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The purpose of this study was to test the hypothesis that an individualized exercise training target heart rate (HR) based on a maximal graded exercise test (GXT) is associated with greater improvements in exercise tolerance during cardiac rehabilitation (CR) compared with no GXT. In this retrospective study, we identified patients who completed 9 to 36 visits of CR between 2001 and 2016, with a length of stay ≤18 weeks and a visit frequency of 1 to 3 days per week. Patients were grouped based on whether their exercise was guided by a target HR determined from a GXT. To assess the relation between GXT and change in exercise training metabolic equivalents of task (METs), we used generalized linear models adjusted for age, gender, race, referral reason, CR visits, CR frequency, METs at start, CR location, and year of participation. Out of 4,455 patients (37% female, 48% White, median age = 62 years), 53% were prescribed a target HR based on a GXT. Compared with no GXT, a GXT was associated with a significantly greater increase in covariate-adjusted METs during CR and percentage change from start (+0.44 METs [95% confidence interval [CI] 0.38 to 0.51] and +17% [95% CI 14% to 19%], respectively). In a sensitivity analysis limited to patients with 24 to 36 visits at ≥2 days per week (n = 1,319), a GXT was associated with a significantly greater increase in covariate-adjusted exercise training METs (+0.51 [95% CI 0.36 to 0.66]; +19% [95% CI 13% to 24%]). In conclusion, to maximize the potential increase in exercise capacity during CR, patients should undergo a GXT to determine an individualized exercise training target HR.   © 2022 Elsevier Inc. All rights reserved. (Am J Cardiol 2022;175:139−144)

Introduction

In patients with heart disease, participation in phase 2 (early) cardiac rehabilitation (CR) is associated with ~25% lower risk for secondary cardiac events and is the standard of care for secondary prevention of heart disease.[1,2] An important component of CR is exercise training aimed at increasing exercise capacity.[3,4] Greater increases in exercise capacity during CR are associated with lower morbidity and mortality.[5−8] Increasing exercise capacity is dependent on an exercise training intensity that provides sufficient stimulus (i.e., overload principle) to elicit an exercise training response.[3,9] Exercise training intensity is best prescribed based on an individual's exercise capacity and other data (e.g., heart rate [HR] response) determined during a sign and symptom-limited maximal graded exercise test (GXT).[4] However, most patients in the United States participate in CR without a GXT.[10] This may be due, in part, to a lack of empirical data supporting the importance of a GXT to prescribe exercise intensity. The purpose of this study was to test the hypothesis that patients who are provided an individualized exercise training target HR

based on a GXT will have greater increases in exercise tolerance during CR compared with patients who do not undergo a GXT.

Methods

This was a retrospective, observational study of patients who participated in the Henry Ford Hospital and Medical Group phase 2 CR program between 2001 and 2016. The cohort was identified from the Henry Ford Preventive Cardiology Outcomes database. Select patient characteristics and program outcomes were prospectively entered into this database on all patients who participated in CR. Inclusion criteria for this study were age = 18−80 years old, 9 to 36 visits of CR, length of stay in CR ≤18 weeks, and attendance frequency of 1 to 3 days per week. The lower limit for visits was 9 because we believed this is the minimal dose (~4 week) that might result in a meaningful exercise training response. Exclusion criteria were recent or current atrial fibrillation, cardiac transplant, and left ventricular assist device. For patients who participated in CR more than once during the study period, only the first encounter was used. This study was approved by the Institutional Review Board of the Henry Ford Health System.

This phase 2 CR program is offered in Detroit, Michigan, and at 2 suburban locations in the metropolitan-Detroit area. Staffed by clinical exercise physiologists, CR is an outpatient program offered in a group setting 3 days per week. Each session includes an educational lecture and at least 30 minutes of aerobic exercise training (plus 5 minutes each of warm-up and cool-down). Multiple exercise modes

(e.g., treadmill, stationary bike) are available during each visit. Patients are encouraged to exercise on 2 modes for ≥15 minutes each. Consistent with recommendations from professional organizations,[4,9,11,12] individualized exercise training intensity is prescribed at 50% to 80% of measured HR reserve determined from a GXT. If a recent GXT is not available, exercise intensity is set at HR at rest plus ≤20 to 30 beats.[11,12] In both situations, ratings of perceived exertion (i.e., Borg 6 to 20 scale) is a secondary method used to guide intensity. Using these methods, exercise training workloads are selected by patients with guidance from CR staff. Staff regularly encourage patients to progress their exercise workloads based on the patient's HR and perceived exertion.

If a recent GXT is not performed before starting CR, staff are encouraged to order one on those patients who do not have an obvious limitation to full participation in exercise or the GXT (e.g., skeletal muscle impairment). Staff can order a GXT at any time during a patient's participation in CR. Whether or not an individualized exercise target HR was determined based on a GXT is captured in the outcomes database.

Exercise workloads during CR are described in metabolic equivalents of task (METs; where 1 MET represents $3.5 \text{ ml O}_2 \times \text{kg}^{-1} \times \text{min}^{-1}$). METs are calculated based on the speed and grade recorded by staff from the treadmill during typical CR visits using existing equations for walking.[11] Exercise training METs at the start of CR (mean of visits 2 and 3) and discharge from CR (mean of the last 2 visits) are captured in the outcomes database.

The primary outcome was change in exercise tolerance based on exercise training workloads expressed in METs from start to discharge from CR. Patients were grouped based on whether they were prescribed an individualized exercise training target HR from a GXT. Reasons for referral to CR were categorized as (1) coronary artery bypass graft surgery; (2) myocardial infarction without coronary artery bypass graft surgery; (3) percutaneous coronary intervention without myocardial infarction or coronary artery bypass graft surgery; (4) valve repair or replacement only; (5) heart failure only; and (6) medical therapy only, which includes patients with stable angina pectoris.

Because continuous data were not normally distributed, they are presented as median (10th, 90th percentile). The Kolmogorov-Smirnov and Mann-Whitney U tests were used for within-group and unadjusted between-group comparisons, respectively. Nominal data were compared using chi-square. Covariate-adjusted change in METs (start to discharge from CR) and percentage change in METs was calculated (including 95% confidence interval [CI]) using generalized linear models. Covariates were age, gender, race, the reason for referral, total visits completed, attendance frequency (days per week), METs at start, CR location, and year of participation (2001 to 2004, 2005 to 2008, 2009 to 2012, 2013 to 2016). The year of participation was included to adjust for potential changes in patient etiologies, co-morbidities, and GXT referral rates over the study period. Stratified analyses were performed by gender, age (median and quartiles), the reason for referral, and year of participation. A sensitivity analysis was performed limited to patients who completed 24 to 36 visits with an attendance frequency ≥2 days per week. Alpha level was set at 0.05. IBM SPSS Statistics for Windows version 24.0 (Armonk, New York) was used for all analyses.

Results

During the study period, 8,004 patients participated in our phase 2 CR program. Of these, 4,455 patients met the criteria for this study and had complete data. Overall, 53% had an individualized exercise target HR based on a GXT. There was significant variation in the prevalence of GXT over the study period (2001 to 2004 = 78% [n = 955 of 1220], 2005 to 2008 = 50% [n = 549 of 1,096], 2009 to 2012 = 45% [n = 488 of 1,085], 2013 to 2016 = 34% [n = 355 of 1,054], p <0.001). Each of the patient characteristics listed in Table 1 was significantly different between the GXT groups. The largest differences

Table 1
Cohort characteristics

Characteristic	All patients (n= 4,455)		Individualized target heart rate based on a graded exercise test				P-value*
			No (n= 2,108)		Yes (n= 2,347)		
Age (years)	62	(47, 76)	65	(50, 77)	60	(45, 74)	<.001
Female	1,626	(37%)	812	(39%)	814	(35%)	.01
Race							<.001
White	2,142	(48%)	1,094	(52%)	1,048	(45%)	–
Black	1,951	(44%)	823	(39%)	1,128	(48%)	–
Other	362	(8%)	191	(9%)	171	(7%)	–
Reason for referral to cardiac rehabilitation							<.001
CABG	907	(20%)	452	(21%)	455	(19%)	–
MI (no CABG)	1,507	(34%)	699	(33%)	808	(34%)	–
PCI (no CABG or MI)	631	(14%)	305	(15%)	326	(14%)	–
Valve only	197	(4%)	128	(6%)	69	(3%)	–
Heart failure only	465	(10%)	218	(10%)	247	(11%)	–
Medical therapy only	748	(17%)	306	(15%)	442	(19%)	–

Data are median (10th, 90th percentile) or n (% of group).
CABG = coronary artery bypass graft; MI = myocardial infarction; PCI = percutaneous coronary intervention.
*Between group comparison by graded exercise test group (no vs. yes).

Table 2
Cardiac rehabilitation outcomes

| Characteristic | All patients (n= 4,455) | | Individualized target heart rate based on a graded exercise test | | | | P-value* |
			No (n= 2,108)		Yes (n= 2,347)		
Visits	18	(12, 36)	18	(12, 36)	16	(12, 36)	<.001
LOS (weeks)	7.6	(4.1, 15.0)	8.4	(4.1, 15.3)	7.0	(4.1, 14.6)	<.001
Visit frequency (d•wk^{-1})	2.5	(1.6, 3.0)	2.5	(1.6, 2.9)	2.5	(1.6, 3.0)	.06
Exercise training METs							
Start	2.6	(1.8, 3.7)	2.5	(1.7, 3.3)	2.8	(2.0, 3.9)	<.001
Discharge	3.7	(2.4, 5.9)	3.3	(2.2, 5.3)	4.0	(2.8, 6.4)	<.001
Change	1.0	(0.2, 2.7)	0.7	(0.1, 2.2)†	1.1	(0.2, 3.0)†	<.001
% Change	38	(7, 96)	32	(6, 89)†	41	(7, 104)†	<.001

Data are median (10th, 90th percentile).

LOS = length of stay; METs = metabolic equivalents of task.

*Unadjusted between group comparison by graded exercise test group (yes vs. no).

† P<.001; within group comparison.

were seen with age and race. The GXT group was younger and had a greater prevalence of patients who were Black and a lower prevalence of women and patients who were White.

Apart from CR visit frequency, all CR outcomes were significantly different between GXT groups (Table 2). Patients in the GXT group attended fewer CR visits, had a shorter length of stay, started at higher exercise training METs, and had a greater increase (unadjusted) in METs during CR. Both groups had a significant increase in METs (absolute and percent change) from start to discharge during CR (Table 2).

The covariate-adjusted change in exercise training METs during CR by the GXT group is shown in Figure 1. Compared with no GXT, the GXT group had a significantly greater change in covariate-adjusted exercise METs in all patients and analyses stratified by gender and median age. In the entire cohort, patients who had a GXT exhibited nearly half a MET greater increase in their exercise workloads (adjusted between-group difference 0.44 METs [95% CI 0.38 to 0.51 METs], p <0.001) from start to discharge during CR. In addition, a GXT was associated with a significantly greater percent change from start METs during CR (adjusted between-group difference 17% [95% CI 14% to 19%], p <0.001). The adjusted between-group difference for change in exercise METs during CR was significantly greater in those with a GXT within each study period (2001 to 2004 = 0.27 METs [95% CI 0.15 to 0.40 METs]; 2005 to 2008 = 0.50 METs [95% CI 0.38 to 0.63 METs]; 2009 to 2012 = 0.42 METs [95% CI 0.29 to 0.56 METs]; 2013 to 2016 = 0.45 METs [95% CI 0.29 to 0.62 METs]).
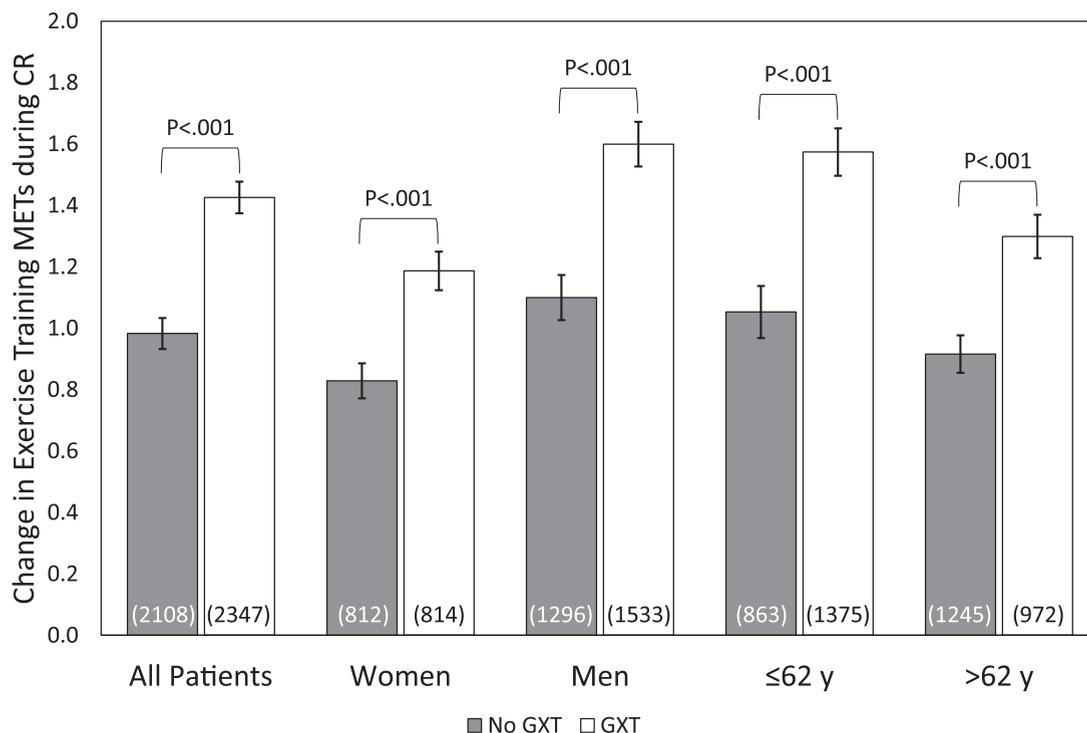

Figure 1. Covariate-adjusted change in exercise training METs from start to discharge during CR by GXT group. Bars represent mean and 95% confidence interval. Values in parentheses represent sample size of each group.
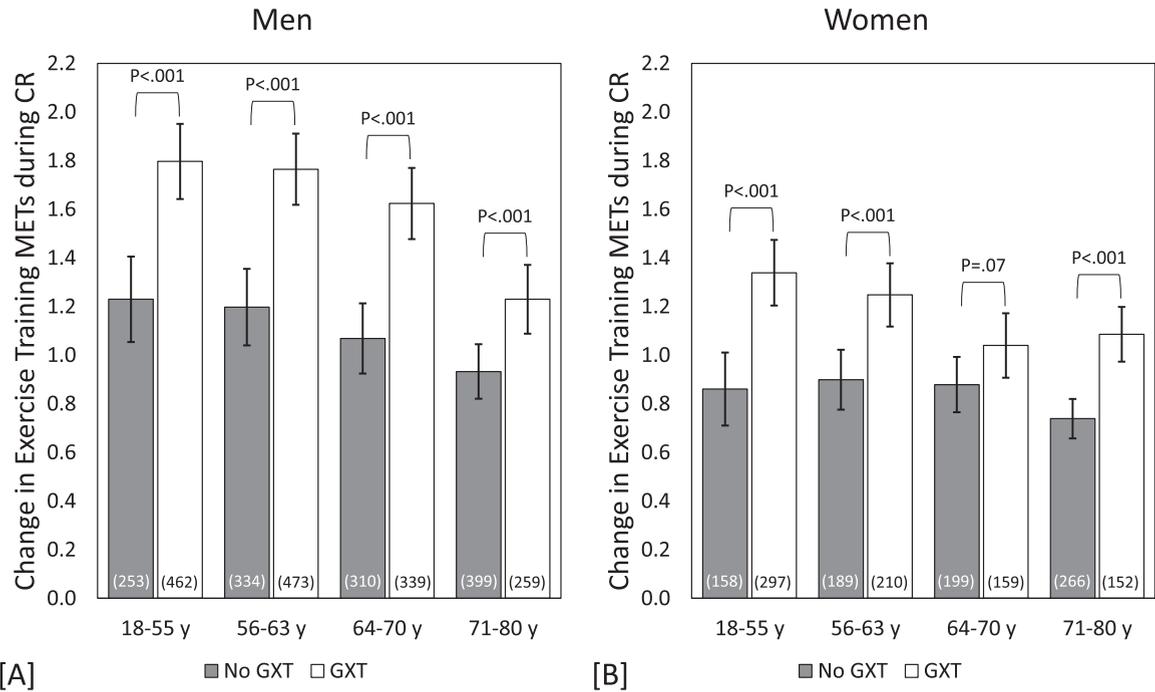
Figure 2. Covariate-adjusted change in exercise training METs from start to discharge during CR associated with a maximal GXT by age quartiles in men (*left pane [A]*) and women (*right pane [B]*). Bars represent mean and 95% confidence interval. Values in parentheses represent sample size of each group.

The GXT group had significantly greater improvements in covariate-adjusted exercise training METs during CR in all gender and age subgroups except women aged 64 to 70 years (Figure 2). This was also observed in all subgroups by gender and reason for referral to CR except for women who had coronary artery bypass graft surgery (Figure 3).

In the sensitivity analysis limited to patients who completed 24 to 36 visits of CR with an attendance frequency ≥2 days per week (n = 1,319), a GXT was associated with a significantly greater increase in covariate-adjusted exercise training METs during CR (adjusted between-group difference = 0.51 [95% CI 0.36 to 0.66], p <0.001) and percent
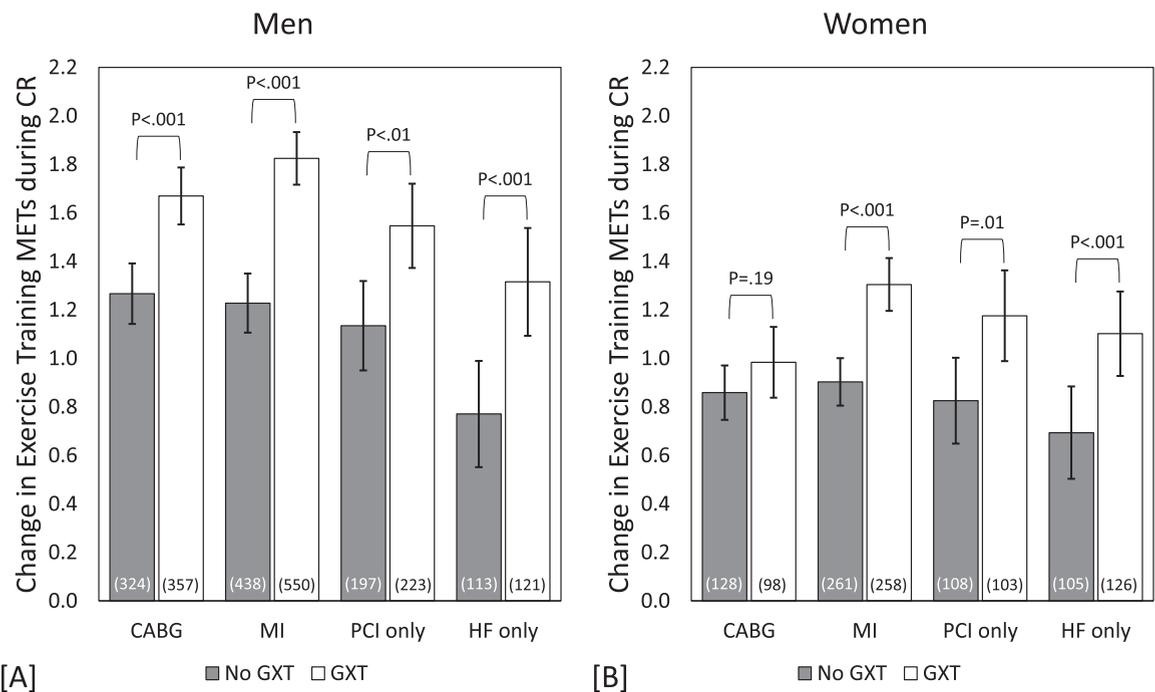

Figure 3. Covariate-adjusted change in exercise training METs during CR associated with a GXT by reason for referral to CR in men (*left pane [A]*) and women (*right pane [B]*). Bars represent mean and 95% confidence interval. Values in parentheses represent the sample size of each group. CABG = coronary artery bypass graft; HF = heart failure; MI = myocardial infarction; PCI = percutaneous coronary intervention.

change from start METs (adjusted between-group difference = 19% [95% CI 13% to 24%]; p <0.001).

Discussion

We showed that patients who were provided an individualized exercise training target HR established from a GXT experienced greater increases in exercise tolerance during CR than patients without a GXT. Patients who performed a GXT exhibited ~0.5 METs (+0.44 to 0.51 METs) greater improvement in exercise training workloads and a 17% to 19% point larger improvement from start CR. This effect was observed in nearly all subgroups. To our knowledge, this is the first study to provide data supporting the importance of a GXT to prescribe exercise intensity in patients in CR.

Although the magnitude of the effect on exercise training workloads shown in this study might not seem large, it is clinically meaningful. Each MET of exercise workload at discharge from CR is associated with a 28%[6] to 40%[13] lower adjusted risk for all-cause mortality. Based on these estimates, 0.5 MET greater improvement might translate to an additional 15% to 23% lower risk for all-cause mortality. This benefit is significant considering that the cost of a GXT (i.e., exercise stress electrocardiography) is $300 to $400. In comparison, β-blocker therapy after myocardial infarction is associated with a ~25% reduction in all-cause mortality with an annual cost of $432 per year (weighted average cost for 1998).[14] Thus, the cost-benefit of a GXT to prescribe exercise intensity in CR may be favorable to β-blocker therapy, a well-established cost-effective therapy.[14]

The importance of a GXT in conjunction with CR has been acknowledged since the 1970s. It is consistently recommended in professional guideline statements for patient risk assessment (e.g., ischemia, arrhythmias) and individualized exercise prescription.[4,10] A GXT has been described as essential to determine an effective exercise training intensity in all patients in CR.[15] Finally, a GXT meets appropriate use criteria before CR for patients with stable ischemic heart disease, with and without coronary revascularization.[16]

Without a GXT, exercise intensity is based on a one-size-fits-all approach using HR (e.g., at rest +20−30 beats) and/or patient-reported perceived exertion (e.g., Borg scale).[11,12] HR at rest +20−30 beats results in an exercise intensity at or below the recommended minimal intensity in most patients.[17,18] Although ratings of perceived exertion can be a reliable and valid method to guide exercise intensity, it is influenced by multiple factors, including age, gender, exercise experience, and self-efficacy.[19] In addition, discordance has been reported between ratings of perceived exertion and exercise HR in patients with heart disease.[20] Exercise intensity methods that are not based on a GXT may lead to self-selected pace[21] and suboptimal exercise training intensity.[22] For example, in 385 patients who completed CR, 21% failed to show an increase in peak oxygen uptake.[22] This nonresponse was associated with a lower exercise training intensity than the responders despite similar ratings of perceived exertion.[22]

Over the past 15+ years, there has been a declining rate of GXTs in CR. In 2005 (New York), the rate of GXTs in CR was 90%;[23] 70% in 2007 (Ohio);[24] 33% in 2017 (Midwest United States);[25] and 17% in 2020 (n = 246 programs in the United States).[10] We showed a similar decrease over our study period (78% to 34%). The reason for this decrease is likely multifactorial and may include equipoise in the value of a GXT for CR,[10] low event rates in CR,[26,27] and a lack of data on the benefits and risks of CR with and without a GXT, respectively.

We are aware of just 2 related studies. First, in a retrospective study of 500 patients who attended CR with and without a GXT, there was no significant between-group difference in estimated caloric expenditure during CR after 12 weeks.[28] Exercise training workloads were not reported, so it is unknown whether the change in caloric expenditure was due to changes in workloads, exercise duration, or exercise mode. Second, in a trial of 78 patients with heart disease who were randomized to (1) a target HR from a GXT, (2) a target HR from a GXT plus ratings of perceived exertion, or (3) ratings of perceived exertion after 2 sessions guided by a target HR from a GXT, there was no significant difference for change in exercise capacity across groups.[29] Because the perceived exertion group had a GXT and were familiarized with an HR-based intensity, they are not representative of patients who participate in CR without a GXT. Despite this, the 8% greater increase in exercise capacity after 1 month of CR in the HR groups than in the perceived exertion group[29] is consistent with the present study (+17% after 2 months).

This study is not without limitations. First, there is a potential selection bias that may have resulted in healthier, more functional patients being scheduled for a GXT more often than less healthy patients. However, consistent with national trends, the prevalence of GXTs in our cohort decreased over time (from 78% to 34%), and the effect of GXT on change in exercise training METs was constant over the study period, suggesting that any selection bias was heterogeneous. We attempted to control for this bias by adjusting for characteristics that might be related to exercise response. Second, we were limited to available data in our outcomes database. Physical activity habits outside of CR and the timing of the GXT relative to the start of CR are 2 examples that might minimize residual confounding. A prospective trial in which patients are randomized to participate in CR with versus without a GXT would address these limitations.

In conclusion, an important component of CR is exercise training to increase exercise capacity. To maximize the potential increase in exercise capacity, patients should undergo a maximal GXT to determine an individualized exercise training target HR.

Disclosures

The authors have no conflicts of interest to declare.

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