The Cost Implications of Off-Pump Versus On-Pump Coronary Artery Bypass Graft Surgery at One Year

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Background. **The purpose of this study was to determine the cost implications of the Coronary Artery Bypass Graft Off or On Pump Revascularization Study (CORONARY) at 1 year.**

Methods. **Country-specific healthcare costs were obtained from public databases or local experts from each country in the CORONARY trial. Purchasing power parities were applied to these costs of consumed healthcare resources. Analyses of subgroups included in the CORONARY clinical trial were also conducted. Costs are reported in US dollars.**

Results. **After 1 year, the total cost per patient in the off-pump coronary artery bypass graft surgery (CABG) arm was $9,650 ($9,216 to $10,285) compared with $9,583 ($9,239 to $9,988) for the on-pump CABG arm; that resulted in a nonsignificant increase of $68 (−$575 to $710). Similar findings were noted for various subgroups. There were also no differences due to late conversions.**

Conclusions. **The CORONARY trial demonstrated that off-pump CABG was clinically as safe and effective as on-pump CABG with no difference in costs. Thus, the decision as to which method to choose is free from costs considerations and should be based on patient preference and surgeon expertise (Coronary Artery Bypass Graft [CABG] Off or On Pump Revascularization Study [CORONARY]; clinicaltrials.gov NCT00463294).**

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The use of coronary artery bypass graft surgery (CABG) as a common procedure in reducing mortality in patients with serious coronary artery disease is well established [1]. On-pump CABG, which uses a cardiopulmonary bypass pump, is the most common form of this procedure but has been associated with cardiovascular complications [1]. Because many of the complications stem from the use of the pump itself, off-pump CABG techniques were developed to improve patient outcomes.

The Coronary Artery Bypass Graft Off or On Pump Revascularization Study (CORONARY) is the largest, randomized, controlled surgical trial to date that was designed to evaluate the safety and long-term outcomes of CABG patients who underwent either off-pump or on-pump surgery. At 1 year, no significant difference was observed between either method of CABG surgery in the primary composite outcome [3].

Although the results of the CORONARY trial showed no significant differences, determining the cost implications associated with both methods is an important step to optimizing the use of scarce healthcare resources by decreasing costs where possible without compromising the clinical outcomes. In this paper, we estimated costs of both techniques as they evolve over a 1-year period and discuss the results.

Material and Methods

CORONARY Trial

The CORONARY trial recruited 4,752 patients from 79 centers in 19 countries. Full details of this trial are published elsewhere [2–4]. In short, CABG patients who underwent median sternotomy and had one or more of the following risk factors were randomly assigned to either off-pump or on-pump CABG procedures: age 70 years or more, peripheral arterial disease, cerebrovascular disease, or carotid stenosis of 70% or more of the luminal diameter, or renal insufficiency. Patients 60 to 69 years of age were eligible if they had at least one of the

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following risk factors: diabetes mellitus requiring treatment with an oral hypoglycemic agent or insulin, need for urgent revascularization after an acute coronary syndrome, left ventricular ejection fraction of 35% or less, or recent history of smoking (less than 1 year before randomization); patients aged 55 to 59 years were eligible if they had at least two of those risk factors.

The primary outcome of the CORONARY trial is a composite index including rate of death, nonfatal stroke, nonfatal myocardial infarction, or nonfatal new renal failure requiring dialysis. There was no significant difference in this outcome between the two groups (9.8% versus 10.3%; 95% confidence interval [CI]: 0.79 to 1.14; $p = 0.59$) at 30 days after randomization [3] and at 1 year (12.1% versus 13.3%; 95% CI: 0.77 to 1.07; p = 0.24) [4].

Cost Study Design

We hypothesized in the trial protocol that the use of off-pump CABG in the CORONARY trial would be either cost neutral or cost saving compared with on-pump CABG. As previously published [5], we define cost neutrality as (1) an incremental cost that included 0 in the confidence interval, and (2) a difference in cost that is 5% or less of the total cost of standard care (to avoid a type 2 error).

Costs per participant consisted of two components: healthcare services utilization and unit costs for these services. Drug utilization and events from all patients collected in the trial were used. All analyses used the results up to the 1-year follow-up visit. Because the cost data we are reporting does not span more than a year, there is no need to discount.

Healthcare Utilization

Healthcare utilization is divided into initial hospitalization period and the postdischarge period. The initial hospitalization period included costs associated with CABG and percutaneous coronary intervention as well as length of stay costs in intensive care unit (ICU) and ward settings until discharge. The CABG costs consisted of the cost of running an operating theater for one case as well as the cost of an intraaortic balloon pump if it was necessary. Physician costs were not included because the variability of staff reimbursement models in all participating countries would be difficult to capture and implement in our model. The impact of this is likely negligible as the salaries or fee for service are usually very similar or the same for both forms of CABG. Costs for surgical supplies consumed, such as retractors, were also not captured in this analysis. These costs, although important, are difficult to accurately reflect in our analysis because globally, hospitals may have differing policies regarding the use of key bypass surgical supplies (ie retractors and bypass pumps) as well as varying, often confidential pricing with suppliers, and in the case of retractors, have the choice of being either reusable or nonreusable.

The postdischarge period consisted of medication prescribed at discharge, procedures conducted after discharge, and event costs. Data for both initial hospitalization and the postdischarge period were recorded in the study case report forms and collected during the trial. Resource utilization data were generally limited to hospitalizations; data regarding items such as doctor visits and out of hospital tests were not collected. Because data collected during the follow-up period were less detailed than during the initial hospitalization, events (such as myocardial infarctions and strokes) are based on a "typical" event cost and do not reflect actual length of stay during the trial. It was assumed that patients who had indicated use of concomitant medication through the study were taking their medications daily until it was indicated they had stopped. Because doses for these medications were not recorded, typical doses were applied.

Unit Costs

Healthcare resource use was recorded prospectively during the trial. We sought to obtain country-specific unit costs for the majority of included events, procedures, and medications for all countries in the trial, using a method we have used previously [6]. Different countries use different methodologies for determining the cost of clinical events (event costs). Some countries provided costs based on their local diagnosis-related group system whereas others used their hospital's account system. Regardless of the sources, all costs were converted into US dollars using purchasing power parities [7]. These purchasing power parities convert all costs to a single currency and reflect differences in the purchasing power of funds between countries. It allowed us to aggregate the cost figures from different countries to arrive at an average cost per participant for the duration of the study in each arm. Because unit costs were not always easily accessible, the authors enlisted the help of national investigators or local experts to help provide unit costs using a standardized questionnaire.

As the CORONARY trial recorded drug classes and not medications, specific examples for each class were chosen for the questionnaire after consulting with experts. Drug costs were based on the generic version of the drug if available in that country. In this analysis, the authors chose to use the least expensive form all medications normally available to patients in each country.

It was not always possible to collect all the desired unit costs from all countries; however, the costs for most expensive events or procedures were obtained. To impute missing data in this analysis, we divided the countries in the CORONARY trial into five groups based on their geographic location and overall status represented by their GDP per capita. The 19 CORONARY trial countries were grouped into North America (2), South America (5), Western Europe (6), Eastern Europe (4), and Asia (2).

Costs for strokes were exceptions to the prevailing costing methodology. Unlike other events in which consumption is limited to a defined acute period, strokes often require care for months or years after the initial hospitalization. Therefore, it is important that the cost for these events reflect the additional continual care inherent to these events. To represent this reality, we applied a single time cost of stroke that reflects a 1-year period.

Indirect costs assumed by patients and their families/caregivers were not recorded and hence were not included. These costs are unlikely to differ between both groups because the results of the clinical trial demonstrated that there was no significant difference in events or repeat coronary revascularization.

Statistical Analysis

Categorical data were reported as frequencies and continuous data as mean ± SD. Total costs were estimated as the mean cost per patient in each group, including the 95% CIs. Because cost data tend to not be normally distributed, the bootstrap method (5,000 samples) was used to calculate standard errors and 95% CI [8]. The bias corrected and accelerated method was used for CIs [9]. Cost differences (ie, incremental costs) were calculated as the difference between the mean costs per patient in the on-pump arm minus the mean cost per participant in the off-pump arm. All analyses were completed using SAS (version 9.1; SAS Institute, Cary, NC).

Sensitivity Analyses

To determine the potential impact of off-pump and on-pump surgical supplies, sensitivity analyses were conducted that assumed a difference in cost of surgical supplies of ±$500 and ±$1,000. That was done by assuming that the cost of on-pump supplies was $1,000 and varying the cost of off-pump supplies from $0 to $2,000.

Subgroup Analyses

Most subgroups that were evaluated in the CORONARY clinical trial were considered in our economic analysis. Certain subgroups were not included if they were a very small subset of the overall study or did not appear to show any clinical significant in the clinical trial.

Results

During the initial hospitalization period, patients in the off-pump group cost $8,626 compared with $8,567 for the on-pump group, a nonsignificant difference of −$59 (95% CI: −$660 to $542) more for off pump. For the follow-up period, this trend of neutrality continued with the difference in cost between discharge and 6 months ($37 more for off pump; 95% CI: $122 to $195) and 6 months to 1 year ($28 less for off pump; 95% CI: −$113 to $169) also being nonsignificant. At 1 year, the cumulative total cost for the off-pump group was $9,650 (95% CI: $9,216 to $10,285) compared with a cost of $9,583 (95% CI: $9,239 to $9,988) for the on-pump group. That resulted in a slight, nonsignificant increase in cost of only −$68 (95% CI: −$710 to $575). There was no significant difference between both groups in any of the categories that made up the average total cost per patient. Details of the cost analysis results are displayed in Table 1.

A per protocol analysis (ie, excluding patients who had a conversion) was also conducted. No significant difference in cost was noted, with off pump being slightly less expensive than on pump ($40; 95% CI: −$623 to $704).

Table 1. Mean In-Trial Costs for On-Pump and Off-Pump Coronary Artery Bypass Graft Surgery

Variable	On-Pump Mean Cost (95% CI)	Off-Pump Mean Cost (95% CI)	Difference (On-Pump − Off-Pump)
Subtotal initial hospital costs	8,567 (8,264–8,948)	8,626 (8,223–9,242)	−59 (−660 to 542)
Initial hospital CABG	1,588.95	1,588.93	0.02
Operating room	1,555.96	1,550.38	5.58
Intraaortic balloon pump	32.98	38.55	−5.57
Initial hospital PCI	5.92	38.54	−32.62
With stent	0.00	30.64	−30.64
Without stent	5.92	7.90	−1.98
Initial hospital ICU	4,385.54	4,364.20	21.34
Initial hospital ward	2,586.74	2,634.38	−47.64
Subtotal discharge to month 6	515 (429–646)	551 (456–701)	−37 (−195 to 122)
Drugs	284.40	292.32	−7.92
Procedures	35.92	58.71	−22.79
Events	194.45	200.37	−5.92
Subtotal month 6 to year 1	501 (419–635)	473 (397–595)	28 (−113 to 169)
Drugs	284.40	292.32	7.92
Procedures	35.33	34.91	0.42
Events	180.92	145.59	35.33
Overall total study costs	9,583 (9,239–9,988)	9,650 (9,216–10,285)	−68 (−710 to 575)

Costs are in US dollars.

CABG = coronary artery bypass graft surgery; CI = confidence interval; ICU = intensive care unit; PCI = percutaneous coronary intervention.

Sensitivity Analyses

Results of the sensitivity analyses show that when off-pump supplies were $1,000 less than on-pump supplies, off-pump CABG was a cost saving $932 ($290 to $1,575). Increasing the cost of off-pump supplies from $0 to $2,000 by $500 increments showed a linear increase in the incremental cost by an equivalent amount up to a maximum incremental cost of $1,068 (−$1,710 to −$425) more for off-pump surgery (Fig 1).

Subgroup Analyses

The results for all analyzed subgroups are displayed in Tables 2 and 3. None of the subgroups evaluated showed any significant difference in cost, either statistically or magnitude of the mean difference in cost, with the exceptions of women (n = 908) and patients with grade 2 left ventricular ejection fraction (n = 1,103).

At the end of the trial, female patients who underwent off-pump CABG surgery saved an average of $928.21 compared with those who had on-pump surgery ($10,439 versus $11,366, off pump versus on pump, respectively). This difference in cost is largely driven by a longer ICU length of stay and by additional strokes among women who had on-pump CABG. The ICU cost for female off-pump patients was $744 less than for those who had on-pump CABG, and average stroke costs from initial discharge to 1 year were also $396 less for off-pump female patients. Patients with a left ventricular ejection fraction between 35% and 49% demonstrated similar economic benefit using off-pump CABG. At 1 year, off-pump CABG cost $774 less than on-pump CABG. As for the female subgroup, these savings were also associated with a shorter length of stay, $424 less in the ICU and $354 in the ward.

The mean difference in cost in the geographical regions looked at in the CORONARY trial was generally small, and in all cases was not statistically significant (Table 3). The difference in cost for a combined regional group consisting of North America, Eastern Europe, and Western Europe was only $162 favoring on-pump CABG whereas South America saved $189 in favor of off-pump surgery.

Comment

The CORONARY trial was overall clinically neutral as no significant difference was noted in the rate of the primary composite outcome at 1 year. Therefore, it is not surprising that our cost analysis also reflects this neutrality, with off-pump CABG costing only $68 (−$710 to $575) more than on-pump, a difference both statistically and financially not significant. The bulk of expenses occurred during the initial hospitalization, with both groups incurring fewer costs from discharge to 1 year. At the 1-year mark, both groups showed little cost difference from each other; however, with the longer follow-up results of the CORONARY trial anticipated in 2016, clinical differences may emerge that could impact policy recommendations.

Conversely, the Randomized On/Off Bypass (ROOBY) trial, the only other large clinical trial to date to report on both the clinical outcomes and the corresponding costs of off-pump versus on-pump CABG, demonstrated that in Veterans Affairs hospitals, off-pump CABG was worse than on-pump surgery (1-year composite adverse event rate of 9.9% for off pump versus 7.4% for on pump; $p = 0.04$) [10]. The negative clinical findings subsequently resulted in an adjusted cost for off-pump CABG of $59,623 compared with $56,023 for on-pump, a difference that the ROOBY study group found to be significant ($p = 0.046$) [11]. As described in the published results of the CORONARY clinical trial [3], this difference in the results could be due to differences between the CORONARY trial and the ROOBY study. The CORONARY study was a larger trial (4,752 patients versus 2,203 for the ROOBY study). The CORONARY trial patients were also more ethnically diverse owing to the study's recruitment from 19 countries around the world, compared with the ROOBY trial, which was based on the US Veterans Affairs' population. Surgeons in the CORONARY trial were also required to have a higher level of experience with off-pump CABG compared with

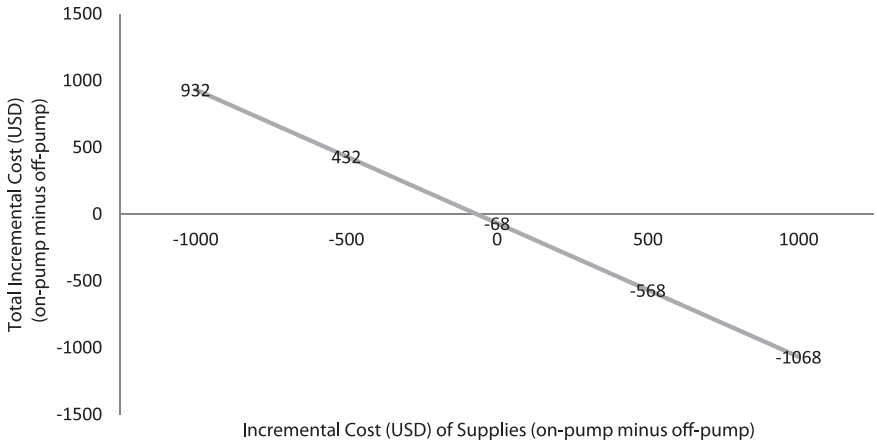

Fig 1. Impact of differences in cost of on-pump and off-pump supplies to overall incremental cost per patient. Note: The difference in cost of surgical supplies ranged from −$1,000 (off-pump supplies costing $1,000 more) to $1,000 (off-pump supplies costing $1,000 less). Revised total incremental costs were then calculated using these estimates. (USD = US dollars.)

Table 2. Mean In-Trial Costs for Subgroups Analyzed in the CORONARY Trial

Subgroup	No. of Patients	Cost On Pump	No. of Patients	Cost Off Pump	Cost Difference (On-Off)
Age					
< 70 years	1,408	8,953	1,407	8,787	166
≥ 70 years	968	10,501	967	10,911	−410
Sex					
Female	434	11,367	474	10,438	928
Male	1,942	9,185	1,901	9,454	−268
Diabetes mellitus					
Yes	1,128	9,278	1,100	9,128	149
No	1,248	9,861	1,275	10,100	−239
Left ventricular ejection fraction					
Grade 1 (≥50%)	1,651	9,750	1,643	10,068	−318
Grade 2 (35-49%)	543	9,230	560	8,455	774
Grade 3 (20-34%)	126	9,840	118	8,884	955
Grade 4 (<20%)	5	8,325	6	19,242	−10,916
Diseased vessels					
Left main	487	10,890	514	10,731	159
Single vessel only	49	7,633	70	6,019	1614
Double vessel only	381	7,904	436	8,237	−333
Triple vessel only	1,405	9,741	1,306	9,887	−146
EuroSCORE					
0–2	660	8,204	679	8,464	−260
3–5	1,288	9,554	1,229	9,498	56
6+	399	11,726	429	11,868	−143
Off-pump experience of surgeon					
< 350 cases	769	8,052	723	8,356	−304
350–900 cases	795	11,091	782	10,370	721
> 900 cases	775	9,489	836	10,150	−661
Renal failure requiring dialysis					
Yes	25	8,692	41	13,760	−5,068
No	2,303	9,636	2,291	9,580	56
Peripheral arterial disease					
Yes	196	10,162	189	10,305	−143
No	2,180	9,532	2,186	9,594	−62
Cerebrovascular disease					
Yes	241	13,249	215	13,193	56
No	2,136	9,169	2,160	9,298	129

Costs are in US dollars. None of the subgroup differences were statistically significant.

CORONARY = Coronary Artery Bypass Graft Off or On Pump Revascularization Study; EuroSCORE = European System for Cardiac Operative Risk Evaluation.

Table 3. Mean In-Trial Costs for Geographic Subgroups Analyzed in the CORONARY Trial

Region	No. of Patients	Cost On Pump	No. of Patients	Cost Off Pump	Cost Difference (On-Off)
South America	419	8,415	424	8,226	189
NA/EE/WE	913	10,587	908	10,749	−162
India	654	4,323	653	4,415	−92
China	391	17,286	390	17,407	−121

Costs are in US dollars. None of the subgroup differences were statistically significant.

CORONARY = Coronary Artery Bypass Graft Off or On Pump Revascularization Study; NA/EE/WE = North America/Eastern Europe/Western Europe.

those in the ROOBY trial, and that may have resulted in better patient outcomes.

There are some limitations to our analysis. The first important limitation is that cost data regarding CABG-specific supplies (off-pump retractors and cardiopulmonary bypass circuits) were not included in our analysis because, on a global scale, differing policies regarding the use of these supplies, varying and often confidential pricing between hospital systems even within the same geographic region, and different types of off-pump retractors (disposable or reusable) make accurately collecting these costs extremely difficult. That our results show very similar costs for on-pump and off-pump procedures—a difference of only $68—emphasizes that the potential cost savings will depend largely on the institutions and their local environment. That is shown in our sensitivity analyses in which we varied the difference in cost of surgical supplies from $1,000 less for off-pump CABG to $1,000 more in $500 increments and saw that certain surgical supplies such as retractors for off-pump CABG and the cardiopulmonary bypass circuits for on-pump CABG can drastically alter the cost of the procedure, depending on the negotiated price and the hospital's policy regarding use. Therefore, the final determination as to which procedure is cost saving locally is dependent on the cost of these supplies in each hospital.

Additionally, there was a large variation in the collected unit costs, resulting in a correspondingly large standard error in costs of the bootstrap samples and wide 95% CIs. Moreover, that a global versus a country-specific perspective was taken means that the analysis does not account for different patterns of practice and reimbursement policies. Furthermore, our costs did not take into account differences in the length of each procedure evaluated in the CORONARY trial; however, this difference is believed to be insignificant as most off-pump procedures were 20 minutes shorter than on-pump procedures.

The issue of late conversions is an additional variable that was not entirely captured in our analysis because the use of off-pump retractors or bypass pumps for on-pump CABG were not included specifically for late conversions. Although most conversions are not an issue, because in this intent-to-treat analysis, depending on the timing of conversion, it is possible that both off-pump and on-pump equipment had been prepared and thus "used" in the operating room for the same patient. In the off-pump group, only 63 of 184 conversions were converted during coronary grafting, thereby potentially using retractors first and cardiopulmonary bypass later. In the on-pump group, 147 of 150 patients were converted before coronary grafting. It is likely that for most, if not all, of these 147 patients, the bypass machine was already primed and thus could not be used again. The estimated impact of these conversions on our findings are expected to be minimal, given the large number of patients in the CORONARY trial; however, conversions may result in additional costs for each technique depending on the surgeon's expertise and local operating room management.

Lastly, this analysis only considers the direct healthcare costs incurred during the study. Costs such as out of hospital costs and productivity losses for patients and their caregivers were not included but are unlikely to have a significant impact on our results, as clinical results were similar.

In conclusion, the CORONARY trial demonstrated that, contrary to the findings of contemporary trials comparing off-pump and on-pump surgical techniques, off-pump CABG was clinically as safe and effective as on-pump surgery, with no additional costs from measured outcomes. Given the clinical and cost neutrality of both techniques, determination of which technique should be used in any given situation should not be based on costs, but rather, on a combination of dialogue between the surgeon and the patient to determine which method is best suited for the patient and consideration of the individual preferences of both parties.

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