Does Sex Also Influence Antibiotic Penetration Into Presternal Subcutaneous Tissue?

To the Editor:

We have read the great article by Andreas and colleagues [1], which showed that harvesting of the internal mammary artery impaired local antibiotic penetration during coronary artery bypass grafting. In their research, the authors measured antibiotic penetration in presternal subcutaneous tissue with microdialysis probes in 2 female and 6 male patients [1]. We were curious to see whether there are sex differences in antibiotic penetration patterns. On average, total body water, extracellular water, intracellular water, total blood volume, plasma volume, and red blood cell volume are greater in male individuals [2]. Therefore, if an average adult man and an average adult woman are exposed to the same dose of a watersoluble drug, the volume of distribution will be increased in the man, thus decreasing drug concentration [2].

Blood distribution and regional blood flow, which affect pharmacokinetics, are different between male and female individuals [2]. Blood flow to skeletal muscle is greater in male individuals, whereas blood flow to adipose tissue is greater in female individuals [2]. Body composition is also different; body fat as a percentage of total body weight is higher in women than in men [2, 3]. All the aforementioned parameters affect drug distribution. We thought that sex differences might lead to differences in antibiotic penetration because drug distribution differs by sex. In addition, Andreas and colleagues measured antibiotic penetration in the subcutaneous tissue, where the regional flow differs between male and female individuals.

In conclusion, we ask whether the patterns of antibiotic penetration into subcutaneous tissue were different between male and female patients.

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References

The Reliable Change Index for Assessment of Cognitive Dysfunction After Coronary Artery Bypass Graft Surgery

To the Editor:

We read the article by Bruce and colleagues [1] regarding cognitive impairment defined with reliable change indices (RCIs) after coronary artery bypass graft (CABG) surgery. The authors state that “we are unaware of any previous studies that have used the RCI to examine the cognitive performance of individual CABG surgical patients.” This is indeed a curious comment considering the authors [1] cite Andrew and colleagues [2] and Raymond and colleagues [3], both of whom used the RCI to determine cognitive impairments after CABG surgery. Preceding these papers still, the use of RCI to determine the incidence of cognitive impairments was published in 1998 by Kneebone and colleagues [4].

Kneebone and colleagues [4] highlighted the importance of inspecting individual and meaningful change in cognitive function after CABG surgery, thereby overcoming some methodologic issues inherent to analyses of group change. Bruce and colleagues [1], however, have predominantly analyzed group changes, and unfortunately nowhere in their report were the study limitations clearly acknowledged. For example, there was no specified power calculation. It is questionable whether this study was sufficiently powered to reliably calculate the RCI from a small control group (N = 15) as applied to an equally small CABG surgery (N = 16) and thoracic surgery group (N = 15). A second point relates to the alleged “confounding effects” of psychological distress on cognitive dysfunction after CABG surgery as stated by Bruce and colleagues [1]. The authors recruited a CABG group who were, on average, in the moderate and clinically significant range for self-reported anxiety and stress and were in the mild range for depression [5]. Such depression, anxiety, and stress scores greatly exceed those reported by Andrew and colleagues [2] in a comparable CABG surgery group. Given such high clinical distress levels in the CABG group, it is unlikely that a representative CABG group was recruited or, alternatively, that the cognitive assessments were done at a time of heightened emotional distress, thereby potentially limiting the conclusions of the cognitive assessment.

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References


Reply

To the Editor:

We thank Drs Tully and Baker [1] for highlighting our finding [2] that the apparent cognitive impairment in a significant proportion of coronary artery bypass graft (CABG) patients [3] may be an artifact of experimental design. Our innovative study included both a surgical control group and a nonsurgical control group, and postsurgical performance was normalized to presurgical performance using the reliable change index (RCI), to control for learning effects. The inclusion of appropriate control groups ensures an accurate understanding of the extent of cognitive change that occurs after surgery [4]. The sample size (46 participants) had ample statistical power to support the analyses performed, and we are confident of the veracity of our principal findings.

We found that CABG patients display more cognitive impairment before surgery than the other groups. Although this difference is maintained after surgery, it does not become greater. This finding suggests that CABG patients sustain permanent brain injury before surgery, and it raises the question of whether CABG surgery ought to be performed sooner.

Another important finding was that emotional state (e.g., stress, anxiety, depression) influences cognitive performance before and after surgery, and that emotional state is largely responsible for the observed decrements in cognitive performance. This finding is consistent with Andrews and colleagues [5], who reported that “preoperative levels of anxiety, depression and stress were related to deficits in neuropsychological function and that once mood state was accounted for this relationship disappeared.” Furthermore, Tully and colleagues [6] reported that in CABG patients “the prevalence of clinical depression is consistently reported at around 20%” and “subthreshold depressive symptoms in the absence of diagnostic interview is reportedly high, between 32% and 43%.” We confirmed these findings and extended them to patients undergoing thoracic surgery. The strength of this effect in two surgical groups highlights its generality and emphasizes the need to control carefully for emotional state in future studies that assess the effect of surgery on cognition.

Previous studies used the RCI to compare the incidence of cognitive impairment between patient groups [5, 6], whereas we also used the RCI to compare the extent of cognitive impairment between individual patients. We found that group changes are driven by large changes in a minority of individuals: many patients display no cognitive impairment after surgery, whereas individuals who are impaired at 1 week generally improve to baseline by 8 weeks.