Participation in Cardiac Rehabilitation and Survival After Coronary Artery Bypass Graft Surgery

A Community-Based Study

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Background—Cardiac rehabilitation (CR) is recommended for all patients after coronary artery bypass surgery, yet little is known about the long-term mortality effects of CR in this population.

Methods and Results—We performed a community-based analysis on residents of Olmsted County, Minnesota, who underwent coronary artery bypass surgery between 1996 and 2007. We assessed the association between subsequent outpatient CR attendance and long-term survival. Propensity analysis was performed. Cox proportional hazards regression was then used to assess the association between CR attendance and all-cause mortality adjusted for the propensity to attend CR. We identified 846 eligible patients (age 66±11 years, 76% men, and 96% non-Hispanic whites) who survived at least 6 months after surgery, of whom 582 (69%) attended CR. During a mean (±SD) follow-up of 9.0±3.7 years, the 10-year all-cause Kaplan-Meier mortality rate was 28% (193 deaths). Adjusted for the propensity to attend CR, participation in CR was associated with a 10-year relative risk reduction in all-cause mortality of 46% (hazard ratio, 0.54; 95% confidence interval, 0.40–0.74; $P<0.001$) and a 10-year absolute risk reduction of 12.7% (number needed to treat=8). There was no evidence of a differential effect of CR on mortality with respect to age (≥65 versus <65 years), sex, diabetes, or prior myocardial infarction.

Conclusions—CR attendance is associated with a significant reduction in 10-year all-cause mortality after coronary artery bypass surgery. Our results strongly support national standards that recommend CR for this patient group. **(*Circulation*. 2013;128:590-597.)**

Key Words: coronary artery bypass grafting ■ mortality ■ patient compliance ■ propensity score ■ rehabilitation

Each year, more than 300 000 patients undergo coronary artery bypass grafting (CABG) surgery in the United States.[1] Although the introduction of percutaneous coronary intervention (PCI) has decreased the use of CABG in the past decade,[1,2] CABG remains the most common cardiac surgery and is the standard of care for patients with either left main or severe 3-vessel coronary artery disease. After CABG, national guidelines strongly recommend cardiac rehabilitation (CR) for all patients.[3,4]

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Although a survival advantage has been well demonstrated with CR in patients with myocardial infarction (MI)[5] and PCI,[6,7] surprisingly only a small handful of studies have examined the mortality impact of CR after CABG. These studies were either small and not statistically significant,[8,9] involved only older patients,[10] used billing data,[10] or did not account for participation bias.[11] In addition, to the best of our knowledge, no randomized controlled trials have ever specifically tested CR after CABG. Lastly, based on the results of one recent controversial trial in patients with a recent MI,[12] new doubts have arisen regarding the effectiveness of CR in the era of modern medical therapy for coronary artery disease.

Consequently, the aim of the present study was to determine the influence of CR participation on all-cause mortality after CABG in a contemporary, community-based, mixed-age cohort using detailed patient-level data.

Methods

We used the database of the Division of Cardiovascular Surgery, Mayo Clinic, Rochester, MN, to identify consecutive residents of Olmsted County who underwent CABG from January 1996 to December 2007 and were discharged alive. We excluded patients who were not residents of Olmsted County, had undergone a combined procedure, lacked a valid research consent (per Minnesota law), or

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were discharged to a long-term care facility. Because Mayo Clinic is the only center in Olmsted County performing CABG and also has the only CR program in the county, the present study closely approximates a community-based study.[13] This study was approved by the Mayo Clinic Institutional Review Board.

Standard definitions for risk factors and comorbidities were used according to the Society for Thoracic Surgery database.[14] The Charlson index was calculated from 16 clinical variables known to be predictive of mortality.[15] Renal failure was defined as a baseline creatinine level ≥2.0 mg/dL and renal complication as a creatinine level ≥2.0 mg/dL with a doubling from baseline or need for temporary or permanent dialysis. Arrhythmia was defined as the presence of or prior treatment for atrial fibrillation, atrial flutter, ventricular fibrillation, ventricular tachycardia, or third-degree heart block. Neurological complication was defined by a new stroke, transient ischemic attack, or postoperative delirium with hallucinations. Functional status was a combination of New York Heart Association class and Canadian Cardiovascular Society class, graded on a scale of I to IV. This database did not have CR referral information for the majority of patients, nor did it have sufficiently available and reliable morbidity events (subsequent MI, PCI, or stroke) to allow a proper analysis of these outcomes.

In addition, we obtained socioeconomic factors known to affect CR attendance from the general medical record. Distance from home to CR was determined with an online Web-based mileage calculator. Insurance status was classified in 4 groups: Medicare, Medicaid, commercial, or self-pay/uninsured. Medical "connectedness" was estimated by tabulating all outpatient physician visits in the year before CABG. These factors were used as important baseline socioeconomic variables in all analyses.

Patients were considered to have participated in CR if they attended at least 1 outpatient session within 6 months of the index CABG surgery, as previously done.[10] Attendance was ascertained by use of the Mayo Clinic CR database. All nonparticipants' medical records were checked to ensure they had not attended CR within 6 months after CABG surgery.

All patients attending CR underwent conventional exercise training and lifestyle counseling according to American Association Cardiovascular and Pulmonary Rehabilitation guidelines. Most patients underwent a baseline 6-minute walk as part of an exercise prescription. Patients typically exercised for 30 to 45 minutes 3 times per week but were also encouraged to exercise for 30 minutes per day on days when not attending CR. This program also included evaluation and management of any active symptoms, arrangement of follow-up appointments and laboratory testing, and management of risk factors such as hypertension, hyperlipidemia, and tobacco dependence in coordination with the patient's primary care physician.

After CABG surgery, all patients were encouraged to participate in a long-term, nurse-administered disease-management program.[16] Participating patients were more likely to be CR participants (because of encouragement from CR staff), but this was not uniformly the case and was not recorded. In this program, follow-up typically occurred at 6, 9, 12, 18, and 24 months after surgery and annually thereafter. Consequently, to evaluate the adherence patterns of patients in the present study with regard to healthcare follow-up after CABG, we tabulated all outpatient physician visits that occurred between 6 and 24 months of follow-up. Similarly, we obtained low-density lipoprotein (LDL) cholesterol levels taken between 6 and 18 months of follow-up and considered any LDL level <100 mg/dL controlled.

The primary outcome was the 10-year incidence of all-cause mortality, which was ascertained by a 2-stage approach. First, vital status was extracted from the Mayo registration database, in partnership with the Minnesota State Death Tapes. For anyone not indicated as deceased according to Mayo records, death information was pulled from the Accurint system.[17] Patients with no record of death from either source were ultimately censored (indicated as alive) on October 25, 2011, 1 month before the Accurint pull.

Statistical Analysis

Cox proportional hazards regression analysis was used to test the association between CR attendance and long-term mortality. An individual was considered a CR participant if he or she attended at least 1 session within 6 months of surgery. We used a landmark approach such that subjects who died or were lost to follow-up within 6 months were excluded. Conditioning on 6-month survival allowed all patients in the analysis to have the same opportunity to attend CR and allowed testing of CR participation as a "baseline" factor in the Cox proportional hazards modeling.

To control for CR participation bias, propensity score methods[18] were used. Using logistic regression, we fit a nonparsimonious multivariable model (which included any significant 2-way interactions) to assess the influence of all available baseline factors on the likelihood of being a CR participant. The propensity score is a function of the predicted probability of CR participation from this model. We controlled for the propensity score using 3 different approaches: (1) Regression adjustment that treated the propensity score as a covariate, (2) stratification by propensity score levels, and (3) caliper matching on propensity scores. All available variables were included in the propensity model with the exceptions of postoperative MI, resuscitation, shock, and postoperative angiogram. These factors were excluded because of low event rates, concerns about model convergence, and missing data.

For the stratification approach, we examined the distribution of propensity scores from both groups and "trimmed" the nonoverlapping tail ends, reducing the sample to those within a common range of scores. The retained subjects were then divided into 5 equally sized strata by use of propensity score quintile values. The influence of CR participation on mortality was assessed within each stratum by Kaplan-Meier methods and Cox proportional hazards regression modeling, as well as in the combined group via stratified Cox proportional hazards regression. To assess the effectiveness of the stratified propensity approach, CR participants were compared with nonparticipants within the 5 strata for each significant factor in the overall propensity model. To test the effect of the trimming, we also performed a sensitivity analysis that included all patients.

For the propensity-matching approach, CR participants were individually matched to nonparticipants within the same caliper (width based on 0.10 of the SD of propensity score) and closest in terms of propensity score. This analysis included only individuals with a suitable match, and because of a relative shortage of nonparticipants in the overall cohort, the majority of those unmatched (362 of 406, or 89%) were CR participants.

For secondary analyses, logistic regression was used to test for a linear trend in CR participation rates over the study time period. The year of surgery was the independent variable, and a patient was considered to have attended CR if they attended for a single session anytime in the subsequent 6 months. Poisson regression was used to test for a difference in the annualized rate of outpatient physician follow-up visits between participants and nonparticipants. We also tested for group difference in the proportions with an LDL level drawn and controlled at 1-year follow-up using a χ^2 test. $P<0.05$ was considered statistically significant. All analyses were performed with the SAS statistical software package (version 9.2, SAS Institute Inc, Cary, NC).

Results

We identified 869 consecutive Olmsted County residents consent who underwent isolated CABG during the study period. A total of 23 patients (2.6%) were excluded, 13 of whom died in the first 6 months (only 3 attended CR), 7 for whom the vital status could not be verified, and 3 because of unknown CR status. Consequently, a total of 846 subjects were used in all CR-related analyses. Baseline characteristics, socioeconomic factors, and operative, postoperative, and surgical complications are reported in Table 1. During a mean follow-up of 9.0±3.7 years, the 10-year all-cause Kaplan-Meier mortality rate was 28% (193 deaths). The unadjusted 10-year cumulative incidence of all-cause mortality for the non-CR and CR groups was 45% (100 deaths) and 20% (93 deaths), respectively ($P<0.001$).

The majority of patients began CR within 1 month after hospital discharge (median [quintile 1, quintile 3] time to start CR was 10 [5–17] days), and all patients started CR within 6

Table 1. Baseline Characteristics

Patient and Clinical Characteristics	No CR (n=264)	CR (n=582)	*P* Value
Age, y	68.3±11.0	64.4±10.3	<0.001
Male sex	192 (73)	456 (78)	0.07
White race	245/254 (96)	550 (95)	0.46
Surgery year*	2001 (1997, 2004)	2001 (1998, 2004)	0.71
Any prior cardiac operations	9/180 (5)	5/415 (1)	0.005
Total # of diseased coronary arteries			0.08
0	0 (0)	1 (<1)	
1	13 (5)	24 (4)	
2	37 (14)	119 (20)	
3	214 (81)	438 (75)	
Left main disease >50%	82 (31)	179 (31)	0.94
Charlson index (ordinal categories)			<0.001
0	42 (16)	132 (23)	
1–2	93 (35)	235 (40)	
3–4	64 (24)	124 (21)	
≥5	65 (25)	91 (16)	
Ejection fraction, %	53.3±13.5	56.0±13.3	0.010
Functional status classification			0.11
1	11 (4)	25 (4)	
2	25 (9)	95 (16)	
3	116 (44)	233 (40)	
4	112 (42)	229 (39)	
Preoperative risk factors			
Body mass index, kg/m^2	29.4±5.6	29.5±5.2	0.74
Body mass index categories, kg/m^2			0.67
<25	51 (19)	108 (19)	
25 to <30	109 (41)	229 (39)	
30 to <35	62 (23)	160 (27)	
≥35	42 (16)	85 (15)	
Family history of coronary artery disease	110/258 (43)	264/564 (47)	0.26
Diabetes	95 (36)	157 (27)	0.008
Hypercholesterolemia	223 (85)	516 (89)	0.10
Smoking			0.13
Never	78 (30)	200 (34)	
Current	50 (19)	82 (14)	
Past	136 (52)	300 (52)	
Renal failure	19 (7)	16 (3)	0.003
Hypertension	203 (77)	417 (72)	0.11
Peripheral arterial disease	62 (23)	71 (12)	<0.001
Cerebrovascular disease	47 (18)	81 (14)	0.14
Prior cardiovascular intervention	100 (38)	194 (33)	0.20
Prior myocardial infarction	137 (52)	257 (44)	0.037
Prior congestive heart failure	33 (13)	29 (5)	<0.001
Angina	232 (88)	528 (91)	0.20
Cardiogenic shock	6 (2)	12 (2)	0.84
Resuscitation	0 (0)	2 (<1)	0.34
Arrhythmia	49 (19)	71 (12)	0.014
Preoperative β-blocker use	209 (79)	491 (84)	0.06
Social factors			
Type of insurance:			<0.001
Medicare	160 (61)	275 (47)	
Medicaid	13 (5)	24 (4)	
Commercial/Mayo	76 (29)	279 (48)	
Self-pay/uninsured	15 (6)	4 (1)	
Distance to CR facility, miles*	3.3 (1.8, 9.9)	3.6 (2.3, 7.1)	0.60
Distance to CR facility >10 miles	65 (25)	118 (20)	0.15
No. of visits in 1 year before CABG*	4 (1, 8)	5 (2, 8)	0.035
Operative characteristics			
Intra-aortic balloon pump used	26 (10)	26 (4)	0.003
Cross clamp time (minutes)	45.6±21.3	48.7±20.5	0.048
Elective status	179 (68)	416 (71)	0.28
Internal mammary artery used as graft	245 (93)	561 (96)	0.023
Postoperative complications			
Length of hospitalization stay ≥1 wk	165 (63)	270 (46)	<0.001
Postoperative angiogram	1/211 (0)	11/487 (2)	0.10
Reoperation for bleeding	10 (4)	17 (3)	0.51
Myocardial infarction	0 (0)	2 (<1)	0.34
Neurological complication	32 (12)	28 (5)	<0.001
Renal complication	10 (4)	11 (2)	0.10

N (%) reported for all categorical variables; for those with any missing data, the denominator of subjects with observed data is reported and was used to compute the percentage. Other values are mean±SD or median (quintile 1, quintile 3) as indicated.

CABG indicates coronary artery bypass grafting surgery; and CR, cardiac rehabilitation.

*Median (quintile 1, quintile 3); *P* value from Wilcoxon rank sum test.

months. Median time (quintile 1, quintile 3) from first to last CR session was 55 (42, 69) days. Overall attendance during the time frame was 69% (annual rates ranged from 55%–76%), and the median number of CR sessions (quintile 1, quintile 3) per patient was 14 (9, 19.) There was no significant linear trend for change in CR attendance over the study time frame by univariate analysis (*P*=0.79; online-only Data Supplement Figure S1.

Table 2 lists the baseline variables and their effects on CR participation from a multivariable logistic regression model, from which the predicted probabilities were used to derive propensity scores. Specifically, smoking, renal failure, lack of insurance, and having a perioperative neurological

Table 2. Propensity Factors for Attendance at Cardiac Rehabilitation

Patient and Clinical Characteristics	Multivariable Result: OR (95% CI) [*P* Value]
Age (per 10 y)*	
Hospitalization ≤1 wk	0.96 (0.69–1.33) [0.786]
Hospitalization >1 wk	0.58 (0.43–0.77) [<0.001]
Male sex	1.20 (0.79–1.81) [0.396]
Surgery year	0.94 (0.88–1.01) [0.094]
White race	1.02 (0.43–2.42) [0.966]
Any prior cardiac operations	0.31 (0.09–1.11) [0.072]
Total # of diseased coronary arteries	0.90 (0.65–1.27) [0.559]
Left main disease >50%	1.14 (0.79–1.66) [0.485]
Charlson index (categorized)	0.85 (0.69–1.05) [0.123]
Ejection fraction	1.00 (0.99–1.02) [0.531]
Functional status classification	0.95 (0.72–1.24) [0.683]
Preoperative risk factors	
BMI categories, kg/m^2	*F* test *P*=0.473
<25	1.0 (Reference)
25 to <30	0.86 (0.54–1.38) [0.541]
30 to <35	1.12 (0.67–1.89) [0.660]
≥35	0.77 (0.43–1.37) [0.371]
Family history of coronary artery disease	1.14 (0.77–1.69) [0.500]
Hypercholesterolemia	1.19 (0.72–1.97) [0.499]
Smoking	*F* test *P*=0.021
Never	1.0 (Reference)
Current	0.46 (0.27–0.80) [0.006]
Past	0.82 (0.56–1.22) [0.328]
Renal failure	0.43 (0.18–0.99) [0.046]
Hypertension	0.96 (0.64–1.44) [0.844]
Peripheral arterial disease	0.64 (0.41–1.01) [0.054]
Cerebrovascular disease	1.20 (0.74–1.93) [0.460]
Prior cardiovascular intervention	0.92 (0.63–1.35) [0.678]
Prior myocardial infarction	1.24 (0.84–1.82) [0.284]
Congestive heart failure	0.75 (0.40–1.41) [0.370]
Angina	1.13 (0.61–2.12) [0.692]
Arrhythmia	0.73 (0.46–1.17) [0.196]
Preoperative β-blocker used	1.39 (0.90–2.14) [0.137]
Operative characteristics	
Intra-aortic balloon pump used	0.64 (0.32–1.28) [0.205]
Cross clamp time, min	1.01 (1.00–1.01) [0.223]
Elective status	0.83 (0.52–1.32) [0.428]
Internal mammary artery used as graft	1.64 (0.78–3.47) [0.193]
Postoperative complications	
Reoperation for bleeding	0.84 (0.33–2.08) [0.700]
Neurological complication	0.52 (0.27–0.98) [0.042]
Renal complication	1.06 (0.38–2.97) [0.916]
Social factors	
Insurance	*F* test *P*=0.017
Medicare	1.0 (Reference)
Medicaid	0.97 (0.40–2.34) [0.942]
Commercial/Mayo	1.14 (0.68–1.91) [0.611]
Self-pay/uninsured	0.15 (0.04–0.53) [0.003]
Distance of CR center >10 miles	0.92 (0.61–1.38) [0.677]
No. of visits in prior 1 year†	
No diabetes	1.28 (0.98–1.68) [0.071]
Diabetes	2.14 (1.47–3.12) [<0.001]

BMI indicates body mass index; CI, confidence interval; CR, cardiac rehabilitation; and OR, odds ratio.

*A significant interaction was detected between age and length of hospital stay; younger age was predictive of CR attendance among those hospitalized ≤1 week but not among subjects whose hospital stay was >1 week.

†To satisfy regression assumptions, a log transformation was applied to the total number of visits in the 1 year before coronary artery bypass graft surgery; a significant interaction was detected between number of visits and diabetes, such that a higher (log-transformed) number of visits was associated with nonattendance, although more so in diabetic subjects.

complication were significantly associated with not attending CR (*P*<0.05 for each).

Table 3 summarizes the differences across propensity quintiles for the prediction of attendance at CR. As can be seen, none of these factors differed significantly between the 2 groups in any of the 5 quintiles, which suggests adequate group balance to perform within-strata comparisons of survival or to estimate an overall stratified effect of CR on survival.

The associations between CR attendance and mortality are summarized in Table 4 based on unadjusted, propensity-adjusted, propensity-stratified, and propensity-matched analyses. With the propensity score method of covariate adjustment, CR was associated with a 46% reduction in hazard of 10-year mortality (hazard ratio, 0.54; 95% confidence interval [CI], 0.40–0.74; *P*<0.001), conditional on surviving the first 6 months. Both the stratified and matched propensity score methods produced a nearly identical effect for CR attendance as reflected by a 45% reduction in hazard of mortality (stratified: hazard ratio, 0.55; 95% CI, 0.40–0.75; *P*<0.001; matched: hazard ratio, 0.55; 95% CI, 0.36–0.84; *P*=0.007.) Stratum-specific effects of CR on long-term mortality are also reported in Table 4 and illustrated in the Figure for each of the 5 propensity score quintiles. Based on a 10-year adjusted mortality rate of 35.7% in nonparticipants and 23.0% in participants, the absolute risk reduction was 12.7%, and the number needed to treat to prevent 1 death over 10 years was 8. Among those who attended CR, the number of sessions attended was not associated with long-term mortality, after adjustment for age, sex, and Charlson index (*P*=0.41). When trimmed patients (34 total, 4%) were included as part of the sensitivity analysis, results were nearly identical (hazard ratio, 0.54; 95% CI, 0.40–0.74; *P*<0.001). There was no significant differential effect of CR on mortality when tested by age (≥65 or <65 years; *P*=0.87), sex (*P*=0.86), prior MI (*P*=0.74), or diabetes (*P*=0.61).

Compared with nonattendees, CR attendees were significantly more likely to have had an LDL level drawn at approximately 1 year after CABG (83% versus 52%, *P*<0.001) and to have that LDL level be <100 mg/dL (72% versus 60%, *P*=0.006). Furthermore, the annualized rate of total outpatient clinic visits in the 2 years after CABG was higher on average

Table 3. Comparison of Patient and Clinical Predictors of Attendance at Cardiac Rehabilitation by Propensity-Matched Quintiles

Patient and Clinical Characteristics	Propensity Quintile	Variable Subgroup	No CR	CR	*P* Value
Age, y	1	…	71.7±10.2	70.7±10.9	0.55
	2	…	68.7±9.4	69.3±8.4	0.68
	3	…	66.4±11.1	66.5±9.6	0.96
	4	…	61.1±11.3	64.1±8.7	0.14
	5	…	61.0±12.0	59.5±9.4	0.53
Smoking status	1	Never	28 (27)	15 (25)	0.82
		Current	21 (21)	15 (25)	
		Past	53 (52)	31 (51)	
	2	Never	22 (31)	21 (23)	0.19
		Current	17 (24)	17 (18)	
		Past	31 (44)	54 (59)	
	3	Never	14 (31)	35 (30)	0.79
		Current	6 (13)	21 (18)	
		Past	25 (56)	62 (53)	
	4	Never	5 (21)	44 (32)	0.24
		Current	5 (21)	14 (10)	
		Past	14 (58)	80 (58)	
	5	Never	8 (40)	67 (47)	0.24*
		Current	0 (0)	14 (10)	
		Past	12 (60)	61 (43)	
Diabetes	1	…	42 (41)	27 (44)	0.70
	2	…	28 (40)	32 (35)	0.50
	3	…	16 (36)	35 (30)	0.47
	4	…	3 (13)	29 (21)	0.33
	5	…	4 (20)	32 (23)	0.80
Peripheral vascular disease	1	…	35 (34)	25 (41)	0.39
	2	…	17 (24)	18 (20)	0.47
	3	…	9 (20)	16 (14)	0.31
	4	…	1 (4)	7 (5)	1.00*
	5	…	0 (0)	4 (3)	1.00*
Hospital stay >1 wk	1	…	82 (80)	49 (80)	0.99
	2	…	46 (66)	62 (67)	0.82
	3	…	20 (44)	50 (42)	0.81
	4	…	7 (29)	39 (28)	0.93
	5	…	7 (35)	48 (34)	0.92
Renal failure	1	…	13 (13)	8 (13)	0.95
	2	…	4 (6)	4 (4)	0.69
	3	…	2 (4)	0 (0)	0.07*
	4	…	0 (0)	3 (2)	1.00*
	5	…	0 (0)	1 (1)	1.00*
No. of visits in 1 year prior†	1	…	3.0 (1.0, 7.0)	4.0 (1.0, 7.0)	0.31
	2	…	5.0 (2.0, 9.0)	4.0 (1.0, 8.0)	0.63
	3	…	6.0 (2.0, 9.0)	5.0 (2.0, 9.0)	0.72
	4	…	2.0 (1.0, 5.5)	4.0 (2.0, 7.0)	0.08
	5	…	6.5 (2.5, 15.5)	5.0 (3.0, 9.0)	0.44
Neurological complication	1	…	21 (21)	15 (25)	0.55
	2	…	8 (11)	6 (7)	0.27
	3	…	1 (2)	4 (3)	1.00*
	4	…	1 (4)	1 (1)	0.28*
	5	…	0 (0)	1 (1)	1.00*
Type of insurance	1	Medicare	74 (73)	44 (72)	0.48
		Medicaid	6 (6)	3 (5)	
		Commercial	10 (10)	10 (16)	
		Self-Pay	12 (12)	4 (7)	
	2	Medicare	46 (66)	63 (68)	0.83
		Medicaid	3 (4)	5 (5)	
		Commercial	21 (30)	24 (26)	
	3	Medicare	25 (56)	71 (60)	0.82
		Medicaid	2 (4)	6 (5)	
		Commercial	18 (40)	41 (35)	
	4	Medicare	9 (38)	64 (46)	0.70*
		Medicaid	0 (0)	3 (2)	
		Commercial	15 (63)	71 (51)	
	5	Medicare	6 (30)	31 (22)	0.22*
		Medicaid	2 (10)	6 (4)	
		Commercial	12 (60)	105 (74)	

Values are n (%) or mean±SD unless otherwise indicated.
CR indicates cardiac rehabilitation.
**P* value obtained from Fisher exact test because of low cell counts.
†Median (quintile 1, quintile 3); Wilcoxon rank sum test.

among CR attendees (rate=7.8 visits per person per year; 95% CI, 7.6–7.9) than nonattendees (rate=6.2 visits per person per year; 95% CI, 5.9–6.4; *P*<0.001).

Discussion

We found in our large contemporary, community-based, mixed-age, post-CABG cohort that CR participation was significantly associated with an approximate 45% reduction in all-cause mortality. This finding was demonstrated by 3 different techniques to adjust for the propensity to attend CR and was not significantly different by sex, age ≥65 or <65 years, presence/absence of diabetes, or prior MI. The number needed to treat with CR to prevent 1 death after CABG at 10 years was 8. These findings support national guidelines and coverage policies that recommend CR participation after CABG.[3,4]

The present study adds to the small number of published studies that have assessed the relationship between CR participation and mortality after CABG. Suaya et al[10] demonstrated a 5-year, 28% relative risk reduction using a large Medicare claims database, but their study was limited by lack of detailed patient information and an elderly cohort. Hansen et al[11] demonstrated

Table 4. Effect of Cardiac Rehabilitation on All-Cause Mortality, by Propensity Approach

Propensity Method	CR+/CR–	N (No. of Deaths)	10-Year Cumulative Incidence of Death, %*		CR Participation Effect,† HR (95% CI) [*P* Value]
			CR Participants	Nonparticipants	
Unadjusted					
Overall	582/264	846 (193)	20.3	44.6	0.36 (0.27–0.47) [<0.001]
Adjustment					
Overall	582/264	846 (193)	23.0	35.7	0.54 (0.40–0.74) [<0.001]
Stratification					
Overall	551/261	812 (192)	23.9	36.5	0.55 (0.40–0.75) [<0.001]
Quintile 1	61/102	163 (70)	40.9	54.6	0.66 (0.40–1.10) [0.113]
Quintile 2	92/70	162 (47)	31.3	38.9	0.76 (0.43–1.35) [0.348]
Quintile 3	118/45	163 (36)	17.4	51.1	0.27 (0.14–0.52) [<0.001]
Quintile 4	138/24	162 (25)	18.2	30.9	0.54 (0.22–1.36) [0.191]
Quintile 5	142/20	162 (14)	10.5	19.9	0.50 (0.14–1.79) [0.288]
Matching					
Overall	220/220	440 (130)	26.9	42.7	0.55 (0.36–0.84) [0.007]

CI indicates confidence interval; CR, cardiac rehabilitation; CR+, attended cardiac rehabilitation; CR–, did not attend cardiac rehabilitation; and HR, hazard ratio.
*Cumulative incidence rates obtained from Kaplan-Meier method; rates in the overall group for all 3 propensity methods reflect adjustment for the propensity score.
†Effect of CR participation on 10-year mortality was assessed via Cox proportional hazards regression conditional on 6-month survival.

a 2-year, 87% relative reduction in mortality risk using patient-level data, but participation bias was not accounted for. Hedback et al[8] found a 54% reduction in 10-year all-cause mortality after CABG, but this did not meet statistical significance, likely because of the small sample size (n=147; *P*=0.06.)

To the best of our knowledge, there are no randomized controlled trials that have specifically tested CR in CABG, although these patients have generally been included in general post-MI trials. Among these trials, meta-analyses have demonstrated a 20% to 25% reduction in all-cause mortality seen in patients with either MI or PCI.[19–21] Unfortunately, most randomized trials of CR are now >20 years old.[21] In addition, one recent controversial trial[12] suggests that CR after an MI may not be effective in the era of modern medical therapy for coronary artery disease. Furthermore, it appears unlikely that additional randomized trials of CR will be completed given the problematic ethical considerations of withholding this guideline-endorsed therapy. Consequently, carefully controlled cohort studies (such as the present study) have an important role in evaluating the modern effects of comprehensive CR.

Compared with the above studies, the present results showed a smaller impact of CR on all-cause mortality risk than was noted by Hansen et al,[11] similar to the results of Hedback et al,[8] larger than the results of the study by Suaya et al,[10] and larger than the meta-analyses of randomized controlled trials performed in mixed coronary artery disease populations.[19–21] Furthermore, the present findings are consistent with previously published cohort studies from Olmsted County, Minnesota, and Calgary, Alberta, Canada, that found that CR participation was significantly associated with a 40%

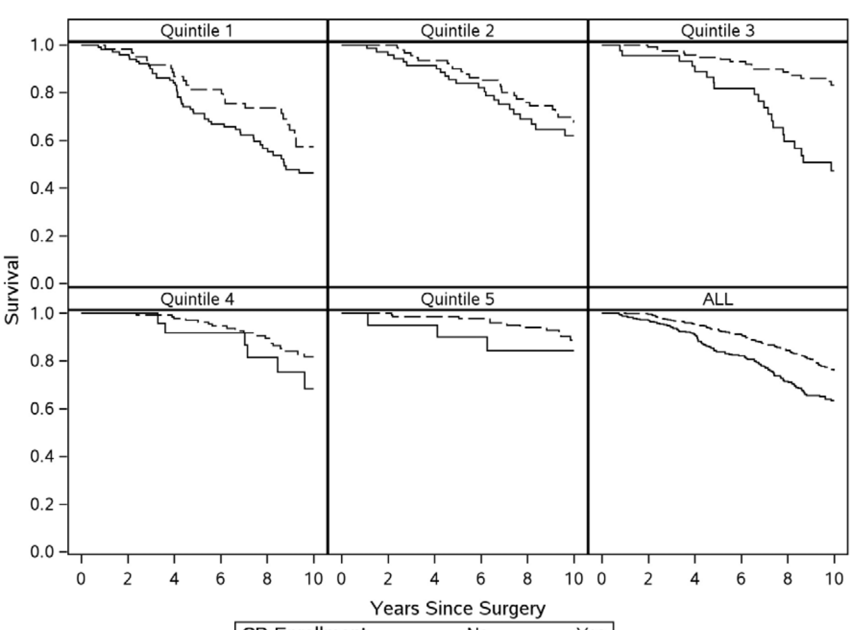

Figure. Association between cardiac rehabilitation (CR) and survival in patients undergoing coronary artery bypass graft surgery. Kaplan-Meier survival plots by propensity score quintile and for strata-combined group, comparing rates over time between patients attending and not attending CR.

to 50% reduction in mortality risk after MI,[13] PCI,[6] or a new diagnosis of coronary artery disease.[22]

What, then, might explain our findings? Two possible explanations are worth consideration. First, we contend that the present findings reflect a true association between CR and substantial reduced mortality risk, related to the direct effects of CR on the short- and long-term delivery of effective secondary prevention therapies in CABG patients. Previously published studies support this concept, showing that CR participation is associated with improvements in coronary heart disease risk factor control,[20] as well as long-term follow-up and adherence to secondary prevention medications.[16,23] We confirmed these concepts in the present study by demonstrating improved rates of LDL measurement, LDL control, and outpatient follow-up in the first 2 years after CABG. We maintain that these results are a direct consequence of participation in a comprehensive CR program and one of several possible explanations for CR participants having improved outcomes. In addition, given that patients undergoing CABG typically have more severe coronary artery disease and risk factors, they likely derive a greater benefit from CR than patients with more limited coronary artery disease.

A second possible explanation for the present findings is the presence of a "healthy cohort" bias, such that CR participants were healthier and more motivated to maintain optimal health than those who did not participate in CR. Certainly, the present data show that CR participants were generally younger and healthier than those who did not participate in CR. To help address this concern, we used multiple propensity score techniques. Although the final result remained statistically significant, this adjustment substantially attenuated the effect of CR, likely reflecting the removal of such bias. Furthermore, we also assessed the potential role for instrumental variable analysis (ie, adjusting for factors that are associated with "accessibility" of CR but that are not necessarily related to mortality risk), which in similar studies has further reduced the point estimate.[10] We found, however, that the instrumental variables we could identify (driving distance to CR and medical "connectedness") did not differ significantly between those who participated in CR and those who did not, likely because of the short distance (<10 miles) that most patients needed to travel to attend CR. Consequently, we were unable to perform the planned instrumental analysis. Lastly, and most importantly, we found no differences in the key predictor variables for CR attendance when comparing our propensity quintiles across study groups as demonstrated in Table 3. In summary, even after adjusting for identifiable factors that were associated with a possible "healthy cohort" bias and "accessibility" of CR, we found a persistent significant association between CR participation and reduced all-cause mortality risk.

We did not find an association between the numbers of CR sessions attended and reduced mortality in the present cohort, which differs from recent findings that suggested an approximate 1% reduction in mortality for each session of CR attended.[22,24] However, we believe this is primarily because during the study period, Mayo Clinic CR individualized the recommended number of CR sessions per patient depending on progress toward goals. Healthier patients were allowed to graduate earlier, whereas more frail and sick patients were encouraged to complete 36 sessions. Therefore, a higher number of CR sessions attended may in part reflect poorer underlying health.

CR participation rates in the present study were high (68%) and compare favorably to national participation rates of 20% to 30%.[10] This implies that nationally, higher participation rates are clearly achievable, and that many more patients would attend CR if given the opportunity. In addition, participation rates in the present study compared favorably with previously reported rates from Olmsted County, Minnesota, during a similar time period in persons recuperating from MI or PCI (55% and 40%, respectively).[6,13] This higher relative participation for patients undergoing CABG compared with MI or PCI is likely attributable to increased disease severity and the need for surgical revascularization and has been noted previously.[10] However, it remains unclear why 32% of patients did not participate, and more importantly, whether this participation rate could be improved through additional quality improvement projects.

Study Limitations

The present study included data from only 1 county in Minnesota and thus may have limited generalizability. Subgroup analyses (such as those for individual propensity strata) may have been underpowered because of smaller sample sizes. Referral to CR was unknown, and thus, the present results may reflect some element of referral bias. Our database did not include a number of behavioral factors and attitudes that might affect attendance at CR or adherence to other recommended therapies. Our follow-up system with nurse case management may have favorably biased the present results, but we note that the GOSPEL study (Global Secondary Prevention Strategies to Limit Event Recurrence After Myocardial Infarction) tested a 3-year program of intensive follow-up after CR and found no difference in either cardiovascular or all-cause mortality.[25] Our use of landmark analysis limits the generalizability of the present results to patients who survive the first 6 months after CABG. Lastly, because our data were observational in nature, it is possible that the present results may have been affected by bias in our population sample (eg, healthy cohort bias). Despite our best efforts to adjust for bias in the study population, it is possible that unidentified sources of potential bias still exist in the present data. The present results, therefore, may overestimate the true association between CR participation and mortality risk after CABG. However, even if as much as half of our effect size was attributable to undetected residual bias, there would still be a substantial and important protective association between CR attendance and subsequent mortality after CABG.

Conclusions

We found in a community-based, mixed-age cohort that CR participation after CABG was associated with a significant reduction in long-term mortality. The present results support the recently released clinical practice guidelines that strongly recommend CR for all patients after CABG surgery.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Cardiac rehabilitation (CR) is a program of structured exercise training, aggressive risk factor control, and lifestyle management for patients recovering from a recent cardiac event. There is strong evidence from both randomized controlled trials and observational studies that CR reduces mortality among patients with myocardial infarction and percutaneous coronary intervention; however, the evidence is less well established among patients with coronary artery bypass graft (CABG) surgery, and there has been some recent controversy about the effectiveness of CR. No randomized controlled trial has ever specifically tested CR among patients with CABG. Observational studies have either been small or limited to elderly patients. Consequently, we performed a community-based detailed analysis of the long-term, all-cause mortality changes associated with CR participation after CABG in 846 mixed-age patients. After 10 years of follow-up, CR attendance was associated with a 45% reduction in long-term mortality. Our findings support national guidelines that strongly recommend referral to CR for all patients after CABG.

Participation in Cardiac Rehabilitation and Survival After Coronary Artery Bypass Graft Surgery: A Community-Based Study

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Supplemental Material

Participation in Cardiac Rehabilitation and Survival Following Coronary Artery Bypass Graft Surgery: A Community Based Study

[Intended for online publication]

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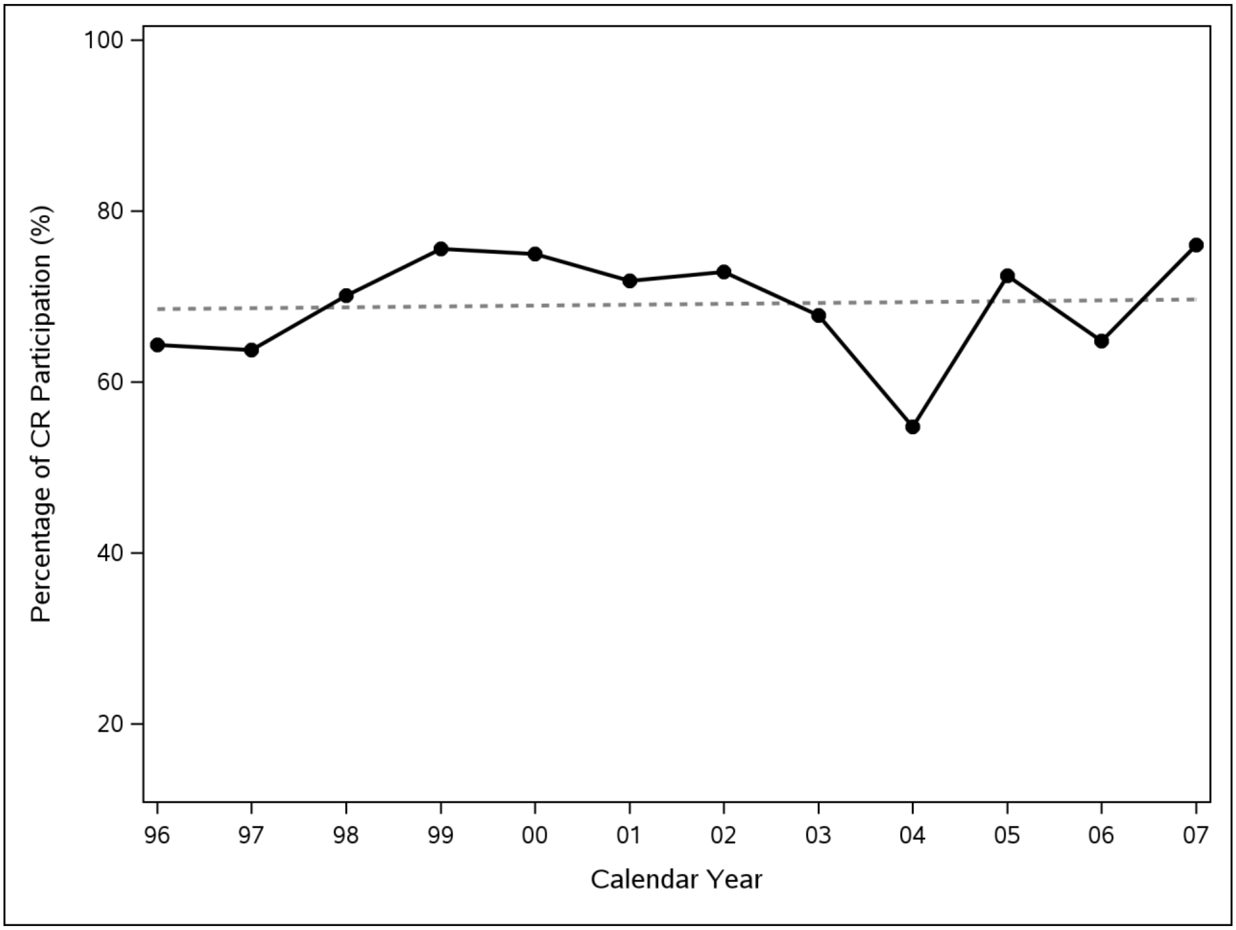
Figure S1. Time Trends in Cardiac Rehabilitation Participation among patients with Coronary Artery Bypass Graft Surgery in Olmsted County, MN.



As seen, participation in CR remained consistently high for the duration of the study with only minimal year to year variability.