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Body mass index is inversely associated with mortality in patients with peripheral vascular disease

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ABSTRACT

Background: Current guidelines contain no advice on how to manage obesity and underweight in patients with peripheral vascular disease (PVD).
Objectives: The aim of this study was to assess the association of underweight, overweight and obesity with mortality in patients with PVD.
Patients and Methods: We recruited 1472 patients with a broad range of presentations of PVD. Underweight, overweight and obesity were defined by body mass index (BMI) and associated with mortality using Kaplan Meier and Cox proportional hazard analyses.
Results: Survival at 3 years was 37.5, 78.1, 86.8 and 87.0% for patients that were underweight, normal weight, overweight and obese at recruitment, respectively, $p < 0.001$. Patients that were underweight had approximately twice the risk of dying (RR 2.15, 95% CI 1.31–3.55, $p = 0.003$), while patients that were overweight (RR 0.67, 95% CI 0.49–0.91, $p = 0.011$) or obese (RR 0.59, 95% CI 0.41–0.85, $p = 0.005$) had approximately half the risk of dying, after adjustment for other risk factors and using normal weight subjects as the reference group. 823 patients had waist circumference measured at recruitment. Patients with waist circumference in the top quartile had half the risk of dying (RR 0.50, 95% CI 0.26–0.98, $p = 0.045$). In 267 patients we assessed the relationship between BMI and abdominal fat volumes using computed tomography. BMI was highly correlated with both intra-abdominal and subcutaneous fat volumes.
Conclusions: Obesity whether assessed by BMI or central fat deposition is associated with reduced risk of dying in patients with established PVD. Underweight is highly predictive of early mortality in patients with PVD.

Obesity is an important risk factor for cardiovascular events and mortality in the general population [1–3]. Current guidelines recommend weight loss in patients who are obese or overweight with coronary heart disease (CHD) [4,5]. In contrast obesity has been associated with improved outcomes in patients with a range of established chronic diseases [6–16].

Peripheral vascular diseases (PVD) are a group of conditions affecting the vessels outside the heart [17–20]. In general PVD has received less attention than CHD, with a number of studies suggesting that risk factors in patients with PVD are frequently managed less intensively than those in CHD patients, despite equal or worse prognosis [21–23]. Current guidelines for treating PVD scarcely mention obesity, weight management and nutrition, thus it is not clear how these should be addressed in this patient group [17–20]. The prognostic importance of anthropometric measures in predicting survival in patients with PVD is controversial [24–44]. Large waist circumference, as part of the metabolic syndrome, has been associated with increased incidence of cardiovascular events in some studies [24–29]. While other studies have associated overweight and obesity with reduced mortality [30–36], or found no association between body mass index (BMI) and survival [37–44]. Given the inconsistency in previous reports regarding the association of anthropometric measures with outcome in patients with PVD the current study was designed to examine the association of BMI with survival in a diverse cohort of PVD patients. The primary aim of this study was to assess the association of underweight, overweight and obesity with survival in PVD patients. Secondary aims were to assess the association of waist circumference with survival and to examine the relationship between BMI and central fat deposition.

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1. Methods

1.1. Study design

This study was designed as an on-going prospective cohort investigation of patients with PVD designed to assess risk predictors of PVD presence and outcome commencing in 2002. Due to the previous conflicting results on the association of obesity with outcome in patients with PVD sample size calculations were not straight forward and no formal calculation was performed [24–44]. For the current analysis aimed at assessing the association of BMI with mortality 1472 patients were included. Monte-Carlo simulations suggest that a multivariate regression model is powered sufficiently when 10 outcome events per degree of freedom of the predictor variables are observed [45]. We estimated that at 1 year mortality would be approximately 15% and planned to adjust for 11 variables (age >69 years, male sex, hypertension, diabetes, smoking, CHD, presenting complaint, statin prescription, aspirin prescription, angiotensin converting enzyme inhibitor prescription and angiotensin receptor blocker prescription) in our regression model. Based on these estimates we felt that our sample size was adequate.

1.2. Patients

Patients were recruited from in- and out-patient vascular services at The Townsville Hospital and The Mater Hospital Townsville. Patients with all types of PVD were considered for inclusion. All patients classified as having any type of PVD by a Royal Australasian College of Surgeons accredited vascular specialist were considered for inclusion into the study. Inclusion criteria for the current study included a diagnosis of PVD, the assessment of both height and weight at recruitment, (to enable the calculation of BMI) and at least one follow-up assessment as an in- or out-patient. Ethical approval for the study was granted by the local Institutional Ethics Committees at The Townsville Hospital, The Mater Hospital Townsville and James Cook University. Written informed consent was obtained from all participants.

1.3. Definition of presenting complaint

Presenting category was broadly defined into one of seven groups namely venous disease; miscellaneous PVDs; asymptomatic carotid stenosis; mild lower limb or upper limb peripheral athero-thrombosis; aneurysm of the aorta or peripheral arteries; symptomatic carotid artery stenosis; and critical lower limb ischaemia as previously described [46–51]. Details of the definition of these presenting groups are given in the on-line Supplementary data. For patients with more than one presenting complaint classification was determined by the complaint which was deemed most severe.

1.4. Height and weight

A nurse measured patients' height and weight. Patients were asked to remove shoes and bulky clothing and then stand backwards against a wall mounted measuring tape. Height was measured to the top of the head to the nearest cm. Patients were then asked to stand on weighing scales and weight measured in kg to two decimal places. The accuracy of the weighing scales was checked for validity compared to a known weight at approximately 3 monthly intervals.

1.5. Definition of other risk factors

Hypertension was defined by a history of high blood pressure or receiving treatment to reduce blood pressure [48–50]. Diabetes was defined by a fasting blood glucose concentration ≥7.0 mM, or history of, or treatment for hyperglycaemia [48–50]. Smoking status was classified as current smokers (smoked within the last month), ex-smokers (given up for more than 1 month) and never smokers; and later simplified as ever and never smokers [48–50]. Coronary heart disease (CHD) was defined by a history of myocardial infarction, angina or treatment for coronary artery disease [48–50].

1.6. Medications

At the time of recruitment a list of patients' medications was recorded including whether they were prescribed statins, aspirin, angiotensin converting enzyme inhibitors and angiotensin receptor blockers.

1.7. BMI and waist circumference

Body mass index was calculated as weight in kg divided by height in m^2 [52]. Patients' BMI at recruitment was used to define them as underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.50–24.99 kg/m^2), overweight (BMI 25.00–29.99 kg/m^2) or obese (BMI ≥30.00 kg/m^2) according to the World Health Organisation (WHO) definition [53]. In a sub-set of patients in which a trained research nurse was available the patients' waist circumference was measured at entry in accordance with the International Society for the Advancement of Kinanthropometry guidelines [29,52]. Waist circumference was measured with a tape measure at a point half way between the lowest rib and the anterior superior iliac spine by a trained nurse. Waist and hip measurements were recorded to the nearest cm.

1.8. Follow-up

Patients were followed up through attendance at out-patient clinics and/or as an in-patient as part of their normal medical care. Patients with venous disease and miscellaneous PVD were followed up as needed depending on the severity of their presenting complaint and any medical intervention planned. Patients with limb athero-thrombosis and carotid artery stenosis were generally reviewed 6 months after their initial assessment and then yearly unless symptoms or imaging findings changed [47–49]. Patients with small aneurysms or large aneurysms that had been repaired were followed up yearly or at 6 months if the aneurysm was nearing a diameter at which intervention was indicated [50,51].

1.9. Recording of outcome data

The primary outcome event was death. Charts and hospital electronic records were reviewed for the date of any deaths and cause recorded when available. For surviving patients follow-up was concluded at the date of last in- or out-patient review. Cardiovascular events, particularly admission for myocardial infarction and stroke, were also recorded (see Supplementary data available on-line for further information).

1.10. Assessment of abdominal fat from computed tomography imaging

A sub-set of patients underwent computed tomography angiography (CTA) around the time of recruitment. The CTAs were