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Effect of Chronic Kidney Disease and Supplemental Polyunsaturated Fatty Acid Use on Exercise Levels During Cardiac Rehabilitation in Patients With Coronary Artery Disease

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Abstract

PURPOSE—The correlation between chronic kidney disease (CKD) and increased cardiovascular disease-related mortality is well established. Cardiac rehabilitation (CR) improves exercise capacity, quality of life, and risk factors in patients with coronary artery disease (CAD). Data on the benefits of CR in patients with CKD are sparse.

To compare outcomes after CR in patients with CAD but normal renal function, versus those with CAD and CKD.

METHODS—We studied 804 patients with CAD entering an exercise-based CR program. Demographics, risk factors, exercise capacity in metabolic equivalent levels (METs), and estimated glomerular filtration rate (GFR) were recorded before and after the 3-month CR program. Use of polyunsaturated fatty acid (PUFA) was determined by medical records review. Stage III–V CKD (GFR <60 mL/min/1.73 m²) was present in 167 patients at baseline.

RESULTS—After CR, METs improved in all patients, although increases in patients with a GFR 30 to 59 mL/min/1.73 m² (1.6) and a GFR <30 (1.3) were smaller than those in patients with a GFR ≥60 (2.6, $P < .05$ vs GFR 30–59 and GFR <30). In patients with a GFR ≥60 mL/min/1.73 m², PUFA use was associated with a 20% greater increase in MET levels compared with nonusers (3.0 vs 2.5, $P = .02$); and in patients with a GFR 30 to 59, PUFA use was associated with 30% increase in MET level compared with nonusers (2.0 vs 1.4, $P = .03$). These observations persisted after multivariable adjustment for baseline MET level, demographics, and risk factors.

CONCLUSIONS—Potential mitigation by PUFA of the smaller improvement in exercise capacity with decreasing GFR requires confirmation in prospective randomized trials.

Keywords

cardiac rehabilitation; fish oil; kidney disease; polyunsaturated fatty acids

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Chronic kidney disease (CKD) is increasing in prevalence in the United States.^{1,2} Previous studies have shown that prevalent CKD is an independent risk factor for subsequent cardiovascular disease and correlates with both an increased cardiovascular and all-cause mortality.^{3,4} Impaired exercise tolerance is common with CKD for several reasons specific to that condition. In CKD, both structure and function of skeletal muscle are deranged,^{5–7} which may be exacerbated by the associated metabolic acidosis.⁵ In addition, energy production by mitochondria is also reduced in CKD.^{8–14} Despite these physical derangements, exercise capacity may be improved in such patients.^{15,16} Cardiac rehabilitation (CR) improves exercise capacity and outcomes among patients with coronary artery disease (CAD),¹⁷ but the effect of CR on patients with coexisting CKD is sparse.¹⁸

The aim of this study was therefore to compare the outcomes after CR in patients with CAD and normal renal function with those of patients with both CAD and CKD.

Polyunsaturated fatty acids (PUFAs) have been reported to improve exercise capacity in patients with cardiovascular disease and chronic obstructive pulmonary disease.^{19,20} There have also been some suggested benefits of PUFA in patients with CKD.^{21,22} Therefore, the use of fish oil during CR was assessed to identify any effect on outcomes in our patients.

METHODS

Between 2004 and 2012, 804 patients were enrolled in an outpatient CR program at Wake Forest Baptist Medical Center. Serum creatinine levels were measured within 30 days before they began CR. The Wake Forest Baptist Medical Center Institutional Review Board approved the use of patients' medical records to collect clinical data.

Patients CR had undergone interventions for CAD, including cardiac catheterization, percutaneous coronary intervention, and/or coronary artery bypass surgery. Glomerular filtration rate (GFR) was estimated using the isotope dilution mass spectrometry-traceable Modification of Diet in Renal Disease (MDRD) Study method and collected within 30 days before the start of CR and within 30 days after the last CR session. The "4-variable" modification of the MDRD Study equation uses age, sex, race (African American vs non-African American), and serum creatinine (Cr) as follows: $GFR (mL/min/1.73 m^2) = 175 \times (S_{Cr})^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$.²³ Patients were stratified into 3 groups on the basis of a $GFR > 60 mL/min/1.73 m^2$ (non-CKD patients and Stage I-II CKD, $n = 634$); 30 to $59 mL/min/1.73 m^2$ (Stage III CKD, $n = 148$); and $< 30 mL/min/1.73 m^2$ (Stage IV–V CKD and/or on dialysis, $n = 22$, 16 of whom were dialysis patients). CKD stages were defined according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI)²⁴ (Figure 1). The diagnosis of Stage I CKD ($GFR > 90 mL/min/1.73 m^2$) and Stage II CKD ($GFR 60–89 mL/min/1.73 m^2$) requires urine findings, structural abnormalities, or presence of genetic traits suggestive of kidney disease; these factors were not assessed during this study. For simplicity, patients with a $GFR \geq 60 mL/min/1.73 m^2$ are referred to as non-CKD patients, although these patients could have Stage I or Stage II CKD.

Details of our CR program have been previously reported.²⁵ It lasted 12 weeks (three 30- to 40-minute sessions per week of upper and lower body exercises with exercise machines). Clinical status was used by an exercise physiologist to develop an individualized exercise plan.²⁶

At each visit, vital signs were recorded before each session, including height, weight, systolic and diastolic pressures, and heart rate. In our program, exercise comprises upper and lower body training methods including walking laps on a track, cycle ergometry, treadmills, and stair climbers. The emphasis is on a mixture of modes of aerobic exercise although as well as light resistance exercises using elastic bands are used at the end of each session.

Metabolic equivalent (MET) levels were recorded at each session and obtained either automatically from exercise devices or using a standardized and validated MET formula from the American College of Sports Medicine²⁷ during the aerobic phase of exercise after the participants were roughly half-way through each session. The goal is to increase exercise over the previous session as tolerated to a rating of perceived exertion of 11 to 14 on a 6- to 20-point Borg scale.²⁷ The MET level for that, and each subsequent, visit was the greatest level of exertion for the patient for that visit. The MET level at the first visit was the baseline. We noted the highest MET level attained at any time after baseline measurement. The difference between this and the baseline level is the change, and this is what we report in the various groups. In this manner, we were able to track temporal escalation of sessional MET levels as the patients advanced through the program.

Hypertension was defined according to the guidelines JNC 7.²⁸ Baseline blood pressure was defined as the first measurement taken, and the postblood pressure was the last measurement for each patient. The Ferrans and Powers Quality of Life Index²⁹ was tested by questionnaires. This validated instrument³⁰ tests overall quality of life, health and functioning, psychological well-being, social and economic satisfaction, and family contentment. It was administered routinely by nursing staff in our program. Quality-of-life scores were calculated before and after CR. Left ventricular function was measured by standard techniques.³¹ Lipid goals were defined in accordance with the Adult Treatment Panel III guidelines.³² The use of fish oil (PUFA) by each patient was determined by medical record review.

Statistical Analysis

Descriptive statistics (frequency and percentage for categorical variables, mean and standard deviation for continuous variables) were calculated and compared at baseline for statistical significance using χ^2 or Fisher exact tests for categorical variables and *t* tests for continuous variables. For baseline statistics we used standard deviations, and for absolute differences we used 95% CI. Absolute changes were calculated as mean (95% CI) of postrehabilitation minus baseline levels, and compared using analysis of variance with F-testing. We evaluated all patient demographic and clinical variables from Table 1 for the multivariate models. The dependent variable was absolute change in METs from baseline accounting for baseline differences between the groups. Multivariable linear regression models were constructed with increase in METs from baseline as the dependent variable. Independent predictors were selected for inclusion using a backward selection methodology. All potentially significant

univariate predictors of exercise capacity ($P < .10$) were included in the model, and the least significant covariates were removed individually until all remaining covariates were statistically significant predictors of exercise capacity. Two- and 3-way interaction terms between independent predictors in the final models were further tested for statistical significance. A P value of .05 was considered statistically significant. The SAS version 9.3 statistical software package (SAS Institute, Cary, NC) was used for all statistical analyses.

RESULTS

Baseline patient demographics and clinical characteristics by GFR are shown in Table 1. Compared with patients with a GFR ≥ 60 mL/min/1.73 m², those with a GFR < 60 were more likely to be of nonwhite race and had a lower body mass index ($P < .05$ for both). A GFR < 60 mL/min/1.73 m² was also associated with higher prevalence of diabetes, more single-vessel disease, lower quality of life, and lower exercise capacity ($P < .05$ for all). PUFAs were used by approximately 25% of all patients, regardless of GFR ($P > .05$).

After CR, all patients saw statistically significant improvements in exercise capacity, quality of life, and weight, regardless of baseline GFR. Patients with a GFR ≥ 60 mL/min/1.73 m² had significant improvements in all usual CR metrics (Table 2). Increase in exercise capacity was greatest in patients with a baseline GFR ≥ 60 mL/min/1.73 m². Significant correlation between the baseline MET and both the change and highest MET was found (Spearman coefficient $r = 0.22$, and $r = 0.69$, $P < 0.001$ for both). Patients with a GFR < 60 mL/min/1.73 m² also saw significant improvements, albeit to a lesser degree. Patients with a GFR ≥ 60 mL/min/1.73 m² had the greatest improvement in low-density lipoprotein (LDL); patients with a GFR < 30 mL/min/1.73 m² showed little to no improvement in LDL. High-density lipoprotein (HDL) improved in patients with a GFR ≥ 60 mL/min/1.73 m² and in those with a GFR 30 to 59 mL/min/1.73 m², but not in those with a GFR < 30 mL/min/1.73 m².

Within patients with a GFR ≥ 30 mL/min/1.73 m², PUFA use was associated with significantly greater improvements in MET levels regardless of GFR (Table 3). Among patients with a GFR ≥ 60 mL/min/1.73 m² and in those with a GFR 30 to 59 mL/min/1.73 m², PUFA use was associated with a statistically significant increase in MET level compared with nonusers. In addition, in those with a GFR 30 to 59 mL/min/1.73 m² greater weight loss occurred among PUFA users compared with non-users (4.0 vs 1.5, Figure 1). There were insufficient data in patients with a GFR < 30 mL/min/1.73 m² to assess any effects of PUFA use.

Following multivariable adjustment, a GFR 30 to 59 mL/min/1.73 m² was independently associated with decreased improvement in MET levels relative to a GFR ≥ 60 mL/min/1.73 m² ($\beta = -0.39$), while controlling for other covariates in the model. In addition to decreased GFR, increased age, female sex, increased baseline body mass index, and ejection fraction $< 35\%$ were significant independent predictors of decreased exercise capacity. Baseline MET, PUFA use, and total number of CR sessions attended were significant independent predictors of increased exercise capacity. The details of the multivariate analysis of change in exercise capacity are shown in Table 4.

The outcomes, which we have included in our results, are shown with those of previous studies for comparison in Table 5.

DISCUSSION

The literature on CR in patients with CKD remains sparse, and data are difficult to compare because of population differences and varying endpoints.^{18,33,34} In our patients, we found that CKD was common. Furthermore, CKD negatively impacted the improvement in exercise capacity in patients with CAD, but this could be partially mitigated by the use of PUFA.

In a previous study, Venkataraman et al¹⁸ reported on 115 patients with CKD undergoing CR; however, weight, diastolic blood pressures, statin usage, effects on renal function, and outcomes in dialysis patients were not reported. In a recent registry-based study from Germany, Völler et al³⁴ described outcomes in more than 35 000 patients with CKD who had undergone CR. These patients were older (mean age 72 years) and 97% had undergone a 3-week in-hospital CR program. Takaya et al³³ reported the effects of a 3-month outpatient-based CR program on renal function. There were notable baseline differences compared with other studies: the mean body mass index of the patients in the Japanese study was 22.9 (compared with 26 in Germany,³⁴ 30 in the year 2005 in Alabama,¹⁸ and 28 in our current study). In addition, in the Japanese study, 70% were smokers, 5 to 10 times greater than other studies. These authors did not report the effects of CR on risk factors. The effects of CR on risk factors and GFR in these studies are displayed in Table 5 (findings in our study are also shown for ease of comparison). Some of the differences may be due to differences in practice guidelines and/or program duration. For example, in our study, between 80% and 90% of our patients were taking a statin, whereas Venkataraman et al¹⁸ did not report data on statin usage, and in Germany, the CR program usually lasted only 3 weeks.³⁴

In common with the other studies of CR,^{18,33,34} and with observations of CKD in general,^{35,36} our patients began at a lower exercise capacity than those with normal renal function. Venkataraman et al¹⁸ used a 6-minute walk and showed an improvement in exercise capacity with CR in patients with CKD, similar to that of Völler et al.³⁴ Takaya et al³³ demonstrated an increase in $\dot{V}O_2$ using cycle ergometry. In our patients with Stage III CKD, using estimated MET levels, exercise capacity also increased and, although this improvement was less than in patients with no CKD, may have been further enhanced by the use of PUFA although the mechanism(s) are unclear. Decreased exercise capacity in patients with CKD is multifactorial. Skeletal muscular dysfunction plays an important role,^{37–39} and dysfunction of mitochondria, the primary source for energy production, may contribute.^{9–11,13,40} Increased exercise capacity in PUFA users with chronic obstructive lung disease and nonischemic cardiomyopathy^{19,20} may be due to improved muscle metabolism²⁰ and/or mitochondrial synthesis and function.^{41–43} Regardless of the mechanism, the findings are consistent with a beneficial effect of PUFA use on exercise capacity in patients with CKD,^{21,22,44} an area of active investigation in this patient group.⁴⁵

In previous studies,^{18,33,34} no data on patients on dialysis were reported. We found no outcome differences between patients with a GFR less than 30 (not on dialysis) and those on

dialysis and merged their data in statistical analyses, and so included them together. Despite other improvements, we found no significant change in LDL, HDL, triglycerides, or blood pressure after CR. We could not assess the effect of PUFA in the dialysis group as only 3 patients were users.

Limitations of the current study are that it was at a single site and retrospective with possible inherent selection bias especially for PUFA use. Serial creatinine levels were not recorded, so we could not document sustained renal impairment for a minimum of 3 months, the criterion for CKD according to the NKF KDOQI.²⁴ Renal pathology, renal imaging, or proteinuria was not evaluated to identify patients with a GFR < 60 mL/min/1.73 m² with Stage I or Stage II CKD. Differences between normal estimated GFR and patients with CKD included an increase of 8 years in mean age and higher proportion of women (33% vs 24%) in patients with CKD although the main findings remained robust after adjustment in multivariate analysis. PUFA use during CR was determined by medical records review and is given here as a dichotomous variable as details of dose and type of pharmaceutical preparation were not available in all patients. Reported MET levels were calculated from moderate-intensity exercises without more precise formal stress or metabolic testing. In addition, the same exercise device was not used for each patient for each MET level. However, our previously reported investigations without stress tests^{25,46} concur qualitatively with other studies using formal treadmill exercise testing.^{47,48} Finally, we did not evaluate muscle function, which may be adversely affected in patients with CKD. CR nevertheless benefits patients with CKD, even in those receiving dialysis, enhancing exercise capacity and improving weight. Furthermore, these effects may be enhanced by the adjunctive use of PUFA. The hypothesis generated by our data should be formally tested, avoiding these shortcomings, in well-designed prospective, randomized clinical trials.

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Figure 1.

Effect of fish oil on exercise and weight loss in patients with a GFR 30 and 59 mL/min/1.73 m² showing greater weight loss among PUFA users compared with nonusers (4.0 vs 1.5) in patients with CKD and CAD undergoing cardiac rehabilitation. Abbreviations: CAD, coronary artery disease; CKD, chronic kidney disease; GFR, glomerular filtration rate; METs, metabolic equivalents; PUFA, polyunsaturated fatty acid.

Table 1Baseline Patient Characteristics by Renal Function at Start of Cardiac Rehabilitation^a

	GFR, mL/min/1.73 m ²		
	60 (n = 634)	30–59 (n = 148)	<30 or on Dialysis (n = 22)
Demographics			
Age, y	60.1 ± 11.1	68.3 ± 10.4 ^b	64.4 ± 10.8
Male sex	484 (76)	99 (67) ^b	14 (64)
Nonwhite race	91 (14)	15 (10)	11 (50) ^c
Clinical			
Quality of life	22.4 ± 4.5	22.6 ± 3.9	19.9 ± 4.7 ^c
Current smoker	65 (10)	10 (7)	4 (18)
Blood pressure			
SBP, mm Hg	121.0 ± 17.7	121.0 ± 22.2	136.7 ± 24.7 ^c
DBP, mm Hg	70.7 ± 9.6	67.7 ± 11.0 ^b	73.7 ± 11.5
Resting HR, bpm	76.6 ± 14.1	74.4 ± 13.3	77.7 ± 17.6
Lipids			
LDL, mg/dL	101.4 ± 41.6	95.4 ± 37.2	88.4 ± 70.2
HDL, mg/dL	40.1 ± 17.0	39.1 ± 10.9	39.3 ± 14.1
TG, mg/dL	149.1 ± 125.7	161.2 ± 118.3	139.0 ± 77.2
Diabetes mellitus	172 (27)	59 (40) ^b	15 (68) ^c
Glucose, mg/dL	107.2 ± 32.9	105.0 ± 25.1	122.8 ± 46.0
Ejection fraction, %	49.1 ± 11.6	46.9 ± 14.3	48.9 ± 13.3
Multivessel CAD, n (%)	454 (72)	112 (76)	12 (55) ^c
BMI, kg/m ²	29.3 ± 5.9	28.8 ± 5.5	26.6 ± 5.8 ^b
Weight, lb	196.8 ± 42.7	190.3 ± 40.3	176.5 ± 45.8 ^b
Waist circumference, in	40.9 ± 5.3	40.9 ± 5.2	39.1 ± 6.8
Serum creatinine, mg/dL	0.9 ± 0.2	1.4 ± 0.3 ^b	4.7 ± 2.8 ^b
GFR, mL/min/1.73 m ²	90.1 ± 29.4	50.6 ± 7.1 ^b	19.5 ± 12.4 ^c
BUN, mg/dL	14.7 ± 5.4	22.5 ± 8.8 ^b	40.2 ± 18.5 ^c
Reason for referral			
PCI	352 (56)	74 (50)	7 (32) ^b
CABG	181 (29)	42 (28)	5 (23)
Other	101 (16)	32 (22)	10 (45) ^c
Medications, n (%)			
β-Blockers	583 (92)	129 (87)	20 (91)
ACE inhibitors	403 (64)	102 (69)	16 (73)
Statins	568 (90)	133 (90)	18 (82)
PUFA	146 (24)	38 (26)	5 (23)
METs	2.8 ± 0.9	2.4 ± 0.8 ^b	2.1 ± 0.4 ^c

	GFR, mL/min/1.73 m ²		
	60 (n = 634)	30–59 (n = 148)	<30 or on Dialysis (n = 22)
CR sessions attended, n	26.4 ± 12.0	26.5 ± 12.1	23.9 ± 12.8

Abbreviations: ACE, angiotensin-converting enzyme; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CR, cardiac rehabilitation; DBP, diastolic blood pressure; GFR, glomerular filtration rate; HDL, high-density lipoprotein; HR, heart rate; LDL, low-density lipoprotein; METs, metabolic equivalents; PCI, percutaneous coronary intervention; PUFA, polyunsaturated fatty acid; SBP, systolic blood pressure; TG, triglycerides.

^aData expressed as number (%) or mean ± standard deviation.

^b $P < .05$ versus GFR ≥ 60.

^c $P < .05$ versus GFR 30 to 59 and ≥ 60.

Table 2

Metrics After Cardiac Rehabilitation by Baseline Renal Function

	GFR, mL/min/1.73 m ²					
	60 (n = 634)			30–59 (n = 148)		
	n	Mean Difference (95% CI)	n	Mean Difference (95% CI)	n	Mean Difference (95% CI)
METs achieved	634	2.6 (2.4 to 2.8)	148	1.6 (1.3 to 1.8) ^a	22	1.2 (0.6 to 1.8) ^a
Quality of life	243	1.9 (1.5 to 2.2)	75	1.9 (1.2 to 2.5)	6	3.2 (0.3 to 6.0)
Weight, lb	534	−3.5 (−4.1 to −2.8)	132	−2.2 (−3.4 to −0.9)	16	−2.0 (−4.0 to 0.0)
BMI, kg/m ²	510	−0.6 (−0.7 to −0.5)	124	−0.4 (−0.7 to −0.2)	15	−0.2 (−0.6 to 0.2)
SBP, mm Hg	553	−4.0 (−5.4 to −2.5)	133	−0.9 (−4.3 to 2.4)	16	−6.2 (−21.4 to 9.0)
DBP, mm Hg	550	−1.7 (−2.6 to −0.8)	132	0.1 (−2.2 to 2.4)	16	−2.9 (−9.4 to 3.5)
LDL, mg/dL	427	−20.5 (−24.2 to −16.8)	96	−16.3 (−23.0 to −9.6)	15	−6.1 (−25.1 to 13.0)
HDL, mg/dL	440	1.3 (0.2 to 2.3)	101	3.2 (1.6 to 4.9) ^a	15	3.9 (−7.3 to 15.1)
TG, mg/dL	438	−28.5 (−39.8 to −17.1)	101	−10.7 (−35.0 to 13.5)	15	−4.5 (−41.5 to 32.6)
Serum creatinine, mg/dL	125	0.1 (0.0 to 0.1)	40	0.0 (−0.1 to 0.1)	8	0.9 (−1.0 to 2.9)
GFR, mL/min/1.73 m ²	125	−81 (−12.2 to −4.1)	40	1.9 (−2.0 to 5.8) ^a	8	0.1 (−3.6 to 3.7) ^a
BUN, mg/dL	124	3.0 (1.1 to 5.0)	40	2.0 (−0.6 to 4.6)	8	6.8 (−18.5 to 32.0)

Abbreviations: BMI, body mass index; BUN, blood urea nitrogen; DBP, diastolic blood pressure; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; METs, metabolic equivalents; SBP, systolic blood pressure; TG, triglyceride.

^a $P < .05$ versus GFR 60 mL/min/1.76 m².

Metrics After Cardiac Rehabilitation by Renal Function at Baseline and Polyunsaturated Fatty Acid Use^a

Table 3

	GFR 60 mL/min/1.73 m ² (n = 618) ^b			GFR 30–59 mL/min/1.73 m ² (n = 148)		
	PUFA (n = 146)	No PUFA (n = 472)	P Value ^c	PUFA (n = 38)	No PUFA (n = 110)	P Value ^c
METs achieved	3.0 (2.6 to 3.4)	2.5 (2.3 to 2.7)	.02	2.0 (1.4 to 2.5)	1.4 (1.1 to 1.7)	.03
QoL	1.3 (0.6 to 2.0)	2.1 (1.6 to 2.5)	.12	3.0 (1.6 to 4.4)	1.4 (0.7 to 2.2)	.03
Weight, lb	−3.6 (−4.9 to −2.3)	−3.4 (−4.2 to −2.6)	.48	−4.0 (−6.1 to −1.8)	−1.5 (−3.0 to 0.0)	.07
BMI, kg/m ²	−0.7 (−1.0 to −0.4)	−0.6 (−0.7 to −0.4)	.27	−0.6 (−0.9 to −0.2)	−0.4 (−0.7 to −0.1)	.28
SBP, mm Hg	−2.4 (4.8 to 0.0)	−4.4 (−6.2 to −2.6)	.29	−0.5 (−5.7 to 4.8)	−1.1 (−5.3 to 3.0)	.83
DBP, mm Hg	−0.3 (−1.7 to 1.2)	−2.1 (−3.2 to −1.0)	.10	1.3 (−2.5 to 5.0)	−0.4 (−3.2 to 2.5)	.62
LDL, mg/dL	−19.5 (−27.5 to −11.5)	−21.8 (−26.1 to −17.5)	.60	−20.4 (−34.5 to −6.2)	−14.8 (−22.5 to −7.0)	.47
HDL, mg/dL	2.6 (0.8 to 4.4)	0.8 (−0.5 to 2.1)	.13	3.1 (−0.1 to 6.3)	3.3 (1.3 to 5.3)	.70
TG, mg/dL	−31.0 (−47.9 to −14.2)	−28.7 (−43.2 to −14.2)	.22	−27.2 (−61.3 to 6.9)	−4.4 (−35.6 to 26.8)	.38

Abbreviations: DBP, diastolic blood pressure; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent; PUFA, polyunsaturated fatty acid; QoL, quality of life; SBP, systolic blood pressure; TG, triglyceride.

^aData expressed as mean difference (95% CI).

^b16 patients with no PUFA data.

^cWilcoxon rank sum test of PUFA versus no PUFA.

Table 4

Multivariate Predictors of Significant Change in METs From Baseline

Model, n = 775 ^a	Parameter Estimate	Standard Error	P Value
MET, 1	0.40	0.08555	<.0001
GFR 30–59 vs 60, mL/min/1.73 m ²	−0.465	0.18043	.030
Age, per 10 y	0.514	0.06889	<.0001
Female sex	−0.750	0.15982	<.0001
Baseline BMI, kg/m ²	−0.037	0.01214	.002
Ejection fraction <35%	−0.496	0.21185	.020
PUFA use	0.416	0.15723	.008
CR sessions attended	0.082	0.00578	<.0001

Abbreviations: BMI, body mass index; CR, cardiac rehabilitation; GFR, glomerular filtration rate; MET, metabolic equivalent; PUFA, polyunsaturated fatty acid.

^aOnly patients with no missing data for covariates included in the model. Parameter estimates indicate the multivariable-adjusted absolute mean change in metabolic equivalents from baseline associated with each covariate.

Table 5
Comparison of Risk Factor Change With Cardiac Rehabilitation in Current and Previous Studies

eGFR, mL/min/1.73 m ²	LDL, mg/dL	HDL, mg/dL	TG, mg/dL	SBP, mm Hg	DBP, mm Hg	Wt, lb	BMI, kg/m ²	eGFR, mL/min/1.73 m ²
Pflum et al								
60	-20.5	1.3	-28.5	-4.0	-1.7	-3.5	-0.6	-8.1
30-59	-16.3	3.2	-10.7	-0.9	-0.1	-2.2	-0.4	1.9
<30	-6.1	3.9	-4.5	-6.2	-2.9	-2.0	-0.2	0.1
Takaya et al ³³								
60	— ^a	—	—	—	—	—	-0.2	0.0
<60	—	—	—	—	—	—	-0.2	3.0
Venkataraman et al ¹⁸								
60	-17.0	1.0	-18.0	-2.0	—	—	-0.5	—
<60	-14.0	0.5	-13.0	-2.0	—	—	-0.2	—
Völler et al ³⁴								
60	-28.0	0.0	-21.0	—	—	—	—	—
<60	-27.0	1.0	-19.0	—	—	—	—	—

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; —, change after cardiac rehabilitation; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; TG, triglyceride;

^aNot reported.