

In-Hospital Outcomes of Pedicled Bilateral Internal Mammary Artery Use in Diabetic and Nondiabetic Patients Undergoing Off-Pump Coronary Artery Bypass Grafting: Single-Surgeon, Single-Center Experience

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ABSTRACT

Objective: A common perception is that use of pedicled bilateral internal mammary arteries (BIMA) increases the risk of sternal wound complications in diabetic patients undergoing coronary artery bypass grafting (CABG). The purpose of this study was to compare the in-hospital outcomes of CABG using pedicled BIMA in diabetic and nondiabetic patients.

Methods: From September 1998 to September 2010, 390 consecutive diabetic patients and 519 nondiabetic patients underwent isolated off-pump CABG using pedicled BIMA. The 2 groups had comparable preoperative demographics except for a higher prevalence of acute myocardial infarction (18.9% versus 6.1%, $P = .01$), peripheral vascular disease (17.2% versus 2.7%, $P = .001$), an ejection fraction $<30\%$ (17.7% versus 8.5%, $P = .02$), and chronic renal failure (4.5% versus 0.9%, $P = .01$) in the diabetic patients.

Results: The operative mortality rate of the diabetic patients was comparable to that of the nondiabetic patients (2.8% versus 2.1%, $P = .87$). The in-hospital outcomes, including occurrence of superficial and deep sternal wound infections, were similar except for an increased occurrence of wound infection at the vein harvest site (6.6% versus 1.1%, $P = .04$) and a need for hemofiltration (11.8% versus 2.1%, $P = .02$) in the diabetic patients.

Conclusions: Pedicled BIMA use is associated with comparable incidences of sternal wound complications and other outcomes in diabetic patients and nondiabetic patients. Strict perioperative glycemic control, adherence to meticulous closure technique, and postoperative management of surgical wounds can make pedicled BIMA use a default strategy for diabetic patients.

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INTRODUCTION

Evidence from observational studies suggests that the use of bilateral internal mammary arteries (BIMA) is associated with better clinical outcomes, compared with the use of a single IMA [Lytle 1999; Berreklouw 2001; Ioannidis 2001; Burfeind 2004]. A systematic review of observational studies including 15,962 patients (comprising 11,269 single-IMA and 4693 BIMA patients matched or adjusted for age, sex, ventricular function, and diabetes) reported a survival advantage for patients who underwent their surgeries with BIMA grafts (hazard ratio for death, 0.8; 95% confidence interval, 0.70-0.94) [Taggart 2001; Kappetein 2010]. Nevertheless, there is a wide discrepancy between these findings in the literature and the rates of adoption of BIMA use. In the United States, BIMA use is only approximately 4%, and it is 12% in Europe [Kappetein 2010]. One of the principle reasons for these low adoption rates is the common perception that BIMA use is associated with an increased rate of sternal dehiscence, particularly in diabetics [Savage 2007].

On the other hand, patients with diabetes are those with potentially the most to gain from BIMA grafts, because they often have more severe, diffuse, and distal disease [Raja 2004]. Skeletonization of the IMA is a strategy that has been claimed to lower the risk of deep sternal wound infection in diabetes patients who undergo BIMA grafting [Peterson 2003]. Despite the actual and potential advantages of skeletonization, it is technically more demanding than pedicled IMA harvesting. Skeletonization takes longer than the pedicle technique and has a definite learning curve. Small arterial branches can be inadvertently avulsed by excessive downward retraction, leading to injury to the artery and compromising long-term patency [Raja 2004]. Finally, skeletonization probably induces a greater degree of spasm [Raja 2004; Malinowski 2008].

We routinely use pedicled BIMA for patients needing multi-vessel coronary artery bypass grafting (CABG), and we undertook this study to compare the in-hospital outcomes of CABG using pedicled BIMA for both diabetic and nondiabetic patients.

MATERIALS AND METHODS

Study Sample

This study constituted a retrospective analysis of a prospectively collected cardiac surgery database (PATS; Dendrite

Table 1. Preoperative Patient Characteristics*

Variable	Diabetics (n = 390)	Nondiabetics (n = 519)	P
Age, y	66.3 ± 14.2	68 ± 12.9	.42
Male sex, n	253 (64.8%)	348 (67.0%)	.53
Diabetes, n			
Diet-controlled	37 (9.5%)	0	—
Oral therapy	242 (62.0%)	0	—
Insulin therapy	111 (28.5%)	0	—
Hypertension, n	196 (50.3%)	291 (56.1%)	.27
Hypercholesterolemia, n	135 (34.6%)	193 (37.2%)	.58
Smoker, n	119 (30.5%)	150 (28.9%)	.79
Previous PCI, n	76 (19.5%)	103 (19.8%)	.91
Previous MI, n	112 (28.7%)	97 (18.7%)	.03
AMI, n	74 (18.9%)	32 (6.1%)	.01
COPD, n	54 (13.8%)	67 (12.9%)	.84
Renal insufficiency, n	17 (4.5%)	5 (0.9%)	.01
PVD, n	67 (17.2%)	14 (2.7%)	.001
CVA, n	21 (5.4%)	20 (3.9%)	.32
IABP, n	19 (4.9%)	22 (4.2%)	.79
LMS stenosis >50%, n	112 (28.7%)	136 (26.2%)	.73
Two-vessel disease, n	132 (33.8%)	185 (35.6%)	.69
Three-vessel disease, n	258 (66.2%)	334 (64.4%)	.64
No. of diseased vessels	2.95 ± 0.25	2.92 ± 0.27	.81
LVEF, n			
50%	204 (52.3%)	332 (63.9%)	.06
30%-50%	117 (30%)	143 (27.5%)	.67
<30%	69 (17.7%)	44 (8.5%)	.02
Surgery, n			
Urgent	86 (22.1%)	91 (17.5%)	.39
Elective	304 (77.9%)	428 (82.5%)	.27
Logistic EuroSCORE	4.8 ± 1.1	4.2 ± 1.8	.53

*Data are presented as the mean ± SD where indicated. PCI indicates percutaneous coronary intervention; MI, myocardial infarction; AMI, acute MI; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; CVA, cerebrovascular accident; IABP, intra-aortic balloon pump; LMS, left main stem; LVEF, left ventricular ejection fraction.

Clinical Systems, Ltd, Oxford, UK). Owing to its retrospective, observational nature, informed consent was waived for this study. The PATS database captures detailed information on a wide range of preoperative, intraoperative, and hospital postoperative variables (including complications and mortality) for all patients who undergo cardiac surgery in our institution. The database was collected and reported in accordance with the database criteria of the Society for Cardiothoracic Surgery in Great Britain and Ireland. In addition, the medical notes and charts of all the study patients were reviewed. From September 1998 to September 2010, 390 consecutive diabetic and 519 nondiabetic patients underwent isolated off-pump CABG with pedicled BIMA by the same surgeon (M.A.). Supplemental

grafts were constructed with either a long saphenous vein or a radial artery. Grafting strategy was influenced by the surgeon's preference. The patient characteristics for the 2 groups are shown in Table 1. Indications for CABG were determined at a weekly review by cardiologists, cardiac surgeons, and cardiac radiologists. Patients were placed on a specific waiting list according to the urgency of their procedure. All patients with significant left main stem stenosis or double- or triple-vessel coronary artery disease (defined as significant [>50%] stenosis in 2 or 3 [left anterior descending, circumflex, and right coronary] territories) who underwent first-time, isolated off-pump CABG were included in this study. Surgeries carried out on pump were excluded to minimize surgical variability.

Elective diabetic patients with poorly controlled diabetes as determined in the surgical preassessment clinic were referred to the diabetic clinic for optimization of their glycemic control prior to admission for surgery. Emergency patients were commenced on insulin infusion to achieve normoglycemia in accordance with the institutional protocol, and insulin therapy was continued in the postoperative period until a consultant diabetologist or diabetic nurse specialist assessed that an appropriate oral therapy or insulin regimen could commence.

Operative Technique

We have previously described our operative technique in detail [Raja 2009]. All interventions were performed via a midline sternotomy, with a suction stabilizer. Left and right IMA were harvested as pedicled grafts with minimal trauma and treated with papaverine solution before use. The great saphenous vein was harvested with an open technique or with a vein stripper before 2007 and endoscopically thereafter. The radial artery was harvested from the nondominant arm and treated before use with a flushing solution that consisted of 50 mg phenoxybenzamine, 20 mL blood, and 2000 U heparin.

All sternums were routinely closed with a standard double-wiring technique, in which 8 to 10 single wires were placed either parasternally or transsternally, with adjacent wires on the same side twisted together initially and then twisted with their counterparts on the opposite side.

Since 2007, we have routinely been using gentamicin-collagen sponge (Collatamp; EUSA Pharma [Europe], Oxford, UK) between the 2 halves of the sternum in all patients, including diabetics, who were deemed to be at high risk for sternal wound infection.

Postoperative Management

All patients received intravenous nitroglycerin infusions (0.1–8 µg/kg per minute) for the first 24 hours, unless the patient was hypotensive (systolic blood pressure, <90 mm Hg). The choice of inotropic agents was dictated by the hemodynamic data. Other routine medications included daily aspirin and the resumption of cholesterol-lowering agents and β-blockers. All diabetic patients were commenced on an insulin infusion immediately after surgery to maintain normoglycemia. The dosage of the insulin infusion was adjusted according to the patient's blood glucose level and in accordance with an institutional protocol. The insulin infusion was stopped once regular oral hypoglycemics and subcutaneous insulin therapy were commenced.

Variables and Data Collection

Preoperative variables of interest included age, sex, smoking history, chronic obstructive pulmonary disease, diabetes, hypercholesterolemia, renal insufficiency (preoperative serum creatinine, 200 µmol/L), hypertension, peripheral vascular disease, cerebrovascular disease, left ventricular ejection fraction, urgency (operation performed at <24 h versus >24 h from the time of referral), previous myocardial infarction, prior percutaneous coronary interventions, number of diseased vessels, preoperative intra-aortic balloon pump use, and logistic EuroSCORE. Intraoperative variables of interest included types of grafts used, number of grafts per patient,

conversion to cardiopulmonary bypass, and index of completeness of revascularization (ICOR). ICOR was defined as the total number of distal grafts constructed divided by the number of the affected coronary vessels reported on the preoperative coronary angiogram [Lattouf 2008]. Complete revascularization was assumed when the ICOR value was 1.

Postoperative variables of interest included in-hospital mortality, postoperative intra-aortic balloon pump use, stroke or transient ischemic attack, prolonged ventilation (>24 hours), atrial fibrillation, deep sternal infection, superficial sternal infection, mediastinitis, infection at the vein harvest site, blood product use, hemofiltration, inotropes used on leaving the operating room, chest infection, return to the operating room for bleeding, gastrointestinal complications, and lengths of intensive care unit and hospital stays. Previously published guidelines [El Oakley 1996] for reporting sternal wound infections were used to standardize definitions.

Statistical Analysis

Summary results for numeric variables were presented as the mean ± SD. Summary results for categorical variables were presented as a frequency and percentage. Group differences in numeric variables were evaluated by use of the Student t test or the Wilcoxon rank sum test, as appropriate. Group differences in categorical variables were evaluated by use of the 2 test or the Fisher exact test. A significance level of <.05 was used throughout. All analyses were performed with the Statistical Analysis Systems software package (Release 9.1.3; SAS Institute, Cary, NC, USA). The authors had full access to the data and take responsibility for its integrity. All authors read and agreed to the manuscript as written.

RESULTS

From September 1998 to September 2010, we identified 909 consecutive patients who received BIMA and underwent off-pump CABG performed by a single surgeon (M.A.). Of these patients, 519 (57.1%) were nondiabetics, and the remaining 390 patients (42.9%) were diabetics. The patient characteristics for the 2 groups are summarized in Table 1. In summary, diabetic patients had a higher prevalence of acute myocardial infarction (18.9% versus 6.1%, $P = .01$), peripheral vascular disease (17.2% versus 2.7%; $P = .001$), an ejection fraction <30% (17.7% versus 8.5%; $P = .02$), and chronic renal failure (4.5% versus 0.9%; $P = .01$).

ICOR values were similar for the 2 groups ($P = .76$), and no difference was noted in the mean number of grafts per patient ($P = .81$). The overall rate of conversion to cardiopulmonary bypass for the entire cohort was 1.1%. Table 2 summarizes the intraoperative data.

The unadjusted in-hospital mortality rate was 2.8% for the diabetic group and 2.1% for the control group ($P = .87$), for an overall mortality rate of 2.4%. Causes of in-hospital death were acute myocardial infarction in 4 patients, ischemic bowel in 3 patients, respiratory failure/acute respiratory distress syndrome in 3 patients, suspected hypoperfusion syndrome/low cardiac output syndrome in 2 patients, resistant vasoplegia in 2 patients, overwhelming sepsis in 1 patient, and multiorgan failure in 7 patients.

Table 2. Intraoperative Data*

Variable	Diabetics (n = 390)	Nondiabetics (n = 519)	P
In situ BIMA, n	317 (81.3%)	438 (84.4%)	.67
Y-graft BIMA, n	45 (11.5%)	62 (11.9%)	.87
Y-graft RIMA-SVG, n	11 (2.8%)	12 (2.3%)	.84
Y-graft RIMA-RA, n	12 (3.1%)	4 (0.8%)	.08
RIMA-aorta, n	5 (1.3%)	3 (0.6%)	.10
SVG, n	134 (34.4%)	211 (40.6%)	.09
Radial artery, n	96 (24.6%)	103 (19.8%)	.21
SVG + RA, n	28 (7.2%)	20 (3.9%)	.07
No. of grafts/patient [†]	3.37 ± 0.89 (2-4)	3.39 ± 0.92 (2-4)	.81
ICOR [‡]	1.14 ± 0.27	1.16 ± 0.22	.76
Conversion to CPB, n	5 (1.3%)	5 (0.9%)	.73

*BIMA indicates bilateral internal mammary artery; RIMA, right internal mammary; SVG, saphenous vein graft; RA, radial artery; ICOR, index of completeness of revascularization; CPB, cardiopulmonary bypass.

[†]Data are presented as the mean ± SD (range).

[‡]Data are presented as the mean ± SD.

The combined rates of superficial sternal infection, deep sternal infection, and mediastinitis for the diabetic group (3.8%, 15/390) and the control group (3.7%, 19/519; $P = .87$) groups were similar, for an overall sternal infection rate of 3.7%. The occurrence of wound infection at the vein harvest site was higher in the diabetic patients (6.6% versus 1.1%, $P = .04$).

The remaining in-hospital outcomes were similar, except for an increased need for hemofiltration in the diabetic patients (11.8% versus 2.1%, $P = .02$). Table 3 summarizes the in-hospital outcomes.

DISCUSSION

Despite compelling evidence of prolonged survival and decreased cardiac events, the majority of surgeons avoid BIMA grafting because of the increased risk of sternal infection, especially in patients with diabetes [Grossi 1991; Borger 1998; Nakano 2008]. This risk is perceived to be higher if BIMA are harvested in a pedicled fashion [Nakano 2008], and the technically demanding technique of skeletonization is recommended as a strategy to reduce this risk and increase BIMA usage in diabetics [Peterson 2003; De Paulis 2005]. Contrary to this common perception, our study reports similar rates of sternal wound complications with pedicled BIMA harvesting for diabetics and nondiabetics and validates the safety and efficacy of the use of pedicled BIMA for diabetics.

We attribute our results to meticulous pedicled IMA harvesting, careful wound closure (especially in obese patients), aggressive surgical management of deep sternal wound infection with early debridement and primary closure over suction drains, and continuous and aggressive blood glucose monitoring and management in the postoperative period. Our rates

Table 3. Postoperative Data*

Variable	Diabetics (n = 390)	Nondiabetics (n = 519)	P
Inotropes on leaving OR, n	44 (11.3%)	48 (9.2%)	.71
Stroke/TIA, n	7 (1.8%)	6 (1.2%)	.64
Atrial fibrillation, n	89 (22.8%)	97 (18.7%)	.68
Postoperative IABP, n	2 (0.5%)	4 (0.8%)	.78
Ventilation >24 h, n	14 (3.6%)	16 (3.1%)	.89
Superficial sternal infection, n	6 (1.5%)	8 (1.5%)	1.0
Deep sternal infection, n	7 (1.8%)	9 (1.7%)	.89
Mediastinitis, n	2 (0.5%)	2 (0.4%)	.89
Vein harvest site infection, n	26 (6.6%)	6 (1.1%)	.04
Blood product use, n	42 (10.8%)	58 (11.2%)	.76
Hemofiltration, n	46 (11.8%)	11 (2.1%)	.02
Return to OR for bleeding, n	12 (3.1%)	14 (2.7%)	.81
Chest infection, n	38 (9.7%)	46 (8.8%)	.67
Pleural effusion, n	16 (4.1%)	22 (4.2%)	.91
Tracheostomy, n	3 (0.8%)	2 (0.4%)	.10
GI complications, n	6 (1.5%)	7 (1.3%)	.79
Length of ICU stay, d	1.4 ± 0.3	1.1 ± 0.5	.23
Length of hospital stay, d	5.9 ± 1.4	5.6 ± 1.2	.11
In-hospital mortality, n	11 (2.8%)	11 (2.1%)	.87

*Data are presented as the mean ± SD where indicated. OR indicates operating room; TIA, transient ischemic attack; IABP, intra-aortic balloon pump; GI, gastrointestinal; ICU, intensive care unit.

of sternal wound infections decreased significantly in the last few years, and we have not witnessed mediastinitis in our practice since 2007. This decline in wound infection rates in both diabetics and nondiabetics despite the use of pedicled BIMA suggests that attention to surgical technique, as well as attention to postoperative wound management and attempts to achieve normoglycemia, are issues that must be addressed to maximize the use of pedicled BIMA and minimize the rates of sternal wound infections. Results similar to ours have been reported by Agrifoglio et al [2008] and by Choo and associates [Choo 2009]. They attribute their low rates of sternal wound infections to the aforementioned reasons for the decline in sternal wound complications following pedicled BIMA harvest in diabetics.

Proponents of skeletonized BIMA harvest claim that the sternal blood supply is preserved with this technique, perhaps contributing to a lowering of the incidence of sternal wound complications in general and in diabetics in particular [Peterson 2003; De Paulis 2005; Nakano 2008]. This concept stems from animal studies, which have reported greater residual retrosternal blood flow after minimized retrosternal tissue mobilization with the skeletonization technique [Parish 1992; Fokin 2004], as well as from a small randomized study that used nuclear imaging [Boodhwani 2006]. This concept has recently been contradicted by Nishi and colleagues [2011].

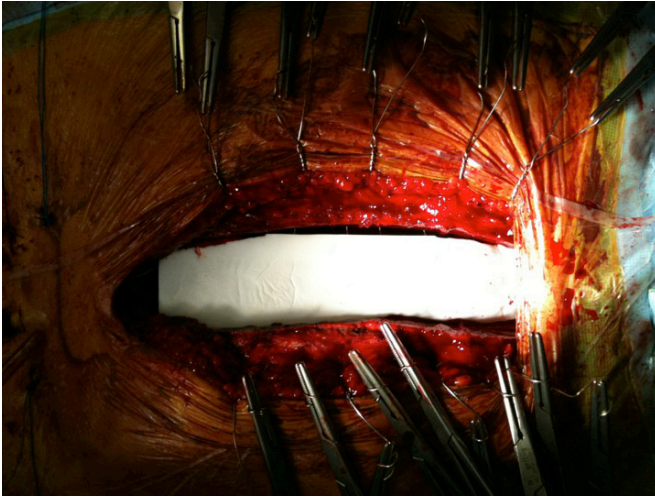


Figure 1. The sternal-wiring technique exerts force both from top to bottom and across the midline, thereby achieving a secure closure and fixing any fractures at the same time. A single Collatamp sponge (20 × 5 × 0.5 cm) is implanted retrosternally without premoistening.

Using a novel laser Doppler flow meter, these investigators showed that the degrees of sternal microcirculation damage after IMA harvesting for skeletonized IMA patients and pedicled IMA patients are not different, suggesting that skeletonization is not advantageous for maintaining the sternal microcirculation. Furthermore, IMA skeletonization is technically more demanding and more time-consuming than pedicled IMA harvesting. It has a surgical learning curve, and there are no current data on long-term patency rates [Raja 2005]. All of these reasons are sufficiently strong to preclude the routine adoption of this technique.

We clip all the side branches during IMA harvesting and use the point-hemostasis technique to minimize leaving charred tissue on the inside of the chest wall, which has the potential to act as a culture medium for microbes. We routinely wash the chest cavity at the end of the procedure with at least a liter of warm saline to remove all debris, and we use a double-wire technique to close the sternum. Our aforementioned sternal-wiring technique exerts force both from top to bottom and across the midline, thereby achieving a secure closure and fixing any fractures at the same time (Figure 1). We firmly believe that the occurrence of a deep wound infection might be due to technical pitfalls, most predominantly a suboptimal sternal-wiring technique [Raja 2005]. Again, we standardized this wiring technique in 2007, and that could have contributed to the decline in sternal wound complications in our experience. At about the same time, we started using gentamicin-collagen sponge (Collatamp) with BIMA harvesting for all high-risk patients, including diabetics. Before closure of the sternum and after placement of the sternal wires, a single Collatamp sponge (20 × 5 × 0.5 cm, with 1 cm² of the sponge containing 2.8 mg native collagen fibrils of equine origin and 2 mg gentamicin sulfate, which is equivalent to 1.10–1.43 mg gentamicin) is implanted retrosternally without premoistening (Figure 1) in all cases deemed high risk for sternal wound complications. The sternal wires are then

tightened. Evidence from a number of randomized controlled trials suggests that Collatamp reduces the incidence of sternal wound infections [Bottio 2003; Eklund 2005], and our experience supports the findings of these trials. In addition to these intraoperative measures, we keep all our surgical wounds (sternotomy and vein harvest site) covered with a waterproof, bacteria-proof dressing with a see-through absorbent pad (OpSite Post-op Visible; Smith & Nephew, London, UK) for 2 weeks postoperatively (Figure 2). The greater visibility and superior absorbency of this dressing allows us to monitor the progress of the wound as often as we like without unnecessary dressing changes. This feature reduces disturbance to the wound bed, minimizes the risk of infection, and helps to provide a cost-effective solution. It also allows the patient to shower with the dressing in situ without unnecessary dressing changes. Our rationale for keeping the wound covered for 2 weeks is that the majority of wounds become infected by cross-contamination in the immediate postoperative period, and keeping them covered during this period minimizes the risk significantly.

Finally, we have aggressively focused on achieving normoglycemia in all diabetics, both pre- and postoperatively, and we have adopted a policy of keeping all sternal wounds covered for a minimum of 2 weeks after cardiac surgery to further

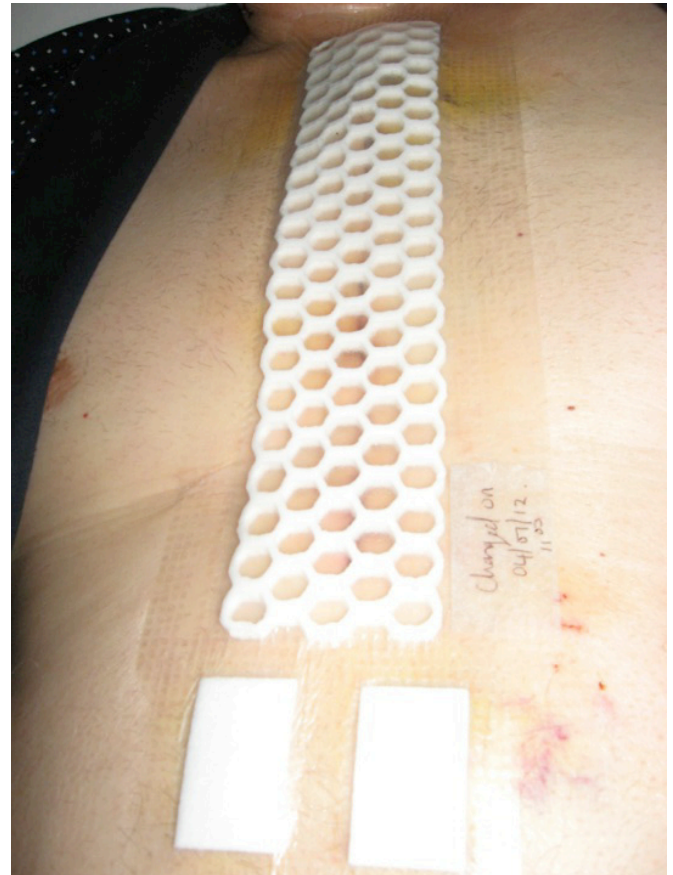


Figure 2. All surgical wounds (sternotomy and vein harvesting site) are covered with a waterproof, bacteria-proof dressing with a see-through absorbent pad (OpSite Post-op Visible) for 2 weeks postoperatively.

reduce the incidence of wound infection. Evidence suggests that better control of postoperative blood glucose levels in diabetes patients after cardiac surgery lowers the incidence of sternal wound complications, particularly deep sternal wound infections [Furnary 1999; Friberg 2005].

We report an increased occurrence of wound infections at the vein harvest site in our diabetic cohort. All infections at the vein harvest site occurred in patients who had undergone traditional open vein harvesting. Traditional longitudinal saphenectomy is a recognized risk factor for the development of leg wound complications [Allen 2000]. Endoscopic vein harvesting modifies the risk factor profile for wound complications [Allen 2000]; therefore, we have adopted it since 2007 as a standard of care in our institution for all patients who require a venous conduit for CABG. There has been a concomitant drop in rates of leg wound infections since the adoption of endoscopic vein harvesting and the aforementioned preventive measures.

The primary limitation of the study is its retrospective nature. The retrospective nature of the study cannot account for the unknown variables affecting the outcome but not correlating strongly with the measured variables. Despite the retrospective and observational nature of the study, we have provided previously unreported data for a large cohort of diabetics and nondiabetics who underwent off-pump CABG with the use of pedicled BIMA, and we have demonstrated the safety of pedicled BIMA harvesting in diabetics. Lastly, we admit the fact that our study has emanated from a single institution and is a single surgeon's experience. Undoubtedly, any validation of the findings will require prospective multicenter studies.

Despite these limitations, we conclude that pedicled BIMA use in diabetic patients and nondiabetic patients is associated with similar incidences of sternal wound complications and other outcomes. Strict perioperative glycemic control, adherence to a meticulous closure technique, and postoperative surgical wound management can make pedicled BIMA use a default strategy for diabetic patients.

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