CORRESPONDENCE

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Diabetes and Not Lack of Treatment with Atenolol Predicts Decreased Survival after Noncardiac Surgery

To the Editor:—The response provided by Wallace regarding the study on perioperative atenolol and myocardial ischemia[1] did not provide an adequate clarification of the statistical results in their previous reports.[2,3] Wallace *et al.* claimed that their previous report demonstrated that perioperative administration of atenolol decreases the incidence of death after surgery during a 2-yr follow-up period.[2] However, their study did not provide statistical support for such a claim. In a univariate analysis (*i.e.*, an analysis in which the effect of a single "independent" parameter is evaluated), the hazard (odds) ratio for death was 0.4 with a confidence interval of 0.2–0.9. This result suggested that the likelihood of death is 2.5-fold less when atenolol was given and that the effect of atenolol was statistically significant. However, in all analytic studies, confounding variables must always be considered as an alternative explanation for study findings, as was done by Mangano *et al.* In the multivariate analysis model, the hazard ratio for atenolol was 0.5 with a confidence interval of 0.2–1.1. Because the confidence interval now included 1.0, this indicated that the effect of atenolol was *not* different from that of placebo, *i.e.*, no influence of atenolol on survival. In fact, in this model, diabetes mellitus proved to be the most important predictor of death with a hazard ratio of 2.8 (confidence interval, 1.4–6.2). Stated differently, when the effects of diabetes have been considered, there is no longer an effect of atenolol.

Because the message that "patients with or at risk for coronary artery disease who are treated perioperatively with β-adrenergic blocking agents have reduced incidence of morbidity and mortality" cannot be supported by the current studies,[2,3] physicians caring for such patients should reevaluate the validity of recommending perioperative beta blockade for improved survival that was based solely on the current study findings. Furthermore, because the clinical treatment of these 200 patients after hospital discharge was completely out of the study protocol control, the effects of other confounding factors cannot be determined and assessed.

When studies involve complicated statistical modeling, it is a responsibility of the authors to understand the technique used to provide an accurate and meaningful interpretation of their results. Unfortunately, the recent popularized use of perioperative beta blockade is based on misinformation.

Jacqueline M. Leung, M.D., M.P.H.
Associate Professor of Anesthesia
University of California, San Francisco
San Francisco, California
Department of Anesthesia
UCSF Mount Zion Medical Center
San Francisco, California
jmleung@itsa.ucsf.edu

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In Reply:—Thank you for allowing me to respond to Dr. Leung's comments about the two studies.[1,2]

In February 1998, Dr. Leung wrote to Anesthesiology with six criticisms of Anesthesiology and *New England Journal of Medicine* articles. These criticisms included suggestions that it was inappropriate to withhold study drug from patients who might have a side effect, questions concerning the statistics in the *New England Journal of Medicine* article, requests for more postoperative hemodynamic data, questions about the withholding of beta blockade, interactions of diabetes and atenolol, and the lack of women in the study. I responded to all of these criticisms in writing, and those comments were published in Anesthesiology.[3] Dr. Leung was dissatisfied with the results of the letter to Anesthesiology and has sent a second letter to Anesthesiology with more criticisms, including:

1. "Their study did not provide statistical support for such a claim."
2. ". . . this indicated that the effect of atenolol was not different from that of placebo, *i.e.*, no influence of atenolol on survival.
3. "β-adrenergic blocking agents have reduced incidence of morbidity and mortality can not be supported by the current studies."
4. ". . . the recent popularized use of perioperative beta blockade is based on misinformation."
5. "Physicians caring for such patients should reevaluate the validity of recommending perioperative beta blockade for improved survival."

We strongly disagree with Dr. Leung and her misunderstanding of the results of the two manuscripts.[1,2] The primary end-point of the atenolol[2] study was the reduction of perioperative myocardial ischemia by atenolol. Perioperative administration of atenolol for 1 week to patients at high risk for coronary artery disease significantly reduced the incidence of postoperative myocardial ischemia (P = 0.029). Furthermore, a secondary finding was that reductions in perioperative myocardial ischemia were asso-