Published in final edited form as:

Am Heart J. 2008 March ; 155(3): 478–484. doi:10.1016/j.ahj.2007.10.026.

Weight Change after Myocardial Infarction - the ENRICHD Experience

Francisco Lopez-Jimenez, M.D.^{*}, Colin O. Wu, PhD^{**}, Xin Tian, PhD^{**}, Chris O'Connor, M.D.^{***}, Michael W. Rich, M.D.^{****}, Matthew M. Burg, Ph.D.[#], David Sheps, M.D.^{*##}, James. Raczynski, Ph.D.[°], Virend K. Somers, M.D., PhD.^{*}, and Allan S. Jaffe, M.D.^{*}, @

^{*}Division of Cardiovascular Diseases, Mayo Clinic and Mayo Clinic, Rochester, MN.

@ Department of Laboratory Medicine and Pathology, Mayo Clinic and Mayo Clinic, Rochester, MN.

^{**}Office of Biostatistics Research, NHLBI, Bethesda, MD.

^{***} Duke University School of Medicine, Durham, NC

^{****}Washington University School of Medicine, St. Louis, MO

[#]Yale University School of Medicine, New Haven, CT, and Columbia University School of Medicine, NY, NY

^{*##} University of Florida School of Medicine, Gainesville, FL

[°]University of Alabama School of Medicine, Birmingham, AL

Abstract

Background: The relationship of changes in weight to outcomes in patients post myocardial infarction (MI) is controversial.

Methods: From the Enhancing Recovery in Coronary Heart Disease patients (ENRICHD) trial data, we assessed weight change, and the associations of baseline weight and change at follow-up outcomes and interactions between psychosocial factors.

Results: At baseline 73.6% of patients ($N=1706$) were overweight or obese; 134 patients had BMI ≥ 40 . Underweight patients were more likely to die or suffer nonfatal recurrent MI. After controlling for covariates, overweight and obese patients had similar outcomes to normal weight patients.

Eighteen percent of patients gained $> 5\%$, 27% lost $> 5\%$ and 55% had $< 5\%$ change in weight. Compared with weight loss $< 5\%$, the risk of death (adjusted hazard ratio [HR] = 1.74, $p=0.01$), and cardiovascular death (HR=1.79, $p=0.04$) were increased with weight loss $> 5\%$. After propensity matching, weight loss $> 5\%$ remained as a significant risk factor for death and CV death. There was no interaction between weight change and depression and/or social support at baseline or follow up. Weight change was not associated with recurrent MI or cardiovascular hospitalizations.

© 2007 Mosby, Inc. All rights reserved.

Corresponding author: Francisco Lopez-Jimenez, M.D., M.Sc. 200 First Street SW, Rochester, Minnesota 55905 Telephone: (507) 284-8087 Facsimile: (507) 266-3623 lopez@mayo.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

This report is an ENRICHD databank study.

Conclusions: A large proportion of patients lose or gain >5% of body weight after an MI. The association between obesity and lower mortality is modulated by comorbidities. Weight loss after MI is associated with worse outcomes and is not related to depression or social support.

BACKGROUND

Excess body weight, being overweight or obese, is a prevalent risk factor in patients with acute myocardial infarction (AMI).¹ The cardiologic societies recommend identification and management of obesity as key components of primary prevention because of the greater risk for cardiovascular events and all cause mortality in this group. Data assessing the impact of obesity on outcomes in patients with established CAD however, are controversial. Studies of patients undergoing revascularization have shown better outcomes or no increased risk in overweight and obese patients.²⁻⁶ Many studies have shown either no association or a favorable effect of obesity in patients with MI; others only a modest association with recurrent events.^{1, 7-10} A pooled analysis of CAD patients has shown an inverse J curve with patients with BMI between 30-35 having the lowest long-term mortality.¹¹

Weight change after MI could affect the disease trajectory. Prior studies have not assessed the effects of weight change on outcomes post MI. Furthermore, no study has examined the role of psychosocial factors on this issue. Depression and social isolation are associated with adverse clinical events after an MI and have been linked to weight changes in the general population.¹² The present analysis was undertaken to evaluate the magnitude, direction, and determinants of weight change following MI, its effect on outcomes, and its relationship to depression and social isolation in the ENRICH study population.

METHODS

The methods¹³ and results of ENRICH have been reported previously.¹⁴ ENRICH was an NIH-sponsored randomized clinical trial in patients with acute MI and either depression or social isolation. The primary study end point was all cause mortality and recurrent MI; secondary endpoints included all cause mortality, coronary revascularization and cardiac hospitalizations. Criteria for recurrent myocardial infarction were as defined for enrollment except for after revascularization procedures. There were 599 primary endpoint events during a median of 29 months of follow-up.

Exclusion Criteria

We excluded patients without a measure of body weight or height at baseline. Patients with BMI ≥ 60 or a weight change > 40%, were assumed to be errors in documentation. We also excluded patients without a six-month evaluation and those in whom it occurred at > 270 days.

Body weight measurements

Baseline body weight came from the clinical record. Body weight was measured during follow-up visits using standard scales. Body Mass Index (BMI) was calculated by dividing the weight in kilos by the square of the height in meters. We created five groups according to BMI: Underweight (BMI < 20), normal weight (BMI ≥ 20 but < 25), overweight (BMI ≥ 25 but < 30), obese (BMI ≥ 30 but < 40), and morbidly obese (BMI ≥ 40). Follow-up weight was recorded a median of 186, IQR = 98 to 270 days. Patients with clinical events in the first 6 months of follow up were excluded. Change in weight was defined in as: a) delta weight, (change in weight from baseline to first follow-up); b) slope weight (change in weight from baseline to follow-up divided by days of follow-up, times 180); and c) percent weight change (change in weight from baseline to follow-up, relative to baseline weight). Creatinine clearance was calculated by Cockcroft-Gault equations.¹⁵

Statistical analysis

Differences among weight groups were examined by Pearson's chi-squared test and the ANOVA F-tests. Cox analysis was used to analyze the combined outcome of recurrent MI or death, all cause mortality, death from cardiovascular disease, fatal or nonfatal MI, nonfatal MI, and cardiovascular hospitalization.

Covariates in the regression models incorporated baseline clinical, demographic, and psychosocial information. (Table 1).¹⁶ Baseline BMI was considered as a continuous variable and as a categorical variable. The incidence rates per 100 patient-years of follow-up were calculated for each group.

To assess associations between weight changes and outcomes, we used separate Cox models for: a) delta weight, b) slope weight, and c) 5% weight change, all adjusted for potential predictors used in previous ENRICHD analyses.¹⁶ Kaplan-Meier survival curves were generated for weight change groups. To account for imbalances in confounding variables of weight change, we constructed logistic regression models in which the weight loss >5% was a dependent variable and the variables in Table 2 were independent variables. We then estimated the propensity score, defined as the conditional probability of having a weight loss >5% given all known measured covariates except outcome, for each patient.¹⁷ Patients with or without a weight loss > 5% were matched based on propensity scores.

Patients with missing covariates were excluded. Regression analyses using multiple imputation for missing covariates had similar results. Analyses were performed using SAS 9.0 (SAS Institute Inc., Cary, NC).

RESULTS

From the cohort of 2481 patients, 163 were excluded because of missing information or because baseline BMI was ≥ 60 . Patients without follow-up weight information ($n=549$), 85 patients with follow-up visit > 270 days window for the 6 month follow up, and 8 patients with a weight change > 40% were excluded, leaving 1676 patients.

Baseline Characteristics

At baseline, 73.6% of patients ($n=1706$) were overweight or obese; 134 patients were morbidly obese ($BMI \geq 40$). Associations are shown in Table 1.

Weight change after MI

The average BMI was 28.95 ± 6.02 at baseline and 28.41 ± 5.72 at follow-up. Eighteen % ($n = 301$) had $\geq 5\%$ weight gain, and 27% ($n = 460$) had $\geq 5\%$ weight loss. Six-month weight change (both loss and gain) was associated with baseline BMI, age, hypertension, revascularization after the index MI, heart failure and other comorbidities, antidepressant use, smoking history and smoking cessation during follow-up (Table 2).

Baseline BMI and clinical outcomes

Event rates for baseline BMI groups appear in Table 3. Underweight patients had higher rates compared with normal weight, overweight and obese patients ($p<0.001$, $p<0.001$ and $p=0.004$, respectively). Table 4 shows the adjusted hazard ratios and 95% confidence intervals for baseline BMI groups. After adjusting for confounders, being underweight was only marginally associated with all cause mortality ($HR=1.77$, $p=0.046$). Obese patients had the lowest all-cause and cardiovascular mortality in unadjusted analysis (Table 3). After controlling for confounders, overweight and obese patients were not significantly different from the normal

weight group in regard to the primary endpoint of death or nonfatal MI, or all cause mortality, but were borderline significantly different for cardiovascular mortality (HR= 0.60, p=0.047).

Regression models adjusted for the creatinine clearance to provide a more accurate estimate of renal function (table 4) indicate that baseline BMI was not associated with all cause mortality or cardiovascular mortality, while creatinine clearance was a highly significant predictor (data not shown).

Weight change and clinical outcomes

Kaplan-Meier survival curves of all cause and cardiovascular mortality and the combined outcome of death and recurrent MI are shown in Figure 1 and hazard ratios for weight changes adjusted for baseline covariates, creatinine clearance, antidepressant use before 6 month, smoking cessation, and depression and social isolation score changes in table 5. Weight loss by all definitions was associated with an increased risk for all-cause mortality, after adjustment for confounders and psychosocial factors. Weight loss of > 5% was associated with 70% increased risk of all-cause mortality and a similar increase in cardiovascular mortality. The interaction terms for weight change and depression and social isolation scores at baseline and during follow-up were not significant, i.e. outcomes were not associated with depression or social support. Weight change was not significantly associated with risk of myocardial infarction (fatal or nonfatal) or cardiovascular hospitalizations (data not shown).

Propensity matching of patients with and without weight loss >5% resulted in propensity scores of 0.71 (C statistic). Multivariate logistic modeling indicated that weight loss > 5% was associated with age, baseline BMI and height, CABG after index MI, and negatively associated with smoking cessation. Of 349 patients with weight loss >5% and nonmissing covariates, 327 patients were matched to patients with the closest propensity score. The characteristics of the propensity matched-pair samples were well matched (Table 2). After adjustment (Table 2), weight loss >5% were associated with increased risk of all cause and cardiovascular mortality. Propensity analysis of patients with or without a weight gain > 5% revealed no significant association (data not shown).

DISCUSSION

Our data indicate that after MI, a large proportion of patients lose or gain >5% of body weight. Furthermore, they indicate that the association between obesity and apparent lower mortality is modulated by differences in comorbidities. In contrast, weight loss is associated with worse outcomes not related to the presence and/or changes in depression or social isolation.

These findings have important implications for understanding the “obesity paradox” in CAD patients.³ In ENRICH, prior to multivariable correction, a similar effect was observed.⁵⁻⁹ After correction for confounders, the association disappeared.

Approximately one third of patients lost >5% of their weight in the first 6 months after MI. Weight loss was associated with increased all-cause and cardiovascular mortality. These associations were not related to depression, social isolation, or changes in smoking. Weight loss was not associated with recurrent myocardial infarction or cardiovascular hospitalizations. Weight gain, which occurred in lower weight individuals did not affect prognosis.

Differential weight change after MI

Most studies and this ENRICH cohort as well indicate that mean weight does not change after acute MI.^{18, 19} However, 27% experienced > 5% weight decrease, and 18% > 5% increase. Weight loss was associated with more co-morbidities at baseline, suggesting weight loss might be a marker of CVD severity or poorer overall health. For example, congestive heart failure

can be associated with increased cachexins, decreased appetite, reduced musculoskeletal activity and loss of muscle mass.²⁰

Association Between Baseline BMI and Medical Outcomes

The association between obesity and better overall and cardiovascular survival is ablated after adjusting for comorbidities and especially differences in creatinine clearance. Thus, previous reports might reflect incomplete adjustment for factors related to low BMI and. prior studies testing did not adjust for creatinine clearance. BMI at baseline was not associated with recurrent MI or cardiovascular hospitalizations; supporting the concept that lower cardiovascular mortality likely reflects non-cardiac comorbidities not accounted in the analyses.

Association Between change in BMI and Long-term Outcomes

The association between body weight change after myocardial infarction and clinical outcomes has not been tested previously. Weight loss is associated with higher all-cause mortality, even after adjustment. Weight loss however, was not associated with reinfarction or cardiovascular hospitalizations.

It is not clear why weight loss is associated with higher mortality, since it is not known why patients lost weight. If weight loss was intentional, it might be that use of inappropriate or unhealthy diets with low intake of micronutrients like omega-3 fatty acids and antioxidants, or high intake of animal fat were responsible for adverse effects. However, we presume weight loss was unintentional and may be a consequence more of non-cardiac comorbidities.

Epidemiologic studies in patients without coronary disease have also shown that *unintentional* weight loss is associated with higher mortality.^{21, 22} This has been attributed to co-morbidities such as depression or malnutrition in the elderly. These factors also are associated with congestive heart failure.

Our findings that 1/3 of patients lost weight and have worse outcomes, may have significant public health implications. However, the ENRICH cohort included more co-morbidities than in most clinical trials of myocardial infarction.¹⁶

Weight gain did not alter prognosis. This is likely because weight gain occurred in lighter patients or was due to residual negative confounding, i.e patients who gained weight were healthier. These observations suggest that comparison groups in the complex area of weight loss and gain must be chosen carefully. Unfortunately, many studies, as ours lack sufficient numbers to compare weight gain and/or loss within each BMI category.

Depression, Social Isolation and Weight Changes After MI

Depression is a cause of weight gain and weight loss.¹² Obesity is also a cause of depression, particularly if severe. We hypothesized that depression would be related to weight change because it is associated with adverse events after MI. However, depression did not interact with BMI at baseline or weight related rates of adverse events or survival. In animals, social isolation contributes to weight loss and this may happen in humans.^{23, 24} Because social isolation is associated with worse outcomes after myocardial infarction, we hypothesized that social isolation would be a confounder as well. However, that was not the case.

Strengths and Limitations

The strengths of our study include analysis of differential weight change providing better ascertainment of the exposure variable of interest. We were able to account for common comorbidities and excluded patients with cancer evident at baseline. We used propensity matching to control for unknown factors that could modulate risk. The use of creatinine

clearance was particularly helpful. Multiple studies have shown that creatinine clearance is one of the strongest predictive factors in patients with coronary artery disease.^{25, 26} To the best of our knowledge, no other study relating BMI to outcomes in patients with cardiovascular disease has adjusted for creatinine clearance. Additionally, our study is the first one to include depression, social isolation, and changes in smoking status.

Potential limitations include the retrospective design and that ENRICHED included only patients with depression and/or social isolation. Therefore, we cannot generalize our results to other populations. Another limitation is the use of BMI as the only measure of obesity. BMI is reproducible and a simple way to assess obesity because it correlates with body fat in middle age people without major comorbidities,^{27, 28} but not in patients with coronary artery disease. We have recently reported that in patients with CAD, BMI fails to detect excess body fat, the true definition of obesity.²⁹ This may be particularly true for elderly patients in whom sarcopenia is prevalent.³⁰ Alternatively, a high muscle mass hampers the specificity of BMI to detect body fat.

Additionally, body fat distribution was not ascertained in ENRICHED. Waist circumference is associated with coronary artery disease and may be more important than BMI alone.¹⁸

Our findings underscore the need for clinical trials using all of these measures to test the effects of intentional weight loss in patients with obesity and cardiovascular disease.

References

1. Lopez-Jimenez F, Jacobsen SJ, Reeder GS, et al. Prevalence and secular trends of excess body weight and impact on outcomes after myocardial infarction in the community. *Chest* 2004;125(4):1205–12. [PubMed: 15078726]
2. Powell BD, Lennon RJ, Lerman A, et al. Association of body mass index with outcome after percutaneous coronary intervention. *Am J Cardiol* 2003;91(4):472–6. [PubMed: 12586271]
3. Gurm HS, Brennan DM, Booth J, et al. Impact of body mass index on outcome after percutaneous coronary intervention (the obesity paradox). *Am J Cardiol* 2002;90(1):42–5. [PubMed: 12088778]
4. Gruberg L, Weissman NJ, Waksman R, et al. The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox? *J Am Coll Cardiol* 2002;39(4):578–84. [PubMed: 11849854]
5. Kuduvali M, Grayson AD, Oo AY, et al. The effect of obesity on mid-term survival following coronary artery bypass surgery. *Eur J Cardiothorac Surg* 2003;23(3):368–73. [PubMed: 12614808]
6. Kim J, Hammar N, Jakobsson K, et al. Obesity and the risk of early and late mortality after coronary artery bypass graft surgery. *Am Heart J* 2003;146(3):555–60. [PubMed: 12947378]
7. Rana JS, Mukamal KJ, Morgan JP, et al. Obesity and the risk of death after acute myocardial infarction. *Am Heart J* 2004;147(5):841–6. [PubMed: 15131540]
8. Krumholz HM, Chen J, Chen YT, et al. Predicting one-year mortality among elderly survivors of hospitalization for an acute myocardial infarction: results from the Cooperative Cardiovascular Project. *J Am Coll Cardiol* 2001;38(2):453–9. [PubMed: 11499737]
9. Kennedy LM, Dickstein K, Anker SD, et al. The prognostic importance of body mass index after complicated myocardial infarction. *J Am Coll Cardiol* 2005;45(1):156–8. [PubMed: 15629390]
10. Nigam A, Wright RS, Allison TG, et al. Excess weight at time of presentation of myocardial infarction is associated with lower initial mortality risks but higher long-term risks including recurrent re-infarction and cardiac death. *Int J Cardiol* 2005;110(2):153–9. [PubMed: 16043245]
11. Romero-Corral A, Montori VM, Somers VK, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet* 2006;368(9536):666–78. [PubMed: 16920472]
12. Wing RR, Phelan S. Long-term weight loss maintenance. *Am J Clin Nutr* 2005;82(1 Suppl):222S–225S. [PubMed: 16002825]

13. The ENRICHD investigators. Enhancing recovery in coronary heart disease patients (ENRICHD): study design and methods. *Am Heart J* 2000;139(1 Pt 1):1–9. [PubMed: 10618555]
14. Berkman LF, Blumenthal J, Burg M, et al. Effects of treating depression and low perceived social support on clinical events after myocardial infarction: the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial. *Jama* 2003;289(23):3106–16. [PubMed: 12813116]
15. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;16(1):31–41. [PubMed: 1244564]
16. Jaffe AS, Krumholz HM, Catellier DJ, et al. Prediction of medical morbidity and mortality after acute myocardial infarction in patients at increased psychosocial risk in the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) study. *Am Heart J* 2006;152(1):126–35. [PubMed: 16824842]
17. Rubin DB. Estimating causal effects from large data sets using propensity scores. *Ann Intern Med* 1997;127(8 Pt 2):757–63. [PubMed: 9382394]
18. Dagenais GR, Yi Q, Mann JF, et al. Prognostic impact of body weight and abdominal obesity in women and men with cardiovascular disease. *Am Heart J* 2005;149(1):54–60. [PubMed: 15660034]
19. De Lorgeril M, Salen P, Martin JL, et al. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation* 1999;99(6):779–85. [PubMed: 9989963]
20. Ciccoira M, Bolger AP, Doehner W, et al. High tumour necrosis factor- α levels are associated with exercise intolerance and neurohormonal activation in chronic heart failure patients. *Cytokine* 2001;15(2):80–6. [PubMed: 11500083]
21. Kuller L, Wing R. Weight loss and mortality. *Ann Intern Med* 1993;119(7 Pt 1):630–2. [PubMed: 8363176]
22. Lee IM, Paffenbarger RS Jr. Is weight loss hazardous? *Nutr Rev* 1996;54(4 Pt 2):S116–24. [PubMed: 8700438]
23. Yamada K, Ohki-Hamazaki H, Wada K. Differential effects of social isolation upon body weight, food consumption, and responsiveness to novel and social environment in bombesin receptor subtype-3 (BRS-3) deficient mice. *Physiol Behav* 2000;68(4):555–61. [PubMed: 10713297]
24. Van Leeuwen SD, Bonne OB, Avraham Y, et al. Separation as a new animal model for self-induced weight loss. *Physiol Behav* 1997;62(1):77–81. [PubMed: 9226345]
25. Dixon SR, O'Neill WW, Sadeghi HM, et al. Usefulness of creatinine clearance in predicting early and late death after primary angioplasty for acute myocardial infarction. *Am J Cardiol* 2003;91(12):1454–7. [PubMed: 12804732]A6
26. Sorensen CR, Brendorp B, Rask-Madsen C, et al. The prognostic importance of creatinine clearance after acute myocardial infarction. *Eur Heart J* 2002;23(12):948–52. [PubMed: 12069449]
27. Marshall JD, Hazlett CB, Spady DW, et al. Validity of convenient indicators of obesity. *Hum Biol* 1991;63(2):137–53. [PubMed: 2019407]
28. Warner JT, Cowan FJ, Dunstan FD, Gregory JW. The validity of body mass index for the assessment of adiposity in children with disease states. *Ann Hum Biol* 1997;24(3):209–15. [PubMed: 9158840]
29. Romero-Corral A, Somers VK, Sierra-Johnson J, et al. Diagnostic performance of body mass index to detect obesity in patients with coronary artery disease. *Eur Heart J* 2007;28(17):2087–93. [PubMed: 17626030]
30. Castillo EM, Goodman-Gruen D, Kritz-Silverstein D, et al. Sarcopenia in elderly men and women: the Rancho Bernardo study. *Am J Prev Med* 2003;25(3):226–31. [PubMed: 14507529]

Figure 1.
Kaplan-Meier estimates of survival for the weight change groups.

Baseline Characteristics According to the Weight Groups by the Body Mass Index (kg/m²).

Table 1

	Underweight (BMI<20) (n=84)	Normal (20~25) (n=528)	Overweight (25~30) (n = 872)	Obese (30 ~40) (n = 700)	Morbid Obese (≥40) (n = 134)	p-value
Age (years)	67.7±13.1	63.4 ± 13.1	61.9 ± 12.0	57.8 ± 11.9	55.7 ± 11.8	<0.0001
Ejection fraction (%)	46.5±12.4	44.1 ± 13.5	44.9 ± 13.0	46.7 ± 13.2	46.8 ± 12.7	0.037
Creatinine (mg/dL)	1.17 ± 1.16	1.27 ± 1.04	1.15 ± 0.66	1.11 ± 0.61	1.15 ± 0.58	0.013
Creatinine clearance	53.8±23.6	65.5 ± 27.7	81.7 ± 31.5	104.4± 40.5	127.1± 48.4	<0.0001
Systolic blood pressure (mm Hg)	118.4±18.3	121.5 ± 19.8	123.2 ± 18.3	124.8 ± 19.4	129.6 ± 21.6	<0.0001
Diastolic blood pressure (mm Hg)	66.1±10.4	69.0 ± 10.3	70.4 ± 10.8	71.3 ± 11.3	73.5 ± 12.5	<0.0001
Comorbidity score	2.15 ± 1.95	2.13 ± 2.08	2.01 ± 1.97	2.43 ± 2.16	2.81 ± 2.16	<0.0001
BDI score	17.2±8.3	15.8 ± 8.4	15.0 ± 8.3	16.3 ± 8.3	17.4 ± 7.7	0.001
ESSI score	22.3±6.2	22.9 ± 6.3	23.3 ± 6.3	23.0 ± 6.5	23.9 ± 6.3	0.313
Gender (% female)	59.5	42.1	37.3	48.4	64.2	<0.0001
Killip class III-IV (%)	10.7	8.6	6.9	8.5	6.5	0.601
Smoking history (%)	59.0	68.8	66.6	64.0	60.6	0.157
Previous MI (%)	38.1	26.9	26.1	28.3	27.3	0.208
CHF history (%)	15.2	16.0	11.4	15.2	19.4	0.041
PVD (%)	12.2	14.3	11.4	12.3	16.7	0.325
Stroke/TIA (%)	14.5	12.1	8.6	8.7	6.8	0.064
Pulmonary disease (%)	23.8	19.8	15.2	20.8	26.9	0.003
Diabetes (%)	17.1	26.1	28.2	42.5	51.5	<0.0001
Hypertension (%)	47.0	51.4	60.4	68.3	79.0	<0.0001
Renal disease (%)	10.8	11.4	10.0	9.0	8.5	0.694
Previous CABG (%)	18.1	15.4	12.7	12.0	6.9	0.048
CABG after index MI (%)	14.6	15.4	19.6	17.3	12.0	0.120
Vasodilators (%)	42.5	42.8	41.8	41.0	44.4	0.948
Lipid lowering drugs(%)	32.1	42.0	43.9	45.8	55.7	0.012
ACE inhibitor (%)	45.6	45.1	49.0	49.5	47.6	0.592
β-Blockers (%)	74.4	71.7	76.6	75.4	77.6	0.325

Note: Values are means ± standard deviation or percentages.

BMI= Body Mass Index, **BDI** = Beck Depression Inventory; **CHF**= congestive heart failure; CABG=Coronary Artery Bypass Graft; **ESSI**= ENRICHD Social Support Instrument; **MI**= myocardial infarction; **PVD** = peripheral vascular disease.

Table 2
Patient Characteristics by the Weight Change at Follow-up Groups.

Characteristic at Baseline	Before Propensity Score Matching			After Propensity Score Matching			
	Weight Loss >5% (n = 460)	Weight change ≤5% (n = 915)	Weight Gain >5% (n = 301)	P-value	Weight Loss >5% (n = 327)	No weight loss (n = 327)	P-value
Age (years)	62.1 ± 12.1	60.7 ± 12.2	56.8 ± 12.2	<0.0001	61.6 ± 12.3	61.8 ± 12.3	0.876
Baseline BMI (kg/m ²)	30.9 ± 6.6	28.6 ± 5.6	26.9 ± 5.5	<0.0001	30.6 ± 6.1	30.7 ± 6.4	0.856
Ejection fraction (%)	44.8 ± 14.4	46.2 ± 12.6	45.5 ± 12.7	0.262	45.4 ± 14.4	46.2 ± 12.7	0.525
Creatinine (mg/dL)	1.18 ± 0.75	1.15 ± 0.76	1.09 ± 0.56	0.224	1.18 ± 0.69	1.20 ± 0.77	0.659
Creatinine clearance	90.7 ± 42.7	85.8 ± 37.2	86.1 ± 34.6	0.090	89.9 ± 42.4	89.0 ± 44.2	0.785
Systolic blood pressure (mm Hg)	126.1 ± 21.3	122.9 ± 18.9	120.8 ± 17.9	0.0007	124.8 ± 19.1	125.8 ± 18.9	0.496
Diastolic blood pressure (mm Hg)	70.8 ± 11.2	70.4 ± 11.0	69.6 ± 9.7	0.325	70.2 ± 11.0	70.9 ± 10.8	0.407
Comorbidity score	2.44 ± 2.16	2.17 ± 2.06	1.90 ± 1.91	0.002	2.34 ± 2.15	2.42 ± 2.12	0.647
Height (m)	1.686 ± 0.102	1.686 ± 0.108	1.692 ± 0.096	0.696	1.69 ± 0.10	1.69 ± 0.11	0.605
BDI score	15.8 ± 8.5	15.4 ± 8.4	16.1 ± 8.2	0.338	15.1 ± 7.9	15.1 ± 8.1	0.973
ESSI score	23.2 ± 6.4	23.2 ± 6.3	23.2 ± 6.6	0.990	23.5 ± 6.6	23.5 ± 6.2	0.993
Gender (% female)	47.6	45.0	39.2	0.071	47.7	48.6	0.814
Killip class III-IV (%)	10.6	6.7	5.7	0.020	8.5	7.2	0.548
Previous MI (%)	25.2	26.3	25.7	0.894	23.6	23.9	0.927
CHF history (%)	16.7	12.2	8.7	0.005	14.7	15.6	0.743
PVD (%)	14.8	13.5	10.2	0.190	13.8	14.1	0.910
Stroke/TIA (%)	9.2	10.1	7.8	0.495	8.9	9.5	0.786
Pulmonary disease (%)	20.2	18.9	16.5	0.449	21.7	24.5	0.404
Diabetes (%)	36.4	31.8	31.8	0.199	34.3	34.6	0.934
Hypertension (%)*	64.9	61.9	50.2	0.0002	64.5	63.6	0.807
Renal disease (%)	11.5	9.1	8.5	0.269	10.7	11.93	0.622
Previous CABG (%)	12.9	13.8	9.1	0.104	11.9	12.5	0.811
CABG after index MI(%)	25.2	15.4	13.7	<0.0001	25.1	23.6	0.649
Lipid lowering drugs(%)	45.3	47.1	49.8	0.490	45.8	45.7	0.977
Antidepressant use <6 month (%)	15.2	13.0	19.2	0.028	14.68	16.21	0.589

Before Propensity Score Matching				After Propensity Score Matching			
	Weight Loss >5% (n = 460)	Weight change ≤5% (n = 915)	Weight Gain >5% (n = 301)	P-value	Weight Loss >5% (n = 327)	No weight loss (n = 327)	P-value
Baseline smoking status							
Non-smoker (%)	39.3	36.1	21.4	<0.0001	39.1	37.3	0.368
Former smoker (%)	38.2	32.8	30.5		35.5	32.4	
Current smoker (%)	22.5	31.1	48.1		25.4	30.3	
Change from baseline							
BDI change	-6.0 ± 9.0	-6.6 ± 8.4	-5.9 ± 9.9	0.456	-5.8 ± 8.6	-5.2 ± 8.2	0.391
ESSI change	2.6 ± 6.0	2.8 ± 5.9	2.2 ± 6.0	0.269	2.4 ± 5.7	2.1 ± 5.9	0.557
Smoking cessation (%)	11.3	12.7	28.2	<0.0001	12.5	12.2	0.906

Table 3

Event Incidence Rates*.

Outcome	Baseline BMI Groups (N = 2318)					p-value [†]
	Underweight (0~20) (n=84)	Normal (20~25) (n=528)	Overweight (25 ~30) (n = 872)	Obese (30 ~40) (n = 700)	Obese 3 (≥40) (n = 134)	
Death or recurrent MI (n = 558)	18.4 (29)	13.7 (146)	11.2 (207)	10.0 (149)	9.3 (27)	0.004
All cause mortality (n = 317)	12.5 (21)	7.5 (90)	6.0 (121)	4.5 (74)	3.4 (11)	<0.001
Cardiovascular mortality (n=197)	6.5 (11)	4.5 (54)	4.3 (87)	2.4 (40)	1.5 (5)	<0.001
Fatal or nonfatal MI (n = 343)	8.3(13)	7.5 (79)	7.1 (130)	6.8 (102)	6.6 (19)	0.9
Recurrent nonfatal MI (n= 317)	7.0(11)	6.9 (73)	6.5 (119)	6.4 (95)	6.6 (19)	0.99
CV Hospitalization (n = 847)	19.9(27)	22.8 (196)	20.3 (308)	21.7 (261)	24.6 (55)	0.6

Note:

* Per 100 patient-years; numbers of events are shown in parentheses.

[†]The p-value of the Chi-squared test for equality of the incidence rates for the five BMI groups.

Table 4
Adjusted Hazard ratios*, with 95% Confidence Intervals (N=1719).

	Death / nonfatal MI (event n = 401)		All cause mortality (event n= 220)		Cardiovascular mortality (event n =133)	
	HR(95% CI)	p-value	HR(95% CI)	p-value	HR(95% CI)	p-value
Model 1: Baseline BMI groups						
Normal (20~25)	1.00		1.00		1.00	
Underweight (<20)	1.54 (0.98-2.41)	0.06	1.77 (1.01-3.12)	0.046	1.31 (0.57-3.02)	0.5
Overweight (25~30)	0.96 (0.74-1.24)	0.8	0.96 (0.69-1.35)	0.8	1.17 (0.77-1.77)	0.5
Obese (>30)	0.83 (0.63-1.10)	0.2	0.74 (0.51-1.07)	0.1	0.60 (0.36-0.99)	0.047
Model 2: Baseline continuous BMI (per 5 unit increase)						
BMI	0.88 (0.80-0.96)	0.005	0.83 (0.73-0.94)	0.004	0.83 (0.70-0.98)	0.03

Note:

* Multivariate Cox regression model included age; gender; creatinine (≥ 1.3 vs. <1.3); systolic and diastolic blood pressure; previous myocardial infarction; CABG; congestive heart failure; peripheral vascular disease; stroke; renal insufficiency; pulmonary diseases; diabetes; BDI scores; CABG treatment after the index MI; baseline use of vasodilators. The regression results were based on N=1719 subjects with nonmissing covariates.

Table 5
Adjusted Hazard ratios*, with 95% Confidence Intervals (N =1242).

	Death /recurrent MI (event n=239)		All cause mortality (event n = 107)		Cardiovascular mortality (event n = 65)	
	HR(95% CI)	p-value	HR(95% CI)	p-value	HR(95% CI)	p-value
Delta weight	0.91 (0.83-0.99)	0.041	Model 1: Weight change at follow-up from baseline (per 5 kg)			
			0.83 (0.72-0.96)	0.011	0.87 (0.73-1.04)	0.1
Slope weight	0.90 (0.81-0.99)	0.030	Model 2: Weight change at 6 months (per 5 kg)			
			0.83 (0.71-0.96)	0.010	0.87 (0.73-1.05)	0.1
Model 3: Weight change groups						
Weight change≤5%	1.00		1.00		1.00	
Weight gain>5%	0.76 (0.52-1.12)	0.2	0.72 (0.38-1.39)	0.3	0.82 (0.37-1.85)	0.6
Weight loss >5%	1.38 (1.03-1.86)	0.032	1.74 (1.13-2.68)	0.012	1.79 (1.02-3.14)	0.043
Model 4: Weight change groups after propensity score matching†						
Weight loss >5%	1.59 (1.11-2.28)	0.012	2.06 (1.20-3.52)	0.009	2.20 (1.06-4.60)	0.035

Note:

* Multivariate Cox regression model included baseline BMI, antidepressant use before 6 month, smoking cessation, baseline smoking history, creatinine clearance as well other covariates as in Table 4. Events that occurred before the 6-month visit were not included. The regression results for model 1-3 were based on N=1242 subjects with nonmissing weight change and covariates. After additional adjustment for ejection fraction, Killip class, depression score change and social isolation score change, the estimates and p-values are similar to above.

† The propensity matched sample of N=654 patients have 129 death/recurrent MI, 68 death, and 39 CV death events, and the weight loss>5% group have 73 (57%) death/recurrent MI, 42 (62%) death, and 25 (64%) CV death events.