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VANCOMYCIN PASTE AND DEEP STERNAL WOUND INFECTIONS— DÉJÀ VU ALL OVER AGAIN

Reply to the Editor:

In their letter, Lander and colleagues state that they are once again obliged to respond to the misinterpretation of their observational study¹ on the effect of vancomycin paste on deep sternal wound infection (DSWI). If the methodology of their study had not been so significantly flawed, there would be no need for further explanations.

Lander and colleagues claim that our previous study on vancomycin paste relied on propensity matching to account for numerous changes in patient acuity, medical care, antibiotic prophylaxis, surgical technique, and glycemic control. This is incorrect. In 2014, my colleagues and I reported our experience with vancomycin paste.² We compared 2190 patients from December 2003 to November 2007 who did not receive vancomycin paste with 1075 patients who did receive vancomycin paste from December 2007 to August 2013. Unlike the study by Lander and colleagues,¹ there were no differences in surgical techniques used to close the sternum, in glycemic control, or in prophylactic perioperative antibiotics. The only difference in our practice was the use of vancomycin paste. Unlike the study of Lander and colleagues,¹ the patient profiles between our groups were similar. There were no statistical differences in age, sex, congestive heart failure, peripheral vascular disease, strokes, chronic obstructive pulmonary disease, renal failure, the urgency of surgery, the presence of myocardial infarction, diabetes mellitus, or the use of single versus bilateral internal thoracic arteries. Patients who received vancomycin paste did have significantly higher incidences of active smoking and endocarditis. The unadjusted outcomes without propensity matching showed that patients who received vancomycin paste had no superficial or DSWI in both patients without diabetes (0% vs 2.3%; $P < .0001$) and patients with diabetes (0% vs 3.3%; $P = .0004$). These results remained significant even after propensity matching.

This was in sharp contrast to the study by Lander and colleagues,¹ in which there were numerous changes during the course of their study from 2003 through 2015 involving perioperative antibiotics, glycemic control, and sternal wound closure techniques. Only 34.5% of their study patients actually received vancomycin paste. High-risk patients such as those with endocarditis, patients undergoing cardiac transplantation, and those requiring placement of assist devices, who stood to gain the most from vancomycin paste, were excluded from the analysis. Lander and colleagues

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state that analysis of low-frequency events such as DSWI in these subgroups is unrealistic, yet they provide no data regarding the incidence of DSWI in this high-risk population. The incidences of superficial wound infections were also not reported, because they state that these are often treated in the community without further hospital admission. I find it hard to believe that a cardiac surgeon would not supervise the wound care of these patients to determine that the infection was indeed “superficial” and to document that the infection was completely resolved—especially if the surgery involved a valve prosthesis or a vascular graft. In their study, Lander and colleagues¹ reported that 9 patients had a DSWI develop between 90 and 365 days, but these patients were also excluded from the analysis. They justify this exclusion by noting that the Society of Thoracic Surgeons requires only 30 days of reporting and that the surveillance period for the Centers for Disease Control and Prevention is 90 days. This is not exactly the case, because the Centers for Disease Control and Prevention considers the insertion of sternal wires as an implant, in which case the surveillance period extends to 1 year. The fact that a DSWI occurred after 90 days and the exclusion of superficial infections that may not have been treated by a cardiac surgeon are both worrisome. Many of these superficial infections may become indolent, infect the sternal wires, and develop areas of osteomyelitis, which can result in DSWIs. Our experience is that vancomycin paste not only prevents DSWI but all the superficial infections that are a source of increased morbidity and medical expenses.

The study by Lander and colleagues¹ prompted Kowalewski and colleagues³ to undertake a meta-analysis on the effectiveness of topical vancomycin to reduce sternal wound infections after cardiac surgery. Even with the inclusion of the study of Lander and colleagues,¹ the meta-analysis of Kowalewski and colleagues³ revealed that the use of topical vancomycin was associated with a 76% significant reduction of any sternal wound infection and a 76% reduction in the incidence of DSWI. Kowalewski and colleagues³ noted that in the study of Lander and colleagues,¹ vancomycin was used in only 25% of patients from 2003 to 2010, when the DSWI rate was 1.29%, but vancomycin use was increased to 53% from 2011 to 2015, during which time the DSWI rate fell to 0.29%: a 5-fold decrease!

I agree with Lander and colleagues that “rigorous attention to perioperative antibiotic administration and glucose management are essential components to minimizing DSWI.” The key here is “components.” To eliminate all sternal wound infections completely, there must be a multifactorial approach. This was the goal of the American Association for Thoracic Surgery (AATS) guidelines for the prevention and treatment of sternal wound infections, which elucidated the key components in the preoperative, intraoperative, and postoperative periods to eliminate all sternal wound infections.⁴ The guidelines discuss the detrimental effects of bone wax when applied to the sternum, which impairs bone healing and serves as a nidus for sternal wound infection, in contrast to vancomycin paste, which has been associated with reduced rates of all sternal infections. Since the introduction of the AATS guidelines, there has been a further reduction in the incidence of DSWI. The most recent data from the Society of Thoracic Surgeons Adult Cardiac Surgery Database give the prevalences of DSWI as follows⁵: coronary artery bypass grafting (CABG), 0.3%; aortic valve replacement, 0.1%; aortic valve replacement plus CABG, 0.3%; mitral valve repair, 0.2%; mitral valve replacement, 0.5%; mitral valve repair plus CABG, 0.1%; and mitral valve replacement plus CABG, 0.03%.

With the implementation of the AATS guidelines, we are closer to ensuring that sternal infections will become a “never event.” In the study by Lander and colleagues,¹ the incidence of DSWI among patients who did not receive vancomycin paste was 1.0%; it was 0.8% among those who did. Rather than continuing to defend a study that may have been well intended but has serious flaws, I would encourage Lander and colleagues to adopt all the AATS guidelines, which include the avoidance of bone wax and the use of vancomycin paste, so that DSWI will also become a “never event” at their institution.

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VANCOMYCIN PASTE IN STERNAL WOUND INFECTION PROPHYLAXIS—A GENUINE DEBATE OR FUTILE ATTEMPTS TO JUSTIFY FLAWED STUDY?

Reply to the Editor:

We read, again with unextinguished enthusiasm, the response letter to our meta-analysis¹ by Dr Body et al,² in which the authors criticize our methodological approaches to the assessment of effectiveness of vancomycin paste applied to the sternal edges to prevent sternal wound infections (SWIs) after heart surgery. Our enthusiasm is driven mainly by the fact that superstitions and different opinions on the matter of topical antibiotics in cardiac surgery, albeit largely resolved in a recent American Association for Thoracic Surgery expert consensus report,³ still add fuel to the fierce debate.

That said, we feel obliged to clarify the issues raised by a recent report in the *Annals of Thoracic Surgery*,⁴ which served as an underpinning for our meta-analysis. Namely, the authors, in contrast to previous reports,⁵⁻⁷ showed that vancomycin paste neither reduced the incidence of deep SWI (DSWI) nor was its use a negative predictor of DSWI in a multivariate analysis. In the meta-analysis, this

particular study was found to be the source of substantial heterogeneity in the analysis of SWIs, the reason being, apart from unbalanced baseline characteristics of the patients, certain methodologic flaws as discussed elsewhere in detail,^{1,8} which beyond doubt suggested a strong influence of factors other than topical vancomycin must have driven the results toward null in the analysis by Lander et al.⁴

Significant unbalance was seen in particular when data were stratified according to time assays. Indeed, vancomycin paste was used only in 25% of patients in the first 7 years of the study period (2321 of 9413 from 2003 to 2010) with a 1.29% rate of DSWI (121 DSWIs in 9413 patients). In the second time period (2011-2015), vancomycin paste was used in 53% of patients (2676 of 5079 patients) with a rate of DSWI cut nearly fivefold (0.29%; 15 DSWIs in 5079 patients).

To better illustrate this, we designed a simple time-based analysis only taking into account data published in the report by Lander et al⁴ (Figure 1). We plotted percentage prevalence of vancomycin paste use against percentage incidence of DSWI across reported time ranges. Even from the chart, it is intuitive to observe that with more vancomycin use, the number of DSWIs significantly decreases. Using simple linear regression: β coefficient = -0.94 (95% confidence interval, -1.18 to -0.70 ; $P < .001$). Of note, risk for developing DSWI in the series was still reduced by 26% (risk ratio, 0.74; 95% confidence interval, 0.51-1.07) although this was not significant.

Dr Body's claim that our meta-analysis fails to appreciate that: (1) 2 previous studies^{5,7} used historical controls, (2) significant publication bias was present in the analysis, and last, (3) propensity matching performed in 2 of the included studies is not enough to account for unmeasured

FIGURE 1. Percentage prevalence of vancomycin paste use and percentage incidence of deep sternal wound infection (DSWI) across reported time ranges in the article by Lander et al.⁴