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ORIGINAL ARTICLE

Association between obesity and health-related quality of life in patients with coronary artery disease

A Oreopoulos[1], R Padwal[2,3], FA McAlister[2,3], J Ezekowitz[3,4], AM Sharma[5], K Kalantar-Zadeh[6], GC Fonarow[7] and CM Norris[1,8]

[1]*Department of Clinical Epidemiology, School of Public Health, University of Alberta, Edmonton, Alberta, Canada;* [2]*Division of General Internal Medicine, University of Alberta, Edmonton, Alberta, Canada;* [3]*Mazankowski Heart Institute, Edmonton, Alberta, Canada;* [4]*Division of Cardiology, University of Alberta, Edmonton, Alberta, Canada;* [5]*Division of Endocrinology, University of Alberta, Edmonton, Alberta, Canada;* [6]*Division of Nephrology and Hypertension, Harbor-UCLA Medical Center, Torrance, CA, USA;* [7]*Division of Cardiology, David Geffen School of Medicine at UCLA, Ahmanson-UCLA Cardiomyopathy Center, Los Angeles, CA, USA and* [8]*Faculty of Nursing, University of Alberta, Edmonton, Alberta, Canada*

Background and Objective: In patients with coronary artery disease (CAD), obesity is paradoxically associated with better survival (the 'obesity paradox'). Our objective was to determine whether this counterintuitive relationship extends to health-related quality of life (HRQOL) outcomes.
Design: Cross-sectional observational study.
Subjects: All adults undergoing coronary angiography residing in Alberta, Canada between January 2003 and March 2006 in the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) registry.
Methods: Patients completed self-reported questionnaires 1 year after their index cardiac catheterization, including the Seattle Angina Questionnaire (SAQ) and the EuroQol 5D (EQ-5D Index). Patients were grouped into six body mass index (BMI) categories (underweight, normal, overweight, mild obesity, moderate obesity and severe obesity). An analysis of covariance was used to create risk-adjusted scores.
Results: A total of 5362 patients were included in the analysis. Obese patients were younger than normal and overweight participants, and had a higher prevalence of depression and cardiovascular risk factors. In the adjusted models, SAQ physical function scores and the EQ Index (representing overall QOL) were significantly reduced in patients with mild, moderate and severe obesity compared with patients with a normal BMI. Patients with severe obesity had both statistically and clinically significant reductions in HRQOL scores. Depressive symptoms accounted for a large proportion in variability of all HRQOL scores.
Conclusions: BMI is inversely associated with physical function and overall HRQOL in CAD patients, especially in patients with severe obesity. High body weight is a modifiable risk factor; however, given the apparent obesity paradox in patients with CAD, it is critical that future studies be conducted to fully clarify the relationships between HRQOL and body composition (body fat and lean mass), nutritional state and survival outcomes.
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Introduction

Two recent meta-analyses in the coronary artery disease (CAD) population have reported counterintuitive associations between obesity and clinical outcomes.[1,2] Specifically, studies have shown that being overweight or obese (body mass index (BMI) of $\geqslant 25\,kg\,m^{-2}$) is associated with greater survival in CAD patients, whereas a normal or 'ideal' BMI confers higher all-cause and cardiovascular mortality, a phenomenon known as the 'obesity paradox' or 'reverse epidemiology'.[3] In addition, an investigation by our group identified the same paradoxical association between BMI and survival in a large cohort of patients with established CAD, irrespective of initial treatment strategy. Patients with mild or moderate obesity treated with either revascularization or medical management were at lower adjusted risk of mortality when compared with patients with a normal BMI.[4]

The previous literature in health-related quality of life (HRQOL) and obesity in CAD is limited to intervention studies, specifically analyzing the effect of weight loss from

Correspondence: Dr R Padwal, Internal Medicine and Clinical Pharmacology, University of Alberta, 2F1.26 Walter C Mackenzie HSC, 8440-112th Street, Edmonton, Alberta T6G2B7, Canada.
E-mail: rpadwal@ualberta.ca
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cardiac rehabilitation on HRQOL.[5–8] Although it has been observed that cardiac rehabilitation is associated with positive changes in HRQOL,[7] previous studies have not separated patients by different degrees of obesity, nor have they compared HRQOL or changes in HRQOL between obese and non-obese subjects. Although it is known that obesity is associated with depression[9] and worse HRQOL outcomes in the general population,[10–12] it is not clear whether the paradoxical relationship between increased BMI and survival in patients with CAD extends to HRQOL outcomes. In other words, we aimed to answer the question: Does increasing BMI lead to better HRQOL in patients with CAD?

Materials and methods

We examined a comprehensive, prospective longitudinal inception cohort of all adult patients undergoing coronary angiography in Alberta, Canada between 1 January 2003 and 31 March 2006 using data from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) registry. The APPROACH registry is a population-based database that prospectively captures all cardiac catheterizations performed in the province of Alberta, Canada (population of $\sim$3.3 million) since 1995. Details of the database and methods of data collection have been previously described.[13] Clinical information (socio-demographics and co-morbidities) as well as the results from catheterization are collected in the APPROACH database in the catheterization laboratory from the patient's charts. Individuals in the registry are followed longitudinally, allowing for assessment of outcomes of quality of life in patients who consent to follow-up.

Eligible subjects included all Alberta residents over the age of 18 years, with at least single-vessel CAD (Duke Coronary Index between 3 and 13)[14], a BMI of $\geqslant 18.5\,kg\,m^{-2}$ and who had not previously undergone catheterization. All eligible patients were approached consecutively for consent at the time of catheterization. Consenting patients who underwent catheterization between 1 January 2003 and 31 March 2006 were studied.

Questionnaire packages were mailed at 1 year after the initial catheterization. Patients could either complete the package and mail the questionnaires back in a stamped addressed envelope or telephone using a toll free line and respond to a verbally administered questionnaire. A second questionnaire package was mailed to non-responders 13 months after catheterization with the same options for completion, and a final reminder at 15 months. The questionnaire package included the Seattle Angina Questionnaire (SAQ), a 19-item disease-specific HRQOL instrument, and the EuroQol 5D (EQ-5D), a generic five-item HRQOL instrument.

Weight and height were collected from the admission assessment on the patients' chart. Patients who were stable from a cardiovascular perspective before catheterization had their weight and height measured by a nurse. Patients who arrived from the emergency department before catheterization had their weight and height established through self-report. The BMI is automatically calculated using the metric formula BMI = weight (kg)/height^2 (m^2), by the APPROACH registry software. Patients with BMI values of $>70\,kg\,m^{-2}$ were excluded from the analysis as these values were deemed likely to be erroneous because of the 200 kg weight limit of the cardiac catheterization table.

Outcome measures

The SAQ is a 19-item HRQOL instrument specific for CAD.[15] The SAQ was used to assess four domains of health status including: physical limitation, angina frequency, treatment satisfaction and disease perception. The SAQ physical limitation scale measures the degree to which daily activities are limited by patients' coronary disease, whereas the anginal frequency scale measures the frequency of angina during the previous 4 weeks. The disease perception scale measures the symptom burden of coronary disease perceived by the patient and its effect on their QOL. Each question is measured on an ordinal scale from 1 to 5. Scale scores are then transformed to a 0–100 range by subtracting the lowest possible score, dividing by the range of the scale and multiplying by 100. A higher score indicates better function, fewer symptoms and better QOL.

The EQ-5D is a five-item generic health status instrument describing mobility, self-care, usual activities, depression and anxiety, and pain/discomfort.[16] Scores for the five health states were converted into a utility index score ranging from 0 to 1.0 (the EQ Index) using scores from value sets (preference weights) elicited from a North American population.[17]

The Centre for Epidemiologic Studies Short Depression Scale (CES-D) was also included in the questionnaire packages. The CES-D is a 10-item scale with four responses each, designed to measure depressive symptoms.[22] A higher total score indicates worse depressive symptomatology, and a CES-D score of $\geqslant 10$ has been used to indicate depression based on DSM III (Diagnostic and Statistical Manual of Mental Disorders, Third Edition) criteria.[23]

These scales have been validated, and are responsive and reliable in patients with CAD.[18–21]

Primary statistical analysis

All patients were grouped according to the World Health Organization (WHO) BMI classification system[24] including: normal weight 18.5–24.9 $kg\,m^{-2}$, overweight 25.0–29.9 $kg\,m^{-2}$, mildly obese 30.0–34.9 $kg\,m^{-2}$, moderately obese 35.0–39.9 $kg\,m^{-2}$ and severely obese $\geqslant 40.0\,kg\,m^{-2}$. Baseline characteristics of patients across the ordered six BMI categories were examined by χ^2 tests for linear trend for nominal variables and Jonckheere–Terpstra tests for trend for

continuous variables. An analysis of patient characteristics of those who did not respond to the surveys was also performed.

Multiple linear regression was conducted to determine whether BMI was an independent predictor of HRQOL of patients with CAD. Separate models were created for the EQ Index and the four domains of the SAQ. All measured potential covariates with a prevalence of $\geqslant 1\%$ were retained in each model to account for confounding. Adjusted scores from the final models were compared across BMI categories with Bonfaroni correction. To determine the effect of the covariates entered, variables were entered as blocks in the following sequence: age, sex, co-morbidities, priority and indication for catheterization, disease severity (APPROACH jeopardy score representing percentage of the myocardium at risk), treatment strategy within the first year of catheterization (percutaneous coronary intervention, coronary artery bypass grafting or medical management only), depressive symptoms (CES-D score) and BMI (as a categorical variable). The adjusted R^2 and F-change values were noted to see the relative contribution of each block of variables in the models.

Statistical significance was set at $P<0.05$. Data were analyzed using SPSS for Windows (version 17.0, SPSS, Inc., Chicago, IL, USA).

Results

A total of 13 369 Alberta residents underwent a coronary catheterization and were sent a HRQOL questionnaire package. Of these, 10 147 patients were eligible for this study among which 6292 (62.0%) patients or family members responded to the mailed questionnaire package. Among responders, 5362 questionnaires were returned with complete data whereas 374 surveys were returned but contained missing outcome data. In addition, 515 surveys were returned informing the investigators that the patient had died before receiving the survey.

A comparison of the differences in the baseline demographic data and clinical characteristics of responders and non-responders is presented in Table 1. Compared with responders, non-responders were younger ($P<0.0001$), more likely to be current smokers ($P<0.0001$), more likely to have diabetes mellitus ($P<0.0001$), hyperlipidemia ($P<0.0001$), an ejection fraction of $<35\%$ ($P<0.0001$), less malignancy ($P=0.01$), more elective cardiac catheterizations ($P<0.0001$) and were more likely to have been treated with medical therapy only during the first year after their index catheterization (24.0 vs 19.3%, $P<0.0001$). In addition, patients with obesity were less likely to respond to the survey.

Table 2 presents the baseline characteristics of patients included in the analysis by BMI category. Patients with obesity were significantly younger and more likely to have hypertension, hyperlipidemia and diabetes mellitus, but a higher ejection fraction compared with patients with a normal BMI. In addition, as the BMI increased, so did the prevalence of depression (CES-D score of $\geqslant 10$), particularly in those with severe obesity.

Table 1 Responders vs non-responders

Variable	*Non-responders*	*Responders*	P-*values*
N	3827	5736	—
Normal (BMI 18.5–24.9 kg m^{-2})	17.6	20.3	0.001
Overweight (BMI 25.0–29.9 kg m^{-2})	42.2	42.7	0.6
Mild obesity (BMI 30.0–34.9 kg m^{-2})	26.5	24.6	0.04
Moderate obesity (BMI 35.0–39.9 kg m^2)	8.8	8.2	0.3
Severe obesity (BMI $\geqslant$40.0 kg m^{-2})	4.5	3.3	0.002
Age (years) (mean ± s.d.)	61 ± 11	65 ± 11	<0.0001
Sex (% F)	21.9	22.8	0.3
Cerebrovascular disease	6.3	6.5	0.7
Pulmonary disease	14.0	14.0	1.0
History of heart failure	8.3	8.7	0.5
Renal disease (serum creatinine >200 μmol l^{-1})	2.9	3.0	0.8
Diabetes mellitus	27.1	21.6	<0.0001
Hypertension	68.0	67.4	0.6
Hyperlipidemia	84.7	82.0	0.001
Malignancy	3.0	4.3	0.01
Peripheral vascular disease	6.7	7.4	0.2
Liver/gastrointestinal disease	7.0	8.0	0.08
Current smoker	34.6	22.2	<0.0001
Previous MI	49.5	50.2	0.5
Ex-smoker	35.4	43.1	<0.0001
Previous CABG	3.2	3.9	0.08
Unstable angina indication for cath	23.2	21.9	0.2
MI indication for cath	38.3	40.1	0.07
Stable angina indication for cath	37.7	36.8	0.6
LVEF <35%	4.0	5.1	0.02
Emergent priority	4.8	9.9	<0.0001
APPROACH jeopardy score (% myocardium at risk) (mean ± s.d.)	45 ± 29	48 ± 29	<0.0001
Medical management only treatment	24.0	19.4	<0.0001
CABG treatment	23.0	24.7	0.05
PCI treatment	53.0	55.9	0.005

Abbreviations: APPROACH, Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease; BMI, body mass index; CABG, coronary artery bypass grafting; cath, catheterization; CES-D, Center for Epidemiological Studies Short Depression Scale; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention. Values are expressed as percentages unless otherwise noted.

Disease-specific health-related quality of life

There were no significant differences in adjusted QOL scores for the SAQ domains of treatment satisfaction, angina frequency or disease perception domains between BMI categories (Table 3). There were, however, statistically significant differences in adjusted scores between BMI categories for the SAQ physical limitation. *Post hoc* analyses revealed that patients with mild, moderate and severe obesity had significantly worse physical function compared with patients with normal BMI, but no significant difference between patients who were overweight and patients of normal BMI. Patients with severe obesity had the lowest SAQ physical limitation scores (74.0 (95% confidence

Table 2 Patient characteristics according to BMI category

Variable	*Normal BMI (18.5–24.9 kg m^{-2})*	*Overweight (25.0–29.9 kg m^{-2})*	*Mild obesity (30.0–34.9 kg m^{-2})*	*Moderate obesity (35.0–39.9 kg m^{-2})*	*Severe obesity (⩾40.0 kg m^{-2})*	P-*value*[a]
N	1097	2310	1331	446	178	—
Age (years) (mean ± s.d.)	68 ± 11	65 ± 11	63 ± 10	62 ± 10	60 ± 9	0.0001
Sex (% F)	29.3	18.1	20.6	29.4	35.4	0.9
Cerebrovascular disease	7.6	6.2	5.9	5.4	7.9	0.2
COPD	15.4	12.5	13.7	14.1	22.5	0.5
History of heart failure	9.5	7.6	7.2	13.0	9.6	0.4
Renal disease (serum creatinine $>200\,\mu mol\,l^{-1}$)	3.0	3.1	2.6	2.9	3.4	0.7
Diabetes mellitus	13.9	18.7	26.7	34.2	36.0	<0.0001
Hypertension	60.3	66.5	70.9	75.3	75.8	<0.0001
Hyperlipidemia	78.5	83.3	82.9	82.3	87.1	0.001
Malignancy	5.3	4.1	3.8	4.7	1.7	0.04
Peripheral vascular disease	7.5	6.9	6.9	9.6	7.3	0.5
Liver/gastrointestinal disease	8.5	7.9	7.8	8.7	7.8	0.8
Current smoker	24.2	20.4	23.3	24.0	21.3	0.7
Previous MI	50.9	50.6	47.0	51.3	54.5	0.6
Ex-smoker	34.5	44.7	45.8	47.3	42.7	<0.0001
Previous CABG	3.6	3.7	3.7	3.1	2.8	0.8
MI indication for catheterization	23.2	21.1	22.8	20.4	19.7	0.3
Unstable angina indication for catheterization	42.5	40.0	39.0	39.9	44.3	0.3
Stable angina indication for catheterization	33.4	37.9	36.8	38.6	36.0	0.09
'Other' indication for catheterization	0.9	1.0	1.4	1.1	0	1.0
LVEF <35%	5.9	5.2	5.3	3.1	1.7	0.007
Emergent priority	12.4	10.0	9.5	6.7	10.1	0.001
Depression (CES-D Score of ⩾10)	14.7	13.4	15.3	18.4	27.0	<0.0001
APPROACH jeopardy score (% myocardium at risk) (mean ± s.d.)	47 ± 29	49 ± 29	47 ± 28	46 ± 29	42 ± 28	0.6
Medical management only treatment	21.2	18.4	17.7	19.0	21.2	0.2
CABG treatment	23.6	25.0	24.3	27.7	17.3	0.6
Days from initial catheterization to CABG	51 ± 85	46 ± 60	59 ± 94	59 ± 102	88 ± 183	0.2
PCI treatment	55.2	56.6	58.0	53.3	61.6	0.5

Abbreviations: APPROACH, Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease; BMI, body mass index; CABG, coronary artery bypass grafting; cath, catheterization; CES-D, Center for Epidemiological Studies Short Depression Scale; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention. Values are expressed as percentages, unless otherwise noted. [a]*P*-values for χ^2 test for linear trend or Jonckheere–Terpstra tests.

Table 3 HRQOL scores adjusted for demographics, co-morbidities, diseases severity, treatment strategy, depressive symptoms and BMI

HRQOL	*Normal BMI (18.5–24.9 kg m^{-2})*	*Overweight (25.0–29.9 kg m^{-2})*	*Mild obesity (30.0–34.9 kg m^{-2})*	*Moderate obesity (35.0–39.9 kg m^{-2})*	*Severe obesity (⩾40.0 kg m^{-2})*	P-*value*
EQ Index	0.890 (0.882–0.897)	0.887 (0.882–0.897)	0.871 (0.865–0.878)[a]	0.869 (0.857–0.880)[a]	0.852 (0.834–0.869)[a,b]	<0.0001
SAQ-PL	83.2 (82.0–84.3)	82.7 (79.5–83.5)	80.5 (79.5–81.5)[a]	79.9 (78.1–81.6)[a]	74.0 (71.2–76.9)[a,b]	<0.0001
SAP-AF	91.3 (90.4–92.3)	91.1 (90.5–91.8)	91.0 (90.2–91.9)	90.9 (89.4–92.4)	90.8 (88.5–93.1)	1.0
SAQ-TS	89.7 (88.9–90.5)	90.9 (90.3–91.4)	90.7 (89.9–91.4)	90.1 (88.8–91.4)	90.2 (88.1–92.2)	0.3
SAQ-QOL	77.4 (76.4–78.5)	78.6 (76.6–79.3)	77.5 (76.6–78.5)	78.9 (77.3–80.6)	77.8 (75.1–80.4)	0.3

Abbreviations: BMI, body mass index; EQ Index, EuroQol 5D; HRQOL, health-related quality of life; SAQ QOL, Seattle Angina Questionnaire quality of life/disease perception; SAQ-AF, SAQ anginal frequency; SAQ-PL, SAQ Physical limitation; SAQ-TS, SAQ Treatment Satisfaction. [a]Statistically different from normal BMI. [b]Clinically different from normal BMI.

interval 71.2–76.9) vs 83.2 (95% confidence interval 82.0–84.3), $P<0.0001$).

General health-related quality of life

There were significant differences in adjusted EQ Index between BMI categories. Similar to the *post hoc* SAQ Physical limitation results, patients with mild, moderate and severe obesity had significantly worse overall QOL compared with patients with normal BMI, with severely obese patients having the lowest EQ Index (0.852 (95% confidence interval 0.834–0.869) vs 0.890 (95% confidence interval 0.882–0.897), $P<0.0001$).

The results of the multivariable analyses showing what covariates were independent predictors of the HRQOL scores are outlined in Table 4. Age, sex, co-morbidities and indication for cardiac catheterization, disease severity, treatment and depressive symptoms were independent predictors

Table 4 Predictors of HRQOL

	Adjusted R^2	*s.e. of the estimate*	*F-change*	P-*value*
EQ Index				
Age	0.002	0.15	10.965	0.001
Sex	0.025	0.14	122.520	<0.0001
Co-morbidities and indication for cath	0.076	0.14	14.280	<0.0001
APPROACH jeopardy score	0.077	0.14	2.350	0.2
Treatment (medical management only, PCI or CABG)	0.081	0.14	12.628	<0.0001
Depressive symptoms	0.343	0.12	2049.309	<0.0001
BMI category	0.347	0.12	6.582	<0.0001
SAQ				
Physical limitation				
Age	0.059	20.67	314.556	<0.0001
Sex	0.089	20.37	165.359	<0.0001
Co-morbidities and indication for cath	0.168	19.55	24.067	<0.0001
APPROACH jeopardy score	0.169	19.55	0.477	0.5
Treatment (medical management only, PCI or CABG)	0.179	19.45	32.177	<0.0001
Depressive symptoms	0.292	18.06	796.506	<0.0001
BMI category	0.299	17.99	10.028	<0.0001
Anginal frequency				
Age	<0.0001	16.67	0.692	0.4
Sex	0.010	16.58	57.370	<0.0001
Co-morbidities and indication for cath	0.027	16.47	5.610	<0.0001
APPROACH jeopardy score	0.029	16.46	11.532	0.001
Treatment (medical management only, PCI or CABG)	0.040	16.39	32.117	<0.0001
Depressive symptoms	0.130	15.60	550.423	<0.0001
BMI category	0.129	15.60	0.185	1.0
Treatment satisfaction				
Age	0.010	14.60	52.490	<0.0001
Sex	0.015	14.6	27.864	<0.0001
Co-morbidities and indication for cath	0.025	14.5	3.701	<0.0001
APPROACH jeopardy score	0.028	14.5	19.000	<0.0001
Treatment (medical management only, PCI or CABG)	0.038	14.4	29.666	<0.0001
Depressive symptoms	0.150	13.5	692.853	<0.0001
BMI category	0.150	13.5	1.452	0.2
Disease perception				
Age	0.021	19.97	112.090	<0.0001
Sex	0.037	19.81	89.059	<0.0001
Co-morbidities and indication for cath	0.065	19.54	8.825	<0.0001
APPROACH jeopardy score	0.067	19.53	9.209	0.002
Treatment (medical management only, PCI or CABG)	0.079	19.47	35.524	<0.0001
Depressive symptoms	0.247	17.60	1158.680	<0.0001
BMI category	0.247	17.60	1.162	0.3

Abbreviations: APPROACH, Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease; BMI, body mass index; CABG, coronary artery bypass grafting; cath, catheterization; EQ Index, EuroQol 5D; HRQOL, health-related quality of life; PCI, percutaneous coronary intervention; SAQ, Seattle Angina Questionnaire.

of SAQ Physical limitation score and the EQ Index in addition to BMI category. Depressive symptoms accounted for a large portion of the variance in HRQOL scores for the EQ Index and each of the domains of the SAQ as shown by the largest F-changes.

Sensitivity analysis. A sensitivity analysis was performed to address 6.5% (374) patients included in the analysis who had incomplete HRQOL outcome data at 1 year. New variables were created, by which the lowest and highest SAQ physical limitation and EQ Index scores were imputed into the missing 1-year responses. Analyses were run as described above with similar results in adjusted SAQ physical limitation and EQ-5D scores after both minimal and maximum imputations.

Discussion

Although studies in the CAD population have consistently shown an 'obesity paradox' by which a higher BMI is associated with lower mortality, the paradox does not extend to HRQOL outcomes. Thus, if the obesity paradox is in fact a valid finding, these potential additional years of life may not be quality years. The results of our study showed that after adjustment for clinical characteristics and depressive

symptoms, obesity remained associated with worse physical function and a lower overall QOL in CAD patients. This underscores the importance of conducting prospective studies that measure overall and disease-specific HRQOL, and how changes in weight, lean body mass or body fat may modify these.

Because even small differences in HRQOL scores can be detected as statistically significant, mean differences can also be described in terms of clinically important differences.[25] Spertus *et al*.[26] have indicated that the minimal clinically important difference in SAQ dimensional scores is between 5 and 8 points. Although the minimal clinically important difference in EQ Index has not been established in CAD, previous research has estimated it to be 0.03 based on an effect size of 0.2[27] (representing a small but meaningful difference). Accordingly, patients with severe obesity (BMI of $\geqslant 40.0\,kg\,m^{-2}$) had statistically and *clinically significant* reductions in physical function and overall QOL when compared with patients with a normal BMI. Psychological interventions such as cognitive therapy, psychotherapy and relaxation therapy may help to improve HRQOL without directly affecting weight loss. Intervention from a physical or occupational therapist may help the patient improve physical function and activities of daily living, which could also improve HRQOL. Perhaps patients with severe obesity should be the highest priority for weight loss, psychological, physical and/or occupational interventions to improve HRQOL. In addition, given that depressive symptoms had such a large influence on HRQOL outcomes, interventions to address depression may be of utmost importance in severely obese patients.

Our results are similar to those of Kalantar-Zadeh *et al*.,[28,29] who reported a negative association between percent body fat and physical and mental HRQOL in chronic hemodialysis patients, and to Evangelista *et al*.,[30] who showed a negative association between higher BMI and lower physical, emotional and overall HRQOL in patients with heart failure, two populations that also exhibit the obesity paradox. Our findings are in contrast to Poston *et al*.,[31] who found that obesity was not associated with statistically or clinically significant differences in SAQ scores, including physical function, at 12 months after PCI. The reason for this discrepancy could in part be due to the lack of a severe obesity category; patients with severe obesity (BMI of $\geqslant 40.0\,kg\,m^{-2}$) were grouped together with the moderate obesity group (BMI of $\geqslant 35.0\,kg\,m^{-2}$).

The effect of weight loss on HRQOL outcomes in patients with established CAD has been studied in the setting of cardiac rehabilitation programs. Decreases in percent body fat, BMI and total weight resulted in significant improvements in overall QOL as measured by the Medical Outcomes Study short form 36 (SF-36) as well as the Kellner Symptom Questionnaire, a measure of depression, hostility, somatization and anxiety.[5,7,32] Data from the general population also show an improvement in HRQOL with weight loss in overweight and obese individuals; in the Women's Health Study,[33] weight loss in overweight women was associated with improved physical function and vitality as well as a reduction in pain. Individuals with obesity have substantial improvements in social, emotional and physical QOL with weight loss either by diet and exercise[34] or with surgical[35,36] intervention. In a recent study, Lavie *et al*.[8] showed improvement in HRQOL with weight loss in 393 overweight or obese CAD patients (BMI of $\geqslant 25.0\,kg\,m^{-2}$) after completing a cardiac rehabilitation and exercise training program, but only a nonsignificant trend for lowered mortality at 3-year follow-up. It is possible, however, that reducing body fat vs BMI or weight alone may lead to lower mortality.[37,38]

There are limitations to our study that should be noted. First, the cross-sectional nature provides associative, not causal, evidence. Second, there was a 1-year lag between measurement of BMI and collection of HRQOL. Furthermore, information was not collected regarding the duration of obesity or whether patients had lost weight. These factors may affect the association between BMI and HRQOL. Previous studies in adults, however, have shown BMI to be stable over this period of time.[39,40] Zavaroni *et al*.[40] showed that approximately 80% of those in the highest BMI quartile were in the upper two BMI quartiles 12 years later. Similarly, 80% of those in the lowest BMI quartile at baseline were in the lower two quartiles when observed 12 years later. In another analysis of over 5500 patients recently diagnosed with CAD from 15 European centers, weight changes at least 6 months after coronary disease seemed to be equally distributed between gains and losses, with the population distribution similar to a normal curve and the majority of patients experiencing very little weight change (mean weight loss was not reported).[41] Thus, we are confident that in this relatively short time span, substantial changes in weight were unlikely to occur. It should also be recognized that because we compared HRQOL between BMI groups, differential changes in weight would have had to occur between BMI groups to bias the results. If our assumptions are erroneous, the direction of bias would depend on the net direction of weight change in the overweight and obese groups relative to the normal-weight groups. For example, we found that a higher BMI was associated with reduced SAQ physical limitation scores in APPROACH. Therefore, if overweight and obese patients gained more weight after catheterization, lower SAQ scores measured 1 year later would have been ascribed to the baseline BMI levels and our results may have been falsely exaggerated. On the other hand, if overweight and obese patients experienced a net weight reduction, then our observed results can be considered conservative. Third, although BMI is the most commonly used epidemiologic measure of obesity, it does not differentiate between adipose and lean tissue or central and peripheral adiposity. Fourth, patients with obesity were less likely to respond to HRQOL questionnaires. Differential response rates across BMI categories may introduce bias and limit external generalizability to all obese patients with CAD. Fifth, 6.5% (374) of the patients included in the analysis had

incomplete or missing HRQOL outcome data; however, a sensitivity analysis showed that these missing responses would not have changed the results. Sixth, our HRQOL analysis included only those patients who survived at least 1 year after their index catheterization to receive the HRQOL questionnaire package. However, the 'obesity paradox' phenomenon is not restricted to those patients with CAD who experience early mortality.[1,4] Seventh, although we had a disease-specific questionnaire for CAD, we lacked an instrument specific to obesity. An obesity-specific questionnaire, such as the Impact of Weight on Quality of Life-Lite (IWQOL-Lite), may have provided more information regarding any differences in psychosocial factors between BMI groups. Finally, differences in the frequency and timing of post-catherization coronary artery bypass graft surgery between BMI groups may potentially affect subsequent QOL after 1 year. However, neither the frequency nor the timing of coronary artery bypass graft surgery after catheterization was significantly different between groups (Table 2).

Summary and implications

We have shown that BMI is inversely associated with physical function and overall HRQOL in CAD patients, especially in patients with severe obesity. Serial annual assessments of disease-specific and general HRQOL may therefore help to identify higher-risk patients who may need more attention and interventions. High body weight is a modifiable risk factor, and proper weight management could potentially improve the HRQOL of patients with obesity. However, given the apparent obesity paradox in patients with CAD, it is critical that future studies be conducted to investigate the relationships between HRQOL and body composition (total body fat, abdominal fat and lean mass), nutritional state and survival outcomes so that appropriate interventions can be developed.

Conflict of interest

The authors declare no conflict of interest.

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