Impact of body mass index on outcomes of enhanced external counterpulsation therapy

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Objectives We evaluated the association of baseline body mass index (BMI) on the outcomes of enhanced external counterpulsation (EECP) therapy for chronic stable angina.

Background We are in the midst of a pandemic of obesity, which is complicating the care of patients with coronary artery disease (CAD).

Methods We examined 2730 patients enrolled from 2002 to 2004 in the IEPR-2. Baseline and outcome variables were stratified by the entry BMI in kilograms per meter squared.

Results Obesity (BMI > 30 kg/m^2) was common (40.6%) among patients with severe CAD referred for EECP. Within the total cohort, 2.6% was underweight (BMI ≤ 20 kg/m^2) and 4.5% was morbidly obese (BMI > 40 kg/m^2). Prevalence of diabetes, hypertension, dyslipidemia, and heart failure (HF) was higher in obese patients. However, the rates of baseline angina and prior revascularization were similar among the groups. The peak diastolic augmentation ratio was similar between groups during the first (0.7 ± 0.4 for lowest and highest BMI) and last hours of treatment (0.9 ± 0.5 and 0.8 ± 0.5). The cumulative hours of treatment, the change in angina class, and the Duke Activity Status Index were similar for all BMI groups. There was a greater reduction in weekly anginal episodes from baseline across ascending levels of BMI (−6.3 ± 13.6 to −9.7 ± 15.8, P = .03). The rates of discontinuation for clinical events were highest (14.3%) with skin breakdown being the most frequent cause (10.1%) in the underweight. The rates of clinical events including myocardial infarction, HF, and death trended higher across ascending levels of BMI (P = .52). Multivariate analysis found that older age, history of stroke, history of HF, and diabetes, but not BMI, were predictors of clinical events.

Conclusions More than 40% of patients with severe CAD referred for EECP were obese. Underweight patients had higher rates of discontinuation of treatment mainly because of skin breakdown. Symptomatic benefit of EECP was similar among all BMI groups. However, despite symptomatic improvement, there was a nonsignificant trend for higher rates of myocardial infarction, HF, and death as BMI increased. (Am Heart J 2006;151:139.e9-139.e13.)

We are in the midst of a rapidly evolving obesity pandemic. Recent data from the ARIC Study indicate that approximately 82% of adult Americans can expect to experience a weight gain during adulthood.[1] This weight gain is usually cumulative and generally does not regress unless intentional weight loss is attempted or chronic illness develops. These data suggest that the obesity pandemic is reaching into populations with coronary artery disease (CAD) and may impact therapies for CAD.[2,3]

Enhanced external counterpulsation (EECP) was cleared for marketing by the Food and Drug Administration in 1995 for use in stable and unstable angina, acute myocardial infarction (MI), and cardiogenic shock, and in 2002 for use in heart failure (HF). The Centers for Medicare and Medicaid Services approved coverage of EECP in 1999 for use in patients with angina refractory to maximal medical therapy and attempts at percutaneous and/or surgical coronary revascularization. Enhanced external counterpulsation is a noninvasive counterpulsation technique that has been shown to reduce angina pectoris, improve quality of life, and extend time to exercise-induced ischemia in patients with symptomatic stable angina.[4]

Previous studies have shown that the degree of diastolic augmentation during EECP can impact the

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Table I. Baseline demographics, clinical characteristics, and cardiac medications according to BMI category

		BMI (kg/m²)					
Factor	**n**	**≤20.0**	**20.1-25.0**	**25.1-30.0**	**30.1-35.0**	**35.1-40.0**	**>40.0**
No.		70	522	1018	690	306	124
Age (y) (mean ± SD)*	2720	68.4 ± 14.2	70.5 ± 11.5	68.5 ± 10.9	65.6 ± 10.6	63.5 ± 9.8	61.8 ± 10.8
Age ≥80 y (%)*	2720	22.9	20.0	12.6	7.1	5.3	2.4
Men (%)†	2730	64.3	71.3	76.1	75.7	70.9	58.1
BMI (kg/m^2) (mean ± SD)	2730	18.1 ± 1.4	23.0 ± 1.3	27.5 ± 1.3	32.1 ± 1.4	36.9 ± 1.3	42.2 ± 1.4
Weight (kg)*	2730	55.9 ± 13.9	74.2 ± 20.9	81.2 ± 10.6	94.0 ± 11.2	105.7 ± 13.7	115.7 ± 16.6
Hypertension (%)†	2683	75.7	78.1	80.3	80.7	87.8	82.8
Hyperlipidemia (%)*	2668	84.1	84.9	92.2	91.1	94.3	94.2
Diabetes (%)*	2666	30.4	34.1	37.9	48.4	64.6	65.3
Heart failure (%)	2625	26.5	31.1	27.3	27.5	29.9	35.9
Prior MI (%)	2675	73.5	73.2	71.9	68.9	71.7	65.9
Prior PCI (%)*	2601	59.7	65.0	68.9	70.7	73.0	76.9
Prior CABG (%)†	2671	62.3	69.9	71.8	73.2	69.9	67.2
Multivessel coronary disease (%)	2313	84.7	80.2	78.5	82.2	79.7	76.3
Left ventricular ejection fraction (%)*	2488	46.5 ± 17.5	44.9 ± 16.3	46.3 ± 14.2	48.6 ± 13.7	48.9 ± 13.6	48.5 ± 14.4
Antiplatelet therapy (%)	2726	77.1	75.6	76.1	77.4	78.7	71.8
Warfarin (%)†	2724	20.0	16.0	12.3	9.0	10.8	12.9
β-Blocker (%)*	2727	71.4	75.9	78.7	83.5	83.6	80.6
Angiotensin-converting enzyme inhibitor (%)	2728	41.4	42.7	47.1	47.5	45.9	52.4
Angiotensin II receptor antagonist (%)†	2728	12.9	12.1	11.1	11.9	16.4	19.4
Nitrates (%)	2727	81.4	74.7	74.7	75.8	74.8	78.2
Diuretics (%)*	2727	40.0	45.4	41.4	48.3	54.4	66.9

CABG, Coronary artery bypass graft surgery.
*P < .0001.
†P < .05.
‡P < .001.

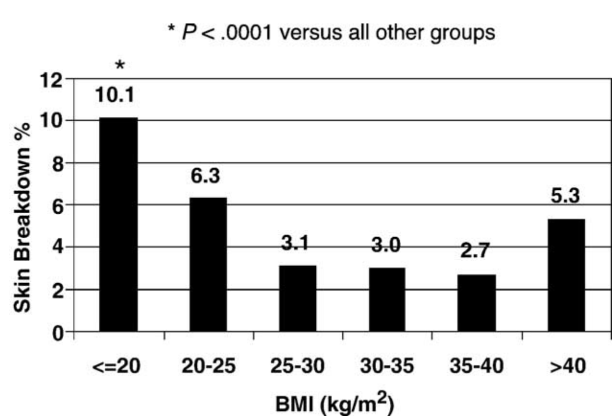
short- and long-term antianginal benefits with this therapy.[5] Because EECP involves placement of cuffs over the calf, thigh, and hip/buttock area, the size of these areas and the degree of subcutaneous fat could impact the degree of augmentation and ultimately the clinical effect of EECP. We set out to explore the relationship between the body mass index (BMI), the best recorded measure for obesity in this population, and the outcomes after EECP.

Methods

Patients

The IEPR-2 enrolled 3218 consecutive patients from January 2002 to October 2004. Data in 2730 IEPR-2 patients who had their weight and height recorded were used for this analysis. Data came from 73 clinical sites where, on average, EECP was performed on each patient one session per day, 5 days a week, for 7 weeks. Because the IEPR was designed to collect data on as broad a range of patients as possible, the criteria for entry were only that the patient gave informed consent and had at least 1 hour of EECP treatment of chronic angina. Body mass index was calculated from the reported height and weight. Body mass index was divided as a dichotomous variable (obese defined as >30 kg/m^2) and into 6 ordinal categories: ≤20.0, 20.1 to 25.0, 25.1 to 30.0, 30.1 to 35.0, 35.1 to 40.0, and >40 kg/m^2. Patients with a BMI ≤20 kg/m^2 were defined as underweight, those >30 kg/m^2 as obese, and those>40 kg/m^2 as morbidly obese.

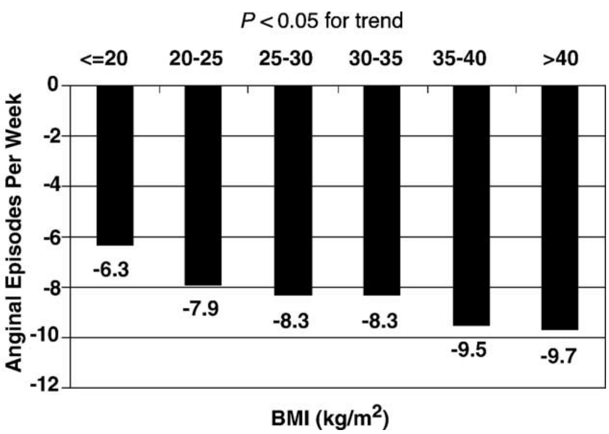
Figure 1



Rates of skin breakdown according to BMI group.

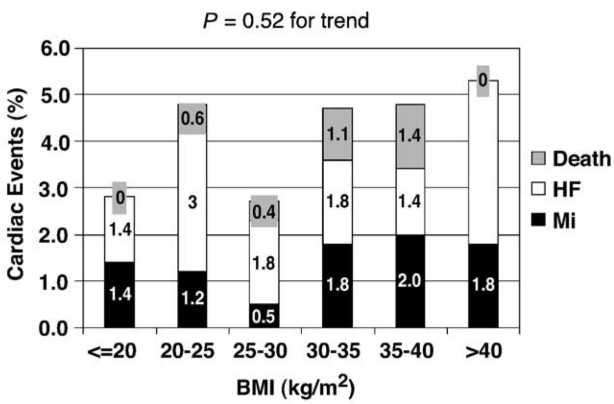
The IEPR methodology has been previously described.[6] All patients gave written informed consent before entry into the Registry. Briefly, the Registry methodology involved collecting patient demographics, medical history, coronary disease status,

Figure 2



Reduction in the number of anginal episodes per week with EECP according to BMI group.

Figure 3



Cardiovascular events during treatment.

and quality of life assessments before EECP treatment. After 35 hours of standard EECP treatment (Vasomedical, Westbury, NY), data on Canadian Cardiovascular Society anginal class, quality of life using the Duke Activity Status Index (DASI), and interim clinical events were collected.

Statistical analysis

Data are presented as percentages for categorical variables or as mean values and SDs for continuous variables. χ^2, χ^2 for trend, and 1-way analysis of variance were used as test statistics as appropriate. A P value <.05 was considered statistically significant. Multivariate analysis was done using a logistic regression model with a backward selection technique. There were 2568 complete cases used in the model and 91 events (composite of death, MI, and HF).

Results

Baseline characteristics

Baseline characteristics according to BMI group are given in Table I. A total of 1110 patients (40.6%) were obese and 4.5% morbidly obese. Age decreased across the BMI groups. However, age ≥80 years was more frequent in the low BMI groups and uncommon in the obese BMI groups. Most of the subjects had multivessel CAD, and there was no difference among the BMI groups. Prevalence of diabetes, hypertension, dyslipidemia, and HF increased with BMI.

Current treatment

Rates of percutaneous coronary angioplasty and bypass surgery were higher across ascending BMI groups. Importantly, there were higher rates of use for β-blockers and diuretics as BMI increased, whereas rates of warfarin use were the highest in the lowest BMI groups. A total of 18.3% of patients were not receiving antiplatelet or warfarin. Consistent with similar severity of angina at baseline, nitrate use was high and not significantly different among the groups.

Procedural results and complications

The peak diastolic augmentation ratio was similar for all groups during the first (0.7 ± 0.4 for lowest and highest BMI) and last hours of treatment (0.9 ± 0.5 and 0.8 ± 0.5, respectively). The cumulative hours of treatment were similar for all groups (31.2 ± 10.4 and 33.3 ± 10.0 hours for lowest and highest BMI groups, respectively).

Rates of skin breakdown noted clinically, which caused either adjustment of placement of cuffs, extra padding, monitoring, or discontinuation of treatment, are shown in Figure 1. The rate of stopping EECP treatment because of an adverse clinical event was highest for underweight patients (P < .001 vs patients with BMI > 20 kg/m^2). The rates of stopping for an adverse clinical event were 14.3%, 6.7%, 6.3%, 6,6%, 7.6%, and 7.3%, respectively, for the lowest to highest BMI groups. Other procedural complications including new arrhythmias, transient ischemic events, and strokes were all infrequent (<2.0%) and similar among the BMI groups (data not shown).

Improvement in symptoms

Figure 2 shows the reduction in absolute numbers of angina episodes per week from baseline and at the completion of EECP 7 weeks later. There was a trend for a greater reduction in angina frequency as BMI increased (Table II). However, there was no difference in the rates of reduction in >1 angina class or improvement in the DASI Score.

Table II. Symptomatic response to EECP according to BMI group

		BMI (kg/m²)					
Variable	**n**	**≤20.0**	**20.1-25.0**	**25.1-30.0**	**30.1-35.0**	**35.1-40.0**	**>40.0**
Angina episodes per week*	2752	11.1	11.1	11.2	11.1	12.6	12.4
Angina class‡	2658						
I		1.5	0.6	2.5	1.0	0.7	1.6
II		5.9	5.0	6.4	3.0	5.1	4.1
III		52.9	65.9	66.1	68.8	66.3	69.7
IV		39.7	28.6	25.0	27.2	27.9	24.6
Duke Activity Status Score (mean ± SD) (before)†	2303	9.9 ± 8.4	11.6 ± 10.3	12.6 ± 11.1	10.4 ± 9.3	9.8 ± 9.2	9.1 ± 9.1
Duke Activity Status Score (mean ± SD) (after)†	2303	15.0 ± 12.1	17.0 ± 12.1	18.3 ± 13.2	16.2 ± 11.3	16.0 ± 12.9	13.6 ± 10.0
Duke Activity Status Score improved (%)	2303	63.2	61.3	62.3	66.3	67.8	61.0

*$P < .05$.
†$P < .001$.

Clinical events

Figure 3 shows the rates of death, the MI, and the development of HF according to BMI group. There was an increase from 2.9% to 4.8% in the composite event rate from the lowest to the highest BMI group ($P = .52$). Deaths were infrequent and evenly distributed in the middle BMI groups with no deaths in either extreme group. Rates of percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery were low and similar among the BMI groups. Multiple logistic regression for the composite out of death, MI, or HF during EECP treatment found older age (OR 1.041, 95% CI 1.02-1.06, $P = .0002$), prior history of stroke or transient ischemic attack (OR 1.80, 95% CI 1.11-2.91, $P = .02$), diabetes (OR 1.76, 95% CI 1.12-2.77, $P = .02$), and prior HF (OR 4.25, 95% CI 2.70-6.71, P, 0.0011), but not BMI (OR 1.02, 95% CI 0.98-1.06, $P = .41$), as significant predictors. There was an interaction found between very old age (≥80 years) and BMI ≥30 kg/m^2 for the composite outcome ($P = .05$).

Discussion

We have demonstrated that more than 40% of patients with severe CAD referred for EECP were obese. Rates of skin breakdown and cessation of therapy before the end of 7 weeks were more common in the underweight. Conversely, rates of MI, development of HF, and death during the course of EECP trended nonsignificantly higher as BMI increased. For those 80 years and older, obesity, which was uncommon, was an independent predictor of clinical events during the course of EECP.

The EECP therapy systems used in the IEPR-2 have cuffs in 5 sizes applied around the calves, thighs, and hips/buttocks of all the patients. Our results suggest that there may be a cushioning effect of adiposity that works to reduce rates of skin breakdown. Hence, only in the underweight was there appreciable skin breakdown likely because of pressure over bony areas including the anterior iliac crests. However, in the obese, excess adiposity and increased overall size of the circulatory system, with greater densities of capillary beds (yet similar size of intravascular volume) to be perfused during each pulse, did not reduce the extent of diastolic augmentation or the symptomatic benefit of EECP.[7,8] Obese patients, if anything, had a slight reduction in the frequency of angina compared with nonobese patients, whereas the percent improvement in the DASI was similar among the groups. This finding is likely to be meaningful because the obese in general have lower self-reported health-related quality of life owing to their angina, dyspnea, or depressive symptoms as compared with persons with normal body weight.[9]

The higher rates of MI, HF, and death seen in the higher BMI groups over the course of EECP therapy may be a reflection of greater overall risk of events related to those with CAD and excess adiposity and more baseline comorbidities.[10] In particular, both HF and diabetes, which are independently related to obesity, were found to be an independent predictors of events during the course of EECP. However, it may be a signal that EECP applied to larger lower extremities and in those with a greater overall systemic circulatory distance may not be optimized for body size. Hence, one practical application from this study would be the new research on the optimization of EECP according to body size to reduce adverse events and possibly improve efficacy of treatment.

We acknowledge several limitations to our study. We relied on self-reported height and weight, which introduced systematic error.[11] Likely, the true BMI is higher for all subjects in the study. We do not have details on cases that were discontinued and whether or not the skin breakdown was the major reason for stopping. However, given the low frequency of other noncardiac events, it is likely that this was the reason for higher discontinuation rates in the underweight. Finally, long-term outcomes are not yet available to determine whether or not the course of EECP had equal durability on symptoms and outcomes across BMI groups.

Conclusions

Obesity was common (40.6%) among patients with severe CAD referred for EECP. Underweight patients had higher rates of discontinuation and skin breakdown. Symptomatic benefit of EECP was similar among all BMI groups. Cardiac complications during the course of EECP therapy appear are not directly related to BMI but are associated with obesity-related comorbidities including HF and diabetes.

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