LETTERS TO THE EDITOR

Regarding "Clinical course of asymptomatic patients with carotid duplex scan end diastolic velocities of 100 to 124 centimeters per second"

I read with great interest the article written by Riles et al[1] regarding the follow-up of 97 asymptomatic patients presenting initially with carotid end-diastolic velocities of 100 to 124 cm/s. The authors should be commended for their efforts to define the natural history of moderate asymptomatic carotid stenosis in a period where endarterectomy is challenged by medical therapy in such cases.[2] Given their results, the authors conclude, "medical management is appropriate in most cases." However, two weaknesses of the study should be pointed out:

First, as stated by the authors, one of the main current criticisms of large prospective randomized studies (Asymptomatic Carotid Atherosclerosis Study, Asymptomatic Carotid Surgery Trial) that demonstrated the benefit of surgery over medical therapy for asymptomatic carotid disease is that current medical therapy is probably more efficient today than it was 20 years ago, especially because of the generalization of statin use. Therefore, the types of medications administered to the 97 patients during follow-up duration should have been provided to the readers of the *Journal of Vascular Surgery* because it seems paramount to correctly interpret the results.

Second, the authors' conclusion is not supported by their results. The fundamental goal of carotid stenosis management in asymptomatic patients is to prevent ipsilateral stroke and death from neurologic cause with regards to the patient's life expectancy. Although the benefit of medical therapy over surgical intervention in these patients might be real, it needs to be confirmed by studies that include follow-up durations exceeding the usual timing of symptoms occurrence. In the study of Riles et al,[1] mean follow-up was 29.1 months (range, 2-116 months), but ipsilateral symptoms occurred in five patients after a mean of 35.3 months (range, 12-58 months). Of note, three of these five patients experienced symptoms at 54, 54, and 58 months, a follow-up duration that largely exceeded the mean follow-up period of the study. Therefore, it is foreseeable that a higher number of patients managed medically would experience ipsilateral symptoms with a longer follow-up. These patients were not captured by the present study, and this weakens the authors' conclusions regarding the efficiency of medical management in asymptomatic carotid disease.

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Reply

We appreciate the comments regarding our clinical study of individuals with moderate asymptomatic carotid stenosis defined by an end diastolic velocity ranging between 100 and 124 cm/sec. I am pleased to respond to the two points made in the letter.

First, although most patients were taking statins, in this retrospective review it was not possible to provide accurate information regarding the compliance of the patients in the study group. A future study with this information would indeed be helpful.

With regards to the second comment, we stand by our conclusion that the risk of stroke among patients in this range is small, and therefore, any intervention that carries >1% risk must be justified on the basis of other criteria and carefully weighed in terms of benefit to the patients. If the converse to this conclusion is to recommend surgery or stent placement for anyone with an end diastolic velocity >100 cm/sec, clearly this would result in many unnecessary procedures. More importantly, if the Carotid Revascularization Endarterectomy vs Stenting Trial data represents the current periprocedural risk for carotid endarterectomy and carotid artery stenting, the result would be more rather than less strokes for this population.

Without question, we need new studies of asymptomatic carotid artery disease to evaluate the effectiveness of current medical therapy *as well as* interventions for the prevention of stroke. We hope this report will lead future investigators to use flow velocity criteria for sub-classification of participants rather than the lumen diameter measurements of earlier studies. Data on the natural history of carotid bifurcation disease based velocity measurements would helpful to clinicians, as Duplex ultrasonography is by far the principle modality for determining which asymptomatic patients need medical therapy, further diagnostic tests, and in many cases, interventional therapy.

As mentioned in our conclusions, we hope this report will lead to a larger prospective study of asymptomatic carotid disease, but strongly urge investigators to sub-classify patients according to flow-velocity criteria so that we can relate their findings to our clinical practices.

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Regarding "Gender trends in the repair of ruptured abdominal aortic aneurysms and outcomes"

We read with great interest a study by Mureebe et al,[1] which concluded that a significant gender difference remained in the outcomes after treatment for ruptured abdominal aortic aneurysm (AAA). Female gender was associated with increased risk of death in multivariate analysis after controlling for age, year, and type of procedure, with an adjusted odds ratio (OR) for open repair of 1.18 (95% confidence interval [CI], 1.15-1.21; $P < .0001$) and an OR for endovascular repair of 1.68 (95% CI, 1.48-1.90; $P < .0001$).

Although a lot of studies have compared mortality in repair of ruptured AAA between women and men, most of them have provided unadjusted (crude) mortality rather than adjusted (controlling for confounding) mortality. A recent meta-analysis[2] combining unadjusted mortality from 25 studies (representing 93,802 patients) demonstrated that the mortality rate was 61.8% for women and 42.2% for men (pooled unadjusted OR, 1.41; 95% CI, 1.22-1.63). We report the results of a meta-analysis of sex differences in perioperative mortality in repair of ruptured AAA, combining not unadjusted but adjusted ORs for death.

To identify all contemporary studies providing adjusted ORs for perioperative death among women compared with men in repair of ruptured AAA, public domain databases, among them

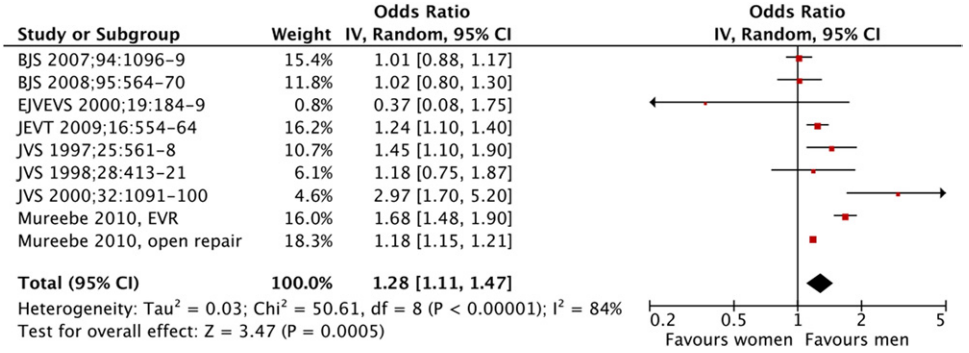

Fig. Forrest plot shows odds ratios and 95% confidence intervals (*CIs*) for perioperative death among women compared with men in repair of ruptured abdominal aortic aneurysm. *BJS,* British Journal of Surgery; *EJVEVS,* European Journal of Vascular and Endovascular Surgery; *EVR,* endovascular repair; *IV,* inverse variance; *JEVT,* Journal of Endovascular Therapy; *JVS,* Journal of Vascular Surgery.

MEDLINE and EMBASE, were searched from January 1995 to May 2010 using Web-based search engines (PubMed and OVID) with exploding keywords including sex, gender, rupture, ruptured, and abdominal aortic aneurysm. Studies considered for inclusion met the following criteria: the study population was patients undergoing repair of ruptured AAA; main outcomes included adjusted ORs for 30-day or in-hospital death among women compared with men; and the adjusted method was appropriate (eg, multivariate logistic regression). We excluded studies providing merely unadjusted mortality or ORs.

Our search identified eight studies, including the study by Mureebe et al,[1] that provided adjusted ORs for perioperative death among women compared with men in repair of ruptured AAA. Pooled analysis (representing 164,883 patients) demonstrated a statistically significant increase in perioperative mortality among women compared with men in the random effects model (pooled adjusted OR, 1.28; 95% CI, 1.11-1.47; $P = .0005$; Fig). There was significant between-study heterogeneity ($P < .00001$) and little difference in the pooled result from the fixed-effects model (pooled adjusted OR, 1.19; 95% CI, 1.17-1.22; $P < .00001$). Exclusion of any single study from the analysis did not substantively alter the overall result of our analysis. There was no evidence of significant publication bias ($P = .60$ by an adjusted rank-correlation test).

The results of our analysis suggest that female gender is associated with increased risk of perioperative death in repair of ruptured AAA, which was robust in sensitivity analyses and strengthens the conclusion of the study by Mureebe et al.[1]

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Reply

This is in response to the letter by Doctors Takagi, Manabe, Matsui, Goto, and Umemoto, entitled "Regarding 'Gender trends in the repair of ruptured abdominal aortic aneurysms and outcomes'". The authors evaluated the contemporary literature examining the risk of death from ruptured abdominal aortic aneurysms (AAAs). The authors both utilized and compared these results to our recently published article in the *Journal of Vascular Surgery.* We are very appreciative of their work and of their findings, which further cement our conclusion that female gender is associated with increased risk of perioperative death after repair of a ruptured AAA. This conclusion endures, even in the setting of significant heterogeneity in the studies the authors examined, furthering this as a universal outcome. As we commented on in our discussion, administrative databases are limited to the ability to dissect out the underlying explanations of this observed difference in mortality from ruptured AAA between men and women.

We thank the authors for their comments and for their efforts in continuing to highlight differences in outcomes. We are hopeful that additional research will expose the bases of this worrisome observation.

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Regarding "Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals"

We read with interest the article by Kent et al[1] in the September 2010 issue of the *Journal of Vascular Surgery.* These important data add to our understanding the risk factors for abdominal aortic aneurysms (AAAs), which have come from large screening trials and a smaller number of prospective population studies.[2-4] We would, however, like to make some points regarding the potential translation of the predictive score set out by the authors. The overall prevalence of AAAs in patients screened by life line screening appears to be extremely low (0.8%) when compared to other data sets. This may be a reflection of the fact that the screened population was a healthier group than the general population (referred to by the authors in the discussion), and if this is the case, then the odds ratios generated by the analysis are likely to be falsely elevated when extrapolated to the general population. Perhaps this is why the authors attempted to predict prevalence in the popula-