# Female Risk Using OPCAB, $\pi$ -Circuit, and Aorta No-Touch Coronary Revascularization

**Sotirios N. Prapas**,<sup>1</sup> Ioannis A. Panagiotopoulos,<sup>1</sup> Mohamed A. Salama Ayyad,<sup>1</sup> Vassilis N. Kotsis,<sup>1</sup> Dimitris A. Protogeros,<sup>1</sup> Ioannis N. Linardakis,<sup>1</sup> Theofanis P. Tzanavaras,<sup>1</sup> Fotini N. Danou<sup>2</sup>

Departments of <sup>1</sup>Cardiac Surgery and <sup>2</sup>Anesthesia, Henry Dunant Hospital, Athens, Greece



Dr. Prapas

### ABSTRACT

**Background:** In this study, we evaluated female sex as a risk factor in the off-pump coronary artery bypass (OPCAB), aorta no-touch technique.

Materials and Methods: From February 2001 to November 2005, 1359 patients in our institution underwent isolated coronary revascularization with the  $\pi$ -circuit technique, which consists of (1) beating heart surgery, (2) OPCAB, (3) no touching of the aorta, (4) use of composite grafts, and (5) arterial revascularization. There were 1159 men (group A) and 200 women (group B). Both groups were compared with respect to preoperative risk factors, intraoperative parameters, and postoperative morbidity and mortality. Follow-up lasted from 4 to 60 months. Data were analyzed with the  $\chi^2$  test, the Fisher exact test, the Kaplan-Meier method, and the Cox model of regression analysis.

**Results:** Female patients were older (P < .0005) and had higher prevalences of obesity (P < .0005), arterial hypertension (P < .0005), and diabetes (P < .0005). Emergency operations were also more frequent in this group (P < .027). There was no difference between the groups in the preoperative use of an intra-aortic balloon pump (IABP). The 2 groups were not significantly different with respect to 30-day mortality (1.1% versus 4%) or 7-day mortality (0.3% versus 0%). The 2 groups had comparable rates of IABP use postoperatively. Cognitive disturbances and strokes were rarely encountered (0.6% in men and 0.2% in women). In the early postoperative phase, women had more pulmonary complications (P < .014), and survival seemed to favor the male group during the follow-up period (P < .001). Further analysis with the Cox

Current address for M.A.S.A.: Cardio-Thoracic Surgery Department, Faculty of Medicine, Assiut University, Assiut, Egypt.

Presented at the 6th Annual Meeting of the Euro-Asian Bridge, Dubrovnik, Croatia, April 27-28, 2009.

Correspondence: Sotirios N. Prapas, MD, Director of Cardiac Surgery Department, Henry Dunnat Hospital, Mesoghion 107, Athens GR 11521, Greece; +30-210-6972877; fax: +30-210-6972745 (e-mail: sprapas@ dunanthospi.gr, sotiriosprapas@yahoo.gr). regression model with exclusion of confounding preoperative morbidity factors (more prevalent in group B) showed that the 2 groups had similar survival rates. As a group, women were 1.06 times more likely to die from a cardiac cause than men (P < .897).

**Conclusions:** The use of the  $\pi$ -circuit, aorta no-touch technique is equally effective and safe for both sexes. Women are more prone to pulmonary complications in the early post-operative phase. The apparent difference in survival favoring men can be attributed to the higher prevalence of pre-operative risk factors in women. In general, we consider the off-pump, aorta no-touch technique an effective method for lowering morbidity and mortality in the relatively high-risk female patient group.

#### INTRODUCTION

Sex differences in open heart surgery have been the focus of numerous publications in recent years. In answer to the contradictions that persist in recommendations for optimal care, especially in coronary bypass surgery, the Society of Thoracic Surgeons recently published practice guidelines in this field [Edwards 2005].



Kaplan-Meier survival curves for the 2 groups after the OPCAB aorta no-touch technique during a 60-month follow-up.

	Group A (Male)	Group B (Female)	
Preoperative Variables	(n = 1159)	(n = 200)	Р
Age, y	64.13 ± 9.79	68.98 ± 9.33	<.0005
Body surface area, m <sup>2</sup>	$\textbf{1.9}\pm\textbf{0.14}$	$\textbf{1.67} \pm \textbf{0.13}$	<.0005
BMI, kg/m²	27.67 ± 3.47	$\textbf{28.09} \pm \textbf{4.25}$	.244
Diabetes, n	347 (29.9%)	90 (45%)	<.0005
Obesity, n	243 (21.0%)	52 (26.0%)	. 115
Cholesterol >250 mg/dL, n	435 (37.5%)	75 (37.5%)	1.000
Stroke, n	37 (3.2%)	4 (2%)	.502
PVD, n	73 (6.3%)	12 (6%)	1.000
TIA, n	20 (1.7%)	3 (1.5%)	1.000
GIT disease, n	58 (5%)	7 (3.5%)	.472
COPD, n	57 (4.9%)	11 (5.5%)	.725
Renal failure, n	99 (8.5%)	10 (5%)	.108
Renal dialysis, n	14 (1.2%)	5 (2.5%)	.182
Arterial hypertension, n	468 (40.4%)	116 (58%)	<.0005
LV function, n			
Good	832 (71.8%)	141 (70.5%)	
Moderate	245 (21.1%)	43 (21.5%)	.882
Poor	82 (7.1%)	16 (8%)	
Preoperative IABP, n	22 (1.9%)	5 (2.5%)	.581
Emergency, n	170 (14.7%)	42 (21.0%)	.027
Redo operations, n	72 (6.2%)	6 (3.0%)	.232

Table 1. Baseline Characteristics of the Patients\*

\*BMI indicates body mass index; PVD, peripheral vascular disease; TIA, transient ischemic attack; GIT, gastrointestinal tract; COPD, chronic obstructive pulmonary disease; LV, left ventricle; IABP, intra-aortic balloon pump.

There is great uncertainty regarding the impact of sex as an independent risk factor for morbidity and mortality following coronary artery bypass surgery. Most studies show that women have a higher risk for morbidity and mortality following coronary artery bypass grafting (CABG) procedures than their male counterparts [Kennedy 1980; Fisher 1982; O'Connor 1993; Tu 1995; Jones 1996; Edwards 1998]. One of the key problems, however, in attempting to compare outcomes for the sexes is the difference in the preoperative clinical characteristics of men and women. A smaller body surface area and smaller coronary arteries could lead to reduced rates of graft patency [Fisher 1982; O'Connor 1993]. Other investigators have documented underutilization of noninvasive and invasive testing in women compared with men that may influence perioperative results [Shin 1999].

Our aim was to study the difference in outcomes between the male and female sexes after CABG with off-pump coronary artery bypass (OPCAB), complete arterial revascularization with composite grafts, and an aorta no-touch technique.

## MATERIALS AND METHODS

Our study is a prospective observational study in the Department of Cardiac Surgery, Henry Dunant Hospital, Athens, Greece. In the period from February 2001 to November 2005, 1359 patients with coronary artery disease requiring CABG surgery underwent operations to achieve coronary revascularization with the  $\pi$ -circuit technique, which consists of the following: (1) beating heart surgery, (2) OPCAB, (3) no touching of the aorta, (4) use of composite grafts, and (5) arterial revascularization.

# Surgical Technique

The standard approach was a median sternotomy. Skeletonized internal mammary arteries and radial artery pedicle (from the nondominant arm) were then harvested. Composite arterial grafts (T graft, Y graft, extensions,  $\pi$  graft, sequential use) were created with one or both internal mammary arteries, with or without use of the radial artery.

Our aim was to achieve complete arterial myocardial revascularization that depended on the native origin of the internal mammary arteries with complete avoidance of any aortic manipulation (aorta no-touch technique). We both decreased the risk of aortic manipulation and circumvented the use of cardiopulmonary bypass (CPB), thus avoiding their known adverse side effects.

Exposure of the left anterior descending artery and the middle portion of the right coronary artery is simple, because these arteries lie on the anterior surface of the heart. To improve the exposure and minimize the heart displacement for the lateral and inferior vessels, we kept the patient in the Trendelenburg position with the bed rotated toward the surgeon. Elevation and rotation of the heart to expose the coronary arteries were achieved by maintaining tension on the pericardial wall with deep pericardial traction sutures.

Stabilization of the anastomotic site was achieved through suction with the aid of the Octopus tissue stabilizer (Octopus II; Medtronic, Minneapolis, MN, USA).

## **Definitions of Variables**

Diabetes is defined as a fasting plasma glucose concentration ≥126 mg/dL. Obesity is defined as body mass index >30 kg/m<sup>2</sup>. Stroke is defined as a cerebrovascular accident, confirmed with computed tomography or magnetic resonance imaging, that leaves the patient with brain damage. Peripheral vascular disease refers to disease of the blood vessels outside of the heart and the brain, as diagnosed by x-ray angiography, Doppler study, or magnetic resonance angiography. Chronic obstructive pulmonary disease occurs in patients with longterm bronchodilators or steroid therapy for lung disease. Renal failure is defined as an increase in the creatinine level to >200 µmol/L on admission or a history of renal transplantation or dialysis. Emergency surgery is defined as the necessity to take the patient to the operating theater on referral before the beginning of the next morning's operation schedule. Pulmonary complication is defined as the occurrence of pleural effusion and/or atelectasis. Psychological changes are defined as changes in the mental condition, as documented by

	Group A (Male) (n = 1159)	Group B (Female) (n = 200)	Р
Stroke, n	3 (0.3%)	0 (0.0%)	1.000
Renal complications, n	25 (2.2%)	5 (2.5%)	.793
Pulmonary complications, n	61 (5.3%)	20 (10.0%)	.014
Prolonged ventilation >48 h, n	30 (2.6%)	9 (4.5%)	.162
Sternal wound infection, n	9 (0.8%)	4 (2.00%)	.111
Postoperative AF, n	236 (20.4%)	37 (18.5%)	.633
Reoperation, n	8 (0.7%)	1 (0.5%)	1.000
Postoperative IABP, n	16 (1.4%)	5 (2.5%)	.248
Cognitive disorders, n	7 (0.6%)	1 (0.5%)	1.000
GIT complications, n	30 (2.6%)	6 (3.0%)	.640
Urine retention, n	8 (0.7%)	0 (0.0%)	.613
Recatheterization, n	25 (2.2%)	7 (3.5%)	.307
Postoperative PTCA	11 (0.9%)	3 (1.5%)	.447

Table 2. Postoperative Complications in the Male and Female Groups\*

\*AF indicates atrial fibrillation; IABP, intra-aortic balloon pump; GIT, gastrointestinal tract; PTCA, percutaneous transluminal coronary angioplasty.

comparison of the mental component summary scales for the short-form health survey (SF-36) taken preoperatively and at 2 weeks postoperatively. Thirty-day death is defined as death within the first postoperative month, and 7-day death is death within the first 7 days postoperatively.

### Anesthesia Technique

Anesthesia was managed according to standard protocol. All patients had a central venous catheter; some even had a Swan-Ganz catheter. Diazepam was administered as a preanesthesia agent. We then used a combined dose of opioid/volatile agents (30 µg/kg fentanyl, 0.2 mg/kg etomidate, and sevoflurane) along with cisatracurium as a neuromuscular blocking agent. Heparin was administered at a dose of 100 IU/kg before the start of the first anastomosis to achieve an activated clotting time of 250 to 350 seconds. On completion of all anastomoses, protamine was administered to reverse the effects of heparin and return the activated clotting time to near preoperative levels. Radial artery, central venous, and pulmonary artery pressures were monitored in all patients.

#### Data Collection and Analysis

The preoperative baseline characteristics of the patients, operative data, and overall postoperative events were recorded. All statistical tests were performed as 2-tailed tests. The Fisher exact test, the  $\chi^2$  test, and the Cox regression model were used for data analysis. A *P* value <.05 was considered statistically significant. Statistical analysis was performed with the commercially available statistical software SPSS (version 13 for Windows; SPSS, Chicago, IL, USA).

# RESULTS

We studied 1359 patients who underwent isolated offpump CABG. There were 1159 male patients, and 200 female patients with a mean  $\pm$  SD age of 64.13  $\pm$  9.79 years for men and 68.98  $\pm$  9.33 years for women. Other baseline characteristics are summarized in Table 1.

All of the patients underwent their operations with the  $\pi$ -circuit technique, which consists of the following: beating heart off-pump CABG, no touching of the aorta, and use of composite grafts with exclusively arterial revascularization.

The 2 study groups (male and female patients) were compared with respect to preoperative and operative data to identify factors that significantly influenced postoperative outcomes. Table 1 summarizes the data for preoperative variables. The mean age was significantly higher in women than in men (68.98 ± 9.33 years and 64.13 ± 9.79 years, respectively; P < .005). Female patients were more affected by diabetes mellitus and arterial hypertension (P < .005 for both variables), and female patients underwent an emergency operation more frequently than male patients (P = .027). The 2 groups failed to show any additional statistically significant differences for any of the other preoperative variables (Table 1).

The 2 groups were compared with respect to postoperative intra-operative balloon pump use, but the differences were not statistically significant. Cognitive disturbances and strokes were rarely encountered (0.6% and 0.2%, respectively). Females had more pulmonary complications in the early postoperative phase (P < .014).

Postoperative events are summarized in Table 2. Total survival favored the male group (Table 3). Analysis with Kaplan-Meier survival curves (Figure) showed a statistically significant difference between the 2 groups in mortality due to cardiac reasons (P = .001).

We noticed in this survey that differences between the female and male sexes in preoperative and intraoperative factors might have influenced the results. Therefore, we used the Cox regression model to evaluate the difference between the 2 groups after excluding the preoperative comorbidities. After the correction for these factors, we perceived no statistically significant differences between the 2 sexes.

Overall, women had a 1.2 times higher mortality rate postoperatively but had a mortality due to cardiac reasons that was only 1.06 times higher.

### DISCUSSION

Coincidentally, it is likely that the proportion of female patients will continue to increase with the continued aging of surgical candidates; therefore, outcomes assessment for women will assume even greater importance [Abramov 2000]. In 2005, 150,000 women are estimated to have undergone CABG, and 360,000 women are estimated to have undergone a percutaneous intervention [American Heart Association 2005]. It is unclear whether worse outcomes for women are related to the increased incidences of comorbidities, unfavorable anatomic characteristics, or the female sex itself [Aldea 1999].

Table	3.	Mortality	after	the	Off-Pump	Coronary	Artery
Bypass, Aorta No-Touch Technique							

	Group A (Male) (n = 1159)	Group B (Female) (n = 200)	Р
Total mortality, n	46 (4%)	19 (9.5)	.002
In-hospital mortality (30 d), n	13 (1.1%)	8 (4%)	.231
7-Day mortality, n	3 (0.3%)	0 (0.0%)	1.000

Single-center databases, multicenter registries, and a few randomized trials have all reported that women have higher prevalences of risk factors, acute coronary syndromes, angina symptoms, and congestive heart failure compared with men, even though women have better preservation of the left ventricular systolic function and a similar or lesser extent of epicardial coronary disease [Edwards 1998; Jacobs 1998]. The emerging data from investigations such as the Women's Ischemia Syndrome Evaluation (WISE) study [Merz 1999] are beginning to reveal explanations for these seemingly paradoxical differences between the sexes.

In our study, women who underwent CABG had more comorbid conditions and risk factors compared with men. These comorbidities included an older age, diabetes, obesity, and emergency operative interference.

OPCAB surgery is a recently developed surgical technique that avoids the deleterious consequences of CPB. High-risk patients have been suggested to be the most likely to benefit from OPCAB, because such patients are at the highest risk of developing complications related to the use of CPB [Brown 2002; Mack 2002].

The technique of OPCAB has been suggested to decrease morbidity and mortality by avoiding the deleterious effects of CPB, particularly in high-risk patients [Bucerius 2005]. In addition, we have used the aorta no-touch technique in the revascularization process to decrease the complications that could occur after a proximal anastomosis on the aorta. With the use of this technique, we seldom encountered any cerebrovascular complications (only 3 male cases).

All patients underwent complete revascularization with one or both internal mammary arteries, a strategy that is reflected in the postoperative results. Use of both internal mammary arteries for revascularization favors good outcomes [Prapas 2002].

Bucerius and associates found that OPCAB surgery in women was associated with a significantly lower prevalence of postoperative respiratory insufficiency than with conventional CABG [Bucerius 2005]. In our study, between-group differences in postoperative outcome variables failed to reach statistical significance, with the exception of postoperative pulmonary complications, which were significantly increased in the women patients. This result may have been related to the greater incidence of comorbidities in women than in men, especially for the significantly higher incidence of preoperative chronic obstructive airway disease in women [Abramov 2000]; however, we found no significant difference in chronic obstructive pulmonary disease between the sexes in our study, even though the incidence of this disease was nominally higher in the women (5.5%) than in the men (4.9%).

This finding is in agreement with a study by Athanasiou et al [2003], in which the higher incidence of postoperative pulmonary complications among the female patients in these investigators' survey was determined by the higher incidence of preoperative pulmonary morbidity (P = .04). In addition, the women patients in that study were more obese and were more often to have been admitted to the hospital before their operation [Athanasiou 2003].

The mortality for women after CABG has been an important issue for the past 3 decades. A decrease in in-hospital mortality observed for women having bypass operations in northern New England has accounted for 44% of the decrease in overall mortality for the entire CABG population. We hope that ongoing efforts at improving the outcomes of surgical revascularization for coronary artery disease will lead to further declines in adverse outcomes for both women and men [O'Rourke 2001].

Brown and associates [2002] found a 42% lower mortality rate in women who underwent OPCAB than in women who underwent on-pump CABG. These results are in accordance with the findings of Mack and associates [2002], which revealed a significantly lower postoperative mortality after OPCAB surgery in a large study population of male and female patients who underwent CABG surgery, even though the mean predicted risk profile was significantly higher in OPCAB patients.

In our study, we found a statistically significant difference in survival for women after CABG due to cardiac reasons. After excluding the preoperative unfavorable risk factors with the Cox regression model, we found no statistically significant difference between the sexes with respect to survival. The apparent difference in survival favoring male patients can be attributed to higher prevalence of preoperative risk factors in the female patients.

Therefore, we can say with confidence that this method of coronary revascularization with the  $\pi$ -circuit technique consisting of (1) beating heart surgery, (2) OPCAB, (3) no touching of the aorta, (4) use of composite grafts, and (5) arterial revascularization can be performed safely in all CABG patients, even in the high-risk female group.

# CONCLUSION

The use of the  $\pi$ -circuit, aorta no-touch technique is equally effective and safe for both sexes. Females are more prone to pulmonary complications in the early postoperative phase. The apparent difference in survival favoring men can be attributed to a higher prevalence of preoperative risk factors in women.

In general, we consider the off-pump, aorta no-touch technique an effective method for lowering morbidity and mortality in the relatively high-risk female patient group.

#### REFERENCES

Abramov D, Tamariz MG, Sever JY, et al. 2000. The influence of gender on the outcome of coronary artery bypass surgery. Ann Thorac Surg 70:800-6. Aldea GS, Gaudiani JM, Shapira OM, et al. 1999. Effect of gender on postoperative outcomes and hospital stays after coronary artery bypass grafting. Ann Thorac Surg 67:1097-103.

American Heart Association. 2005. Heart Disease and Stroke Statistics—2005 Update. Dallas, TX: American Heart Association. Available at: http://www.americanheart.org/downloadable/heart/1105390918119 HDSStats2005Update.pdf. Accessed September 23, 2009.

Athanasiou T, Al-Ruzzeh S, Del Stanbridge R, Casula RB, Glenville BE, Amrani M. 2003. Is the female gender an independent predictor of adverse outcome after off-pump coronary artery bypass grafting? Ann Thorac Surg 75:1153-60.

Brown PP, Mack MJ, Simon AW, et al. 2002. Outcomes experience with off-pump coronary artery bypass surgery in women. Ann Thorac Surg 74:2113-9.

Bucerius J, Gummert JF, Walther T, et al. 2005. Impact of off-pump coronary bypass grafting on the prevalence of adverse perioperative outcome in women undergoing coronary artery bypass grafting surgery. Ann Thorac Surg 79:807-13.

Edwards FH, Carey JS, Grover FL, Bero JW, Hartz RS. 1998. Impact of gender on coronary bypass operative mortality. Ann Thorac Surg 66:125-31.

Edwards FH, Ferraris VA, Shahian DM, et al. 2005. Gender-specific practice guidelines for coronary bypass surgery: perioperative management. Ann Thorac Surg 79:2189-94.

Fisher LD, Kennedy JW, Davis KB. 1982. Association of sex, physical size and operative mortality after coronary bypass in the Coronary Artery Surgery Study (CASS). J Thorac Cardiovasc Surg 84:334-41.

Jacobs AK, Kelsey SF, Brooks MM, et al. 1998. Better outcome for women compared with men undergoing coronary revascularization: a report from the Bypass Angioplasty Revascularization Investigation (BARI). Circulation 98:1279-85.

Jones RH, Hannan EL, Hammermeister KE, et al. 1996. Identification of

preoperative variables needed for risk adjustment of short-term mortality after coronary artery bypass graft surgery. Working Group Panel on the Cooperative CABG Database Project. J Am Coll Cardiol 28:1478-87.

Kennedy JW, Kaiser GC, Fisher LD, et al. 1980. Multivariate discriminant and angiographic predictors operative mortality from the Collaborative Study in Coronary Artery Surgery (CASS). J Thorac Cardiovasc Surg 80:876-87.

Mack M, Bachand D, Acuff T, et al. 2002. Improved outcomes in coronary artery bypass grafting with beating-heart techniques. J Thorac Cardiovasc Surg 124:598-607.

Merz CN, Kelsey SF, Pepine CJ, et al. 1999. The Women's Ischemia Syndrome Evaluation (WISE) study: protocol design, methodology and feasibility report. J Am Coll Cardiol 33:1453-61.

O'Connor GT, Morton JR, Deihl MJ. 1993. Differences between men and women in hospital mortality associated with coronary bypass artery graft surgery. The Northern New England Cardiovascular Disease Study Group. Circulation 88(pt 1):2104-10.

O'Rourke DJ, Malenka DJ, Olmstead EM, et al. 2001. Improved inhospital mortality in women undergoing coronary artery bypass grafting. Northern New England Cardiovascular Disease Study Group. Ann Thorac Surg 71:507-11.

Prapas SN, Anagnostopoulos CE, Kotsis V, et al. 2002. A new pattern for using both thoracic arteries to revascularize the entire heart: the  $\pi$ -graft. Ann Thorac Surg 73:1990-2.

Shin AY, Jaglal S, Slaughter P, Iron K. 1999. Women and heart disease. In: Naylor CD, Slaughter PM, eds. Cardiovascular health & services in Ontario: an ICES atlas. Toronto, Canada: Institute for Clinical Evaluative Sciences. p 335-53.

Tu JV, Jaglal SB, Naylor DC, and the Steering Committee of the Provincial Adult Cardiac Care Network of Ontario. 1995. Multicenter validation of a risk index for mortality, intensive care unit stay, and overall hospital length of stay after cardiac surgery. Circulation 91:677-84.