Potential shift from coronary bypass surgery to percutaneous coronary intervention for multivessel disease and its economic impact in the drug-eluting stent era

Frédéric Poulin MD¹, Stéphane Rinfret MD MSc FRCPC^{1,2}, François Gobeil MD FRCPC¹

F Poulin, S Rinfret, F Gobeil. Potential shift from coronary bypass surgery to percutaneous coronary intervention for multivessel disease and its economic impact in the drug-eluting stent era. *Can J Cardiol* 2007;23(14):1139-1145.

BACKGROUND: Drug-eluting stents (DES) may promote percutaneous coronary intervention (PCI) procedures in patients traditionally referred for coronary artery bypass graft (CABG) surgery and may save money.

OBJECTIVES: The purpose of the present study was to quantify the potential shift from CABG surgery to multivessel PCI in the DES era and to model the economic consequences.

METHODS: Based on predefined criteria, the feasibility of PCI was evaluated in patients with multivessel coronary artery disease who underwent CABG surgery before the availability of DES at the Centre Hospitalier de l'Université de Montréal's Notre-Dame Hospital (Montreal, Quebec). Modelling was used to evaluate the potential cost savings using multivessel PCI instead of CABG surgery. Equal one-year outcomes in both groups were assumed, with the exception of a 10% repeat revascularization (RR) rate in the DES group and a 4% RR rate in the CABG group. The impact of those assumptions was evaluated using 1000 Monte Carlo simulations.

RESULTS: The authors retrospectively evaluated that, of 289 patients who underwent CABG without concomitant valve surgery between January and December 2003, only 22 patients (8%) were good candidates for multivessel DES implantation. The procedures would have involved an average of 3.6 DES per patient. The average cost per revascularization procedure was \$14,402 with surgery and \$11,220 for multivessel DES implantation (using \$2,200 DES), leading to a savings of \$3,182 per patient. However, after including RR procedures, PCI would only have been associated with savings of \$812 per surgery avoided. Monte Carlo analysis revealed that surgery may be less expensive than PCI in 36% of patients.

CONCLUSIONS: Most patients who underwent CABG surgery in 2003 were retrospectively judged to be ineligible for multivessel PCI with DES. In the rare eligible patient, multivessel PCI with DES is not expected to produce savings to health care costs in Canada unless the DES purchase cost continues to decrease.

Key Words: Coronary artery bypass grafting surgery; Drug-eluting stents; Economic analysis; Multivessel disease; Percutaneous coronary intervention

La possibilité de passer d'un pontage aortocoronarien à une intervention coronaire percutanée en cas de maladie plurivasculaire et ses répercussions économiques avec les endoprothèses à élution de médicament

HISTORIQUE : Les endoprothèses à élution de médicament (EEM) peuvent favoriser les interventions coronaires percutanées (ICP) chez les patients subissant habituellement un pontage aortocoronarien (PAC) et permettre d'économiser.

OBJECTIF : La présente étude visait à quantifier la possibilité de passer du PAC à une ICP plurivasculaire avec les EEM et à en modéliser les conséquences économiques.

MÉTHODOLOGIE : D'après des critères prédéfinis, les auteurs ont évalué la faisabilité de l'ICP chez des patients atteints d'une cardiopathie plurivasculaire qui avaient subi un PAC avant que les EEM ne deviennent disponibles à l'Hôpital Notre-Dame du Centre hospitalier de l'Université de Montréal (à Montréal, au Québec). Ils ont utilisé la modélisation pour évaluer les économies potentielles réalisées si on remplaçait le PAC par une ICP. Ils ont postulé des issues équivalentes dans les deux groupes au bout d'un an, à l'exception d'un taux de reprise de la revascularisation (RR) de 10 % au sein du groupe ayant reçu l'EEM et de 4 % au sein du groupe ayant subi le PAC. Ils ont évalué les conséquences de ces hypothèses au moyen de 1 000 simulations Monte Carlo.

RÉSULTATS : Les auteurs ont rétrospectivement évalué que, sur les 289 patients qui avaient subi un PAC sans opération valvulaire concomitante entre janvier et décembre 2003, seulement 22 patients (8 %) étaient de bons candidats à l'implantation d'une EEM plurivasculaire. L'intervention exigeait une moyenne de 3,6 EEM par patient. Le coût moyen par intervention de revascularisation s'élevait à 14 402 \$ par opération et celui des implantations d'EEM plurivasculaire (à l'aide d'EEM de 2 200 \$), à 11 220 \$, ce qui entraînait une économie de 3 182 \$ par patient. Cependant, compte tenu des RR, l'ICP n'assurait qu'une économie de 812 \$ par opération évitée. L'analyse de Monte Carlo a révélé que, chez 36 % des patients, l'opération peut être moins coûteuse que l'ICP.

CONCLUSIONS : Les auteurs ont évalué que la plupart des patients qui ont subi un PAC en 2003 n'étaient pas admissibles à une ICP plurivasculaire associée à une EEM. Chez les rares patients qui étaient admissibles, cette intervention ne devrait pas permettre au système de santé du Canada de réaliser des économies, à moins que le coût des EEM continue de baisser.

¹Centre Hospitalier de l'Université de Montréal; ²Centre Hospitalier de l'Université de Montréal Research Centre, University of Montreal, Montreal, Quebec

Correspondence: Dr Stéphane Rinfret, Pharmacoeconomics and Pharmacoepidemiology Unit, Centre Hospitalier de l'Université de Montréal Research Centre, Interventional Cardiology, Notre-Dame Hospital, 1560 Sherbrooke Street East, Montreal, Quebec H2L 4M1. Telephone 514-890-8000 ext 25018, fax 514-412-7580, e-mail s.rinfret@umontreal.ca

Received for publication December 19, 2006. Accepted June 17, 2007

Percutaneous coronary intervention (PCI) with stent implantation is an effective alternative to coronary artery bypass graft (CABG) surgery in patients with multivessel coronary artery disease (1,2). However, one large randomized controlled trial (3) and a registry from the state of New York (4) revealed that CABG surgery had a slight survival advantage over multivessel PCI. These data were obtained before the advent of drug-eluting stents (DES) and may therefore not be applicable in the current era. By slowly releasing antiproliferative and antimitotic agents to the arterial wall, DES have dramatically reduced the incidence of restenosis in randomized controlled trials (5,6). Despite this, DES are used in fewer than 50% of PCI procedures in Canada because of high acquisition costs and constraint measures.

Improved clinical outcomes with DES compared with CABG surgery or multivessel bare metal stent (BMS) implantation were also seen in the Arterial Revascularization Therapies Study II (ARTS II) (7) and the Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty versus Coronary Artery Bypass Surgery in Multivessel Disease III (ERACI III) (8). These prospective nonrandomized trials compared the outcomes of patients who underwent multivessel DES implantation with historical control groups of patients who underwent multivessel BMS or CABG surgery in previous randomized trials (ARTS [1] and ERACI II [2]). Both studies showed a reduction in major adverse cardiac events with DES even though contemporary candidates treated with DES were at higher clinical and anatomical risk than their surgical counterparts.

If the reduction of restenosis with DES and its associated health consequences (recurrent angina, need for repeat revascularization [RR] and impaired quality of life) is not offset by late stent thrombosis and increased mortality (9-13), multivessel stent implantation is likely to be considered on a growing proportion of patients who were traditionally referred for CABG surgery before the DES era. However, the magnitude of this shift is difficult to quantify and anticipate. In fact, in many CABG versus PCI trials, only a minority of patients were eligible for both revascularization techniques due to anatomical considerations (1,3,14). Treating multivessel coronary disease patients with PCI is likely to put additional strain on Canadian catheterization laboratories' budgets, and it may not be feasible unless additional funds are devoted for such an indication. Nevertheless, a small shift in referral practices may have an economic impact, resulting in health care savings from avoided CABG surgeries if multivessel DES implantation is less expensive than surgery. To date, no study has compared the cost of multivessel PCI and DES with surgery in Canada.

The purpose of the present study was to quantify the potential shift from CABG to multivessel PCI and to model the economic consequences using a cohort of patients with multivessel disease treated with surgery before the introduction of DES.

METHODS

Overall study design

The study is divided into two parts. The first part was a health services research study involving a single-centre retrospective analysis of CABG surgery cases performed at the Centre Hospitalier de l'Université de Montréal's Notre-Dame Hospital (Montreal, Quebec), a large, Canadian teaching hospital. Angiographic data were reviewed by two interventional cardiologists and were evaluated as to which cases could have been treated with DES instead of surgery, had the technology been available at that time. The second part of the study involved a cost comparison between multivessel DES implantation and CABG using available cost data and modelling, as well as a budget impact analysis.

Clinical and angiographic data collection

Clinical data and major in-hospital outcomes were retrospectively collected for consecutive patients who underwent their first CABG surgery without concomitant valve or ventricular surgery between January and December 2003. Patients who underwent valve or ventricular surgery at the same time as their CABG surgery were excluded because they could not have been considered PCI candidates. The year 2003 was selected because it preceded the introduction of DES at the Notre-Dame Hospital. Patients whose surgical indication was the result of a PCI complication or failure were also excluded. Left ventricular ejection fraction was obtained from the most recent preoperative echocardiogram, angiogram or nuclear-gated single-photon emission computerized tomography scan. Left ventricular systolic dysfunction was defined as an ejection fraction below 40%. Chronic renal failure was assumed when serum creatinine was higher than 150 µmol/L. Postoperative myocardial infarction (MI) was defined as a fivefold increase in creatine kinase muscle-brain levels above the upper limit of normal with a new pathological Q wave on an electrocardiogram, or a 10-fold increase without a pathological Q wave within the first 24 h postoperatively (15). Postoperative stroke was considered to be present if there was a loss of neurological function caused by an ischemic or hemorrhagic event with residual symptoms at least 24 h after onset, or that leading to death (16).

Assessment of patient eligibility for multivessel PCI

Two interventional cardiologists (SR and FG) independently reviewed the preoperative coronary angiographic results and had to agree on the feasibility of PCI for a patient to be considered eligible. Exclusion criteria included significant (50% or greater) left main artery disease, chronic total occlusions (CTOs) and predefined high-risk lesions. High-risk lesions included those involving the ostium of the left anterior descending (LAD) or left circumflex (LCX) arteries, those involving high-risk or multiple (two or more) bifurcations, those that were highly calcified or tortuous, or any lesion that was judged to have poor likelihood of acute success with PCI, such as extremely long lesions (longer than 60 mm) that would have required multiple overlapping DES. Patients for whom six or more DES would have been required were also excluded. In the case of initial disagreement, if a consensus was not reached between the two reviewers, the patient was judged to be ineligible for PCI. For a patient to be judged suitable for multivessel DES implantation, the interventional cardiologists had to believe that a complete revascularization could have been accomplished with PCI. Both cardiologists were blinded with regard to clinical data and outcomes, including ejection fraction and diabetes status, to prevent assessment bias at the time of their decision as to the feasibility of PCI.

Virtual PCI procedure description

A virtual procedure was planned for patients considered to be suitable for PCI. The aim was to determine the procedural resources (especially the number of DES) needed to complete a PCI procedure on patients judged to be eligible for multivessel PCI and to assess the complexity of the intervention, which may have an impact on expected clinical outcomes. Based on their visual estimates from careful review of all coronary angiographic results, the two cardiologists described the number, length and diameter of stents that would have been required during the virtual procedure based on the currently available Cypher (Cordis Corporation, USA) or Taxus (Boston Scientific, USA) stents. They also assessed whether any of the stents would have been implanted on a coronary bifurcation or ostium. The American College of

Cardiology/American Heart Association classification was assessed for all lesions (17). The required stent length was estimated based on complete lesion coverage from one normal segment to another, even if this would require multiple overlapping stents; these data were also recorded in the virtual procedure plan. Bifurcation lesions had to be manageable with provisional side-branch stenting, assuming that all would only need one stent. Estimates of the number of DES per procedure based on this analysis were subsequently used in economic models.

Statistical analysis

Continuous data are presented as mean $\pm$ SD, or median and interquartile range (25th to 75th percentile) when not normally distributed. Binary data are presented using the number and percentages. The initial agreement between the two cardiologists as to the feasibility of multivessel PCI was assessed using Cohen's kappa statistic. Statistical comparisons were made between those who were eligible for virtual PCI and those who were not. Continuous data were compared using the *t* test, except for highly skewed data, which were compared using the Wilcoxon rank sum test. Binary data were compared using Fisher's exact test, and multiple categories were compared using the χ^2 test. $P < 0.05$ was considered to be statistically significant. All statistical analyses were performed with SAS for Windows (version 8.2; SAS Institute, USA).

Economic analysis

A cost analysis was performed using spreadsheets. A one-year economic model was designed assuming equal clinical outcomes (death, MI or stroke) in both groups, with the exception of a conservative estimation of a 10% RR rate in the DES group and a 4% RR rate in the CABG group. The RR rate following CABG was derived from the ARTS II and ERACI III studies. The RR rate following DES implantation was also based on the same studies, but was conservatively raised to account for the higher-risk profile of the population of the present study. It was also assumed that for post-PCI RR procedures, 75% would have been CABG surgeries and 25% would have been additional PCI procedures, with all PCI procedures being performed with further DES implantation. All post-CABG RR would have been performed using PCI, because early repeat surgery following discharge has become an exceptional procedure at the Notre-Dame Hospital. CABG surgery costs were obtained from detailed case costing performed at the hospital. To convert inpatient resources into costs, the Module d'Aide à la Gestion de l'Information Clinique (MAGIC) case costing system (MédiaMed Technologies, Canada) was used, which provides hospital case costing based on scenarios of resources used. PCI procedural costs were based on a detailed 'bottom up' system of costing of procedures (all basic and more specialized material, personnel, medication, contrast, etc) that were performed in 2003. Average post-PCI hospital costs in 2003 were obtained with the MAGIC case costing system. It was established that the CABG group needed two days of hospitalization in the intensive care unit and five days in the surgical ward, and that the PCI group needed one day of hospitalization, on average, following the intervention in 2003. Hospitalization costs leading to the decision of revascularization were assumed to be the same in both groups. Physician fees (cardiac surgeon, cardiologist, anesthesiologist and intensive care specialist) were based on the Régie de l'assurance maladie du Québec data. Although results are expressed in 2003 Canadian dollars, the purchase price of DES that was current at the time of writing was used, which was approximately \$2,200, on average, in most Canadian centres. It was also assumed that DES patients

received 12 months of clopidogrel. The perspectives of both the Ministry of Health (MOH) and the hospital chief executive officer were used for this analysis. The horizon of the analysis was limited to one year, and therefore costs were not discounted.

Monte Carlo simulations were used to verify the stability of the base case analysis findings with the model. Important model parameters were varied (cost of CABG, number of stents per procedure, risk of an RR following the index procedure and modality of treatment for restenosis) within plausible boundaries for data based on assumptions or visual estimations (such as for the number of stents per procedure). The budget impact of the shift from CABG to PCI was verified by varying the percentage of PCI in additional simulations. A triangular distribution was assumed, in which the most likely value for a given parameter was its value in the baseline model. In the final simulation, the purchase cost of DES was decreased to \$1,800 to assess its impact on cost savings per CABG surgery averted. These sensitivity analyses were performed with Crystal Ball software (Decisioneering Inc, USA).

RESULTS

Study population

From January to December 2003, a total of 360 patients underwent their first CABG surgery at the Notre-Dame Hospital (Montreal, Quebec). Of these, 42 involved a concomitant valve ($n=35$) or ventricular ($n=7$) surgery and were thus excluded. For 27 patients, coronary angiography results and charts were not available for review. Finally, in two patients, CABG surgery was performed as a consequence of PCI complication or failure; therefore, these patients were also excluded. A total of 289 patients were available for inclusion in the present study.

Potential shift from surgery to PCI

Based on a detailed review of the coronary angiography results, only 22 of the 289 surgical patients (8%) had coronary anatomy that would have also been suitable for complete revascularization with multivessel DES implantation. The kappa statistic between the two observers was 0.84 (95% CI 0.72 to 0.96), demonstrating good initial agreement. Final agreement was reached through discussion, as previously described.

The presence of a CTO (51%) or stenosis of greater than 50% of the left main coronary artery (30%) were the most common reasons for judging the remaining 92% of patients to be ineligible for multivessel PCI. Other reasons for noneligibility included the presence of ostial LAD or LCX lesions (13%), high-risk or multiple bifurcation lesions (13%) and other high-risk lesions (14%). The sum of all proportions exceeds 100% because more than one reason for noneligibility may be attributed to each patient.

Baseline and procedural characteristics and surgical outcomes

Baseline and surgical procedural characteristics of the 289 patients are displayed and compared by eligibility for PCI with DES (Table 1). Most patients were male (78%) and had a mean age of 65 years. Smoking, dyslipidemia, hypertension and diabetes were highly prevalent. Past medical history revealed a previous MI in 33% and PCI in 14%. This was a relatively high-risk surgical cohort, in which 9% had chronic renal failure, 17% had chronic obstructive pulmonary disease and 25% had peripheral vascular atherosclerotic disease. The preoperative mean ejection fraction was 52%, and nearly one-quarter of patients had left ventricular systolic dysfunction. The majority of patients (79%) had three-vessel disease. Compared with patients judged to be ineligible for PCI, patients who would have been good candidates for multivessel PCI with DES were more likely to have had two-vessel rather

TABLE 1
Baseline characteristics of all patients by eligibility for percutaneous coronary intervention (PCI)

	All patients (n=289)	Eligible (n=22)	Not eligible (n=267)	P
Age, years	65±9	63±10	65±9	0.38
Male sex	226 (78)	14 (64)	212 (79)	0.10
Hypertension	205 (71)	15 (68)	190 (71)	0.80
Smoking	178 (62)	18 (86)	160 (60)	0.02
Diabetes mellitus	99 (34)	6 (27)	93 (35)	0.64
Dyslipidemia	186 (64)	12 (55)	174 (65)	0.36
Previous MI	96 (33)	11 (50)	85 (32)	0.10
Previous PCI	39 (14)	5 (23)	34 (13)	0.20
LVEF, %	52±15	54±11	53±14	0.62
LVEF ≤40%	67 (24)	3 (14)	65 (26)	0.30
COPD	48 (17)	7 (32)	41 (15)	0.07
Peripheral vascular disease	71 (25)	3 (14)	68 (26)	0.30
Chronic renal failure	26 (9.0)	0 (0)	26 (9.7)	0.24
Severity of coronary artery disease				0.02
Three-vessel	227 (79)	13 (59)	214 (80)	
Two-vessel	55 (19)	9 (41)	46 (17)	
Single-vessel	7 (2.4)	0 (0)	7 (2.6)	
Surgical indications				<0.01
Stable angina	30 (10)	0 (0)	30 (11)	
Unstable angina/NSTEMI	224 (78)	18 (82)	206 (77)	
STEMI	11 (3.8)	4 (19)	7 (2.6)	
Silent ischemia	24 (8.3)	0 (0)	24 (9)	

Data are presented as mean ± SD or number (percentage). Denominators for each variable vary because of missing data. CAD Coronary artery disease; COPD Chronic obstructive pulmonary disease; LVEF Left ventricular ejection fraction; NSTEMI Non-ST segment elevation myocardial infarction

than three-vessel disease, to have had an acute coronary syndrome or to be smokers ($P<0.05$).

CABG and in-hospital outcomes

As explained earlier, all 289 patients studied underwent a CABG surgery in 2003 before the availability of DES. Details of CABG procedures and associated in-hospital outcomes by eligibility for PCI are shown in Table 2. Most procedures were performed off-pump (81%) and involved mammary artery to LAD artery anastomosis. The median postoperative length of stay was seven days. Among the 289 patients, 12 (4.2%) died during the postoperative period, 15 (5.2%) fulfilled the diagnostic criteria for an MI, 13 (4.5%) suffered from major bleeding and 11 (3.8%) suffered from a stroke. Nineteen patients (6.6%) underwent an emergent reoperation. Although it was not possible to make definitive comparisons of CABG surgery outcomes between PCI candidates and those not eligible for PCI due to insufficient statistical power, none of the virtual PCI candidates died after their CABG surgery. Other adverse events were also extremely rare in these patients. In fact, only one patient of the 22 virtual PCI candidates had a postoperative event (urgent reoperation). The postoperative length of stay was significantly shorter in these patients ($P=0.04$).

Virtual PCI procedures

Details of the virtual PCI in these 22 patients are listed in Table 3. These procedures would have involved the implantation of an average of 3.6 DES per patient, with a mean length of 22 mm and a mean diameter of 2.9 mm per stent. Most lesions were type C

TABLE 2
Coronary bypass procedure actually performed, and associated in-hospital outcomes by eligibility for percutaneous coronary intervention (PCI)

	All patients (n=289)	Eligible (n=22)	Not eligible (n=267)	P
Emergent surgery	29 (10)	2 (9.1)	27 (10)	1.0
Number of distal anastomoses	3.1± 0.9	3.0±1.0	3.1± 0.9	0.74
Mammary graft to LAD	275 (95)	21 (95)	254 (95)	0.95
Complete revascularization	229 (79)	19 (86)	210 (79)	0.58
Off-pump surgery	233 (81)	19 (86)	214 (80)	0.59
Postoperative length of stay, days	7 (5, 9)	6 (5, 7)	7 (5, 10)	0.04
Total length of stay, days	11 (8, 17)	9 (8, 11)	11 (8, 18)	0.06
In-hospital death following CABG surgery	12 (4.2)	0 (0)	12 (4.5)	0.61
Postoperative myocardial infarction	15 (5.2)	0 (0)	15 (5.7)	0.61
Maximum CPK after CABG, U/L	445 (287, 810)	443 (290, 639)	445 (287, 830)	0.48
Urgent reoperation	19 (6.6)	1 (4.6)	18 (6.8)	1.0
Stroke after CABG	11 (3.8)	0 (0)	11 (4.2)	1.0

Data are presented as mean ± SD, median (25th and 75th percentiles) or number (percentage). CABG Coronary artery bypass graft; CPK Creatine phosphokinase; LAD Left anterior descending artery

(54.7%) and many involved a bifurcation (21.8%). Stent overlap would have been necessary in 11.5% of cases.

Economic analysis

Cost savings from CABG averted – base-case analysis: In 2003, based on detailed case costing data, the hospital cost for a CABG surgery at the Centre Hospitalier de l'Université de Montréal was \$11,927. Physician fees were \$2,475 (including the cardiac surgeon, anesthesiologist and intensive care specialist), for a total average cost of \$14,402 per patient from the MOH's perspective. A PCI procedure (\$319 for catheterization laboratory staff, \$219 for basic equipment and coronary angiography, \$431 for PCI equipment with contrast, \$230 for anti-glycoprotein IIb/IIIa inhibitors [assuming 50% received eptifibatide], \$60 for a closure device [used in 30% of patients], and \$732 for bed costs plus 30% overhead, for a total of \$2,570 without stents), involving the implantation of 3.6 DES (cost of \$7,920) and \$730 in physician fees would have cost \$11,220, leading to a savings of \$3,182 per initial revascularization procedure. During the following year, an RR rate of 10% was assumed in the DES group (with 75% being treated with CABG and 25% with PCI) and 4% in the CABG group. The RR procedures would have been performed at an average cost of \$12,652 (assuming up to two new DES implanted for restenosis) per procedure in the DES group and \$7,401 per procedure in the CABG group. Therefore, after one year, the PCI strategy would only be associated with \$812 in savings per initial CABG surgery avoided. From the hospital chief executive officer's perspective, multivessel PCI would save \$375 per CABG avoided, excluding physician fees and the cost of clopidogrel.

Monte Carlo simulations on the cost savings from CABG avoided and budget impact analysis: Monte Carlo simulations were performed from the MOH's perspective, varying important parameters within plausible boundaries and assuming a triangular distribution for all parameters (Table 4). After 1000 simulations, it

TABLE 3
Details of the virtual percutaneous coronary intervention procedure involving multivessel drug-eluting stent implantation in patients who would have been eligible

	Eligible (n=22 patients, 78 lesions)
Number of stents per patient	3.6±0.8
Stent length per lesion, mm	22.0±6.3
Stent diameter per lesion, mm	2.9±0.4
ACC/AHA classification*	
A	0 (0)
B1	20 (27)
B2	14 (19)
C	41 (55)
Stenting of a bifurcation	17 (22)
Need for overlapping stents	9 (12)

Data are presented as mean ± SD or number (percentage). Denominators for each variable vary because of missing data. *The American College of Cardiology-American Heart Association (ACC/AHA) classification was not available for three lesions

was found that multivessel PCI would save \$997±2,757 per CABG surgery avoided after one year. Our findings, however, were very sensitive to the model parameter variations, with 64% of simulations resulting in savings when using multivessel PCI. In the other simulations, surgery was less expensive. However, when using a lower DES price of \$1,800, 84% of simulations resulted in savings when using multivessel PCI, with an average cost saving of \$2,376±2,409 per CABG avoided after one year.

The yearly cost savings for an institution performing 500 CABG surgeries per year were also assessed, now varying an additional parameter, the shift from CABG to multivessel DES implantation, from 5% to 15%. A triangular distribution was assumed, with a most frequent shift of 8%. Using \$2,200 as the cost per DES, 64% of the simulations showed cost savings, with an average savings of \$46±127 thousand. Using \$1,800 as the cost per DES, 84% of simulation showed savings, with average savings of \$118±124 thousand.

DISCUSSION

We retrospectively reviewed the coronary anatomy of patients with multivessel disease referred for CABG surgery before the availability of DES in our institution. Our analysis suggests that multivessel DES implantation is unlikely to become a dominant revascularization alternative unless more complex cases become routinely challenged. Based on angiographic characteristics, we judged that only 8% of patients from this cohort would have been good candidates for complete revascularization with DES, had the technology been available at that time. Anatomical limitations associated with a lower likelihood of acute success are likely to remain central in the selection of surgery over PCI in these patients. These findings underscore the complementary rather than competitive role of surgical and percutaneous revascularization techniques in cardiology. Our retrospective angiographic review, during which we were blinded to relevant clinical data and outcomes, resulted in the selection of a lower-risk cohort for multivessel DES implantation compared with the patients judged to be unsuitable. These 22 patients were more likely to have two-vessel disease, and their surgical outcomes were uneventful in most cases, confirming that CABG surgery was a safe procedure in these patients. Moreover, assuming equal longer-term outcomes, which is still to be confirmed in randomized trials, our

TABLE 4
Model parameters varied in 1000 Monte Carlo simulations

Model parameter	Value in baseline analysis used as the likeliest value in model	Data source	Range of values in Monte Carlo simulations	Assumed distribution in simulations
Cost of CABG*	\$11,927	CHUM case costing system	\$8,000–\$18,000	Triangular
Number of DES per procedure	3.6	Detailed angiographic review	2–6	Triangular
RR rate following CABG	4%	Assumption, based on ARTS II (7)	1%–7%	Triangular
RR rate following PCI with DES	10%	Assumption	7%–13%	Triangular
Patients treated with CABG because of restenosis following multivessel PCI	75%	Assumption	50%–100%	Triangular

*Presented in 2003 Canadian dollars. ARTS Arterial Revascularization Therapies Study; CABG Coronary artery bypass graft; CHUM Centre Hospitalier de l'Université de Montréal; DES Drug-eluting stent; PCI Percutaneous coronary intervention; RR Repeat revascularization

economic analysis suggests that multivessel PCI with DES, in the few who are eligible, may be marginally cost-saving, with \$2,200 per DES; therefore, it is not expected to result in substantial reductions to health care expenditures. Although very few health care interventions actually save costs, we think these costs savings should be taken in a more general budget management context. For example, for a Canadian institution performing 500 CABG surgeries annually without concomitant valve surgery, our base-case model predicts that \$316,800 would be required to buy 144 additional stents to allow 40 eligible patients (8%) to be treated with PCI. This would amount to an annual net savings of only \$32,500 to the MOH, equivalent to 0.5% of the total annual budget for CABG in that institution. We believe that these modest savings, if real, are unlikely to draw further government or other third-party payer's money to buy DES for such an indication. Indeed, with close to 40% of Monte Carlo simulations showing lower costs with CABG, no substantial cost savings should be expected with DES at the present purchase price. However, a further decrease in the cost of DES may certainly make this strategy more attractive economically for hospital managers. Indeed, when decreasing the purchase cost to \$1,800, the majority of the simulations showed cost savings with multivessel DES implantation compared with CABG surgery. With shifts ranging from 5% to 15% and an average of approximately \$2,500 in savings per CABG surgery averted, more important savings are possible, although they remain modest in our view. We think our cost data are applicable to other Canadian institutions. Hospital costs of \$11,948 for off-pump CABG have previously been reported (19). However, data on PCI procedural costs were reported to be higher in other economic analyses (18,19). Therefore, with higher PCI cost data, even lower cost savings from averted CABG surgeries can be expected.

Recently, Griffiths et al (20) estimated that revascularization with DES was technically feasible in 76% of patients in their single-centre multivessel surgical cohort. They clearly used more liberal eligibility criteria in their model. For example, PCI was allowed for favourable CTOs, left main coronary artery disease and other complex lesions (bifurcations and ostial lesions), for which evidence of the safety of DES is lacking. They also allowed incomplete revascularization with DES. Our objective, however,

was to estimate a conservative and reasonable uptake from traditional CABG surgery, as long as a comparable revascularization can be performed with DES. Therefore, we believe that a much smaller proportion of patients (8% in our analysis) traditionally treated with CABG can now be treated with multivessel DES implantation, unless more effective devices and techniques become available to successfully treat high-risk lesions.

For now, the data from recent prospective nonrandomized controlled trials show a favourable outcome with multivessel DES implantation, which gives some multivessel patients the choice of PCI, a potentially better alternative than BMS implantation (7,8). The one-year incidence of major adverse cardiac events in the DES group was 10.5% in ARTS II (7) and 12.0% in ERACI III (8), compared with 11.7% and 19.6% for their respective surgical cohorts. In these same trials (ARTS II and ERACI III), the one-year RR rates were 3.7% and 4.4%, respectively, in the CABG groups, and 8.5% and 8.9%, respectively, in the DES groups. These RR rates in the DES groups are nearly twice as high as the rate of target lesion revascularization of 4.2% reported in a meta-analysis of 14 pooled DES trials (5). In fact, ARTS II and ERACI III data reflect the real-life, off-label practices outside the setting of randomized controlled trials. The percentages of patients with diabetes (27%), patients with three-vessel disease (59%), and the total stented length (76.9 mm) among DES candidates in our study were similar to those seen in ARTS II (26%, 54% and 72.5 mm, respectively) (7). Despite this, we used an even more conservative assumption of the RR rate (10%) because of the higher prevalence of type C lesions (55%) in the patients we considered to be eligible for multivessel PCI (14% in ARTS II [7] and 37% in ERACI III [8]), as well as the high number of overlapping stents, which increase the risk of restenosis (21). This was a reasonable assumption that we also varied in the Monte Carlo simulations. Although in the real world one can expect a lower in-hospital or short-term mortality rate with multivessel PCI than with surgery, our restrictive criteria for PCI interestingly resulted in the selection of a much lower surgical risk cohort who had an actual in-hospital mortality rate of 0% compared with 4.5% in those judged to be ineligible for PCI. Therefore, unless incomplete revascularization with PCI in patients who are at higher surgical risk is performed, we think that multivessel DES implantation will not result in important mortality reductions because of the selection of lower-risk patients who usually do well following CABG. Moreover, concerns have been raised about the long-term safety of DES because of an increased risk of late stent thrombosis and mortality, especially after clopidogrel is discontinued (9-13,22,23). Such complications, associated with the need for prolonged clopidogrel prescription and its associated costs, may offset the initial economic or survival advantage, if any, of PCI over CABG. This is especially true outside the setting of randomized controlled trials.

While DES implantation is considered cost-effective in the United States (24), its economic value remains largely debated in Canada (18,19,25). Most health technology reviews and economic analyses conclude that higher-risk patients, especially patients with diabetes and patients with small vessels (25), are likely to derive the most economic benefit from DES compared with BMS, with a better incremental cost-effectiveness ratio (18,19). However, DES implantation in single de novo lesions does not save money (24,26). Before the present study, no one had evaluated the economic impact of DES in multivessel disease using the appropriate comparison (CABG surgery) in the Canadian context.

Limitations

Our analysis has several limitations that need to be acknowledged. First, the number of eligible patients may have been underestimated. We could have broadened the eligibility criteria by requiring the completeness of DES revascularization to only be equal to that of CABG rather than strictly complete. Superiority of complete revascularization with PCI for multivessel disease on long-term outcomes was inconsistently demonstrated in the pre-DES era (27-32). Another reason for this underestimation may be due to the fact that our interventional cardiologists were already managing a large number of multivessel patients with BMS in 2003, which were not included in the analyses. Second, the retrospective design and lack of quantitative coronary angiography data are definite limitations. However, most interventional cardiologists usually base their decision for PCI on visual estimates, as we did here. This is justified by studies (33-35) that show reasonable correlations between visual and quantitative estimations of lesion length and size. Third, virtual PCI candidates from our surgical cohort were clearly higher-risk patients than those in the most recent DES trials because of a higher prevalence of type C lesions (55%), bifurcating lesions and the need for overlapping stents. We think this would lead to an even lower shift of patients toward multivessel DES implantation, especially if long-term outcomes are not comparable in these higher-risk subsets. Fourth, we did not allow a mixture of DES and BMS to be used in the PCI candidates. Although this would have favourably decreased procedure costs, restenosis rates and follow-up costs might have expectedly been higher. Fifth, our model was limited to a single centre and a one-year follow-up period. It therefore ignored any later risk, benefit or quality of life advantage from either strategy. Finally, we did not consider other physicians', cardiac surgeons' or patients' perspectives in this analysis, which will continue to have an important impact on the selection of CABG or multivessel DES implantation in these patients.

CONCLUSIONS

The present study provides a realistic forecast of the impact of DES on revascularization practices in a large sample of patients with multivessel disease. Anatomical considerations, such as CTOs, left main coronary artery disease and high-risk bifurcations, are likely to remain important limitations for the selection of a complete revascularization with PCI, even in the DES era. CABG surgery is a safe procedure, with low in-hospital mortality, in patients who are candidates for multivessel PCI. In Canada, multivessel PCI with DES, in the few patients who are eligible, is associated with a marginal cost savings compared with CABG surgery. On a large population basis, given the minority of patients who were judged to be eligible for PCI in our analysis, health care policy makers should not expect important cost savings with the use of DES in patients with multivessel disease. However, with future reductions in DES costs, multivessel DES implantation may become economically superior and lead to more significant savings in the few patients who are eligible. Ongoing trial results comparing multivessel DES implantation with surgery are, however, needed to confirm the long-term equivalence in clinical outcomes between these strategies. Economic studies alongside these clinical trials are also awaited.

ACKNOWLEDGEMENTS: The authors gratefully acknowledge Laura McKeeman for the careful assistance with the preparation of the manuscript. Dr Rinfret is a junior clinician-scientist of the Fonds de la recherche en santé du Québec (FRSQ).

REFERENCES

- Serruys PW, Ong AT, van Herwerden LA, et al. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease: The final analysis of the Arterial Revascularization Therapies Study (ARTS) randomized trial. *J Am Coll Cardiol* 2005;46:575-81.
- Rodriguez AE, Baldi J, Fernández Pereira C, et al; ERACI II Investigators. Five-year follow-up of the Argentine randomized trial of coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple vessel disease (ERACI II). *J Am Coll Cardiol* 2005;46:582-8.
- SoS Investigators. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): A randomised controlled trial. *Lancet* 2002;360:965-70.
- Hannan EL, Racz MJ, Walford G, et al. Long-term outcomes of coronary-artery bypass grafting versus stent implantation. *N Engl J Med* 2005;352:2174-83.
- Babapulle MN, Joseph L, Bélisle P, Brophy JM, Eisenberg MJ. A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents. *Lancet* 2004;364:583-91.
- Hill RA, Dündar Y, Bakhai A, Dickson R, Walley T. Drug-eluting stents: An early systematic review to inform policy. *Eur Heart J* 2004;25:902-19.
- Serruys PW, Ong AT, Morice M-C, et al. Arterial Revascularization Therapies Study Part II – sirolimus-eluting stents for the treatment of patients with multivessel de novo coronary artery lesions. *EuroIntervention* 2005;1:147-56.
- Rodriguez AE, Grinfeld L, Fernandez-Pereira C, et al. Revascularization strategies of coronary multiple vessel disease in the drug eluting stent era: One year follow-up results of the ERACI III Trial. *Eurointervention* 2006;2:53-60.
- Bavry AA, Kumbhani DJ, Helton TJ, Borek PP, Mood GR, Bhatt DL. Late thrombosis of drug-eluting stents: A meta-analysis of randomized clinical trials. *Am J Med* 2006;119:1056-61.
- Camenzind E, Steg PG, Wijns W. [Hotline session II]. A meta-analysis of first generation drug eluting stent programs. World Congress of Cardiology 2006. Barcelona, September 2 to 5, 2006. (Abst)
- Stone GW, Moses JW, Ellis SG, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. *N Engl J Med* 2007;356:998-1008.
- Kaiser C, Brunner-La Rocca HP, Buser PT, et al; BASKET Investigators. Incremental cost-effectiveness of drug-eluting stents compared with a third-generation bare-metal stent in a real-world setting: Randomised Basel Stent Kosten Effektivitäts Trial (BASKET). *Lancet* 2005;366:921-9. (Erratum in 2005;366:2086).
- Lagerqvist B, James SK, Stenestrand U, Lindbäck J, Nilsson T, Wallentin L; SCAAR Study Group. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. *N Engl J Med* 2007;356:1009-19.
- Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. *N Engl J Med* 1996;335:217-25. (Erratum in 1997;336:147).
- Califf RM, Abdelmeguid AE, Kuntz RE, et al. Myonecrosis after revascularization procedures. *J Am Coll Cardiol* 1998;31:241-51.
- Cannon CP, Battler A, Brindis RG, et al. American College of Cardiology key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes. A report of the American College of Cardiology Task Force on Clinical Data Standards (Acute Coronary Syndromes Writing Committee). *J Am Coll Cardiol* 2001;38:2114-30.
- Smith SC Jr, Dove JT, Jacobs AK, et al; American College of Cardiology/American Heart Association task force on practice guidelines (Committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty); Society for Cardiac Angiography and Interventions. ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines)-executive summary: A report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty) endorsed by the Society for Cardiac Angiography and Interventions. ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines) – executive summary: A report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty) endorsed by the Society for Cardiac Angiography and Interventions. *Circulation* 2001;103:3019-41.
- Brophy JE, et al. An economic analysis of drug eluting coronary stents: A Quebec perspective. In: des AdEdTe, (AETMIS) MdlleS, eds. AETMIS. Quebec, 2004.
- Shrive FM, Manns BJ, Galbraith PD, Knudtson ML, Ghali WA; APPROACH Investigators. Economic evaluation of sirolimus-eluting stents. *CMAJ* 2005;172:345-51.
- Griffiths H, Bakhai A, West D, et al. Feasibility and cost of treatment with drug eluting stents of surgical candidates with multivessel coronary disease. *Eur J Cardiothorac Surg* 2004;26:528-34.
- Kereiakes DJ, Wang H, Popma JJ, et al. Periprocedural and late consequences of overlapping Cypher sirolimus-eluting stents: Pooled analysis of five clinical trials. *J Am Coll Cardiol* 2006;48:21-31.
- Pfisterer M, Brunner-La Rocca HP, Buser PT, et al; BASKET-LATE Investigators. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents: An observational study of drug-eluting versus bare-metal stents. *J Am Coll Cardiol* 2006;48:2584-91.
- Spertus JA, Kettelkamp R, Vance C, et al. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: Results from the PREMIER registry. *Circulation* 2006;113:2803-9.
- Cohen DJ, Bakhai A, Shi C, et al; SIRIUS Investigators. Cost-effectiveness of sirolimus-eluting stents for treatment of complex coronary stenoses: Results from the Sirolimus-Eluting Balloon Expandable Stent in the Treatment of Patients With De Novo Native Coronary Artery Lesions (SIRIUS) trial. *Circulation* 2004;110:508-14.
- Rinfret S, Cohen DJ, Tahami Monfared AA, Leloir J, Mireault J, Schampaert E. Cost effectiveness of the sirolimus-eluting stent in high-risk patients in Canada: An analysis from the C-SIRIUS trial. *Am J Cardiovasc Drugs* 2006;6:159-68.
- van Hout BA, Serruys PW, Lemos PA, et al. One year cost effectiveness of sirolimus eluting stents compared with bare metal stents in the treatment of single native de novo coronary lesions: An analysis from the RAVEL trial. *Heart* 2005;91:507-12.
- Bourassa MG, Yeh W, Holubkov R, Sopko G, Detre KM. Long-term outcome of patients with incomplete vs complete revascularization after multivessel PTCA. A report from the NHLBI PTCA Registry. *Eur Heart J* 1998;19:103-11.
- Hannan EL, Racz M, Holmes DR, et al. Impact of completeness of percutaneous coronary intervention revascularization on long-term outcomes in the stent era. *Circulation* 2006;113:2406-12.
- Mariani G, De Servi S, Dellavalle A, et al; ROSAI Study Group. Complete or incomplete percutaneous coronary revascularization in patients with unstable angina in stent era: Are early and one-year results different? *Catheter Cardiovasc Interv* 2001;54:448-53.
- Nikolsky E, Gruberg L, Patil CV, et al. Percutaneous coronary interventions in diabetic patients: Is complete revascularization important? *J Invasive Cardiol* 2004;16:102-6.
- van den Brand MJ, Rensing BJ, Morel MA, et al. The effect of completeness of revascularization on event-free survival at one year in the ARTS trial. *J Am Coll Cardiol* 2002;39:559-64.
- McLellan CS, Ghali WA, Labina M, et al; Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) Investigators. Association between completeness of percutaneous coronary revascularization and postprocedure outcomes. *Am Heart J* 2005;150:800-6.
- Danchin N, Juillière Y, Foley D, Serruys PW. Visual versus quantitative assessment of the severity of coronary artery stenoses: Can the angiographer's eye be reeducated? *Am Heart J* 1993;126:594-600.
- Kussmaul WG III, Popp RL, Norcini J. Accuracy and reproducibility of visual coronary stenosis estimates using information from multiple observers. *Clin Cardiol* 1992;15:154-62.
- Gottsauner-Wolf M, Sochor H, Moertl D, Gwechenberger M, Stockenhuber F, Probst P. Assessing coronary stenosis. Quantitative coronary angiography versus visual estimation from cine-film or pharmacological stress perfusion images. *Eur Heart J* 1996;17:1167-74.