

## ORIGINAL ARTICLE

# A Comparison of On-Pump and Off-Pump Coronary Bypass Surgery in Low-Risk Patients

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## ABSTRACT

**BACKGROUND**

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The performance of coronary bypass surgery without cardiopulmonary bypass (“off pump”) may reduce perioperative morbidity and costs, but it is uncertain whether the outcome is similar to that involving the use of cardiopulmonary bypass (“on pump”).

**METHODS**

In a multicenter, randomized trial, we randomly assigned 139 patients with predominantly single- or double-vessel coronary disease to on-pump surgery and 142 to off-pump surgery. Cardiac outcome and cost effectiveness were determined one year after surgery. The uncertainty surrounding the cost-effectiveness ratio (cost differences per quality-adjusted year of life gained) was addressed by bootstrapping.

**RESULTS**

At one year, the rate of freedom from death, stroke, myocardial infarction, and coronary reintervention was 90.6 percent after on-pump surgery and 88.0 percent after off-pump surgery (absolute difference, 2.6 percent; 95 percent confidence interval, -4.6 to 9.8). Graft patency in a randomized subgroup of patients was 93 percent after on-pump surgery and 91 percent after off-pump surgery (absolute difference, 2.0 percent; 95 percent confidence interval, -6.5 to 10.4). On-pump surgery was associated with \$1,839 in additional direct costs per patient (\$14,908 vs. \$13,069 — a difference of 14.1 percent) and an increase in quality-adjusted years of life of 0.83 as compared with 0.82 (difference, 0.01 year; 95 percent confidence interval, -0.03 to 0.04). Off-pump surgery was more cost effective than on-pump surgery in 95 percent of bootstrap estimates.

**CONCLUSIONS**

In low-risk patients, there was no difference in cardiac outcome at one year between those who underwent on-pump bypass surgery and those who underwent off-pump surgery. Off-pump surgery was more cost effective.

**C**ORONARY-ARTERY BYPASS GRAFTING (CABG) has an important role in the management of ischemic heart disease.<sup>1-3</sup> Although excellent clinical results have been reported in a wide range of patients, the safety of CABG is being questioned.<sup>4,5</sup> Data from the National Cardiac Surgery Database of the Society of Thoracic Surgeons (January 1998), encompassing 170,895 patients, showed that only 65.4 percent of patients did not have complications.<sup>6</sup> In addition, health insurance data on 101,812 patients showed that 10.2 percent did not leave the hospital within 14 days after the operation and 3.6 percent were discharged to a non-acute care facility.<sup>7</sup>

Cardiopulmonary bypass with cardiac arrest ("on pump") provides a surgical field free of motion and blood, allowing safe construction of the anastomoses. Yet the use of cardiopulmonary bypass is believed to be a major determinant of perioperative morbidity,<sup>4,5</sup> hospital stay, and costs.<sup>8</sup> As a result, bypass surgery on the beating heart without the use of extracorporeal circulation ("off pump") has been reintroduced into clinical practice,<sup>9</sup> stimulated by the availability of cardiac stabilizers.<sup>10</sup> By immobilizing areas of the beating heart, cardiac stabilizers facilitate the construction of the anastomoses.<sup>11,12</sup>

Off-pump surgery is expected to lower costs by reducing perioperative morbidity and recovery time. Nevertheless, the procedure is technically more demanding, and it is unknown whether off-pump surgery will match the long-term benefits of on-pump surgery. The purpose of this randomized multicenter trial was to compare the cardiac outcome and cost effectiveness of on-pump and off-pump surgery one year after the operation.

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## METHODS

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### STUDY DESIGN AND PATIENTS

The design and methods of the trial have been described in detail elsewhere.<sup>13</sup> In brief, patients with stable or unstable angina (Braunwald class IB or IIB) with normal or moderately impaired ventricular function were randomly assigned to undergo on-pump or off-pump surgery. Patients were eligible if they were referred for isolated coronary bypass surgery for the first time and an off-pump procedure was deemed technically feasible. Patients were excluded if they required emergency or concomitant major surgery, had had a Q-wave myocardial infarction in the preceding six weeks, or had poor left ventricular function.

The study was carried out according to the principles of the Declaration of Helsinki. The ethics committees of the three participating centers approved the study protocol. After patients provided written informed consent, computerized randomization was performed over the telephone. Randomization was stratified according to the center in blocks of 8 to 20 patients.

### SURGICAL TECHNIQUES

The goal of surgery was to obtain complete arterial revascularization, and the surgery was performed by surgeons experienced in both on-pump and off-pump bypass surgery. On-pump surgery used cardiopulmonary bypass in combination with cold crystalloid cardioplegia for myocardial protection. Off-pump surgery used the Octopus stabilizer, described in detail elsewhere.<sup>11</sup> In brief, the distal ends of the two suction arms of the stabilizer are placed on the beating heart on both sides of the target coronary artery. The proximal parts are fixed to the operating table. Through the application of negative pressure, the target area of the heart is sufficiently immobilized to allow the safe construction of the anastomosis of the graft with the recipient artery.

### CARDIAC END POINTS

The primary composite end point was freedom from the following events: death from any cause, stroke, myocardial infarction, and repeated revascularization (surgery or angioplasty). Stroke was defined as a focal brain injury that persisted for more than 24 hours, combined with an increase in disability of at least one grade on the Rankin Scale.<sup>14</sup> Within seven days after surgery, a non-Q-wave myocardial infarction was diagnosed if the serum creatine kinase MB isoenzyme level was more than five times the upper limit of the normal value and a Q-wave infarction was diagnosed if pathologic Q waves appeared concomitantly.<sup>15</sup> Seven days or more after surgery, a non-Q-wave infarction was diagnosed if the ratio of creatine kinase MB isoenzyme to total creatine kinase exceeded 0.1 and a Q-wave infarction was diagnosed if pathologic Q waves appeared. An independent committee whose members were unaware of the patients' treatment assignment evaluated all events.

Secondary end points were freedom from angina and exercise-induced ischemia. Stable angina was defined according to the Canadian Cardiovascular Society classification,<sup>16</sup> and unstable angina according to the Braunwald classification.<sup>17</sup>

At the time of randomization, a subgroup of 110 patients was randomly assigned to undergo angiography one year after surgery. A cardiologist and a cardiac surgeon independently examined the quality of the grafts using the criteria of FitzGibbon.<sup>18</sup>

**COSTS AND COST EFFECTIVENESS**

Direct medical costs were assessed in 1999 Dutch florins and were converted to U.S. dollars using an exchange rate of 2.5 Dutch florins for each \$1. Costs per patient were calculated by multiplying resource use by the unit costs. Follow-up costs are limited to cardiac and other procedure-related costs. The costs of myocardial infarction<sup>19</sup> and stroke<sup>20</sup> after the initial hospitalization were calculated with the use

of unit costs, as assessed by other investigators in the Netherlands. The in-hospital costs of on-pump surgery in the present study were used as an estimate of the cost of repeated CABG during follow-up. The unit costs of coronary angioplasty were previously determined at the University Medical Center Utrecht.

The health-related quality of life was assessed with use of the EuroQol questionnaire and its summary score<sup>21</sup> at base line and 1, 3, 6, and 12 months after surgery. Using linear extrapolation for the periods between measurements, we calculated the quality-adjusted years of life gained by determining the individual area under the curve of the summary score. The cost-effectiveness ratio was calculated by dividing the difference in costs between procedures by the difference in the quality-adjusted years of life.

**STATISTICAL ANALYSIS**

Calculation of the sample size was based on neurocognitive outcome after bypass surgery and has been described elsewhere.<sup>22</sup> All data were analyzed according to the intention-to-treat principle, beginning immediately after randomization. No interim analysis was performed. The risk of an event after on-pump surgery was compared with that after off-pump surgery, and the results are presented as the absolute difference with the corresponding 95 percent confidence interval. Dichotomous data were compared with use of the chi-square statistic. Values are expressed as means ±SD and were compared with use of a two-sample t-test. Continuous variables that were not distributed normally were compared with use of the Mann-Whitney test. All reported P values are two-sided. Event-free survival was graphically compared with use of Kaplan-Meier curves. The uncertainty surrounding the cost-effectiveness analysis was evaluated by means of standard bootstrap techniques.<sup>23</sup>

RESULTS

**CHARACTERISTICS OF THE PATIENTS AND TREATMENT ASSIGNMENTS**

Between March 1998 and August 2000, 139 patients were randomly assigned to undergo on-pump surgery and 142 patients to undergo off-pump surgery. The base-line characteristics of the two groups are summarized in Table 1. Five patients who were randomly assigned to undergo on-pump surgery underwent off-pump surgery. In the case of 10 pa-

**Table 1. Base-Line Characteristics of the Patients.\***

Characteristic	On-Pump Group (N=139)	Off-Pump Group (N=142)
Age (yr)	60.8±8.8	61.7±9.2
Male sex (%)	71	66
One-vessel disease (%)	22	30
Two-vessel disease (%)	50	50
Three-vessel disease (%)	27	20
Normal left ventricular function (%)	79	77
Moderate left ventricular function (%)	21	23
Stable angina (%)		
CCS class I or II	26	32
CCS class III or IV	49	45
Unstable angina, Braunwald class IB or IIB (%)	21	22
Previous myocardial infarction (%)	26	34
History of coronary angioplasty (%)	20	17
Current smoker (%)	14	14
Hypertension (%)	44	40
Hypercholesterolemia (%)	68	68
Family history of coronary disease (%)	58	59
Obesity (%)†	22	18
Peripheral vascular disease (%)	13	7
Diabetes (%)	17	9
History of stroke (%)	3	4
Pulmonary disease (%)	10	9

\* Plus-minus values are means ±SD. Because of rounding, values do not necessarily sum to 100. CCS denotes Canadian Cardiovascular Society.

† Obesity was defined as a score of more than 30 on the Quetelet index, which is the weight in kilograms divided by the square of the height in meters.

tients who were randomly assigned to undergo off-pump surgery, the procedure was converted intraoperatively to an on-pump procedure. One other patient assigned to undergo off-pump surgery underwent coronary angioplasty. Therefore, 265 patients (94 percent) were treated according to the randomization protocol.

The mean number of grafts per patient was 2.6 in the on-pump group and 2.4 in the off-pump group. Complete arterial revascularization was achieved in 76 percent of the patients in the on-pump group and 84 percent of those in the off-pump group. In both groups, 83 percent of the patients underwent revascularization according to the treatment plan, which was defined before randomization. The mean interval between surgery and the 1-year follow-up visit was  $378 \pm 33$  days in the on-pump group and  $375 \pm 29$  days in the off-pump group ( $P=0.42$ ).

#### CARDIAC END POINTS AT ONE YEAR

At one year, 126 patients assigned to undergo on-pump surgery (90.6 percent) and 125 patients assigned to undergo off-pump surgery (88.0 percent) had not had a cardiovascular event (absolute difference, 2.6 percent; 95 percent confidence interval,  $-4.6$  to  $9.8$ ) (Table 2 and Fig. 1). The rate of freedom from angina was 89.0 percent in the on-pump group and 89.3 percent in the off-pump group (absolute difference,  $-0.3$  percent; 95 percent confidence interval,  $-7.7$  to  $7.0$ ). An exercise test was performed in 246 patients (87.5 percent), 19 of whom (7.7 percent) had inconclusive results. The rate of freedom from myocardial ischemia was 79.8 percent (87 of 109 patients) after on-pump surgery and 83.1 percent (98 of 118 patients) after off-pump surgery (absolute difference,  $-3.3$  percent; 95 percent confidence interval,  $-13.4$  to  $6.9$ ). Exercise capacity, expressed in terms of metabolic equivalents (MET), was 9.5 MET in the on-pump group and 9.0 MET in the off-pump group (absolute difference, 0.5 MET; 95 percent confidence interval,  $-0.4$  to  $1.4$ ).

Forty of the 110 preselected patients (36.4 percent) declined to undergo follow-up angiography because they had no symptoms. Angiography was performed in 42 patients (89 grafts) in the on-pump group and 28 patients (69 grafts) in the off-pump group. The overall patency rates (FitzGibbon grade A or B) were 93 and 91 percent, respectively (absolute difference, 2.0 percent; 95 percent confidence interval,  $-6.5$  to  $10.4$ ).

#### COSTS AND COST EFFECTIVENESS AT ONE YEAR

The average direct medical costs per patient per treatment are presented in Table 3. At one year, the total direct costs of on-pump surgery were 14.1 percent ( $\$1,839$ ) higher per patient than those of off-pump surgery ( $\$14,908$  vs.  $\$13,069$ ). Medication accounted for more than 50 percent of the follow-up costs.

The quality of life improved in a similar fashion in the two groups: the EuroQol summary scores increased in both groups from 0.65 at base line to 0.84 three months after surgery (increase, 0.20; 95 percent confidence interval, 0.17 to 0.23). The subsequent scores remained within normal limits (defined as 0.80 in an age-matched cohort in the United Kingdom).<sup>24</sup>

The average quality-adjusted "life time" was 0.83 year after on-pump surgery and 0.82 year after off-pump surgery (absolute difference, 0.01 year; 95 percent confidence interval,  $-0.03$  to  $0.04$ ). The incremental cost-effectiveness ratio for on-pump surgery, as compared with off-pump surgery, was  $\$183,900$  per quality-adjusted year of life gained (i.e.,  $\$1,839 \div 0.01$ ). This ratio indicates that each quality-adjusted year of life gained with the use of a strategy of on-pump surgery rather than off-pump surgery cost  $\$183,900$ . The societal willingness-to-pay threshold is much lower — generally,  $\$20,000$  per quality-adjusted year of life gained.<sup>25</sup> Figure 2 illustrates the bootstrap estimates of differences in costs and quality-adjusted years of life between on-pump and off-pump surgery. The cost-effectiveness ratios were below the defined thresholds in 5 percent of estimates, indicating with 95 percent certainty that off-pump surgery was more cost-effective than on-pump surgery (Fig. 2).

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#### DISCUSSION

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We found no statistically significant difference in cardiac outcome, symptoms, or quality of life at one year between patients who underwent on-pump surgery and those who underwent off-pump surgery. Off-pump surgery, however, was less expensive and more cost effective than on-pump surgery. Therefore, off-pump surgery may be an alternative to conventional CABG. To interpret these results, certain features of our study need to be addressed.

We focused on a relatively low-risk population of patients. The mean age of the patients was 61 years, and the majority had single- or double-vessel disease with preserved ventricular function and

**Table 2. Cardiovascular Events.**

Event	On-Pump Group (N=139)	Off-Pump Group (N=142)	Absolute Difference between Groups (95% CI)*	P Value
	<i>no. of patients (%)</i>		<i>percent</i>	
First event in hospital†				
Death from any cause	0	0	0.0	—
Stroke	2 (1.4)	1 (0.7)	0.7 (–1.7 to 3.1)	0.55
Q-wave and non-Q-wave myocardial infarction	7 (5.0)	7 (4.9)	0.1 (–5.0 to 5.2)	0.97
Repeated coronary revascularization	0	2 (1.4)	–1.4 (–3.3 to 0.5)	0.16
Bypass surgery	0	0	0.0	—
Angioplasty	0	2 (1.4)	–1.4 (–3.3 to 0.5)	0.16
Any event	9 (6.5)	10 (7.0)	–0.6 (–6.4 to 5.3)	0.85
First event during follow-up				
Death from any cause	0	2 (1.4)	–1.4 (–3.3 to 0.5)	0.16
Stroke	0	0	0.0	—
Q-wave and non-Q-wave myocardial infarction	2 (1.4)	0	1.4 (–0.5 to 3.4)	0.15
Repeated coronary revascularization	2 (1.4)	5 (3.5)	–2.1 (–5.7 to 1.5)	0.26
Bypass surgery	1 (0.7)	1 (0.7)	0.0 (–2.0 to 2.0)	0.98
Angioplasty	1 (0.7)	4 (2.8)	–2.1 (–5.2 to 1.0)	0.18
Any event	4 (2.9)	7 (4.9)	–2.1 (–6.6 to 2.5)	0.37
Any first event at 1 yr	13 (9.4)	17 (12.0)	–2.6 (–9.8 to 4.6)	0.48
Primary end point at 1 yr‡	126 (90.6)	125 (88.0)	2.6 (–4.6 to 9.8)	0.48
All cardiovascular events at 1 yr§				
Death	2 (1.4)	2 (1.4)	0.0 (–2.7 to 2.8)	0.98
From cardiac causes	2 (1.4)	0	1.4 (–0.5 to 3.4)	0.15
From noncardiac causes	0	2 (1.4)	–1.4 (–3.3 to 0.5)	0.16
Stroke	2 (1.4)	1 (0.7)	0.7 (–1.7 to 3.1)	0.55
Fatal	1 (0.7)	0	0.7 (–0.7 to 2.1)	0.31
Nonfatal	1 (0.7)	1 (0.7)	0.0 (–2.0 to 2.0)	0.98
Q-wave and non-Q-wave myocardial infarction	9 (6.5)	7 (4.9)	1.5 (–3.9 to 7.0)	0.58
Fatal	1 (0.7)	0	0.7 (–0.7 to 2.1)	0.31
Nonfatal	8 (5.8)	7 (4.9)	0.8 (–4.4 to 6.1)	0.76
Repeated coronary revascularization	4 (2.9)	7 (4.9)	–2.1 (–6.6 to 2.5)	0.37
Bypass surgery	1 (0.7)	1 (0.7)	0.0 (–2.0 to 2.0)	0.98
Angioplasty	3 (2.2)	6 (4.2)	–2.1 (–6.2 to 2.0)	0.33

\* CI denotes confidence interval.

† In the off-pump group, one patient underwent angioplasty while awaiting surgery. In the on-pump group, one patient had a myocardial infarction and another patient had a minor stroke while awaiting surgery.

‡ The primary end point was a composite of freedom from death from any cause, myocardial infarction, and repeated coronary revascularization (surgery or angioplasty).

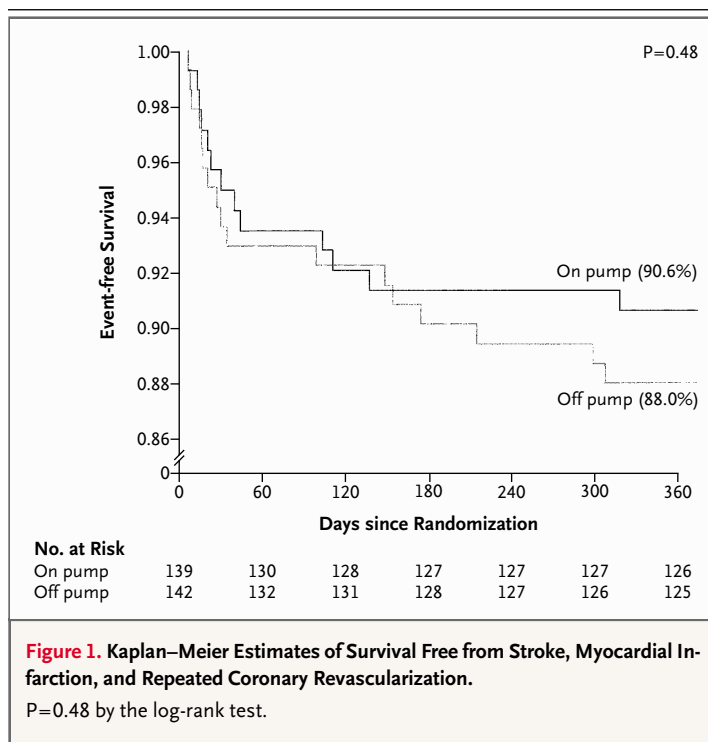
§ All cardiovascular events were included in the analysis. For example, one patient in the on-pump group died postoperatively after a myocardial infarction, and both events (death and myocardial infarction) were counted. In the on-pump group, there were three strokes (one patient had two) and four angioplasty procedures (one patient had two).

a limited number of coexisting conditions. This risk profile may explain why the in-hospital mortality rate was lower (0.7 percent in the on-pump group and 0.0 percent in the off-pump group) than the mortality rate after first-time elective CABG reported by the Society of Thoracic Surgeons (1.8 percent).<sup>6</sup> It may also explain why the one-year mortality rate in this study (1.4 percent in both the on-pump group and off-pump group) was lower than that among patients who underwent conventional CABG in the recent Arterial Revascularization Therapies Study (2.8 percent).<sup>26</sup>

The characteristics of our study population may also account for the low incidence of perioperative stroke after on-pump and off-pump surgery (1.4 percent and 0.7 percent, respectively). It was lower than that reported by Roach et al. (3.1 percent)<sup>5</sup> and by the Society of Thoracic Surgeons (1.7 percent)<sup>6</sup> but is similar to the incidence in a review of observational studies on off-pump surgery involving 1582 patients (0.6 percent).<sup>12</sup>

The use of cardiopulmonary bypass is considered to be a major determinant of perioperative stroke during on-pump surgery.<sup>4,5</sup> Patients who are undergoing CABG today are older and have more coexisting conditions than patients a decade ago.<sup>27</sup> Today's patients are therefore at higher risk for perioperative death and stroke and may thus benefit more from off-pump surgery.<sup>28</sup> This difference may in turn have pronounced effects on costs and cost effectiveness. A retrospective analysis of high-risk patients in the data base of the Society of Thoracic Surgeons showed a lower incidence of stroke after off-pump surgery.<sup>29</sup> The possible benefits and role of off-pump surgery in patients at increased risk for stroke need to be addressed in appropriately designed trials.

The incidence of perioperative myocardial infarction did not differ significantly between treatment groups. The incidence of perioperative Q-wave infarction after off-pump surgery, however, was higher (2.8 percent) than that reported in a recent randomized trial (0.5 percent).<sup>30</sup> Differences in the definition of infarction may explain this discrepancy. In a series of observational studies, myocardial infarction after off-pump surgery was reported in 0.0 percent<sup>28</sup> to 4.0 percent<sup>10</sup> of the patients. We previously reported that as compared with off-pump surgery, on-pump surgery was associated with a much greater (by 41 percent) release of creatine kinase MB isoenzyme postoperatively ( $P < 0.01$ ).<sup>31</sup> The release of troponin I was also significantly greater



after on-pump surgery in another randomized trial.<sup>32</sup> These observations may have important clinical implications, since a lower level of release of creatine kinase MB isoenzyme after CABG<sup>33</sup> and coronary angioplasty<sup>34</sup> is associated with a better prognosis.

The degree of improvement in angina, exercise capacity, and quality of life did not differ significantly between the two approaches to treatment. The difference in the rates of repeated revascularization after on-pump surgery (2.9 percent) and off-pump surgery (4.9 percent) was small. The angiographic data did not show any significant differences in the rate of graft patency or the quality of the anastomoses. Unfortunately, a substantial number of patients declined to undergo follow-up angiography because they had no symptoms. Although it has not been proved, the absence of symptoms may suggest the presence of patent grafts in these patients. The rate of graft patency may therefore have been underestimated. The missing data preclude a precise interpretation of the angiographic results and a comparison of these results with those of other series. Nevertheless, the one-year rate of graft patency after off-pump surgery in our study (91 percent) was similar to the rates of early graft

**Table 3. Average Resource Use and Direct Medical Costs per Patient.\***

Resource	Average Resource Use			Average Costs		P Value
	On-Pump Group (N=139)	Off-Pump Group (N=142)	Unit Cost	On-Pump Group (N=139)	Off-Pump Group (N=142)	
<i>dollars per patient</i>						
<b>Direct costs in hospital</b>						
Staff (operating time)†	3.82 hr	4.17 hr	338	1,290	1,411	<0.01
Intraoperative use of materials						
Off-pump coronary bypass surgery	0.04	0.99	1,235	44	1,226	<0.01
Cardiac stabilizer	0.04	0.99	438	16	435	<0.01
On-pump coronary bypass surgery	0.96	0.08	2,092	2,017	162	<0.01
Cardiopulmonary bypass	0.96	0.08	902	870	70	<0.01
Intensive care unit	1.62 days	1.43 days	1,057	1,712	1,512	0.98
Ward	8.65 days	8.11 days	247	2,134	2,002	0.06
Transfusion blood products‡	1.07	0.85	—	44	35	0.38
Additional investigations§	—	—	—	1,968	1,867	0.02
Subtotal	—	—	—	10,095	8,720	<0.01
<b>Direct costs during follow-up</b>						
Stroke	0.01	—	6,818	49	—	0.31
Myocardial infarction	0.01	—	10,908	157	—	0.15
On-pump coronary bypass surgery	0.01	0.01	10,095	71	71	0.98
Percutaneous coronary angioplasty	0.02	0.03	3,740	91	96	0.73
Angiography (not part of study protocol)	0.05	0.06	809	41	46	0.62
Hospitalization, other cardiac¶	2.17 days	2.46 days	—	827	736	0.47
Intramural rehabilitation	2.20 days	0.68 day	—	322	81	0.05
Outpatient health care**	—	—	—	555	564	0.63
Medication use	—	—	—	2,700	2,755	0.16
Subtotal	—	—	—	4,813	4,349	0.32
<b>Total direct costs at 1 yr</b>	—	—	—	14,908	13,069	<0.01

\* Unless otherwise indicated, values are the costs (in dollars) per patient. The costs per unit have been rounded. P values were calculated with use of the Mann–Whitney rank-sum test.

† Values are costs of all staff: surgeon, anesthesiologist, perfusionist, and nurse.

‡ Values are the costs of all transfusions: erythrocytes, platelets, and fresh-frozen plasma.

§ Values are the costs of blood tests, radiology services, electrocardiography, intraaortic balloon pump, pulmonary-artery catheter, angiography, coronary angioplasty, evaluation for myocardial infarction, consulting physicians, and in-hospital rehabilitation.

¶ Values reflect the costs of hospitalizations: intensive care unit, coronary care unit, and ward.

|| Values reflect the costs of rehabilitation centers and nursing homes.

\*\* Values are the costs of outpatient care: rehabilitation, consulting physician, and nurse.

patency (91 to 99 percent) reported in a review of nonrandomized studies.<sup>35</sup>

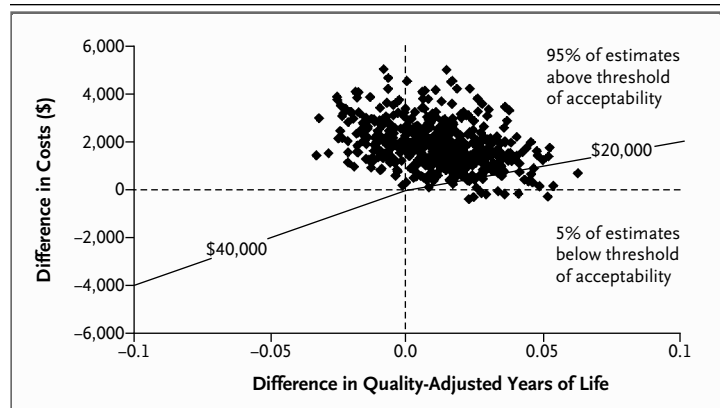
There was no statistically significant difference in cardiac outcome between the treatment groups. Off-pump surgery, however, was less expensive. The absolute difference in the incidence of cardiovascular events (2.6 percent) implies that 38 patients must

undergo on-pump surgery for 1 additional patient to be free of such events at one year. In terms of the difference in direct medical costs (\$1,839 per patient), this result also implies an additional expenditure of approximately \$70,000. Another randomized trial disclosed that off-pump surgery lowered hospital costs by 30 percent, mainly because of a

reduction in perioperative morbidity and hospital stay.<sup>36</sup> Taking into account the number of bypass operations performed annually in the United States (571,000 in 1999)<sup>37</sup> and the expectation that 50 percent of these operations will be performed off-pump by 2005,<sup>38</sup> the savings may be substantial.

For our data to be interpreted properly, the limitations of our study must be addressed. The absolute difference in the cardiac outcome (2.6 percent) was associated with a wide 95 percent confidence interval (-4.6 to 9.8 percent), mainly because of the small number of subjects. Therefore, a significant difference in cardiac outcome favoring one surgical approach may have been missed. Also, the results cannot be extrapolated to patients with more advanced coronary artery disease or a higher preoperative risk (or both). The majority of patients who undergo bypass surgery have three-vessel disease; less than 1 percent have single-vessel disease. This was the case in 23 percent and 26 percent of our patients, respectively. In current practice, however, off-pump surgery is increasingly being performed in patients with single- and double-vessel disease.<sup>39</sup> With respect to costs and cost effectiveness, these data must be interpreted with regard to the setting and the country in which the study was conducted. There may be substantial differences in costs in other practices and countries. This is especially true with respect to the costs of hospital stay, which may be a source of important savings. The details of the costs, summarized in Table 3, may nonetheless help individual physicians appreciate the potential savings in their own environments. Also, the data are limited to a follow-up of one year. A longer follow-up may alter the cost-effectiveness findings.

We conclude that in low-risk patients there was no significant difference in cardiac outcome between on-pump and off-pump coronary bypass surgery. Off-pump surgery, however, was more cost effective



**Figure 2. Bootstrap Estimates of Differences in Direct Medical Costs and Quality-Adjusted Years of Life after On-Pump and Off-Pump Coronary Bypass Surgery.**

The solid lines indicate the threshold values society is “willing to pay” for each quality-adjusted year of life gained (\$20,000) or “willing to accept” for each quality-adjusted year of life lost (\$40,000).<sup>25</sup> The cost-effectiveness ratios were below the defined thresholds in 5 percent of estimates. This finding indicates that off-pump surgery was more cost effective in 95 percent of the estimates.

and may be regarded as an alternative to on-pump surgery.

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The Octopus cardiac stabilizer, which is marketed by Medtronic, was invented at the University Medical Center Utrecht, and the Medical Center receives royalties from the worldwide sale of the device. According to Dutch patent law, university employees cannot own rights to their inventions but are entitled to compensation if an invention is commercialized. This applies to Drs. Jansen and Borst. Dr. Jansen is a member of the European scientific advisory board of Medtronic, and Dr. Borst was a consultant to Medtronic until April 2002. Medtronic was not involved in the study, nor did it receive any draft of the manuscript before publication.

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#### APPENDIX

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