3		
Low risk	54.3	49.8		51.6		
High risk	32.2	33.2		34.6		
Left main	7.6	8.8		8.4		
Missing	0	0.2		0.1		
Indication for catheterization, %			0.410		0.038	0.026
Stable angina	19.7	19.0		22.4		
Myocardial infarction	54.9	53.3		52.4		
Unstable angina	19.5	20.0		20.1		
Other	5.9	7.8		5.0		
Ejection fraction, %			0.0860		0.0007	0.002
>50	67.6	64.1		71.3		
35–50	21.6	22.7		18.9		
20–34	3.3	4.5		3.0		
<20	0.3	0.7		0.3		
Could not be done	0.3	0		0.2		
Not done	5.6	7.2		4.6		
Missing	1.2	0.7		1.8		
Priority at time of catheterization, %			n/a		n/a	0.145
Unknown/missing	2.2	3.4		3.0		
Emergency	25.0	24.6		24.0		
Urgent, in hospital	48.2	46.9		46.5		
Urgent, out of hospital	2.1	2.5		2.3		
Planned	22.4	21.8		23.9		

(*Continued*)

Table 1. Continued

	CR Status					
	Did Not Start (n=2432)	Started, Did Not Complete (n=554)	P*	Completed CR (n=2900)	P*	Overall P†
Quintile of income			0.0134		<0.0001	<0.0001
1 (<$57 161)	23.5	21.3		15.9		
2 ($57 162–$71 031)	23.6	20.2		16.2		
3 ($71 032–$84 173)	19.3	17.9		20.1		
4 ($84 174–$103 330)	17.2	22.2		21.0		
5 ($103 330–$257 989)	14.1	16.6		24.5		
Missing	2.2	1.8		2.3		

CR indicates cardiac rehabilitation; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; MI, myocardial infarction; PCI, percutaneous coronary intervention; and CABG, coronary artery bypass grafting.

*Pairwise difference for each CR group compared with those never enrolled with Bonferroni correction.

†Overall difference across groups as determined by ANOVA or χ^2 test.

models were then adjusted for clinical risk factors (age, sex, ejection fraction, chronic obstructive pulmonary disease, cerebrovascular disease, elevated creatinine, congestive heart failure, dialysis, hypertension, hyperlipidemia, diabetes mellitus, presence of malignancy, current smoking status, former smoking status, prior myocardial infarction, prior percutaneous coronary intervention prior coronary artery bypass grafting [CABG], peripheral vascular disease, liver or gastrointestinal disease), severity of CAD (Duke jeopardy score), and treatment strategy (percutaneous coronary intervention within 1 year of referral, CABG within 1 year of referral). Survival time was calculated from the date of the first CR session for those who attended or the median time to CR attendance for those who did not to the date on which data were censored or an end point occurred. Data were censored if follow-up ended or the patient was still alive at the end of the study; for the hospitalization and ER visit models, data were also censored at the time of death. Cumulative incidence competing risk curves were plotted for hospitalization and ER visits to account for the competing risk of death.[16] Risk-adjusted survival, time to hospitalization, and time to ER visit curves were plotted from the proportional hazards model with the use of the corrected group prognosis method.[17] We deemed the corrected group prognosis method to be acceptable for hospitalization and ER visits because the competing event occurred in only <1% of cases. The proportional hazards assumption was assessed and satisfied for each model by examining the log-log survival curves against time and by comparing Kaplan-Meier and Cox survival curves. The proportional hazards model held for the full follow-up period.

Propensity-Matched Analysis

We developed a nonparsimonious regression model for CR completion using logistic regression to produce a propensity score for completion. This model included all patient characteristics (age, sex, chronic obstructive pulmonary disease, cerebrovascular disease, elevated creatinine, congestive heart failure, dialysis, hypertension, hyperlipidemia, diabetes mellitus, presence of malignancy, current smoking status, former smoking status, prior myocardial infarction, prior percutaneous coronary intervention, prior CABG, peripheral vascular disease, liver or gastrointestinal disease [any], Duke jeopardy score, and ejection fraction), coronary anatomy, interventions (percutaneous coronary intervention within 1 year of referral, CABG within 1 year of referral), socioeconomic status (quintile of income), and interaction terms (age by sex, sex by diabetes mellitus). The model produced a propensity score for each patient for the probability of completing CR that was then used to match CR completers to noncompleters in a greedy 1-to-1 manner using psmatch2 within Stata (version 11; Stata Corp, College Station, TX). Balance in the matched groups was assessed by looking at the standardized differences between groups, with a difference of <10% deemed acceptable.[18] To properly analyze the propensity-matched pairs, hazard ratios (HRs) were then calculated by use of a variance covariance (correlation) matrix (Stata, "vce" command) to account for clustering by matched pair.

Dose-Response Relationship

To assess the relationship between the number of exercise sessions attended and mortality, we additionally constructed survival models including the number of sessions attended as a covariate.

A 2-tailed value of $P<0.05$ was defined as statistically significant. All statistical analyses were conducted with intercooled Stata version 11, with the exception of the corrected group prognosis method, which was undertaken with SAS version 9.2 (SAS Institute Inc, Cary, NC). The study protocol was approved by the ethics review board of the University of Calgary.

Results

Derivation of Study Population

A total of 12 393 subjects were referred to CWIC between July 1, 1996, and January 31, 2009. Patients were excluded owing to reasons outlined in Figure 1, leaving a final study population of 5886 CAD subjects who underwent coronary catheterization and were referred for CR, had timely covariate information, and had a minimum of 1 year of follow-up. Of those subjects, 2900 (49.3%) completed CR and 2986 did not. The median (interquartile range) length of follow-up was 5.37 years (75th percentile, 8.87 years). A total of 5637 subjects entered the study on or after January 1, 1998, and were included in the hospitalization and ER visit analyses. There were no missing data in the final cohort. In defining our study cohorts, we first considered 3 groups: those who did not attend (n=2432), those who attended a baseline assessment but did not complete the program (n=554), and those who completed the program.

The time from referral to enrollment for those who completed the program was 105.8 days; for noncompleters, it was 100.8 days ($P=0.1396$). The median time to enrollment was 84 days. If we consider time from referral to enrollment in the propensity-matched groups, the difference is even smaller: For CR completers, the mean time was 105.5 days; for noncompleters, it was 103.8 days.

Table 2. Baseline Population Characteristics by Cardiac Rehabilitation Completion

	Entire Population				Propensity-Matched Subjects			
	CR (n=2900)	No CR (n=2986)	Standardized Difference	*P*	CR (n=2256)	No CR (n=2256)	Standardized Difference	*P*
Male, %	83.8	74.7	22.4	<0.0001	80.8	80.8	−0.1	0.970
Mean age, y	60.1	61.1	−8.6	0.0010	60.2	60.4	−1.8	0.545
Elderly (age >75 y), %	7.6	13.0	−17.9	<0.0001	8.8	9.4	−1.9	0.500
Hypertension, %	57.1	61.4	−8.9	0.001	58.3	57.5	1.5	0.608
Hyperlipidemia, %	67.1	69.6	−5.3	0.040	68.2	67.9	0.7	0.823
Diabetes mellitus, %	17.8	23.9	−14.9	<0.0001	19.1	19.0	0.3	0.910
Renal disease, %	1.3	2.5	−9.3	0.0004	1.6	1.5	0.3	0.903
On dialysis, %	0.2	0.5	−4.3	0.101	0.3	0.4	−0.7	0.796
Congestive heart failure, %	8.1	10.4	−8.1	0.002	9.0	8.9	0.2	0.958
Peripheral vascular disease	4.5	7.1	−11.1	<0.0001	5.5	5.8	−1.3	0.652
Cerebrovascular disease, %	4.3	5.8	−6.9	0.008	4.5	4.9	−1.8	0.526
COPD, %	10.0	12.5	−8.0	0.002	10.6	10.9	−1.1	0.701
Current smoker, %	24.7	36.0	−24.6	<0.0001	30.1	30.6	−1.3	0.674
Previous smoker, %	39.7	33.5	12.9	<0.0001	36.7	36.6	0.3	0.926
Known malignancy, %	3.3	4.0	−3.6	0.165	3.5	3.5	0.0	1.000
GI or liver disease, %	5.0	6.4	−6.2	0.018	5.3	5.5	−0.8	0.792
Previous MI, %	34.0	34.4	−0.8	0.771	33.8	34.0	−0.3	0.925
Prior PCI, %	4.3	5.8	−6.7	0.010	5.0	5.3	−1.4	0.638
Prior CABG, %	1.8	2.4	−3.8	0.142	2.0	2.1	−0.6	0.833
Treatment within 1 y after cardiac catheterization, %								
PCI	57.9	61.2	−6.6	0.012	59.8	59.5	0.5	0.879
CABG	27.8	23.2	10.5	<0.0001	24.8	25.0	−0.6	0.836
Duke jeopardy score, %								
Normal	2.0	2.6	4.5	0.083	2.4	2.3	−1.0	0.922
<50%	3.3	3.7	−1.7	0.524	3.5	3.7	−1.0	0.750
Low risk	51.6	53.4	−3.8	0.145	52.9	52.6	0.5	0.858
High risk	34.6	32.4	4.7	0.073	34.0	33.4	1.1	0.706
Left main	8.4	7.8	2.1	0.418	7.3	7.8	−2.3	0.430
Missing	0.14	0.03	3.6	0.169	0	0.04	−1.5	0.317
Indication for catheterization								
Stable angina	22.4	19.6	7.0	0.007	21.3	20.8	1.1	0.715
Myocardial infarction	52.4	54.6	−4.4	0.090	53.5	53.2	0.7	0.811
Unstable angina	20.1	19.6	1.5	0.577	19.5	20.1	−1.4	0.627
Other	5.0	6.3	−5.3	0.041	5.7	5.9	−1.0	0.750
Ejection fraction, %								
>50	71.3	67.0	9.4	<0.0001	68.8	69.0	−0.4	0.898
35–50	18.9	21.8	−7.4	0.005	20.7	20.9	−0.4	0.883
20–34	3.0	3.6	−3.3	0.207	3.5	3.3	0.7	0.805
<20	0.28	0.40	−2.2	0.406	0.36	0.40	−0.8	0.808
Could not be done	0.21	0.20	0.1	0.960	0.22	0.27	−1.0	0.763
Not done	4.6	5.9	−5.8	0.025	5.2	4.8	1.8	0.538
Missing	1.8	1.1	5.5	0.035	1.2	1.3	−0.7	0.788
Priority at time of Catheterization, %								
Unknown/missing	3.0	2.4	3.6	0.166	2.6	2.8	−1.1	0.714
Emergency	24.0	24.9	−2.0	0.449	24.5	24.2	0.7	0.808
Urgent, in hospital	46.5	48.0	−3.0	0.247	46.7	46.6	0.1	0.976
Urgent, out of hospital	2.3	2.2	0.9	0.729	2.2	2.2	−0.3	0.919
Planned	23.9	22.3	3.9	0.139	23.8	23.9	−0.4	0.889

(*Continued*)

Table 2. Continued

	Entire Population				Propensity-Matched Subjects			
	CR (n=2900)	No CR (n=2986)	Standardized Difference	*P*	CR (n=2256)	No CR (n=2256)	Standardized Difference	*P*
Quintile of income, %								
1 (<$57 161)	15.9	23.1	−18.2	<0.0001	19.1	19.2	−0.1	0.970
2 ($57 162–$71 031)	16.2	23.0	−17.0	<0.0001	20.0	19.3	1.8	0.549
3 ($71 032–$84 173)	20.1	19.0	2.7	0.296	20.3	21.1	−1.9	0.532
4 ($84 174–$103 330)	21.0	18.2	7.1	0.006	20.0	19.9	0.4	0.882
5 ($103 330–$257 989)	24.5	14.6	25.1	0.9	18.3	18.2	0.1	0.969
Missing	2.3	2.1	0.9	0.729	2.3	2.4	−0.9	0.767

CR indicates cardiac rehabilitation; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; MI, myocardial infarction; PCI, percutaneous coronary intervention; and CABG, coronary artery bypass grafting.

Baseline Characteristics of the Population

There were significant differences in baseline characteristics across the 3 groups, notably in terms of prevalence of diabetes mellitus, peripheral vascular disease, chronic obstructive pulmonary disease, mean age, and the proportion of women in each group (Table 1). However, when pairwise differences were considered, these differences persisted between the completers and those never enrolled but were not present between those never enrolled and noncompleters.

Table 2 shows the characteristics of patients who completed CR relative to those who did not (never enrolled and not completed combined) for the entire study population and the propensity-matched population, for which unmatched cases are dropped. In the entire study cohort, subjects who completed CR were more likely to be male and younger. Of the women referred to CR, only 471 of 1226 (38.4%) completed it compared with 2429 of 4660 men (52.1%; $P<0.001$); of the elderly referred, only 220 of 388 (36.18%) completed CR compared with 2680 of 5278 nonelderly ($P<0.001$). Several comorbid illnesses were more common in the CR noncompleters. From the group, 2256 completers (77.8% of completers) were propensity matched 1-to-1 to noncompleters. After matching, the clinical characteristics of the 2 groups became similar, with standardized differences between completers and noncompleters for each covariable ranging from −2.3% to 1.8%.

There were 522 deaths in the follow-up period, 315 of which occurred in the non-CR group, 249 among those who never enrolled, and 66 among those who started but did not complete CR (Table 3). Of the CR completers, 404 (13.9%) were hospitalized in the first year after CR referral (Table 3). There were significantly more hospitalizations in the first year for the CR noncompleters and those never enrolled. Subjects who completed CR were also more likely to have undergone CABG in the first year after catheterization. For CR completers, only 9 underwent CABG after completing CR; the remainder underwent CABG before CR.

Compared with those who did not enroll in CR, CR completers had significantly improved survival (HR, 0.58; 95% confidence interval [CI], 0.48–0.70), whereas CR noncompleters did no better (HR, 1.08; 95% CI, 0.82–1.42; Figure 2A). Because CR noncompleters and nonenrollers were similar in terms of baseline characteristics and survival, the 2 groups were combined for further analysis. Compared with the amalgamated group of CR noncompleters, CR completion was associated with better survival in all 3 survival analyses that we conducted: unadjusted, adjusted, and propensity matched (Figure 2B–2D). CR was associated with a lower risk of death in the whole population, with an HR of 0.57 (95% CI, 0.46–0.66) and an adjusted HR of 0.59 (95% CI, 0.49–0.70). The association between CR completion and decreased mortality persisted in the propensity-matched group, with an HR of 0.67 (95% CI, 0.54–0.81). If we consider the elderly and women in separate stratified analyses, the unadjusted HR for elderly subjects (n=608) who completed CR versus did not complete CR was 0.54 (95% CI, 0.38–0.79). For women (n=1226), the unadjusted HR for those who completed CR versus those who did not was 0.33 (95% CI, 0.21–0.52). Adjusted HRs were 0.52 (95% CI, 0.36–0.77) for the elderly and 0.41 (95% CI, 0.25–0.65) for women, whereas the

Table 3. Summary of Events Within the First Year of Coronary Catheterization by Cardiac Rehabilitation Status

	CR Never Enrolled (n=2432), n (%)	CR Noncompleters (n=554), n (%)	CR Completers (n=2900), n (%)	*P*
PCI	1492 (61.4)	334 (60.3)	1680 (57.9)	0.038
CABG	550 (22.6)	143 (25.8)	805 (27.8)	<0.0001
Dead	15 (0.6)	6 (1.1)	0 (0)	<0.0001
Cardiac hospitalization	109 (4.5)	26 (4.7)	32 (1.1)	<0.0001
Any hospitalization	622 (25.6)	204 (36.8)	404 (13.9)	<0.0001
Emergency room visit	741 (30.5)	244 (44.0)	724 (25.0)	<0.0001

CR indicates cardiac rehabilitation; PCI, percutaneous coronary intervention; and CABG, coronary artery bypass grafting.

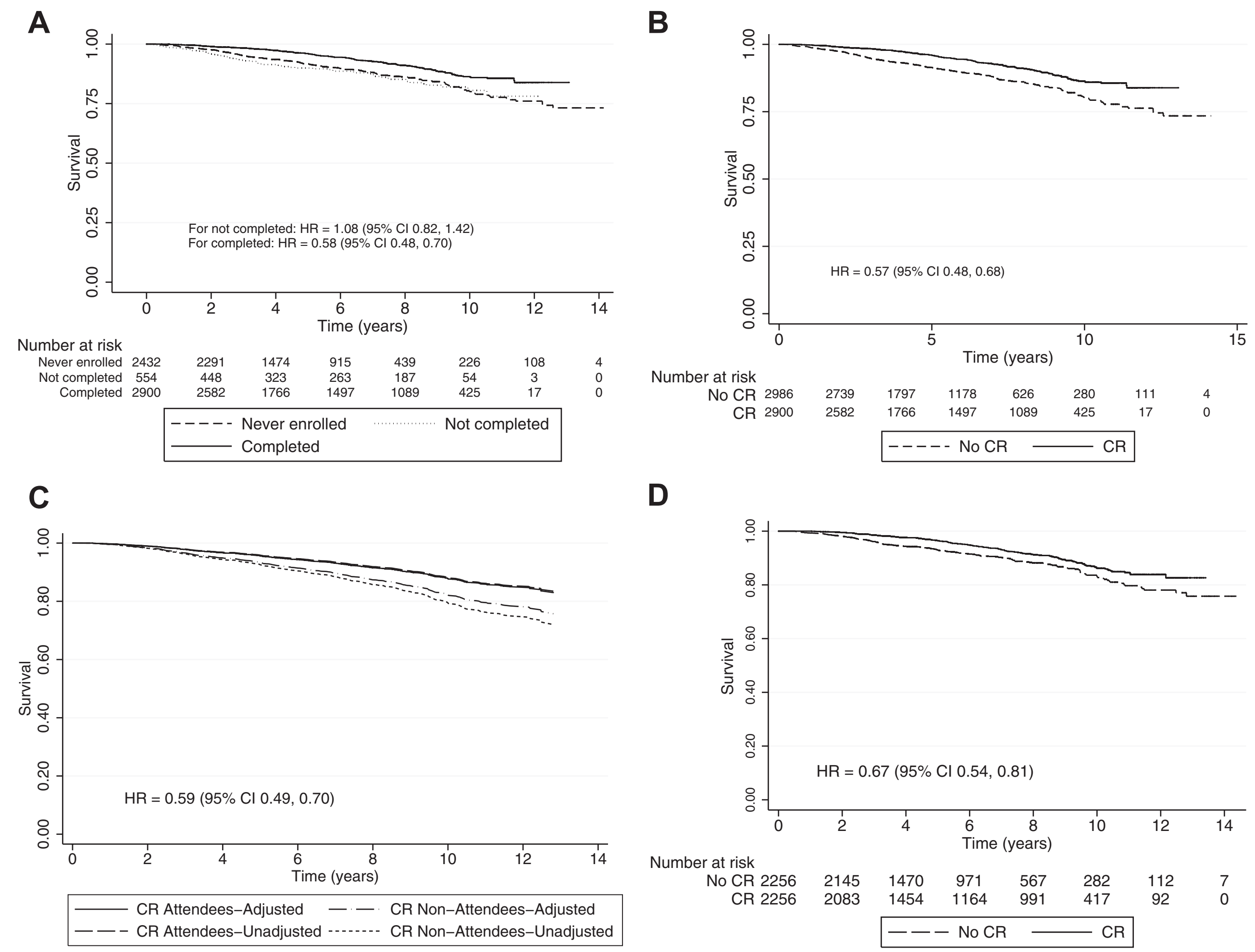

Figure 2. Survival curves: (**A**) Kaplan-Meier survival for those who never enrolled in cardiac rehabilitation (CR) vs those who did not complete CR vs those who completed CR; (**B**) Kaplan-Meier survival for CR completers vs noncompleters; (**C**) survival in CR completers vs noncompleters adjusted for age, sex, clinical factors, treatment strategy, severity of coronary artery disease, and left ventricular ejection fraction; and (**D**) survival in CR completers vs noncompleters in the propensity-matched cohort. HR indicates hazard ratio; CI, confidence interval.

propensity-matched HRs were 0.56 (95% CI, 0.39–0.91) for the elderly (n=409 in propensity-matched cohort) and 0.47 (95% CI, 0.28–0.79; n=867).

Over the study period, 2756 study subjects were hospitalized. Of these hospitalizations, 1156 occurred in those who never enrolled in CR and 325 occurred in those who started but did not complete CR. Curves for cumulative incidence of any hospitalization are shown in Figure 3A and 3B. Relative to those who never enrolled in CR, CR completion was associated with a lower risk of hospitalization (HR, 0.75; 95% CI, 0.69–0.81), a finding that persisted when the entire cohort was adjusted for all covariates (HR, 0.77; 95% CI, 0.71–0.84). However, those who started but did not complete CR were at greater risk for hospitalization than those who never enrolled (unadjusted HR, 1.33; 95% CI, 1.16–1.52; adjusted HR, 1.30; 95% CI, 1.13–1.49). Similar results were seen for cardiac hospitalizations with an unadjusted HR for CR completers of 0.61 (95% CI, 0.51–0.74) and an adjusted HR of 0.68 (95% CI, 0.55–0.83). Subjects who started but did not complete CR were not at significantly increased risk of cardiac hospitalizations relative to those who never enrolled, with an unadjusted HR of 0.87 (95% CI, 0.41–1.18; adjusted HR, 0.87; 95% CI, 0.64–1.19; Figure 3C and 3D). Because there were differences in readmission rates between those who did not complete and did not enroll in CR, these groups were not combined for the purposes of propensity matching to CR completers.

Between the median time to referral and study end, there were 3534 first-time ER visits without admission to hospital, 1411 of these by those subjects who never enrolled in CR and 370 by those who did not complete CR. Relative to those who never enrolled, CR completion was associated with better freedom from ER visits, with an HR of 0.93 (95% CI, 0.87–0.99; Figure 4). This effect was no longer significant when the model was fully adjusted (HR, 0.97; 95% CI, 0.90–1.04), Subjects who started but did not complete CR had a greater risk of ER visits than those who never enrolled (unadjusted HR, 1.31; 95% CI, 1.15–1.48; adjusted HR, 1.29; 95% CI, 1.14–1.47).

Dose-Response Relationship

Of the 3454 people who at least started CR, information on the number of exercise sessions attended was available for 2905 subjects (84%). Subjects who completed CR attended

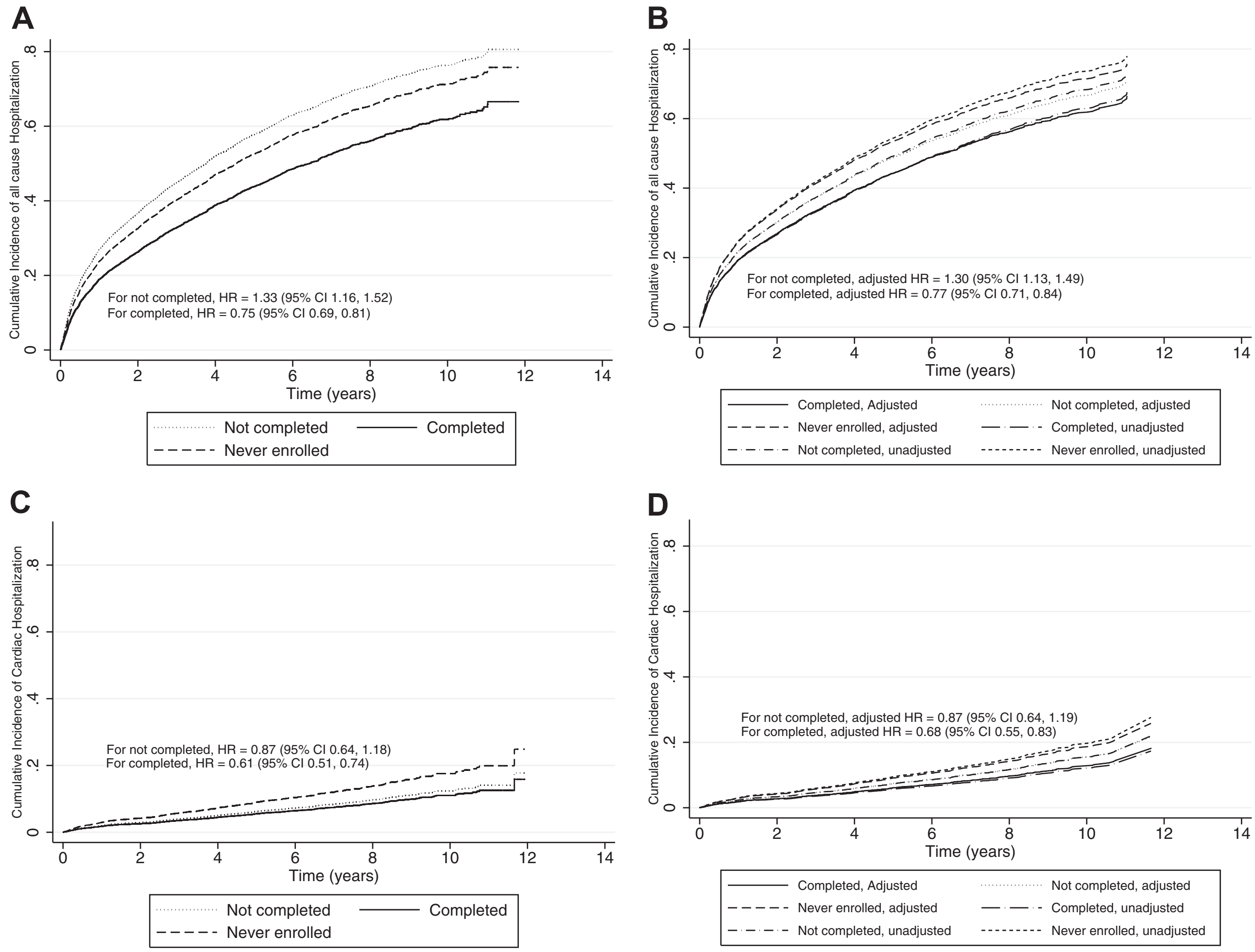

Figure 3. Cumulative incidence curves for subjects who did not enroll in cardiac rehabilitation (CR) vs those who did not complete CR vs those who completed CR: (**A**) Kaplan-Meier freedom from all-cause hospitalization; (**B**) Kaplan-Meier freedom from all-cause hospitalization adjusted for age, sex, clinical factors, treatment strategy, severity of coronary artery disease, and left ventricular ejection fraction; (**C**) Kaplan-Meier freedom from cardiac hospitalization; and (**D**) Kaplan-Meier freedom from cardiac hospitalization adjusted for age, sex, clinical factors, treatment strategy, severity of coronary artery disease, and left ventricular ejection fraction. HR indicates hazard ratio; CI, confidence interval.

an average of 21.9 (SD, 10.2) sessions, and those who did not complete CR attended 6.7 (SD, 9.1 sessions; $P<0.0001$) sessions. Cox proportional hazards models demonstrated that there was a 1% decrease in mortality with each additional session attended (unadjusted HR with number of sessions attended as a continuous variable, 0.99; 95% CI, 0.98–0.99; adjusted HR, 0.99; 95% CI, 0.98–0.995). Within the group of subjects who completed CR, however, the association between number of exercise sessions attended and mortality was not significant (unadjusted HR, 1.01; 95% CI, 1.00–1.03; adjusted HR, 1.01; 95% CI, 0.99–1.03).

Discussion

Prior studies have suggested that CR is associated with better outcomes in CAD patients, and the trials among these prior studies suggest that CR itself produces benefits. In this study, we extend findings of prior studies by studying a larger and unselected cohort of patients than prior studies have, by using propensity-matching methods to tightly control outcome comparisons, by assessing both survival and healthcare resource use outcomes, and by exploring CR use patterns and demonstrating that referral to CR is not sufficient because a substantial proportion of referred patients never attend. Our findings confirm previously published indications of CR benefits by showing that CR completion among those subjects who have undergone coronary angiogram and been referred is associated with decreased risk of mortality and newly showing a reduced frequency of all-cause and cardiac-specific hospitalizations among CR completers. In the context of an increasingly compelling body of evidence in support of CR, the phenomenon of nonattendance is a concerning finding that requires exploration and consideration of interventions to optimize the proportion of eligible patients attending and completing CR.

The observation that CR completion is associated with reduced mortality is not surprising. This finding is consistent with several short-term[19] and medium-term studies.[20] However, this study confirms that these findings are persistent over much longer follow-up, suggesting that the impact of CR on mortality is not time limited. Moreover, the strong survival benefit of CR remained after propensity matching, addressing a gap in the current literature and lending more support for the

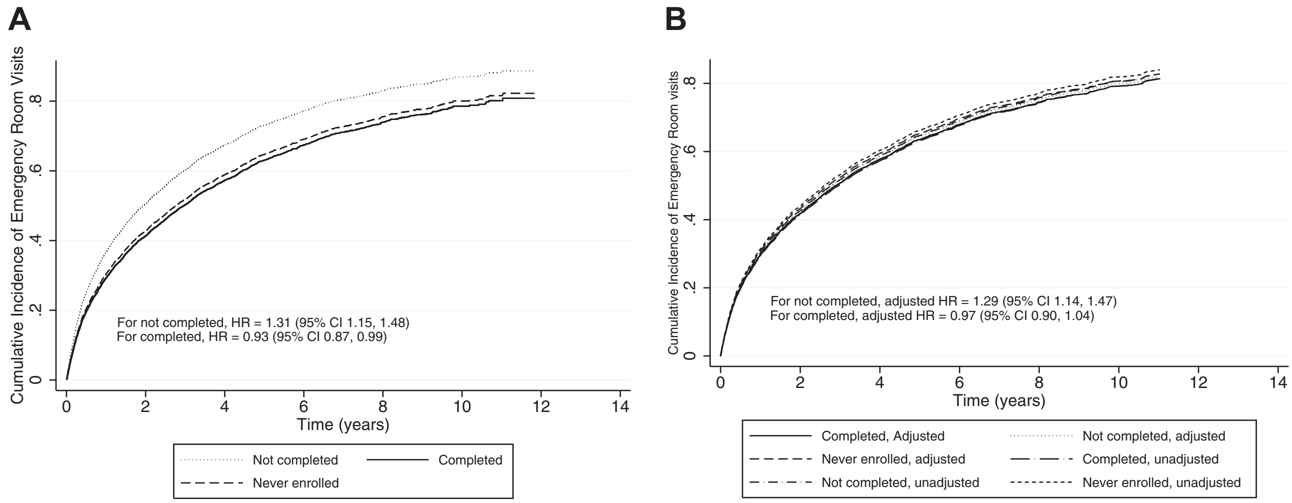

Figure 4. Cumulative incidence curves of emergency room visits for subjects who did not enroll in cardiac rehabilitation (CR) vs those who did not complete CR vs those who completed CR: (**A**) Kaplan-Meier freedom and (**B**) freedom adjusted for age, sex, clinical factors, treatment strategy, severity of coronary artery disease, and left ventricular ejection fraction. HR indicates hazard ratio; CI, confidence interval.

use of CR. CR takes a multimodality approach in helping patients manage their disease,[2] and it is difficult to pinpoint which part is most vital to the clinical impact, especially given that most CR programs are short term. Target-driven CAD risk factor management is likely a piece of the puzzle, and it is also likely that the education participants receive concerning medication and exercise increases long-term adherence to these therapies. In this study, we found, as other authors have,[21,22] that the number of exercise sessions attended was associated with reduced mortality, but this effect disappeared in subjects who completed the program. Recent work from the Organization to Assess Strategies in Acute Coronary Syndromes study demonstrated that receiving behavioral advice and adhering to it was associated with a lower risk of recurrent cardiovascular events in subjects with acute coronary syndromes.[23]

The positive impact of CR on both patient and health system outcomes is sizeable. In the context of such notable CR benefits, the attendance rate of <50% seen in this study and even lower rates in other studies[24] are concerning findings. As part of developing the propensity model, we determined a number of significant predictors of CR completion among our referred population. Men and younger subjects are more likely to complete CR than women and the elderly. Only a third of the women who were referred for CR completed it compared with half of the men; similarly, only a third of the elderly subjects who were referred to CR completed it compared with half of the nonelderly group. These numbers are low but not out of keeping with other studies.[21,25] Work investigating barriers to attendance in smaller cohorts found that not initiating CR referral or discussing CR in the hospital predicts poor attendance, as do female sex, older age, and inability to drive.[26] For women in particular, socioeconomic status and lower levels of education have been associated with poor attendance.[25] In our propensity model, we found that higher income was a major predictor of CR attendance among those referred. These barriers should be considered when subjects are referred to CR. Furthermore, formal evaluation of system interventions to increase CR referral and attendance should be undertaken.[24] In this study, we could consider only those who actually received a referral to CR. There is likely a large cohort of subjects who are never even referred.

The association between CR completion and decreased resource use is an important clinical consideration and a novel finding. Previously, rates of hospitalization in CR patients had been assessed only in congestive heart failure patients, in whom hospitalization was reduced.[27] Given that significant costs are associated with running and attending CR programs, this finding is particularly notable. If rates of downstream resource use can be decreased through participation in CR as shown in this study, a strong economic argument can also be made to continue to support CR participation. The cost of administering CR is poorly studied, with only a few small studies in the area.[28] A simplified cost analysis with some attendant assumptions was included as part of a recent Canadian CR study. The cost-utility ratio those investigators found for CR ($6000 per life-year gained) was within an economically attractive threshol" for cost-effectiveness.[20] This area is in need of further study, especially in the current context of fiscal restraint that may threaten funding for programs like CR. Additionally, subjects who start but do not complete CR deserve attention and further assessment. Subjects who do not complete the program are perhaps especially high risk because they are more likely to be rehospitalized and to visit the emergence department. They warrant close follow-up, and further study is required to characterize who is most at risk for noncompletion at the time of CR enrollment.

Our study has some limitations. Because this was not a randomized controlled trial, it is impossible to draw any conclusions about causation. We excluded all subjects who did not survive the first 6 months after catheterization because they would not have had a chance to attend CR. Additionally, all subjects in our study underwent coronary catheterization. Furthermore, there may be some unmeasured functional differences between subjects who completed CR and those who did not. Part of the impact of CR may be secondary to the healthy user effect or attendance bias; ie, those who attended are possibly healthier than those who did not.[29] However, we have controlled for all available clinical characteristics, including extensive data on cardiovascular function and disease severity, covariates that have not been considered in other recent cohort studies, lending a robustness to our findings. The depth and breadth of available clinical information on each subject are also strengths of this study. We believe our findings are generalizable to other centers, in part because the cohort study design reflects real-world experience more closely than randomized controlled trials.

Conclusions

In this analysis of one of the largest CR cohorts ever studied, we have demonstrated that CR completion among those subjects with CAD who are referred to CR is associated with a decreased risk of mortality and resource use. Our findings have potentially significant clinical implications given the rigorous procedures used to match CR participants to nonparticipants.

CR forms an important part of secondary CAD prevention. Recent efforts by North American authorities recognize the importance of health behaviors in primary and secondary prevention of cardiovascular disease.[5,30] Given the significant clinical and potentially economic benefits that may be derived from CR, greater attention needs to be focused on increasing referrals, reducing barriers to attendance, and ascertaining the economic benefits of reductions in CAD morbidity and mortality from CR completion.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Cardiac rehabilitation (CR) is a well-endorsed but underused modality for treating patients with known coronary artery disease. The objectives of this study were to examine the use of CR by assessing CR attendance after referral and to assess the relationship between completion of CR and outcomes of mortality and resource use in a large cohort of CR patients referred for CR. A prospective analysis of a well-described cohort of subjects referred for CR was undertaken. Of 5886 subjects referred to CR, only 2900 (49.3%) completed the program, with men more likely to complete CR than women (52.1% vs 38.4%; $P<0.001$). Median follow-up was 5.37 years (interquartile range, 3.24 to 8.87 years). CR completion was associated with reduced mortality (hazard ratio, 0.57; 95% confidence interval, 0.46–0.66), reduced hospitalization (hazard ratio, 0.75; 95% confidence interval, 0.69–0.81), and reduced cardiac hospitalization (hazard ratio, 0.61; 95% confidence interval, 0.51–0.74). Using propensity scores, we matched 2256 CR completers to noncompleters. In the propensity-matched cohort, CR remained associated with improved mortality (hazard ratio, 0.67; 95% confidence interval, 0.54–0.81). These findings confirm reduced mortality in association with CR as seen in other studies, but in a larger, better-described population, while also newly demonstrating a significant reduction in hospitalization. Given the increasing number of subjects surviving initial cardiac events, the importance of completing a CR program to reduce future risk of hospitalization and mortality needs to be recognized.

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