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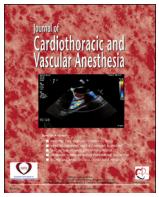

Original Article

# Bleeding-Related Complications and Readmission Rates Associated With Fibrin Sealant Use in Patients Undergoing Coronary Artery Bypass Graft Surgery in the United States

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*Objectives:* To compare the clinical and economic outcomes of EVICEL (Ethicon, Inc., Somerville, NJ) and TISSEEL (Baxter Healthcare Corporation, Westlake Village, CA) use in patients undergoing primary coronary artery bypass graft (CABG) surgery.
*Design:* Retrospective database analysis.
*Setting:* Premier prospective hospital database (June 2009 through March 2014) covering approximately 20% of hospital discharges in the United States.
*Participants:* Adults undergoing primary CABG surgery who received either EVICEL or TISSEEL on the day of surgery (index date).
*Interventions:* Two intervention groups were formed, EVICEL and TISSEEL. Clinical outcomes compared included postoperative bleeding complications (International Classification of Diseases, Ninth Revision, Clinical Modification code: 998.1) and number of blood transfusions received on the index day. Economic outcomes compared included hospital length of stay, hospital costs, and 30-day readmission rates. Propensity-score matching was used to control for patient and hospital characteristics.
*Measurements and Main Results:* A total of 129,014 primary CABG surgery patients were identified; 986 patients (mean age: 64 years, 73% male) received EVICEL and 6,340 patients (mean age: 65 years, 75% male) received TISSEEL on the index day. After propensity-score matching, patients who received EVICEL compared with TISSEEL had significantly fewer postoperative bleeding complications (3.0% *v* 5.0%, $p = 0.0197$), index-day blood transfusion rates (19% *v* 34%, $p < 0.0001$), readmission rates (18% *v* 32%, $p < 0.0001$), and costs ($40,736 [standard deviation $19,465] *v* $46,005 [standard deviation $24,049], $p < 0.0001$). Results from a sensitivity analysis using a generalized linear model to control for other hemostatic agent use also favored EVICEL over TISSEEL.
*Conclusion:* Results from this real-world retrospective database analysis showed fewer bleeding complications and lower costs in patients undergoing primary CABG surgery who received EVICEL compared with TISSEEL.


*Key Words:* bleeding complications; CABG surgery; fibrin sealants; coagulation; transfusions; hospital costs; clotting

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IN 2010, AN ESTIMATED 395,000 coronary artery bypass graft (CABG) surgeries were performed in the United States.[1] Morbidity and mortality rates are increased in cardiac surgery patients who experience bleeding complications.[2] Bleeding events associated with cardiac surgery are frequent, with estimates suggesting that 10% to 15% of the blood supply in the United States is consumed by cardiac surgery patients.[3] Cardiac surgery patients who experience bleeding-related complications have longer intensive care unit and hospital stays and higher hospital costs compared with cardiac surgery patients who do not experience bleeding-related complications.[4] Cardiac surgery patients requiring blood transfusions have been found to have longer times to extubation, longer intensive care unit stays, more postoperative complications, and higher mortality than patients not requiring blood transfusions.[5]

Several strategies can be used to control bleeding in the intraoperative and postoperative periods. Conventional surgical strategies such as manual compression, suture ligation, and cauterization commonly are used to control bleeding during surgery. Prophylactic and therapeutic approaches also are used to decrease the risk of postoperative blood transfusion.[6,7] However, in some situations, these conventional methods are impractical or ineffective, and additional strategies are required.[8] Topical hemostatic agents such as fibrin sealants are another option to control bleeding during surgery.[9]

Fibrin sealants contain both fibrinogen and thrombin[10] and work by mimicking the final stages of the blood coagulation process.[9] Fibrin sealants are used to promote hemostasis in patients undergoing a broad range of surgical procedures, such as cosmetic, cardiovascular, head and neck, neurologic, orthopedic, noncardiac thoracic, and vascular surgery. They are effective across a broad range of bleeding circumstances, such as venous oozing, diffuse raw surface bleeding, and hemorrhage from anastomotic graft sites during vascular surgery.[8,10] At the site of bleeding, fibrin sealants increase the local concentration of fibrinogen and thrombin; the thrombin cleaves the fibrinogen to fibrin, which polymerizes and crosslinks, progressing from a soluble mesh to a stable clot.[11]

Little is known about the real-world clinical and economic outcomes of patients treated with fibrin sealants during cardiac surgery. Such data increasingly are being requested by healthcare decision makers who make policies and payment decisions.[12] To the authors' knowledge, no real-world studies have compared the clinical outcomes and economic burden of patients treated with the fibrin sealants EVICEL (Ethicon, Inc., Somerville, NJ) and TISSEEL (Baxter Healthcare Corporation, Westlake Village, CA). Among the available forms of fibrin sealants in the United States, EVICEL and TISSEEL have the same function (hemostatic) and source (human pooled plasma).[13] A detailed comparison of these 2 products is described in Appendix 1. A few studies have compared the properties of EVICEL versus TISSEEL and clinical implications of the differences. Hickerson et al[16] suggested that the superior clot strength and resilience obtained with EVICEL relative to TISSEEL may be due to the difference in factor XIII concentration. Other differences include the higher thrombin activity in the EVICEL formulation and the presence of plasminogen and aprotinin in the TISSEEL formulation.[16]

The objective of this study was to compare the clinical outcomes (eg, postoperative bleeding events), healthcare resource utilization (eg, hospital length of stay [LOS] and blood transfusion number), and costs between patients who received EVICEL or TISSEEL during CABG surgery.

## Methods

### *Data Source*

The Premier Prospective hospital data set contains information from more than 700 hospitals throughout the United States (www.premierinc.com), covering an estimated 20% of hospital discharges. Data elements include hospital and patient identifiers, primary and secondary International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis coding system diagnoses and procedure codes; LOS; admission types and primary payer information. Also available are data elements for patient demographic characteristics, such as age and race, and hospital characteristics, such as provider geographic location, hospital bed size, teaching hospital status, and hospital location.

### *Patient Selection*

Adult patients 18 years or older who underwent primary CABG surgery from January 2009 to March 2014 and received either EVICEL or TISSEEL during the primary CABG surgery were identified in the Premier database. Patients who underwent a CABG procedure were identified using the ICD-9 procedure codes (Appendix 2). Patients were excluded if they received both EVICEL and TISSEEL at any time during the same hospitalization or underwent both CABG and valve surgeries during the same hospitalization. Patients with incomplete hospital stay data (admission and discharge day) during the study time frame also were excluded.

## Measures

### *Outcomes*

Clinical outcomes evaluated included bleeding complications (ICD-9 diagnosis 998.1: hemorrhage or hematoma or seroma complicating a procedure) after CABG surgery and blood transfusions during 3 time frames. ICD-9 diagnosis codes (99.0x, V58.2), standard charge codes, and current procedural terminology codes were used to identify clinical outcomes during the following 3 time frames: (1) entire index hospitalization, (2) day of index CABG surgery, and (3) after index hospitalization. Economic outcomes evaluated included hospital overall LOS (ie, number of days from hospital admission until discharge), total hospitalization costs, and 30-day readmission rate.

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