Evaluation of the PAS-Port Proximal Anastomosis System in coronary artery bypass surgery (the EPIC trial)

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Objective: During coronary surgery, proximal vein graft anastomoses have been performed by using an aortic partial occlusion clamp to allow for a hand-sewn anastomosis. The purpose of this multicenter, prospective, randomized trial was to evaluate the efficacy of the PAS-Port device (Cardica, Inc, Redwood City, Calif), which allows an automated proximal anastomosis to be performed without aortic clamping.

Methods: Between June 22, 2006, and March 22, 2007, 220 patients requiring coronary artery bypass grafting with at least 2 vein grafts were enrolled. Within each patient, 1 graft was randomly assigned to receive a PAS-Port device, and the other was assigned to receive a hand-sewn anastomosis to the ascending aorta. The primary end point was angiographic patency (<50% stenosis) 9 months after surgical intervention. Secondary end points included average time to complete each anastomosis and 9-month freedom from major adverse cardiac events.

Results: One hundred eighty-three patients received matched grafts that were angiographically assessed at 9 months. The 9-month graft patency was 82.0% (150/183) for hand-sewn and 80.3% (147/183) for PAS-Port grafts. The patency rate of PAS-Port anastomoses was statistically noninferior to that of hand-sewn anastomoses (95% lower confidence limit for difference, –7.95%). The freedom from major adverse cardiac events at 9 months was 97.7% for PAS-Port (95% confidence interval, 94.5%–99.0%) and 98.2% for hand-sewn (95% confidence interval, 95.1%–99.3%) grafts. The PAS-port device was associated with a 4.6 ± 3.9–minute reduction in anastomotic time compared with that seen with a hand-sewn anastomosis ($P < .001$).

Conclusions: The PAS-Port proximal anastomotic device produces an effective anastomosis with a 9-month patency rate that is comparable with that of a hand-sewn anastomosis. It allows for construction of a proximal anastomosis without aortic clamping and requires less time than a hand-sewn anastomosis.

The traditional approach for coronary artery bypass surgery has been to use the left internal thoracic artery to graft the left anterior descending coronary artery and saphenous vein grafts to bypass other diseased vessels. Although arterial revascularization might provide a more durable revascularization strategy,[1,2] venous conduits are still commonly used. For both venous grafts and arterial grafts not harvested in situ, a proximal anastomosis to the ascending aorta must be constructed in addition to a distal anastomosis to the coronary artery target. This has traditionally required clamping of the aorta to perform a hand-sewn anastomosis. However, manipulation of the aorta with a partial occlusion (side-biting) clamp for off-pump procedures and a crossclamp with or without a side-biting clamp for on-pump procedures can be associated with aortic atheroemboli.[3-5] Aortic manipulation is independently associated with an increased risk of postoperative stroke.[6,7]

Facilitating devices have been developed to allow for construction of a proximal anastomosis without clamping the aorta.[8-10] These devices are commonly used during off-pump procedures to allow for a no-clamp coronary bypass procedure. However, these devices still require a hand-sewn anastomosis to be performed between the graft and the aorta and are associated with some blood loss. Hand-sewn anastomoses with these facilitating devices can be time-consuming, increasing operative and anesthesia times. Furthermore,

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Abbreviations and Acronyms
FDA = US Food and Drug Administration
MACE = major adverse cardiac event

hand-sewn anastomoses are dependent on the particular anatomy of the patient and the skills of the surgeon.

The PAS-Port Proximal Anastomosis System (Cardica, Inc, Redwood City, Calif) was specifically designed to create a consistent anastomosis between a saphenous vein and the aorta during either on- or off-pump coronary bypass surgery. It is a fully integrated, automated system that cuts the aortotomy and attaches the vein graft to the aorta in seconds, producing consistent and reproducible anastomoses independent of surgical technique and skill.

The objective of this prospective, randomized, multicenter trial (the Evaluation of the PAS-Port in Coronary Surgery [EPIC] trial) was to evaluate the safety and efficacy of the PAS-Port System in creating a clampless proximal aortic connection and to compare the patency of PAS-Port anastomoses with that of anastomoses constructed by using a standard hand-sewn technique with an aortic clamp.

MATERIALS AND METHODS

Compliance, Ethical Review, and Informed Consent

The study protocol was designed to assess the patency of the index grafts and document any adverse effects related to device use. The study was conducted in accordance with current Good Clinical Practices and the ethical principles of the Declaration of Helsinki. The study protocol and amendments, the subject information/consent form, and any materials used to recruit subjects were submitted to and approved by institutional review boards in the United States or independent ethics committees in Germany (European Union). Before the start of the study, approval was obtained in compliance with the requirements of the Clinical Investigation of Medical Devices for Human Subjects. All patients signed informed consent forms before enrollment.

Study Design

This study was a prospective, randomized, multicenter trial conducted in 12 hospitals in the European Union and the United States. Two hundred twenty subjects were enrolled with the intention to place at least 2 aortocoronary venous bypass grafts. The revascularization strategy for these grafts was determined preoperatively and confirmed intraoperatively before randomization. After satisfying all intraoperative inclusion criteria, including that both vein segments were within specifications for use with the PAS-Port device, the randomization envelope was opened. The 2 saphenous vein graft–coronary target pairings were identified as grafts 1 and 2 and assigned to one of 2 methods for creation of the anastomosis: the hand-sewn control group or the PAS-Port treatment group. The randomization strategy for assignment of the anastomotic method to the 2 index saphenous vein grafts was conducted by using a random number generator. The randomization envelope contained a 6-digit alphanumeric number that was documented on the case report form. With this information, the surgeon was instructed as to which type of anastomotic technique to use for each of the 2 index grafts.

Both on-pump and off-pump surgical procedures were allowed at the discretion of each investigator/surgeon. Facilitating devices (eg, the Maquet Heartstring, Maquet Cardiovascular LLC, San Jose, Calif, or the Novare Enclose, Novare Surgical Systems, Inc, Cupertino, Calif) were allowed for the execution of the hand-sewn index proximal anastomoses to avoid the need for aortic clamping in subjects undergoing off-pump coronary artery bypass at the surgeon's discretion. Intraoperative graft patency was evaluated based on transit time Doppler blood flow measurements. Patients were asked to return for follow-up visits at 3 and 9 months after the operation. A coronary angiogram was performed at 9 months after the operation to document index graft patency.

Study Population

The study population consisted of male and female patients, 50 to 85 years of age, who required nonemergency bypass of at least 2 coronary arteries. Patients were required to have an ejection fraction of greater than 30%, as measured by means of ventriculographic analysis, nuclear imaging, or echocardiographic analysis. Patients were required to have native coronary artery stenosis of greater than 70% in each on the intended index grafts. Exclusion criteria included the following: previous cardiac surgery, dialysis-dependent renal failure, serum creatinine value of greater than 2.3 mg/dL within 30 days before the operation, need for ongoing immunosuppressive therapy, New York Heart Association class IV heart failure symptoms, presence of systemic infection, preoperative intra-aortic balloon counterpulsation, aspirin allergy, history of thromboembolic disease requiring anticoagulation therapy, cerebrovascular accident within 2 weeks before the operation, and life expectancy of less than 1 year.

Populations for Analysis

Successfully treated patients who (1) had 2 grafts randomized, (2) completed the 9-month angiogram, and (3) had both index grafts (matched pair) studied angiographically at 9 months and were assessable by the angiographic core laboratory constituted the per-protocol population. The intent-to-treat population consisted of patients who had 2 grafts randomized, regardless of whether the grafts were successfully anastomosed to the aorta. For patency, this included all patients with and without 9-month angiograms. For safety, this included all patients regardless of when the subject's grafts were censored. The as-treated population included all randomized patients regardless of the method used for the proximal anastomosis or whether the anastomotic methods were successful.

Intraoperative Data Collection

During the surgical procedure, the time to complete the proximal hand-sewn anastomoses, time to use facilitating devices, and loading and deployment time for the PAS-Port system were recorded. All patients received standard anticoagulation management with heparin and protamine reversal in the operating room.

Surgical Technique

Any concomitant procedures, as well as any other planned nonindex grafts, were performed at the discretion of the surgeon while adhering to the following general guidelines: (1) partial occlusion clamps were not to be placed on the aorta after the PAS-Port anastomosis was created; (2) all proximal anastomoses were to be completed first before completing any distal anastomoses; and (3) facilitating devices were permitted (eg, the Maquet Heartstring or Novare Enclose) for the hand-sewn anastomosis but were to be used and removed before deployment of the PAS-Port Anastomosis System. Different techniques were permitted and documented and included off-pump coronary artery bypass, beating heart supported with cardiopulmonary bypass, and traditional on-pump coronary artery bypass with cardioplegic arrest. Different saphenous vein harvesting techniques were also documented and included endoscopic techniques, bridging skin incisions, or open continuous incisions.

The PAS-Port device (Figure 1) was designed to allow surgeons to load the bypass graft and rapidly complete an automated anastomosis. This device creates the aortotomy and attaches the vein graft to the aorta by means of an automated mechanism, all housed in a single unit. This mechanism allows for a proximal aortic anastomosis to be completed without aortic clamping. Compared with earlier devices, the PAS-Port system allows the endothelium of the