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Results of the Prospective Multicenter Trial of Robotically Assisted Totally Endoscopic Coronary Artery Bypass Grafting

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Background. Robotic technology has been proven safe and efficacious in the performance of mitral valve repair and atrial septal defect repair. This report describes a Food and Drug Administration-sanctioned multicenter study of the safety and efficacy of the da Vinci system (Intuitive Surgical, Inc, Mountain View, CA) for totally endoscopic coronary artery bypass (TECAB) surgery.

Methods. Patients requiring left anterior descending (LAD) coronary artery revascularization were eligible. The procedure was performed with femoro-femoral cardiopulmonary bypass (CPB), endoaortic balloon occlusion, and thoracoscopy. All aspects of the procedure were performed with the robotic system, from internal mammary artery harvest to coronary anastomosis.

Results. Ninety-eight patients requiring single-vessel LAD revascularization were enrolled at 12 centers. Thirteen patients (13%) were excluded intraoperatively (eg, failed femoral cannulation, inadequate working space). In 85 patients (69 men, age 58 ± 10 years) who underwent

TECAB, CPB time was 117 ± 44 minutes, cross-clamp time was 71 ± 26 minutes, and hospital length of stay was 5.1 ± 3.4 days. There were five (6%) conversions to open techniques. There were no deaths or strokes, one early reintervention, and one myocardial infarction (1.5%). Three-month angiography was performed in 76 patients, revealing significant anastomotic stenoses ($> 50\%$) or occlusions in 6 patients. Overall freedom from reintervention or angiographic failure was 91%.

Conclusions. Robotic TECAB was accomplished with no mortality, low morbidity, and angiographic patency and reintervention rates comparable with published data. Although the use of CPB was a limitation of the technique, this experience represents a step toward more advanced procedures, such as multivessel or off-pump TECAB.

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Computer (robotic) enhancement has emerged as a potential facilitator of minimally invasive surgical procedures. Initial applications of this technology were limited to providing enhanced (including voice-activated) endoscopic camera control [1] during minimal access procedures. A more advanced iteration of this technology is represented by the da Vinci surgical system (Intuitive Surgical, Sunnyvale, CA), a computerized telemanipulator that allows a surgeon to control two or three "wristed" endoscopic instruments from an operating console, while viewing the operative field through a three-dimensional endoscopic camera. Two Food and Drug Administration (FDA)-sanctioned Inves-

tigational Device Exemption (IDE) trials have validated the safety and efficacy of this device for mitral valve repair [2] and atrial septal defect closure [3].

Loulmet and colleagues [4] and Falk and colleagues [5] have described the technique of totally endoscopic coronary artery bypass (TECAB), in which the da Vinci robotic surgical system is used to perform an entire coronary bypass procedure (including coronary anastomosis) in a closed chest environment. Notwithstanding the feasibility demonstrated by these and other pioneering investigators [6–8], the TECAB operation has not been subjected to evaluation in a clinical trial. This report describes the results of a multicenter, FDA-sanctioned IDE trial investigating the safety and efficacy of arrested-heart, single-vessel TECAB.

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Dr Argenziano discloses that he has a financial relationship with Intuitive Surgical.

Table 1. Inclusion Criteria

1. Suitable candidate for nonemergent, first time single vessel LIMA to LAD myocardial revascularization. Eligibility will be determined through preoperative coronary angiography conducted prior to enrollment of each patient
or
Suitable candidate for undergoing a combination of stent placement or percutaneous transluminal coronary angioplasty (PTCA) and LIMA to LAD myocardial revascularization (hybrid approach)
2. Subjects between the ages of 18 and 80 years (inclusive)
3. Willingness and ability to provide informed consent, and undergo the prescribed follow-up regimen

LAD = left anterior descending; LIMA = left internal mammary artery.

Material and Methods

Trial Design

Patients with single-vessel coronary artery disease involving the left anterior descending (LAD) coronary artery referred for surgical revascularization were eligible for this study. The study protocol was approved by the FDA as IDE #G010011 in December 2001, and the multicenter trial began enrolling patients in January 2002. The protocol was also approved by the Institutional Review Board of each participating institution. Between January 2002 and July 2004, 98 patients were enrolled at 12 institutions. All patients gave informed consent for totally endoscopic coronary artery bypass surgery using the da Vinci robotic surgical system.

Training Protocol

All investigators participating in the trial were required to undergo a stepwise training program before enrolling patients in the trial. By requiring the demonstration of proficiency at each training level before allowing continuation to the next level, the minimum level of technical proficiency was standardized. The stages of the TECAB training requirements were the following: stage 1 – basic da Vinci surgical system training; stage 2 – robotically assisted IMA mobilization; stage 3 – minimally invasive cardiopulmonary bypass (CPB) experience; stage 4 – TECAB specific training; stage 5 – TECAB training cases.

Inclusion and Exclusion Criteria

Patients were considered eligible for enrollment in the trial if deemed appropriate candidates for nonemergent, first time single-vessel left internal mammary artery (LIMA) to left internal descending (LAD) myocardial revascularization. Complete inclusion and exclusion criteria are listed in Tables 1 and 2.

Procedure Details

General anesthesia is established with double-lumen intubation, to allow for selective lung ventilation. External defibrillator patches are placed on the chest, and the patient positioned supine with the left chest elevated 30 degrees with the aid of a small bolster under the left chest. The femoral vessels are exposed. After establishment of single left lung ventilation, the three trocars of the da Vinci robotic system are inserted into the left hemithorax, with carbon dioxide (CO₂) insufflation to a pressure of 6–14 mm Hg. The robotic system is used to harvest the LIMA from the subclavian vein to the internal mammary artery (IMA) bifurcation, and to open the pericardium and identify the target vessel. After systemic heparinization, the distal LIMA is skeletonized and clipped distally. The LIMA is divided, spatulated, and prepared. Next, the femoral artery is cannulated with an endoaortic balloon cannula system, and the balloon is positioned in the ascending aorta with transesophageal echocardiographic guidance. The femoral vein is cannulated with a long venous cannula that is directed into the right atrium. At this point, the endoaortic balloon system is deployed to cross-clamp the aorta and to deliver antegrade cardioplegia. Once cardiac arrest is confirmed, the robotic system is used to perform the coronary arteriotomy and the LIMA to LAD anastomosis. The endoaortic balloon clamp is removed, with external defibrillation if necessary. The robotic system is removed, the patient is weaned from cardiopulmonary bypass, and after protamine administration, the femoral vessels decannulated and closed. Chest tubes and pacing wires are placed, and all wounds are closed. A schematic representation of the flow of the TECAB operation is provided in Figure 1.

Once enrolled patients were taken to the operating room, an additional set of intraoperative criteria were utilized to exclude patients from robotic TECAB for technical or anatomic reasons that were not identifiable preoperatively. Examples of these exclusionary criteria include dense pleural adhesions, hemodynamic intolerance of CO₂ insufflation, or intramyocardial coronary target. A complete listing of intraoperative exclusion criteria are listed in Table 3. In contrast, intraoperative conversions were defined as cases in which a TECAB procedure in progress had to be abandoned and converted to an alternative approach because the surgeon could not proceed endoscopically, for reasons such as patient instability, LIMA injury, unsatisfactory anastomosis, excessive bleeding, or robotic system malfunction.

Intraoperative Exclusion Versus Conversion

Study Endpoints

Study Endpoints

The primary efficacy endpoint of the study was the composite endpoint of LIMA-LAD graft patency and

Table 2. Preoperative Exclusion Criteria

1. Body mass index > 35.0 kg/m²
2. Left ventricular ejection fraction < 0.30
3. Decompensated congestive heart failure (NYHA class III or IV)
4. Acute pulmonary edema
5. Severe uncontrolled hypertension
6. Severe peripheral vascular disease limiting vascular access (eg, femoral, iliac, or aortic aneurysm, dissection or occlusive disease)
7. Acute stroke
8. Aortic valve endocarditis
9. Severe coagulopathy (bleeding diathesis)
10. Digitalis intoxication
11. Severe anemia
12. Severe symptomatic electrolyte imbalance
13. Documented anaphylactic reaction to angiographic contrast media
14. Acute renal failure
15. Chronic renal failure secondary to diabetes
16. Active gastrointestinal bleeding
17. Unexplained fever, which may be due to infection
18. Untreated active infection
19. Severe lack of cooperation by patient due to psychological or severe systemic illness
20. Severe concomitant illness that drastically shortens life expectancy or increases risk of therapeutic interventions
21. Acute myocardial infarction requiring emergent CABG or postinfarction angina or early angina after non-Q wave infarction
22. History of acute myocardial infarction in preceding 30 days prior to proposed coronary artery surgery
23. Moderate to severe aortic and mitral valve disease
24. Hemodynamic instability (cardiogenic shock: systolic blood pressure <90 mm Hg, LVEDP >20 mm Hg, cardiac index <2.5 L/min/m²)
25. Severe ascending and/or aortic arch calcification as determined by radiographic or echocardiographic studies
26. Severe cerebrovascular disease including a history of prior stroke (within 1 month) and/or stenosis (>70%) of either internal carotid artery
27. Connective tissue disease
28. Anatomy unsuitable for endoscopic visualization of the thorax (eg, morbid obesity with remarkable axillary adiposity or physical deformities of or effecting the thorax; eg, scoliosis, kyphosis)
29. History of median sternotomy, left thoracotomy, or radical mastectomy
30. Undergone previous radiation therapy of the mediastinum or thorax
31. History of severe asthma, emphysema, chronic obstructive pulmonary disease, or pulmonary fibrosis
32. Pleural adhesions or symphysis visible on the chest x-ray
33. Uncontrolled diabetes mellitus (>2 serum glucose concentrations of >350 mg/dL within 7 days)
34. Pregnancy
35. Participating in another competing investigational protocol
36. Patient unwilling or unable to comply with any protocol requirements (including return for follow-up visit)
37. Use of gastroepiploic artery bypass grafts

CABG = coronary artery bypass grafting; LVEDP = left ventricular end-diastolic pressure; NYHA = New York Heart Association.

freedom from target vessel reintervention during the period of observation. For the purposes of this evaluation, a patent graft was defined as a graft with 50% or less stenosis of the distal anastomosis as determined by 3-month postoperative follow-up coronary angiography [9]. The primary safety endpoints of the study were freedom from major adverse cardiac events, including mortality, target vessel reintervention, and myocardial infarction.

These and other clinical endpoints, including intraoperative conversion rates and other adverse events, were compared with a historical cohort of patients who under-

went conventional single-vessel, arrested heart coronary artery bypass grafting (CABG) surgery. This comparison was based on data obtained from a specific query of the Society of Thoracic Surgeons (STS) National Database for the years 2000–2002 [STS Adult Cardiac National Database; Core Data Elements Summary, Custom Query version 2.41, Adult Coronary Artery Bypass Procedures 2000–2002].

Follow-up and Data Collection

PREOPERATIVE ASSESSMENT. Patients referred for coronary artery bypass surgery had a preoperative visit consisting of a medical history, physical examination, and

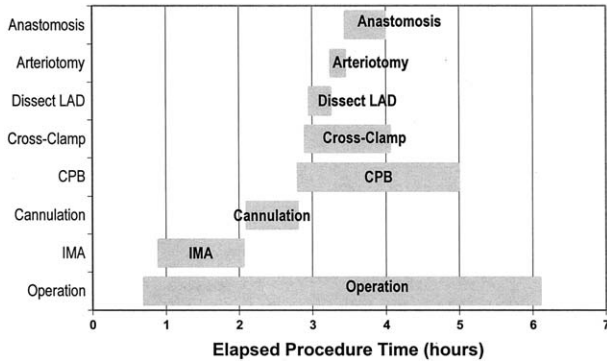


Fig 1. Typical flow of totally endoscopic coronary artery bypass (TECAB) procedure. (CPB = cardiopulmonary bypass; IMA = internal mammary artery; LAD = left anterior descending.)

diagnostic tests, including but not limited to coronary angiography, transthoracic echocardiography, stress electrocardiogram (ECG), resting 12-lead ECG and chest x-ray. Based on this information and the established inclusion-exclusion criteria, the investigator determined the need for surgical revascularization and the appropriateness of the patient for robotically assisted TECAB.

INTRAOPERATIVE AND INTENSIVE CARE UNIT (ICU) ASSESSMENT. For each case, intraoperative times were determined based on perfusion, anesthesia, and operative records or were explicitly recorded during the operation. The details of the surgical procedure, including revascularization scheme, steps of the surgical procedure that were completed robotically, conversion to alternate techniques, time to conversion and reason for conversion, were documented in the operative case report forms.

IMMEDIATE POSTOPERATIVE ASSESSMENT. Immediate postsurgical clinical information was recorded per standard hospital practice and as indicated by the investigator as a part of routine postoperative cardiac care. A postoperative resting 12-lead ECG, chest x-ray, and cardiac enzymes were obtained per standard of care at that institution.

FOLLOW-UP POSTOPERATIVE ASSESSMENT. Patients had a follow-up visit approximately 3 months postoperatively, at which point angiograms were obtained. Supplemental postoperative studies, such as a stress ECG, transthoracic

echo, resting 12-lead ECG, and physical exam were obtained in order to complete the clinical assessment of the patient.

Core Laboratory Review of Angiographic Studies

A primary core laboratory at the Hoag Heart Institute reviewed all preoperative and postoperative angiographic studies. The core laboratory reviewer was masked to the individual institution’s assessment of graft patency.

Data Collection, Entry, and Verification

Clinical information for patients enrolled in the study was collected at all participating institutions and verified against the patients’ medical records by qualified personnel designated by the study sponsor. All applicable information from the medical charts was recorded onto standardized case report forms and entered into a database.

Statistical Methods

All continuous variables were analyzed using a nonparametric, Wilcoxon rank sum test for two group comparisons. Categorical data were analyzed using χ^2 tests for association with or without continuity correction. In the case of small cell comparisons a Fisher’s exact test was used. In all cases 2-tailed *p* values of less than 0.05 are considered significant. The binomial distribution was used for the assessment of binary outcomes (ie, patency) with Agresti’s formula used for the computation of one-sided 95% confidence intervals. Conversion rate comparisons were made with those seen in a literature survey of published conversion rates based on similar cardiac operations of comparable complexity. Comparisons of the incidence of significant adverse events were made between da Vinci TECAB and coronary artery bypass as reported in a customized query from the STS National Database (2000–2002) for single-vessel arrested heart sternotomy CABG. For these comparisons, a normal approximation to the da Vinci arrested heart TECAB summary statistic was used. Generalized estimating equations were used for analyzing the learning curve effects associated with times to complete various tasks associated with CABGs. This method takes into consideration the underlying correlation structure of repeated

Table 3. IntraOperative Exclusion Criteria

1. Blood pressure drop of greater than 20% of baseline or less than 80 mm Hg (systolic) for greater than 15 minutes at insufflation pressure of <10 mm Hg
2. Adhesions between pericardium and chest wall severely limiting visibility (≤ 3 cm between anterior surface of pericardium and chest wall after insufflation [max. 10 mm Hg pressure])
3. Working space 3 cm between anterior surface of pericardium and chest wall
4. Intraoperative complications pertaining to cardiopulmonary bypass (catheter positioning, excessive bleeding at cannulation site, defective cannulation equipment, complications associated with aortic occlusion or cardioplegia delivery)
5. Intramyocardial LAD previously not identified on coronary angiogram or target LAD diameter less than 1.5 mm

LAD = left anterior descending (coronary artery).

Table 4. Patient Demographics

No.	85
Age (yrs)	
Mean	58.4
SD	9.6
Range	34.3-77.1
BMI (kg/m ²)	
Mean	27.6
SD	3.7
Range	19.5-39.1
Gender n (%)	
Female	16 (18.8)
Male	69 (81.2)

BMI = body mass index.

measurements (ie, a given surgeon's case experience over time).

Data Safety Monitoring Board Review of Clinical Trial Safety

Data from the study were reviewed by a cardiac surgeon who was not an investigator in the study. All adverse events, including all conversions and reinterventions in this study were reviewed. The reviewer was blinded to the institution at which each case was performed and to the surgeon who performed each case.

Results

Training Phase

A total of 18 institutions entered the training program with the intention of participating in the multicenter TECAB trial. All 18 sites completed stages 1 and 2 of the training program, and 12 of these completed all 5 stages and were allowed to proceed to enrollment of TECAB patients. At the twelve sites completing stage 5 of the protocol, 21 training cases (stage 5) were performed, with anastomosis times averaging 24 ± 9 minutes (range, 14-49 minutes).

Demographics

A total of 98 patients were enrolled in the trial (not including stage 5 training cases) at 12 centers (see Appendix). Of these, 13 were excluded intraoperatively and did not undergo TECAB. The reasons for these exclusions will be discussed in the next section. Demographics and baseline characteristics of the remaining cohort of 85 patients undergoing TECAB are summarized in Tables 4 and 5.

Intraoperative Exclusions and Conversions

Thirteen of 98 enrolled patients (13%) were excluded from the trial intraoperatively. Ten patients were excluded for inability to establish effective peripheral cannulation (6 patients with prohibitive peripheral vascular disease, 2 with poor venous cannula position and inadequate drainage, and 2 with endoaortic balloon migra-

tion). Two others were excluded for deeply intramyocardial coronary targets that could not be visualized epicardially, and one was excluded for dense pleuropericardial adhesions. Of the 13 excluded patients, 10 underwent coronary bypass surgery by left minithoracotomy (arrested or beating heart minimally invasive direct coronary artery bypass [MIDCAB]), and 3 underwent sternotomy. Five of the remaining 85 patients (5.9%) undergoing TECAB required intraoperative conversion to another approach. In these cases, conversion was prompted by damage of the LIMA graft (2 patients) or inadequacy of the coronary anastomosis (bleeding in 1 case, poor graft flow in 2 cases), and these patients were converted to sternotomy.

Operative and ICU Data

In the 85 patients undergoing TECAB, total operative time was 353 ± 89 minutes (mean \pm SD), with a range of 200 to 600 minutes. Notable subcomponents of this operative time included internal mammary artery harvest time (60 ± 24 minutes; range, 26-187 minutes), cardiopulmonary bypass time (117 ± 44 minutes; range, 41-254 minutes), aortic cross-clamp time (71 ± 26 minutes; range, 30-140 minutes), and coronary anastomosis time (28 ± 11 minutes; range, 14-82 minutes). Postoperative ventilation time was 14 ± 28 hours (range, 0-217 hours), ICU length of stay was 35 ± 37 hours (range, 4-288 hours), and hospital length of stay was 5.1 ± 3.4 days (range, 1.2-25.5 days). Twenty-six of 85 patients (31%) received blood products perioperatively.

Completeness of Follow-Up

Of the 85 patients undergoing TECAB, all were followed through to study completion. One patient underwent

Table 5. Preoperative Characteristics

Characteristics	No. (%)
	85
Smoking	57 (67.1)
Hypertension	47 (57.3)
Diabetes	18 (21.9)
Family history of CAD	41 (50.3)
Dyslipidemia	68 (80.9)
Myocardial infarction	32 (37.6)
Arrhythmia	9 (11.9)
Cerebrovascular disease	3 (3.5)
Peripheral vascular disease	2 (2.5)
Chronic renal failure	1 (1.1)
Angina	67 (79.7)
Dyspnea	18 (21.7)
Average preoperative LVEF	
Mean	56.2
SD	10.2
Range	(30-85)

CAD = coronary artery disease; LVEF = left ventricular ejection fraction.

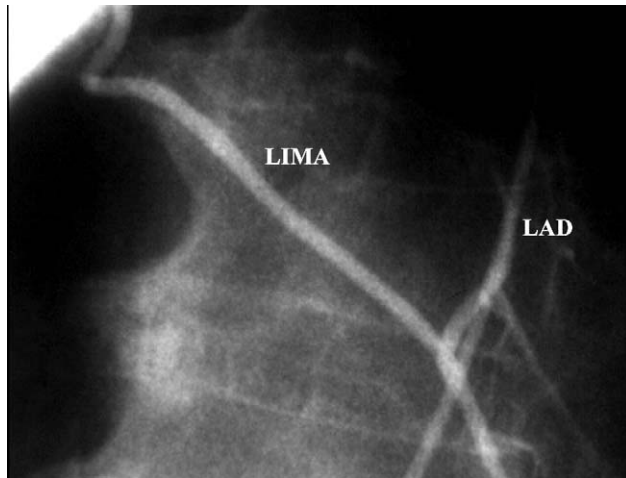


Fig 2. Postoperative angiogram 3 months after totally endoscopic coronary artery bypass. (LAD = left anterior descending; LIMA = left internal mammary artery.)

target vessel reintervention for graft occlusion. Three-month postoperative angiography was performed in 76 of the 85 patients (89%), echocardiography in 72 (85%), and stress testing in 58 (68%). A frame from a representative 3-month angiogram is shown in [Figure 2](#).

Efficacy Endpoints

Of the 85 patients undergoing TECAB, 5 (6%) were converted to other techniques. One patient (1%) required reintervention of the target vessel on the first postoperative day, for graft occlusion. Three-month angiography was performed in 76 patients, and revealed anastomotic

occlusion in 2 cases and significant anastomotic stenosis ($\geq 50\%$) in 4 others. Of these 6 patients, only one (who was symptomatic) underwent reintervention after the three-month angiogram. Thus, a total of 7 of 80 patients having TECAB had either target vessel reintervention or angiographic documentation of graft failure. Because 5 patients had neither a reintervention nor an angiogram, this corresponds to a freedom from graft failure or a reintervention rate of 68/75, or 91%.

Safety Endpoints

Major adverse cardiac events (MACE) were defined as all-cause mortality, myocardial infarction, or target vessel reintervention. There were no deaths from any cause in the cohort during the study period. There was one perioperative myocardial infarction, and 4 target vessel reinterventions (as described above), corresponding to 5 MACE events in 85 patients (5.9%). The incidence of these and other adverse events in the study group is listed in [Table 6](#), along with corresponding incidences from a query of the STS database for similar patients undergoing single-vessel coronary bypass on the arrested heart by sternotomy in 2000–2002. The comparison indicates that our study cohort compared favorably with the STS database cohort. There were 5 groin infections, which did not result in major morbidity but were a TECAB-specific complication not usually associated with conventional approaches, which only infrequently utilize femoral cannulation. Finally, the transfusion rate of 31% was higher than expected, and may reflect the effects of longer cardiopulmonary bypass times in some patients.

Table 6. Adverse Events

Description of Event	TECAB Trial	STS Database (2000–2002)	p Value ^a
No. (%)	85	11,382	
Mortality - all causes	0	(2.5)	0.03
Myocardial infarction	1 (1.1)	(8.2)	<0.05
Target vessel reintervention	4 (4.7)	(2.6)	NS
Cardiac arrest	1 (1.2)	(1.2)	NS
Heart failure	1 (1.2)	52 (8.6)	<0.05
Postop AFIB (new onset)	1 (1.2)	1,909 (16.8)	<0.05
Ventricular tachycardia	1 (1.2)	-	-
Iliac/femoral artery dissection	0 (0)	14 (0.12)	NS
Pleural effusions requiring thoracentesis	3 (3.5)	-	-
Reop for bleeding	3 (3.5)	197 (1.7)	NS
Postcardiotomy syndrome	2 (3.1)	-	-
Respiratory failure (>48 hours)	2 (3.1)	542 (4.8)	NS
Postop renal failure	1 (1.2)	235 (2.0)	NS
Gastrointestinal complications	2 (3.1)	187 (1.6)	NS
Pulmonary embolus	1 (1.2)	189 (1.7)	NS
Groin infection	5 (5.9)	-	-

^a STS database point estimates were compared against study group estimates based on second-order approximation to the 95% confidence interval of each rate.

AFIB = atrial fibrillation; STS = Society of Thoracic Surgeons.

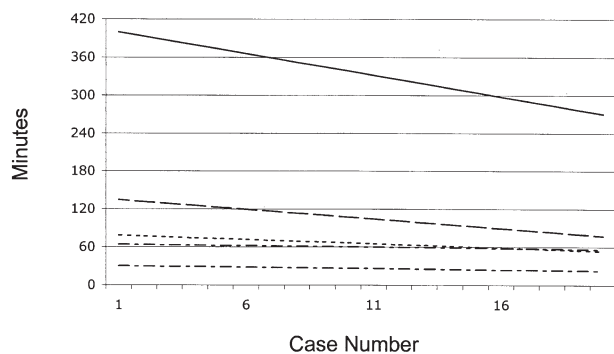


Fig 3. Operative time learning curves. (— = total operating room; --- = cardiopulmonary bypass; ···· = cross-clamp; - · - · = internal mammary artery; - - - - = anastomosis.)

Learning Curve Analysis

The “learning curve” refers to the phenomenon of improved performance with increasing experience. By plotting each surgeon’s individual operative time data against his level of experience (ie, case number), scatter plots were generated, from which best-fit equations were generated. The results of this analysis are depicted graphically in Figure 3. The mean reduction of time with increasing experience was statistically significant for total operative time, cardiopulmonary bypass time, cross-clamp time, and anastomosis time, but not for IMA harvest time.

Comment

Enthusiasm for minimally invasive cardiac surgery has recently been bolstered by the introduction of a new category of technologic achievement: the computerized telemanipulator. In 1997 the first intracardiac procedures (mitral valve repairs) were performed using a prototype of the current da Vinci system [10]. These operations were performed through small thoracotomy incisions, since the “micro-wrists” allowed the surgeons to complete complex maneuvers without placing their hands within the chest. Over subsequent years, the da Vinci system was tested in FDA IDE trials of robotically assisted mitral valve repair [2] and atrial septal defect repair [3].

The technical dexterity and three-dimensional visualization afforded by robotic technology has also been applied to CABG. In 1999, Loulmet and colleagues reported the first use of the da Vinci system for coronary bypass surgery [4]. According to this pioneering report, the robotic system was used to harvest internal mammary artery grafts in four patients, and to complete the remainder of the CABG operation in two of these patients by a totally endoscopic approach (TECAB). A year later, Falk and colleagues [5] reported a much larger experience of robotically assisted CABG surgery, which included 22 patients undergoing TECAB. Subsequent reports of similar experiences by Kappert and colleagues [11] and Dogan and colleagues [8] have supported the feasibility of robotically assisted TECAB. Notwithstand-

ing the achievements of these and other pioneering surgeons, early outcome data were available only in the form of anecdotal single-center reports, and selection criteria for TECAB, as well as technical details of the procedures (on-pump versus off-pump, arrested versus beating heart, target vessel and conduit selection, etc), were not standardized. Therefore, prior to granting approval of TECAB as an indication for use of the da Vinci system, the Food and Drug Administration required the evaluation of this new operation in a controlled clinical safety and efficacy trial.

The present study demonstrated that TECAB can be performed with acceptable safety. In 85 patients, there were no deaths, and only one postoperative myocardial infarction. Other adverse events, such as target vessel reintervention, renal failure, and reoperation for bleeding occurred with equal or lesser frequency than in patients undergoing similar coronary bypass procedures by conventional approaches.

Efficacy in this study was defined as freedom from the composite endpoint of target vessel reintervention or angiographic graft failure after three months. By this definition, after excluding 5 intraoperative conversions and 5 patients without angiographic follow-up data, 68 of 75 evaluable patients, or 91%, had effective procedures. Three of the intraoperative conversions were due to mammary artery damage or anastomotic bleeding, while two were from poor graft flow as assessed by intraoperative angiography.

These results compare reasonably with available data from studies of coronary bypass surgery by minimally invasive and conventional approaches. In a study by Diegeler and colleagues [12], in which a cohort of 271 patients underwent LIMA-LAD bypass by a minithoracotomy, beating heart approach (MIDCAB), angiography revealed a graft patency rate of 88.2% at hospital discharge and of 91.5% at 6 months. In a similar study by Mack and colleagues [13], the graft patency rate after MIDCAB was 91%. Jatene and colleagues [14] reported the angiographic follow-up of 120 patients who had off-pump coronary artery bypass (OPCAB) by sternotomy or minithoracotomy (MIDCAB). In cases performed without a cardiac stabilization device, early (pre-discharge) graft patency was only 79%; when a stabilizer was used, the patency rate improved to 90%. In a sub-study of the International Multicenter Aprotinin Graft Experience (IMAGE) trial [15], in which all patients underwent on-pump CABG by sternotomy, Berger and colleagues found that early angiographic LIMA-LAD patency was 90.9%. Finally, in a recent randomized study by Khan and colleagues [16] published in the *New England Journal of Medicine* in 2004, off-pump CABG resulted in an observed 3-month angiographic patency rate of 92% for IMA grafts and for grafts to the left anterior descending artery. Although these grafts in patients undergoing conventional, on-pump CABG had a patency rate of 100%, the authors concede that “our rate ... in the on-pump group is at the high end of the reported range,” citing the paper by Nathoe and colleagues [17], published a year earlier in the same journal,

in which the angiographic graft patency rate after on-pump CABG was 93%.

There were five conversions in the trial, corresponding to a rate of 6%. These were cases in which intraoperative difficulties prompted the choice of an alternative approach in order to complete the coronary bypass operation. All converted patients had three-month angiography documenting graft patency, and none underwent reintervention of the target vessel postoperatively. This conversion rate compares favorably with studies of other novel minimal access operations, such as MIDCAB [18, 19], minimally invasive aortic valve replacement [20], and thoracoscopic IMA harvest [21], in which conversion rates ranged from 3.9% to 8.3%.

A unique component of our trial was the mandatory, stepwise training program that required prospective investigators to achieve minimum standards of proficiency in specific tasks in order to "graduate" to the full TECAB operation. The enforcement of this program achieved several goals. First, surgeons unable or unwilling to master basic but important components of the TECAB operation, such as robotic IMA harvesting and peripheral perfusion with endoaortic balloon clamping, never entered the trial, minimizing technical failures. Second, the learning curves for certain tasks were established prior to trial entry; as an example, our analysis confirms that IMA harvest times for surgeons in the trial had reached a plateau before the first TECAB was ever performed. Finally, in the face of the recent FDA approval of robotically assisted CABG (which was attained on the basis of data from this study), our stepwise training plan will serve as a prototype in the development of a larger scale training program.

Our study has its limitations. Patients were not randomized to different minimally invasive techniques, such as OPCAB and MIDCAB, so that comparative evaluation of TECAB safety and efficacy data is dependent on intrinsically imperfect historical data. Furthermore, although TECAB is often proposed as a less invasive alternative to OPCAB and MIDCAB, two "off-pump" procedures, safety concerns led to the decision that the trial would study TECAB in the "on-pump," arrested heart setting. This fact somewhat limits the extrapolation of our results to other "more desirable" descendants of arrested heart single-vessel TECAB, such as beating heart TECAB and multivessel TECAB. This is unfortunate, since it is difficult to support the concept of an "on-pump" operation for single-vessel coronary disease as anything more than a steppingstone to beating heart or multivessel TECAB. Finally, although complication rates in our trial compare favorably with those reported to the STS database for patients undergoing single-vessel CABG, we must be cautious in deriving strong conclusions from this comparison, as the two patient cohorts were not prospectively randomized or retrospectively matched. Notwithstanding these limitations, the experience obtained in this trial is certain to further the development of other TECAB variants. Early proof of this is the fact

that several of our trial investigators have already accumulated a significant experience in multivessel and beating heart TECAB since the trial's end.

In conclusion, our multicenter, prospective evaluation of robotically assisted, totally endoscopic coronary bypass surgery demonstrated that this operation can be performed with acceptable safety and efficacy by surgeons who undertake a structured and rigorous training program. Although TECAB will make its greatest impact when applied in an off-pump setting and/or for multivessel disease, this trial confirms the feasibility of coronary bypass surgery by robotic means and suggests a continued role for robotic technology in the pursuit of ideal procedures that will deliver maximal efficacy and safety in the treatment of cardiovascular disease with minimal invasiveness.

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Appendix

Participating Centers

Onze Lieve Vroux Clinic
Aalst, Belgium
Leopold Franzen Hospital
Innsbruck, Austria
Odessa Regional Hospital
Odessa, Texas
Henrico Doctors Hospital
Richmond, Virginia
Saint Agnes Medical Center
Fresno, California
Lenox Hill Hospital
New York, New York
Columbia University Medical Center
New York, New York
St. Joseph's Hospital of Atlanta
Atlanta, Georgia
Carilion Roanoke Memorial Hospital
Roanoke, Virginia
St. Lukes Medical Center
Milwaukee, Wisconsin
Sacred Heart Medical Center
Spokane, Washington
Hospital University of Pennsylvania
Philadelphia, Pennsylvania

DISCUSSION

DR FRANK SELKE (Boston, MA): You take young patients with good LV (left ventricular) function and give them an 88% graft patency at six months, all in six hours of operating. Do you think this has a future?

DR ARGENZIANO: That is a very good question. There really is a two-part answer. The first question is do we think that a six-hour operation which requires cardiopulmonary bypass and femoral cannulation has a future for single vessel disease, and I think the answer is no, because in fact there are very few people who have had to do that after the trial. The stipulation was that we had to prove that this was safe in a more comfortable on-pump setting. There is no question that this is really a steppingstone in that the MIDCAB (minimally invasive direct coronary artery bypass) or the mini ThoraCAB, whatever you want to call it, the endo-ACAB, certainly achieves similar goals without the cardiopulmonary bypass.

With respect to your question about the success rate or the efficacy end point, again, if you ask any cardiac surgeon, well, what is your LIMA (left internal mammary artery) to LAD (left anterior descending) patency rate, they will say, oh, it is 100% or 99%. There was Mrs. Nussbaum. The problem is we don't know what mammary patency rates are, and if you look at the literature, if you look at every study, including the large aprotinin study, which looked at angiographic patency rates, and some of the MIDCAB trials and some of the OPCAB (off-pump coronary artery bypass) trials, any study that has ever looked at vein or mammary patency rates has found the patency rates, in reality, to be much less than people think. So do I think that 88% is a good success rate? I don't, but I suspect that if we took our patients in our practices and did routine three-month angiograms we might be surprised at what would be found.

DR SUDHIR P. SRIVASTAVA (Odessa, TX): I have a comment on your earlier question, and I think it is a very relevant question. Of course the trial, as Mike has pointed out, was really a springboard to get to the next stage, and I think since then the beating heart and da Vinci coronary revascularization is being done, and in fact in many centers those timings have really come down. We have done about 50 cases since July since the FDA (Food and Drug Administration) cleared the coronary anastomosis, and our single vessel timings are down to around two to two and a half hours, and these patients, many of them go home the next day, and we have 100% graft patency. So I think it was an evolutionary step for a later purpose.

DR ARGENZIANO: Sudair should be really congratulated. Dr Srivastava was one of the investigators in our study, and he and a few others have really kind of taken the lead that of course was established by our European colleagues, some of whom were in the trial, some of whom weren't, in moving to the next step, and of course, beating heart TECAB is being performed in Europe and at several centers here in the United States. And frankly, there are learning curves associated with all these procedures. Of the 12 centers that were involved, eight of the surgeons in the center did at least five cases, but there were some who did less. So obviously learning curve is important.

DR OMAR M. LATTOUF (Atlanta, GA): Dr. Argenziano, I have a couple of comments for you. Six patients in your group were converted out of the planned TECAB because of peripheral vascular disease. Did you perform femoral ultrasound in advance, preoperatively, for those patients and would you do that now based on your experience? The second point, you had a 10% stenosis or occlusion rate. Did you use a shunt in the LAD, or

would you use a shunt in the LAD to keep that patent and give you a better chance of graft patency?

DR ARGENZIANO: With respect to the femoral cannulation, all patients did not receive ultrasounds but in fact there was a peripheral vascular exam involving pulses and Dopplers and history. As you know, patients with coronary disease do have some incidence of significant peripheral vascular disease of the iliofemoral system. There was no specific criterion for that, and I think that was something that we did learn. There was significant incidence of this. This is really a problem that doesn't need too much of a solution because, of course, the goal is to do this without cannulation.

You were talking about intracoronary shunts. We didn't because this was an arrested heart trial, and so it was cardioplegic arrest and it was a still heart. Certainly, for the surgeons that are performing beating heart TECAB, the shunt has been helpful, as it is in other forms of OPCAB.

DR INDERJIT S. GILL (Cleveland, OH): The angiograms that you had in the study, were they analyzed in a single core lab or were they done in individual hospitals?

DR ARGENZIANO: All angiograms were sent to a primary core laboratory which rendered an independent blinded assessment, but they were also evaluated by the individual cath labs in the member hospitals, and if there was a disagreement between the primary core lab and the institutional lab, then those studies were referred to a secondary core lab for adjudication.

DR GILL: And a second question. How many of these patients had hybrid diseases?

DR ARGENZIANO: Approximately 30% to 40% of the patients in the study were participants in some form of hybrid scheme.

DR DIMITRI NOVITZKY (Tampa, FL): I have concerns about the study because of such a long ischemic and bypass time. My first question, is it ethical to continue with the study? If you yourself will require coronary bypass surgery, which way would you prefer? For myself, I would choose a standard midline sternotomy. I know that we need to be innovative and introduce changes in surgical procedures. The driving force for the patient care should be the surgeon and not the industry. You should not allow yourself to be pushed and therefore compromise the patient outcome.

DR ARGENZIANO: Thank you for your comments. Your questions are all questions that run through our minds any time we engage in innovative work. Without question, from the first use of the cardiopulmonary bypass machine to what we are doing today, there is a certain amount of trepidation that is involved in the changing of a standard. However, without that sort of thinking, innovation certainly has no chance. But I would have to agree with you that from an ethical standpoint we were very careful. We had a data safety monitoring board, which was chaired by a very experienced, minimally invasive surgeon from Europe who was not involved in the trial, and every adverse event was reviewed, and there was specific criteria for halting the trial or modifying the numbers, and those were not achieved.

With respect to whether I would have this operation done, again, as I say, the healthy patient with a good ventricle certainly has a low risk of complications, but this trial was a steppingstone trial, and based on what we have learned, we have already moved ahead to the next step. So the answer to your question, if I had a single vessel that needed to be revascularized, I would not have trouble having a beating heart TECAB performed by a surgeon with experience in that area. But again, the trick is getting the experience.

Results of the Prospective Multicenter Trial of Robotically Assisted Totally Endoscopic Coronary Artery Bypass Grafting

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