Relation Between Topical Application of Platelet-Rich Plasma and Vancomycin and Severe Deep Sternal Wound Infections After a First Median Sternotomy

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Deep sternal wound infections (DSWIs) are serious complications of sternotomy, leading to increased mortality and costs of care. Topical applications of autologous platelet concentrate and vancomycin have both shown promise in preventing DSWIs. From January 1, 1998, to November 30, 2010, 1,866 patients without previous sternotomy underwent cardiac surgery at the Baylor University Medical Center, Dallas, by a single surgeon who systematically adopted application of a paste containing vancomycin, calcium-thrombin, and platelet-rich plasma (PRP paste) to the edges of sternal wounds before closure in December 2005. A propensity-adjusted logistic regression model employing Firth's penalized maximum likelihood method was used to assess the association between the use of the PRP paste (intervention) and the incidence of severe DSWI. Eleven patients (0.59%) developed severe DSWIs. All were among the 1,318 patients in the control group (0.83%); no severe DSWIs developed in the 548 patients in the intervention group. Both the unadjusted and adjusted associations between the study intervention and DSWI were statistically significant (unadjusted p value = 0.021; adjusted p value = 0.005; adjusted odds ratio = 0.05, 95% confidence interval 0.01, 0.50). In conclusion, the PRP paste appears to prevent severe DSWIs. **(Am J Cardiol 2014;113:1415−1419)**

Deep sternal wound infections (DSWIs) are a rare but potentially life-threatening complication after cardiac surgery. DSWIs occur in 1% to 2% of patients who undergo median sternotomy for cardiac surgery and are associated with significant increases in mortality, hospital length of stay, and costs of care.[1−3] Thirty-day mortality is reported to be 7.3% in patients who develop DSWIs compared with 1.6% in those who do not,[1] and length of stay and hospital costs for cardiac surgery patients who develop DSWIs have been reported to double and triple, respectively.[4] Preventing DSWIs is therefore a high priority for all cardiothoracic surgeons, with implications both for improving patient outcomes and for decreasing costs of care. Topical applications of autologous platelet concentrate and of vancomycin have both shown promise for preventing sternal wound infections.[5−8] Although the rate of DSWIs in our practice was lower than many of those reported in 2005, the profound implications of this serious complication made us seek to do even better. Therefore, in December 2005, Baylor University Medical Center started encouraging surgeons in our practice to apply a paste consisting of vancomycin, calcium-thrombin, and platelet-rich plasma (PRP paste) to the edges of sternal wounds before closure. One surgeon in our practice systematically adopted this change, whereas others chose to wait for evidence of its clinical and cost-effectiveness. Here, we describe the impact of this change in practice on the incidence of severe DSWIs in that single surgeon's patient population.

Methods

All consecutive patients (n = 1,866) who underwent cardiac surgical procedures with full sternotomy and who had not previously undergone coronary artery bypass graft, valve surgery, or other procedures requiring sternotomy, performed by one surgeon from January 1998 to November 2010, were included in this study; among them, 548 (29.37%) received the PRP paste and 1,318 (73.63%) were historical controls. All surgeries were performed at the Baylor University Medical Center in Dallas, the 1,026-bed flagship hospital of the Baylor Health Care System. Institutional review board approval was obtained for a retrospective analysis of patient records.

All patients received prophylactic antibiotics in accordance with national guidelines for the prevention of surgical site infections.[9] Antibiotics were started within 1 hour of incision and discontinued 48 hours of surgery. Before 2006, antibiotic selection was based on surgeon choice, and patients usually received vancomycin or ceftazidime. In late 2006, with an increasing focus on standardization of care, cefazolin became the antibiotic of choice.

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Table 1
System for classifying sternal wound infections by severity

Category	Description
1	Suture granuloma or suture reaction or wire reaction
2	Bone click or unstable bone
3	Skin dehiscence or skin-only superficial wound infection
4	Deep tissue infection from the subcutaneous to the bone but no bone involvement
5	Infection including bone involvement
6	Infection including bone involvement plus septicemia

In December 2005, Baylor University Medical Center started encouraging surgeons in our cardiothoracic surgery group to apply a "paste" to the edges of the sternum just before closure. In aiming to produce a paste with a consistency that would allow accurate and reproducible application to the sternal edge without waste, we arrived at the following recipe: (1) combine 5 ml of 10% calcium chloride solution (100 mg/ml; 1.4 mEq of calcium per ml) with 5,000 IUs of topical thrombin (bovine origin), (2) draw 0.6 ml of the resulting suspension and combining it with 3 ml of PRP, (3) add the mixture to 2 g of vancomycin hydrochloride powder, and (4) mix the powder and the liquid together so that it forms a paste-like consistency. The PRP was produced using a Harvest SmartPReP 2 system,[10] which generates an average platelet concentration 4.8 greater than that found in unprocessed, anticoagulated whole blood. We processed 60 ml blood draws to produce ~7 ml of PRP with platelet concentrations in the range of 1.5 to 2 million platelets/μl, which is considered optimal for stimulating angiogenesis.[11]

All the patients undergoing surgery between December 2005 and November 2010 received the "PRP paste" in addition to the routine antibiotic prophylaxis. For most of these patients, the PRP was prepared using the SmartPReP 2 APC+ system manufactured by Harvest Technologies Corp.[12]

Patients who underwent surgery between January 1998 and November 2005 were considered controls, given that they received only the routine antibiotic prophylaxis.

All patients were assessed for the development of sternal wound infections, in hospital, during follow-up office visits, and via telephone calls for 12 months after discharge. Identified infections were classified according to the system we (B.H. and T.T.) developed, listed in Table 1. Infections falling in categories 1 to 4 were considered superficial and not included in this analysis; categories 5 and 6 constituted the severe DSWIs that were of interest here.

Clinical and nonclinical data on the patients' risk factors were collected and entered into the Society of Thoracic Surgeons Adult Cardiac Surgery Database.[13] Data abstraction, collection procedures, and variable definitions used for the Adult Cardiac Surgery Database are standardized and have been described elsewhere.[13] The key Society of Thoracic Surgeons risk of operative mortality[14] factors was considered: age, gender, body surface area (m^2), race, ethnicity, diabetes mellitus, infectious endocarditis, renal failure, creatinine, chronic lung disease, hypertension, peripheral vascular disease, cerebrovascular disease, myocardial infarction, time from last myocardial infarction to surgery, atrial fibrillation, tobacco use, congestive heart failure, previous pace/ implantable cardioverter defibrillator, previous percutaneous coronary intervention, preoperative angina, ejection fraction, left main disease, surgery status, type/ complexity of surgery, and preoperative use of an intra-aortic balloon pump.

Means, SDs, and percentages were calculated to describe the study cohort. Given the very low incidence rate of the outcomes, a logistic regression model employing Firth's penalized maximum likelihood method[15] with the study intervention as the sole independent variable was used to assess the unadjusted association between the intervention and severe DSWI. To account for possible confounders of this association, a propensity score approach was employed.[16] A logistic regression model was fit to estimate the likelihood of receiving the study intervention. Covariates for this logistic model included established risk factors identified by the Society of Thoracic Surgeons,[17] as well as other clinical and demographic factors—these are listed in Table 2. All continuous predictors were modeled with restricted cubic splines.[18–20] Missing data were present in only 4 variables included in the propensity model (body surface area = 0.05%, creatinine = 2.25%, ejection fraction = 13.71%, status = 0.2%) and were accounted for via multiple imputation using predictive mean matching (a total of 200 imputations were performed for each missing value).[21,22] Estimates from the resulting propensity model were then used to adjust the effect of the study intervention on DSWI in a logistic regression employing Firth's penalized maximum likelihood method.[15] All analyses were performed using the R software, version 2.15.1.[23]

Results

Characteristics of the study population are listed in Table 2. The incidence of all wound infections, by category, is listed in Table 3. Overall, 11 patients (0.59%) developed severe DSWIs (categories 5 and 6)—all these events were among the 1,318 patients in the control group (incidence 0.83%). The incidence in the intervention group (548 patients) was zero. All severe DSWIs developed within 4 months of surgery.

Both the unadjusted and adjusted associations between the study intervention and the severe DSWI were found to be significant (unadjusted p value = 0.021; adjusted p value = 0.005; adjusted odds ratio = 0.05, 95% confidence interval 0.01, 0.50).

Discussion

We compared the incidence of severe DSWIs before and after instituting use of a PRP paste as standard practice in patients who underwent cardiac surgical procedures. After adjustment for key risk factors, patients who had surgery before implementation of the intervention were 18 times more likely to experience severe DSWI than those who had surgery postimplementation.

Our results are consistent with previous reports of topical application of vancomycin or autologous platelet gel to sternal incisions in cardiac surgery. A 1989 randomized controlled trial in 416 cardiac surgery patients found application of topical vancomycin decreased incidence of