Can the Results be Explained by Poor Randomization and Nonpertinent Comparisons?

To the Editor:

I am writing regarding the article, “Anti-Ischemic and Anti-Anginal Effects of Thoracic Epidural Anesthesia Versus Those of Conventional Medical Therapy in the Treatment of Severe Refractory Unstable Angina Pectoris” by Olausson et al.1

While doing comparative graphs for a lecture, I found several inconsistencies in the article that diminish its scientific value. The main inconsistency is found in Table 1. During a run-in period, the patients were treated with both nitroglycerin and heparin infusions for 82±18 versus 122±20 and 53±7 versus 104±13 hours, respectively, for controls and the group with thoracic epidural anesthesia (TEA). These differences were reported as nonsignificant by the authors. However, when recalculating the statistics, I found values of \( P<0.14 \) and \( P<0.0015 \) for the nitroglycerin and heparin infusions, respectively. Thus, at least in terms of the heparin infusion, it seems that the patients might not have been properly randomized.

In addition, Tables 2 and 3 contain several inconsistencies. For example, in Table 2, the “duration of ischemia per patient with ischemia” was given as 3.1 versus 0.8 minutes for controls versus TEA patients, which seems very low when comparing these values with other numbers in the table. My calculations result in the values 32.2 versus 17.25 minutes (355 minutes/11 patients and 69 minutes/8 patients, respectively). Is this correct, or does the duration of ischemia per patient with ischemia denote something else? Also, on the following line of Table 2, the number 32.2 appears as a measure of ischemic burden (area under the curve). If so, the ST-segment depression must be exactly 1.0 mm (the limit for registration) for the entire duration of 32.2 minutes, which seems strange. This makes me think that the numbers were mixed up.

Table 3 is used by the authors to strengthen their arguments for the comparability of their study with 3 other important studies. However, when comparing their mean “episode duration per patient,” which is 19.7 versus 4.1 minutes for controls and the TEA group, respectively, the authors then give the numbers 21 versus 14 minutes (medians) from the Romeo study.2 The correct numbers from that study are 228 versus 91.6 min (means). Why compare from one study with medians from another? My conclusion is that these studies are not comparable regarding the amount of ischemia in the control groups.

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Response
Dr Blomberg probably used a parametric test for his statistical calculations. Because our data were far from normally distributed, we used a nonparametric test, the Mann-Whitney U test, as stated in the Methods section of our article.1 With this test, the probability values for the nitroglycerin and heparin infusions were 0.121 and 0.255, respectively. Thus, there is no reason to believe that “the patients might not have been properly randomized.”

Dr Blomberg then suggests that “the numbers are mixed up” in Table 2. The numbers in Table 2 are correct, but there is one unfortunate error: the expression “duration of ischemia per patient with ischemia” should be “duration per ischemic episode per patient.”

We think that Dr Blomberg probably misunderstood the way Holter data are processed and presented. The area between the ST trend and the line corresponding to −1 mm (0.1 mV) is calculated. The total accumulated area under the curve is usually referred to as the “total ischemic burden” (TIB). The area under the curve for an ischemic episode could either be caused by a large deviation of the ST trend below −1 mm for a short time period or a small deviation of the ST trend below −1 mm for a longer time period. Dr Blomberg’s statement, “the ST-segment depression must be exactly 1.0 mm. . . for the entire duration of 32.2 minutes. . . ” is obscure.

Unfortunately, in the article by Romeo et al,2 no data are given regarding the mean duration of episodes for a 48-hour period. Therefore, we used the median values as surrogates. Median values are lower than the corresponding mean values in such studies because several patients will not have ischemia. Thus, we most likely underestimated the mean duration of episodes in their study, which, if anything, further supports our statement that “. . . the anti-ischemic treatment of the patients in the control group was as effective as previously documented therapeutic regimens.” Dr Blomberg recalculated the data that Romeo et al2 denote as total ischemic burden per day (TIB/day) and claimed that these data correspond to the mean duration of episodes. Unfortunately, Romeo et al2 did not define TIB in their study. We interpreted (right or wrong) the expression TIB/day as the area under the curve.

Finally, we would like to emphasize that Dr Blomberg’s statement, “I found several inconsistencies in the article that diminish its scientific value,” is invalid.

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