SHORT REPORT

Effect of body size on operative risk of carotid endarterectomy

S R Messé, S E Kasner, Z Mehta, C P Warlow, P M Rothwell for the European Carotid Surgery Trialists

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Many studies have found that women have a higher risk of perioperative stroke or death from carotid endarterectomy. Other vascular surgical procedures have demonstrated that body size and morphology impact on operative risk. We correlated the 30 day operative risk of stroke and death in the European Carotid Surgery Trial (ECST) with height, weight, body surface area (BSA), and body mass index using single variable analyses and multivariable logistic regression. Women were at significantly higher risk of perioperative stroke and death in the ECST. Both height and BSA confounded the effect of sex, implying that the generally smaller size of women may contribute to their increased risk. This finding should be validated in other large datasets.

Carotid endarterectomy (CEA) has been proved to reduce the risk of stroke in selected patients, and is an increasingly common surgical procedure.[1] To determine whether a patient should undergo CEA, the short term risk of perioperative complications must be weighed against the risk of stroke without surgery over the long term. Large endarterectomy trials have consistently identified factors that contribute to operative morbidity and mortality including diabetes mellitus, ipsilateral carotid siphon stenosis, contralateral carotid occlusion, left sided procedure, and hemispheric (as opposed to retinal) symptoms.[2–7] Several studies have also reported higher operative risk in women than men.[6–10] A recent systematic review of 21 studies published between 1980 and 2001 determined the odds of perioperative stroke or death in women to be 40% higher (95% confidence interval (CI) 20% to 60%; $p<0.0001$), without significant heterogeneity ($p = 0.1$) between studies (P M Rothwell, personal communication). However, few biologically plausible explanations have been put forth to account for the influence of sex. Among the many differences between men and women that could impact this difference in surgical risk, body size is both intuitively relevant and easy to measure.

A number of measures may be useful to quantify body size and shape. In addition to height and weight, derivative measures such as body surface area (BSA) and body mass index (BMI) are frequently used. In a variety of vascular procedures, low BSA, low BMI, and high BMI have been associated with increased perioperative risk of complications.[11–16] The relationship between body size and morphology with perioperative complications of CEA has not been explored. As demonstrated in other vascular procedures, we hypothesised that patients with the smallest BSA, are malnourished, or are obese will have the highest risk of complications.

SUBJECTS AND METHODS

The European Carotid Surgery Trial (ECST) compared carotid endarterectomy to best medical management in a total of 3024 patients with carotid territory stroke or transient ischaemic attack (TIA). The details of the trial design have been reported previously.[17] For this study, we used measurements of angiographic stenosis based on North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria.[18] Of the 1811 patients treated with CEA in the ECST, the first 1535 consecutive patients had height and weight measured before surgery. From the height (cm) and weight (kg), we calculated the BMI ($\text{weight}/\text{height}^2$) and BSA ($0.007184 \times \text{height}^{0.725} \times \text{weight}^{0.425}$).

Complications were defined as all strokes and deaths within 30 days of surgery. Details of any strokes or deaths occurring during follow up were obtained at clinical review, classified by a trial neurologist at the main trial center, and reviewed by an independent blinded audit committee.

Statistical analyses were performed based on the combined endpoint of stroke and death. Height, weight, BSA, and BMI were tested individually as continuous variables in single risk variable analyses. The independent effects of sex and body size measurements were also assessed in multivariable logistic regression model adjusting for age. The sample size of ECST was based on detecting a difference between medical and surgical therapy. The sample size for the present study was based on the subset of consecutive ECST patients with height and weight data. Given the number of patients with the primary outcome, this sample should have provided adequate power to analyse up to 12 candidate variables potentially associated with the outcome[19]; we evaluated the four body size parameters, sex, and age. All statistical analyses were performed using Stata version 7.0 (Stata Corp., College Station, TX).

RESULTS

Of 1535 patients (1095 men, 440 women) who underwent CEA, 7.8% (6.4% men, 11.1% women) had a stroke or died within 30 days of surgery. Table 1 gives a summary of the characteristics of the 1535 patients by sex. Women had significantly higher operative risk than men (odds ratio (OR) 1.84, 95% CI 1.25 to 2.69; $p = 0.002$). There was no difference between the sexes in degree of stenosis or use of carotid patching. Compared with men, women had significantly lower height, weight, and BSA ($p<0.0001$) and were older ($p = 0.018$). There was no difference in the BMI between the sexes.

In single risk variable analysis, age was not associated with operative risk ($p = 0.18$). Analyses of body size parameters as continuous variables revealed that greater height (OR 0.97

Abbreviations: BMI, body mass index; BSA, body surface area; CEA, carotid endarterectomy; ECST, European Carotid Surgery Trial

Table 1 Characteristics of the patients who underwent carotid endarterectomy in the European Carotid Surgery Trial and who had height and weight recorded*

	All cases (n = 1535)	Men (n = 1095)	Women (n = 440)
Events	119 (7.8%)	70 (6.4%)	49 (11.1%)
Age	62.2 (8.1)	61.9 (8.0)	63.0 (8.3)
% Stenosis	31.8 (39.3)	30.6 (40.0)	34.7 (37.2)
% Patch	26.7	26.8	26.6
Height (cm)	168.9 (8.4)	172.0 (6.8)	161.1 (6.6)
Weight (kg)	72.5 (11.5)	75.0 (10.6)	66.3 (11.0)
BMI (kg/m^2)	25.4 (3.5)	25.3 (3.2)	25.6 (4.1)
BSA (m^2)	1.82 (0.17)	1.88 (0.15)	1.70 (0.14)

*Continuous variables expressed as mean (SD).
BMI, body mass index; BSA, body surface area.

per cm, 95% CI 0.95 to 0.99; p = 0.003), greater weight (OR 0.98 per kg, 95% CI 0.97 to 1.00; p = 0.027) and larger BSA (OR 0.85 per 0.1 m^2 of BSA, 95% CI 0.76 to 0.96; p = 0.006) were associated with less operative risk. BMI was not associated with operative risk (p = 0.69). Similarly, extremes of BMI—malnutrition (BMI<18.5 kg/m^2) and morbid obesity (BMI>30 kg/m^2)—were not significantly associated with higher operative risk (p = 0.52 and p = 0.86, respectively).

In all multivariable analyses, age did not significantly confound the impact of sex, height, or BSA on operative risk but was retained in the models. Models were developed to assess the effects of sex and body size parameters. When sex and height were analysed together, the independent effect of each was no longer statistically significant, suggesting confounding: the OR for female sex was attenuated by 22% (to 1.48; 95% CI 0.91 to 2.41; p = 0.11). There was no interaction (that is, effect modification) between sex and height (p = 0.57). Figure 1A depicts the relationship between operative risk of stroke or death with sex and height. Similarly, when sex and BSA were analysed together, their independent effects were no longer significant: the odds ratio for female sex was attenuated by 18% (to 1.55; 95% CI 0.91 to 2.43; p = 0.054). There was no interaction between sex and BSA (p = 0.11). Figure 1B depicts the relationship between operative risk with sex and BSA. Neither weight nor BMI was significantly associated with risk or confounded the relationship between sex and operative risk.

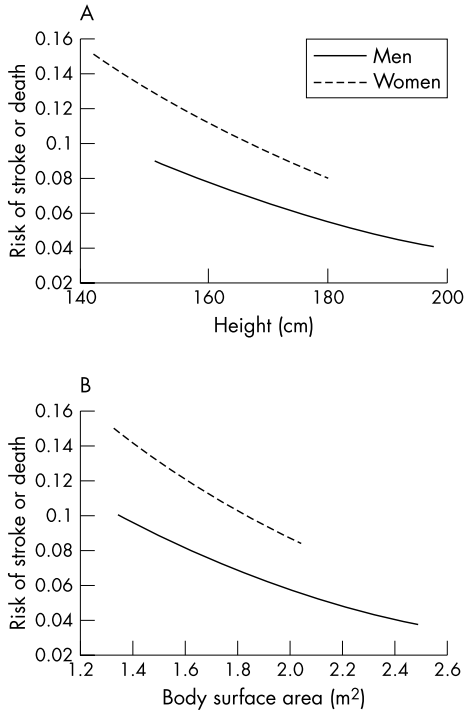

Figure 1 Risk of perioperative stroke or death according to (A) height and (B) body surface area (all values predicted by multivariable logistic regression).

DISCUSSION

The ECST demonstrated that female sex is a major risk factor for operative complications of CEA. This exploratory analysis of the ECST data revealed that shorter height and smaller BSA were associated with greater operative risk of stroke and death, and that these effects appeared to confound and attenuate the role of sex. Thus, the higher risk of perioperative complications in women is, at least in part, due to the fact that they are generally shorter and smaller than men.

Body size may have a direct impact upon technical issues of surgery such as limited access to the surgical field and the inherent challenge of operating on smaller vessels. Both BSA and height have been shown to correlate closely with the diameter of the common carotid artery.[20] Thus, the complications associated with smaller BSA and shorter height may be due to relatively smaller arteries, resulting in more technically challenging surgery and a higher occlusion rate in the postoperative period. A review of coronary endarterectomies demonstrated that patients with smaller BSA were at higher risk for graft occlusion.[15] Similarly, a review of 517 femorodistal bypass grafts for peripheral vascular disease showed that patients with smaller BSA were more likely to occlude the graft within one year.[16] Smaller BSA has also been associated with increased mortality risk in patients undergoing coronary artery bypass grafting. A retrospective analysis of over 344 000 patients demonstrated that there was a significant inverse correlation between BSA and operative mortality; the smaller the patient, the higher the risk. Patients in the lowest category of BSA had approximately twice the operative risk as those in the highest.[14]

The ECST demonstrated a strongly significant effect of sex on surgical outcome at 30 days. While we found that smaller height and BSA accounted for a portion of the effect of sex, there are likely other factors involved that are inherent to sex. Vascular anatomy and atherosclerotic plaque distribution differ between men and women. In particular, women have been shown to have relatively larger outflow-to-inflow area ratios in the carotid system and they are more likely to have maximal stenosis proximal to the carotid bulb, and to have stenosis of the external carotid artery.[21]

Previous studies have reported that extremes of body size, denoted by a very large or very small BMI, may be indicative of poor general health status and have been associated with higher rates of perioperative infection, stroke, and death.[11–13] Nevertheless, we did not find any increased risk for stroke or death in patients with high or low BMI, perhaps due to exclusion of patients at extremes of size from this study, as well as limited statistical power.

There are a number of potential limitations to this study. The generalisability of the results of the present study is limited because the ECST included patients with symptomatic carotid stenoses of any degree, and therefore does not accurately represent those patients who undergo CEA today. Furthermore, although the ECST is the largest published series of CEA with follow up by neurologists, the statistical power to reveal associations was limited due to the relative paucity of endpoints.

In conclusion, we found that height and BSA have modest associations with operative risk of CEA in ECST that explain,

at least in part, the increased risk of perioperative stroke and death in women. Further evaluation of these associations in other populations of patients treated with CEA is necessary. Validation of these findings may improve the ability to stratify risk and optimise the selection of patients prior to endarterectomy.

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Authors' affiliations

S R Messé, S E Kasner, Department of Neurology, University of Pennsylvania Medical Center, Philadelphia, PA, USA
Z Mehta, P M Rothwell, Stroke Prevention Research Unit, Department of Clinical Neurology, University of Oxford, Oxford, UK
C P Warlow, Department of Clinical Neurosciences, Western General Hospital, Edinburgh, UK

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Correspondence to: Dr Scott E Kasner, Department of Neurology, Comprehensive Stroke Center, University of Pennsylvania Medical Center, 3W Gates Building, 3400 Spruce Street, Philadelphia, PA 19104, USA; kasner@mail.med.upenn.edu

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