Ingle, L, Rigby, AS, Carroll, S, Butterly, R, King, RF, Cooke, CB, Cleland, JGJF & Clark, AL 2007, 'Changes in body composition in patients with left ventricular systolic dysfunction initiated on beta-blocker therapy' Experimental and Clinical Cardiology, vol 12, no. 1, pp. 46-47.

Changes in body composition in patients with left ventricular systolic dysfunction initiated on beta-blocker therapy

Lee Ingle PhD[1], Alan S Rigby PhD[2], Sean Carroll PhD[1], Ron Butterly PhD[1], Rod F King PhD[1], Carlton B Cooke PhD[1], John GJF Cleland MD[2], Andrew L Clark MD[2]

L Ingle, AS Rigby, S Carroll, et al. Changes in body composition in patients with left ventricular systolic dysfunction initiated on beta-blocker therapy. Exp Clin Cardiol 2007;12(1):46-47.

BACKGROUND: Increasing body mass index, cholesterol and body fat are associated with a better prognosis in patients with left ventricular systolic dysfunction (LVSD). Beta-blocker usage is associated with changes in body composition and increased body fat. The present study investigated 12-month changes in body composition in patients with LVSD initiated on beta-blocker therapy.
METHODS: The relation between beta-blocker use and body composition was evaluated in 91 patients (75% male) with LVSD. Body composition was assessed by bioelectrical impedance.
RESULTS: Seventeen patients died during the study period. There was no statistical difference among beta-blocker usage, beta-blocker type, or changes in body fat, basal metabolic rate, impedance, fat-free mass, fat mass and total body water. There were no significant differences between any of these measures and beta-blocker usage.
CONCLUSION: After 12 months, changes in body composition were not found to be influenced by initiation of beta-blocker therapy in patients with LVSD.

Key Words: *Body fat; Chronic heart failure; Fat-free mass; Fat mass*

Chronic heart failure (CHF) is a prevalent and deadly condition (1). Patients with CHF have an increased resting metabolic rate, which may be related to the development of cardiac cachexia (2). Patients with cachexia have a worse prognosis than patients without cachexia but both experience a similar degree of left ventricular systolic dysfunction (LVSD) (3,4). Conversely, while thinner patients have a poorer prognosis, increasing body mass index (BMI) (4,5) and body fat (6) are associated with a better outcome.

Beta-blocker therapy is undoubtedly beneficial to patients with CHF, irrespective of symptom severity (7). Previous work has shown that long-term beta-blocker use is associated with increased weight gain compared with placebo-controlled patients following acute myocardial infarction (8). A recent pilot study (9) claimed that beta-blockers may increase body fat mass and total body fat in patients with CHF, and short-term beta-blocker use was associated with reversal of muscle protein catabolism in children suffering from severe burns (10). We aimed to investigate 12-month changes in body composition in patients with CHF initiated on beta-blocker therapy.

METHODS

The Hull and East Riding Ethics Committee approved the study, and all patients provided informed consent for participation. Body composition was determined by bioelectrical impedance assessment (Tanita TBF 410-MA, Tanita Corp, Japan). Patients would step onto the bioelectrical impedance analysis scales, and a safe electrical signal was conducted across the shortest distance between two fixed points (each foot) to measure impedance. The premise of this application is that while body fat resists the electrical signal (impedance), lean tissue (containing more water) allows the signal to pass more easily. Fifty-two per cent of patients were initiated on carvedilol, 36% bisoprolol, 8% atenolol and 4% others.

CHF was defined in accordance with the European Society of Cardiology (11). Left ventricular function was determined from two-dimensional echocardiography and was carried out by one of three trained operators. Left ventricular ejection fraction (LVEF) was calculated using the Simpson's formula from measurements of end-diastolic and end-systolic volumes on apical two-dimensional views, and LVSD was diagnosed if LVEF was 45% or less.

The relation between changes in body fat, body mass, fat mass or fat-free mass, and beta-blocker usage was investigated by least squares regression analysis, taking beta-blocker as a factor at two levels (any versus none) and beta-blocker type (none, atenolol, bisoprolol, carvedilol and any other). The appropriateness of the least squares model was examined by plotting residuals. The residual plots showed no obvious departure from normality. All regression analyses were corrected for age, sex and baseline BMI. Paired samples *t* tests were used to identify differences between baseline and follow-up in surviving patients. An arbitrary level of 5% statistical significance (two-tailed) was assumed.

RESULTS

A total of 91 consecutive unselected patients (75% male) diagnosed with LVSD (mean age 72±11 years; BMI 28.0±5.3 kg/m^2; body mass 80.6±15.0 kg; mean LVEF 32±9%) and body fat (30.9±14.0%), fat mass (24.7±12.3 kg) and fat-free mass (56.6±10.2 kg) were studied .

Of the initial 91 patients, 17 died (19%) before follow-up. The mean follow-up period was 12±2 months. After 12 months,

[1]*Carnegie Research Institute, Leeds Metropolitan University, Beckett's Park Campus, Leeds;* [2]*Department of Academic Cardiology, University of Hull, Castle Hill Hospital, Cottingham, United Kingdom*
Correspondence: Dr Andrew L Clark, Department of Academic Cardiology, University of Hull, Castle Hill Hospital, Cottingham, Kingston-upon-Hull HU16 5JQ, United Kingdom. Telephone 01-482-624012, fax 01-482-624071, e-mail A.Clark@hull.ac.uk
Received for publication April 6, 2006. Accepted September 5, 2006

TABLE 1
Clinical characteristics of patients at baseline and 12 months later

Variable	Baseline	12 months	P
n	91	91	–
Males (%)	75	75	–
Age (years)	72.0±11.1*	73.0±11.1*	–
Body mass index (kg/m^2)	28.0±5.0*	28.4±5.5*	0.27
LVEF (%)	32±9*	39±12*†	0.01
Body fat (%)	30.9±14.0*	31.3±14.2*	0.44
Fat mass (kg)	24.7±12.3*	25.3±13.2*	0.35
Body mass (kg)	80.6±15.0*	81.2±17.0*	0.28
Fat-free mass (kg)	56.6±10.2*	56.3±10.0*	0.52
Basal metabolic rate (kJ)	466±249*	448±134*	0.49
Total body water (%)	41.2±8.1*	42.0±8.3*	0.25
Impedance (ohms)	6349±1304*	6382±1407*	0.46
Diuretics (%)	62	75†	0.01
ACE inhibitor (%)	51	75†	0.001
Atrial fibrillation (%)	26	22	0.35
Smoking status (%)	8	9	0.69
Renal impairment (%)	26	23	0.55

**Values are mean ± SD; †Significant difference (P<0.05). ACE Angiotensin-converting enzyme; LVEF Left ventricular ejection fraction*

mean BMI was 28.4±5.5 kg/m^2, P>0.05; body mass was 81.2±17.0 kg, P>0.05; body fat was 31.3±14.2%, P>0.05; fat mass was 25.3±13.2 kg, P>0.05; and fat-free mass was 56.3±10.0 kg, P>0.05 (Table 1). Therefore, mean body fat increased by 0.4±0.12 kg, fat mass increased by 0.6±0.20 kg, body mass increased by 0.6±0.17 kg and fat-free mass decreased by 0.3±0.06 kg after 12 months.

There was no statistical difference among beta-blocker usage, beta-blocker type, or changes in body fat, basal metabolic rate, impedance, fat-free mass, fat mass and total body water. There was also no difference between beta-blocker usage, beta-blocker type and body composition.

DISCUSSION

In the cohort of patients with LVSD, body mass, fat mass and body fat increased after 12 months, but not significantly. No differences existed between beta-blocker usage or beta-blocker type and changes in body composition. Therefore, after 12 months, changes in body composition were not influenced by initiation of beta-blocker therapy in patients with LVSD.

There are a dearth of studies that have examined temporal changes in body composition in patients with CHF. In a study by Rossner et al (9), 3837 men and women were randomly assigned to receive propranolol or placebo, five to 21 days after acute myocardial infarction, for up to 40 months. A mean weight gain of 1.2 kg (95% CI 0.9 kg to 1.5 kg) was reported. Recently, a study by Lainscak et al (8) reported that treatment with beta-blockers may increase fat mass and body fat in patients with CHF. However, this study included only 41 patients, and the statistical analysis was limited. It was postulated that drug-dependent mechanisms for weight gain included a reduced basal metabolic rate, a reduced thermogenic response and inhibition of lipolysis, which have been reported in other studies (12-15).

To determine if body composition is affected by beta blockade in patients with CHF, it is important to individually determine how long each patient had been prescribed the medication. In our patients, the duration of therapy was not a predictor of changes in body composition. It may have been that the influence of beta blockade on body composition takes longer than 12 months to manifest in CHF. Therefore, further long-term studies (in excess of 12 months) are required. Future investigations should also examine whether temporal changes in body composition affect survival rates in patients with CHF. In conclusion, after 12 months, changes in body composition were not found to be influenced by initiation of beta-blocker therapy in patients with LVSD.

TABLE 2
Relationship between beta-blocker usage and per cent changes in body fat after 12 months in patients with left ventricular systolic dysfunction

Variable	Level	Mean difference (95% CI)	P
Beta-blocker	None	11.9 (10.8,13.3)	
	Any	11.7 (10.7,12.7)	0.61
Type	Atenolol	12.1 (9.9,14.2)	
	Bisoprolol	12.7 (10.9,14.4)	
	Carvedilol	10.8 (9.4,12.3)	
	Other	11.7 (8.5,14.9)	0.79

Mean values are adjusted for age, sex and body mass index. Other beta-blockers were celiprolol, metoprolol, propranolol, sotalol and timolol

REFERENCES

1. Cleland JG, Khand A, Clark A. The heart failure epidemic: Exactly how big is it? Eur Heart J 2001;22:623-6.
2. Obisesan TO, Toth MJ, Donaldson K, et al. Energy expenditure and symptom severity in men with heart failure. Am J Cardiol 1996;77:1250-2.
3. Anker SD, Ponikowski P, Varney S, et al. Wasting as independent risk factor for mortality in chronic heart failure. Lancet 1997;349:1050-3. (Erratum in 1997;349:1258).
4. Davos CH, Doehner W, Rauchhaus M, et al. Body mass and survival in patients with chronic heart failure without cachexia: The importance of obesity. J Card Fail 2003;9:29-35.
5. Horwich TB, Fonarow GC, Hamilton MA, MacLellan WR, Woo MA, Tillisch JH. The relationship between obesity and mortality in patients with heart failure. J Am Coll Cardiol 2001;38:789-95.
6. Lavie CJ, Osman AF, Milani RV, Mehra MR. Body composition and prognosis in chronic systolic heart failure: The obesity paradox. Am J Cardiol 2003;91:891-4.
7. Packer M, Coats AJ, Fowler MB, et al. Effect of carvedilol on survival in severe chronic heart failure. N Engl J Med 2001;344:1651-8.
8. Lainscak M, Keber I, Anker SD. Body composition changes in patients with systolic heart failure treated with beta-blockers: A pilot study. Int J Cardiol 2006;106:319-22.
9. Rossner S, Taylor CL, Byington RP, Furberg CD. Long term propranolol treatment and changes in body weight after myocardial infarction. BMJ 1990;300:902-3.
10. Herndon DN, Hart DW, Wolf SE, Chinkes DL, Wolfe RR. Reversal of catabolism by beta-blockade after severe burns. N Engl J Med 2001;345:1223-9.
11. Remme WJ, Swedberg K. Comprehensive guidelines for the diagnosis and treatment of chronic heart failure. Task force for the diagnosis and treatment of chronic heart failure of the European Society of Cardiology. Eur J Heart Fail 2002;4:11-22.
12. Welle S, Schwartz RG, Statt M. Reduced metabolic rate during beta-adrenergic blockade in humans. Metabolism 1991;40:619-22.
13. Astrup A, Simonsen L, Bulow J, Madsen J, Christensen NJ. Epinephrine mediates facultative carbohydrate-induced thermogenesis in human skeletal muscle. Am J Physiol 1989;257:E340-5.
14. de Jonge L, Bray GA. The thermic effect of food and obesity: A critical review. Obes Res 1997;5:622-31.
15. Koch G, Franz IW, Lohmann FW. Effects of short-term and long-term treatment with cardio-selective and non-selective beta-receptor blockade on carbohydrate and lipid metabolism and on catecholamines at rest and during exercise. Clin Sci (Lond) 1981;61(Suppl 7):433s-5s.