The life and hard times of a coronary surgeon

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BS Goldman. The life and hard times of a coronary surgeon. *Can J Cardiol* 2007;23(3):183-188.

Coronary artery bypass is arguably the most extensively studied operation in surgical history. The technical advances and beneficial effects on symptoms and prognosis have been well documented over four decades. Percutaneous coronary interventions (PCIs) have also evolved through numerous modifications, and symptom relief has been substantiated; both modalities have been challenged by many randomized controlled trials. The rapid growth of PCIs has decreased coronary artery bypass volumes, and resulted in concerns about training, teaching, research, jobs and income. The most important concern, however, is the increasing 'off-label' application of PCIs with drug-eluting stents to a variety of untested coronary lesions. The randomized controlled trials studied a small fraction of those registered and excluded patients who are known to benefit from surgery and, thus, these studies were inherently biased. The results were then extrapolated to 'real-world' patients, who had been misinformed and misled about the performance and prognosis of coronary stents, as was later revealed in various registries. Hospitals should develop a collaborative revascularization strategy to provide patients and families with realistic alternatives.

Key Words: CABG; Coronary artery bypass; Drug-eluting stents; Intracoronary stents; PCI; Percutaneous coronary intervention; Randomized controlled trials

My surgical career essentially began with the first coronary artery bypass (CABG) in Toronto, Ontario, in 1969. Since then, cardiac surgeons have lived through 'the best of times and the worst of times'. My generation faced numerous challenges that required adaptation and change, including the initial skepticism of cardiologists, the early results of the first randomized controlled trials (RCTs), the advent of beta-blockers, as well as vein graft attrition and the introduction of angioplasty (percutaneous transluminal coronary angioplasty [PTCA]) in 1977. When CABG was accepted and case volumes soared, we encountered competition for increased resources, which was ultimately reconciled by increasing wait lists, patient deaths, media attention and political reaction. In the past decade, intracoronary stents and the rapid increase of interventional procedures (percutaneous coronary intervention [PCI]) have resulted in a sharp decline in the rates of CABG (Figure 1).

The increased application of PCI for coronary artery disease (CAD) has resulted in a 20% to 40% drop in CABG volumes in different constituencies (Figure 2).

Younger cardiac surgeons arguably face the most significant challenges today.

La vie et les difficultés d'un chirurgien cardiaque

Le pontage aortocoronarien est sans doute l'opération la plus étudiée de l'histoire chirurgicale. On en a bien documenté les progrès techniques et les effets bénéfiques sur les symptômes et le pronostic depuis 40 ans. Les interventions coronaires percutanées (ICP) ont également évolué et subi de multiples modifications, et on a étayé le soulagement des symptômes. Par ailleurs, de nombreux essais aléatoires et contrôlés ont remis en question ces deux modalités. La croissance rapide des ICP a réduit le volume des pontages aortocoronariens et a soulevé des préoccupations sur la formation, l'enseignement, la recherche, les emplois et les revenus. La principale préoccupation, toutefois, provient de l'application croissante dans une indication non autorisée des ICP en association avec des endoprothèses à élution de médicament pour diverses lésions coronariennes non évaluées. Les essais aléatoires et contrôlés ont porté sur une petite fraction de patients inscrits et exclus pour qui l'une opération est connue pour être bénéfique. Par conséquent, ces études étaient fondamentalement biaisées. Les résultats ont ensuite été extrapolés à des patients « du monde réel » qui avaient été mal informés et induits en erreur quant au rendement et au pronostic des endoprothèses coronariennes, comme l'ont ensuite indiqué divers registres. Les hôpitaux devraient établir une stratégie coopérative de revascularisation pour proposer des solutions réalistes aux patients et à leur famille.

The PCI versus CABG tipping point

If we examine factors that contributed to the PCI versus CABG tipping point, certain realities become evident: cardiac surgeons were too busy, too complacent, and too satisfied with case volumes and income to foresee the tremendous impact of PCI. Of necessity, surgeons had to provide a backup role for PCI complications and be sensitive to cardiology referrals. The surgical community failed to promote the worth of CABG, and the recognition of 20% to 30% restenosis rates for PTCA and bare metal stents implied uncritical acceptance. (Indeed, surgeons smugly assumed that this was potentially a source of later CABG referrals.) Cardiology assumed the 'gatekeeper' role for both diagnosis and intervention without consultation. The public has been conditioned to demand less invasive procedures, and the media popularized the notion of neurocognitive deficit ('pump head') from surgical trauma. The incremental positive changes in revascularization surgery (internal thoracic artery [ITA] to left anterior descending artery [LAD], bilateral ITA grafts, etc) were small and slowly adopted, in contrast to the dramatic and disruptive innovation of PCI, stents and especially drug-eluting stents (DES). PCI

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Received for publication November 24, 2006. Accepted December 29, 2006

Figure 1) Percutaneous coronary intervention (PCI) versus coronary artery bypass graft (CABG) in Ontario. Data at top obtained from the Cardiac Care Network database. Graph reproduced from *Can J Cardiol*

was further fuelled by a multibillion dollar industry with constantly changing technology and claims of lesser cost and resource benefits. This prompted a 'PCI frenzy' and 'DES euphoria', with calls to "put surgeons out of business" (1). Cardiac surgeons went from denial to despair and, in many instances, panic.

Accepted surgical concepts

The rapid shift in coronary revascularization to PCI is at variance with accepted concepts of CABG, which have determined patient care since the 1980s. These include proven durability and survival benefits, superiority of the left ITA-LAD (especially with high-grade proximal stenoses), bilateral ITA, complete revascularization, total arterial conduits, superiority in multivessel disease (MVD), left main stenosis, poor left ventricular function and diabetes – all at acceptable low peri-operative risk (2-4).

The impact of CABG on survival was defined in the 10-year overview of the results of seven RCTs reported in 1994 (5). CABG improved survival and symptoms, particularly in double- and triple-vessel disease, which resulted in greater benefits for severe symptoms, a positive exercise test or poor left ventricular function. The benefits of CABG were underestimated in the early trials because of the intention-to-treat principle, wherein 40% of the medical cohort had crossed over to CABG by 10 years. There was no survival benefit for CABG patients with single- or double-vessel disease and normal left ventricular function, although these are the very patients later included in nearly all subsequent RCTs.

Why has PCI surpassed CABG?

There is no argument about the effectiveness of PCI if applied appropriately; for example, in single- or double-vessel disease. Patients want less invasive treatment. They assume that PCI is as effective as CABG and that it provides a survival benefit, and they are not otherwise informed. Cardiologists accept the need for reintervention; however, they have based their decisions for PCI use on an inappropriate extrapolation of the many RCTs of PCI versus CABG. PCI has been applied almost indiscriminately to patients with complex MVD without evidence-based justification.

Figure 2) Rise and fall of coronary artery bypass (CABG). Yearly number of isolated CABG procedures divided by the yearly number of sites reporting to the Society of Thoracic Surgeons (STS) database (unpublished data)

Disclosure and conflict

At this point, I need to disclose a personal conflict: I have had intracoronary stents successfully deployed for isolated lesions in the proximal right and midcircumflex coronary arteries, with documented patency at two years. Thus, I have personally benefited from stent technology and am grateful for the skills of my colleagues. However, while I respect, admire and have supported interventional cardiology since the introduction of PTCA, I have become disappointed and disillusioned with the direction of PCI and the attitudes and approach of many interventionalists in the treatment of MVD. There are real concerns in the surgical community about overuse, with ultimately higher costs than CABG. The rapid decline in CABG volumes and increasing patient risk profile have negatively affected surgical outcomes, training, teaching and research, as well as income, recruitment and job opportunities. This has resulted in poor morale and pessimism in surgical teams. Cardiac surgical journals have been replete with editorials, lamenting these concerns and the larger issues of adaptation with the need for change and innovation (6).

The real problem

The most significant issue, however, remains cardiology's reliance on the multitude of coronary intervention trials. Taggart (7) articulated the problem best: "the biggest threat to patient care is the increasingly inappropriate (nonevidence-based) use of PCI, rather than CABG, in patients with MVD and left main coronary disease, which not only denies the patient the most effective treatment, but the prognostic benefits of surgery".

Taggart's review is based on a detailed analysis of the major RCTs of PCI versus CABG in MVD and documents the fallacy of the conclusions that have been used by cardiologists to justify intervention. Figure 3 compares the demographics of patients enrolled in the 15 major trials with the CABG population in Ontario in 2005. This illustrates the major differences in patients encountered in surgical practice today versus the summary of the highly selected patient profiles in the RCTs.

As well, late results are often different than trial results. The early results of the Arterial Revascularization Therapies Study (ARTS [8]) revealed the one- and five-year death rates

Trial	Patients, n	Population, %	Stent	Left main, %	Triple-vessel disease, %	Proximal LAD, %	EF >50%	Diabetes mellitus, %	IMA, %
RITA	1011	4	—	0	12	—	—	6	74
ERACI	127	9	—	0	45	—	100	11	75
LAUSANNE	134	3	—	0	0	100	—	12	100
GABI	359	4	—	0	18	—	—	10	37
EAST	392	4	—	0	40	70	100	25	—
CABRI	1054	3	—	0	40	—	100	12	75
MASS	142	69	—	0	—	100	100	21	100
BARI	1829	12	—	0	41	36	100	24	80
TOULOUSE	152	3	—	0	29	—	—	14	58
SIMA	121	—	—	0	—	100	100	11	100
ERACI II	450	2	+	0	56	—	—	17	88
AWESOME	454	—	+	0	45	—	—	—	70
MASS II	408	2	+	0	41	—	—	—	—
ARTS	1205	25	+	0	32	—	100	19	93
SoS	988	25	+	0	38	45	100	14	81
Summary	8826	5	0	0	35	41	100	16	79
CABG				30	>60	90	15	40	90

Figure 3) Patient demographics in 15 randomized controlled trials compared with the 2005 coronary artery bypass graft (CABG) population in Ontario (reproduced from reference 31). Reproduced with permission from reference 7. The green boxes represent the summary of all trials, the red boxes represent Ontario data and the yellow boxes represent those trials that involved percutaneous coronary intervention with stents. ARTS Arterial Revascularization Therapies Study; AWESOME Angina With Extremely Serious Operative Mortality Evaluation; BARI Bypass Angioplasty Revascularization Investigation; CABRI Coronary Angioplasty versus Bypass Revascularization Investigation; EAST Emory Angioplasty versus Surgery Trial; EF Ejection fraction; ERACI Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty Versus Coronary Artery Bypass Surgery in Multivessel Disease; GABI German Angioplasty versus Bypass surgery Investigation; IMA Internal mammary artery; LAD Left anterior descending artery; MASS Medicine, Angioplasty or Surgery Study; SIMA Stenting versus Internal Mammary Artery; RITA Randomised Intervention Treatment of Angina; SoS Stent or Surgery

to be equal for stent versus CABG (2.5% versus 2.5%), but these were different in the Stent or Surgery (SoS) trial (9) in favour of CABG at year one (2.6% versus 0.8%). The five-year mortality in the SoS trial has recently been presented (unpublished data) and shows a striking difference, in favour of coronary bypass (6.6% versus 10.9%, $P=0.016$), although the industry-sponsored trial has not yet made this available for publication. Also in ARTS, 208 patients with diabetes had a marked increase in both death (13% versus 8%) and revascularization rates (43% versus 10%) for stents versus CABG. This was not emphasized in the early results.

A systematic review of the current and available literature (10-12) allowed me to put forward the following observations about the randomized trials of PCI versus CABG (Table 1).

Real-world registries reflect current clinical practice and significant differences from the RCTs. Brenner et al (13) analyzed the Cleveland Clinic experience from January 1, 1995, to December 31, 1999, which included 6033 patients with MVD who underwent PCI ($n=872$) or CABG ($n=5161$) according to their physicians' or their own preference. Although the early mortality was similar, the risk profile was significantly worse in the surgical candidates, and five years later, PCI was associated with an increased risk of death (propensity-adjusted hazard ratio 2.3, 95% CI 1.9 to 2.9, $P<0.0001$). The New York state cardiac registry reported by Hannan et al (14) followed 32,202 patients with MVD who underwent CABG and 22,102 patients who underwent PCI between January 1, 1997, and December 31, 2000. Although the preoperative risk profile was considerably higher in the CABG patients, the adjusted

TABLE 1
General comments on randomized trials of percutaneous coronary intervention (PCI) versus coronary artery bypass (CABG)

- Only a small portion of screened patients (fewer than 5%) are actually randomly assigned
- Trial results are generalized to all patients despite marked differences in risk profiles
- Trials are often underpowered to define significant outcomes
- Lesion sets for PCI in trials are ideal and exclude complex disease
- Rates of major adverse cardiac events are consistently higher for PCI despite ideal lesions, especially in diabetics
- CABG benefit is consistently better in sicker patients
- Changing technology means that trial results are often obsolete, but are applied as justification for current therapy
- Adverse events may appear late after trial completion and are not included
- Trials are inherently biased against prognostic benefits of CABG

three-year survival was better for those with double-vessel disease without LAD involvement (93.3% versus 91.4%), double-vessel disease with proximal LAD involvement (92.1% versus 89.8%) and triple-vessel disease with proximal LAD involvement (89.3% versus 84.4%). Although they were not randomized studies, they do reflect outcomes in current populations. The propensity-score analysis methodology using high numbers of patients is at marked contrast to the randomized trials using small numbers.

Patrick Serruys, arguably the most important PCI proponent in the various RCTs and well respected in cardiology, published the late outcomes after stenting or CABG for MVD as a matched-propensity controlled cohort study in his own centre (15). Absolute survival at eight years was significantly better for CABG than PCI patients (87% versus 82%, $P<0.02$), as was event-free survival (78% versus 64%, $P<0.001$). After adjusting, stenting was an independent predictor of high mortality. Serruys concluded that "in this matched cohort study with an eight-year follow-up, survival was better and less repeat revascularization needed among patients undergoing elective CABG for treatment of MVD compared with the stent group". Nonetheless, the published guidelines for percutaneous interventions of the American College of Cardiology/American Heart Association (16), the European Society of Cardiology (17) and the British Cardiac Society (18) each, in effect, recommend that almost all patients may be treated by PCI, despite having MVD, without discussing or offering the patient the option of CABG (7).

Concerns about PCI today

Extrapolating the role of PCI in single- and double-vessel disease to current patients with multivessel and left main CAD implies a failure to accept or understand the limitations of the RCTs versus real-world patients. The success of primary intervention as rescue therapy for acute myocardial infarction has been extended to 'culprit vessel' angioplasty for unstable patients with MVD. This may well be appropriate for the acutely ill patient presenting with a stenotic vessel serving a significant area of ischemic myocardium or providing important collaterals. However, the 'culprit vessel' philosophy in stable patients with MVD, with subsequent staged interventions, is at odds with the symptomatic and prognostic benefits of

TABLE 2
Percutaneous coronary intervention (PCI) reality

- PCI has become default therapy for multivessel disease, diabetes and left main stenosis in many centres.
- PCI has generally been applied to 'suitable' left main lesions (ostial or midshaft), whereas CABG can bypass any pathology.
- PCI for these suitable left main lesions carries an early 6% and a one-year 17% mortality, with significant risk and complications by 18 months, even with drug-eluting stents (21,22).
- PCI is not associated with less risk of myocardial infarction; there is a reported 10% incidence of significant troponin rise with each intervention (7).
- Repeat PCI results in decreasing left ventricular function as shown by cardiac magnetic resonance imaging, with 5% muscle loss with each intervention resulting in poor candidates for ultimate CABG (7).
- Restenosis rates in diabetes are still problematic – at 10% to 25% (23).
- PCI does not decrease the risk of cerebral injury relative to CABG; cognitive function at one and five years are equal in the Bypass Angioplasty Revascularization Investigation (BARI) (25) and Stent or Surgery (SoS) trials (7).
- There are no data on diffuse disease, long lesions, complex lesions, bifurcations or total chronic occlusions.
- Drug-eluting stenting does not abolish restenosis, with a 10% to 30% incidence, especially in small vessels, long lesions, complex lesions, bifurcations, with edge-narrowing or late incomplete apposition (12,20).
- There are no long-term data on various deployment techniques (ie, crush, kiss or overlap methods).
- Drug-eluting stenting may be associated with late stent thrombosis, cardiac death or myocardial infarction, 4.9% versus 1.3% for bare metal stenting, with a cumulative incidence of 0.6% per year. Camenzind et al (24) summarized all randomized studies to the latest available follow-up at the time of the World Congress of Cardiology meeting in September 2006 and showed a 6.3% rate of death or Q wave myocardial infarction for drug-eluting stenting versus 3.9% for bare metal stenting ($P=0.03$) after discontinuance of antiplatelet therapy.
- The duration of clopidogrel use is uncertain, with significant problems of compliance, cost and possible hypersensitivity reactions (19).
- A response to injury or delayed inflammatory response may precipitate accelerated atherosclerosis or a late catch-up effect, with more extensive coronary disease (25).

CABG Coronary artery bypass

complete revascularization offered by surgery. For patients undergoing diagnostic angiography who are given a loading dose of clopidogrel (600 mg) before identification of CAD and its extent, there is an implied presupposition of ad hoc interventional therapy. This is now performed in up to 60% of patients on the same day, and usually without consultation to the referring cardiologist, let alone a surgical colleague. Cardiologists who perform diagnostic angiography are upset at 'losing' their patients to the interventionists. The lack of truly informed consent, with all options provided, denies the patient a rational and reasonable discussion. In addition, there is apparently no uniform revascularization strategy within a given group of interventionists or institution. The focus on 'fixing the vessel' and accepting procedural success often denies patients with MVD the benefit of a durable procedure with better prognostic outcome (ie, CABG). In this rapidly changing field, there is clearly over-reliance on new devices, heavily influenced by industry, with a regrettable tendency to dismiss earlier results as 'old technology'. There is a lack of a

concurrent PCI database and, thus, limited accountability, compared with the precise and public documentation of results in cardiac surgery. This is compounded by a diffusion of responsibility through an interventional team approach with sequential operators and variable follow-up. Ultimately, the cost of repeat angiography and repeat revascularization is significant and often higher than cardiac surgery, thereby negating any initial cost benefit.

The apparent cavalier approach of many interventionists and some of the disturbing results regarding late stent thrombosis presented at the recent World Congress of Cardiology in Barcelona, Spain, in September 2006 have prompted vigorous physician and media response, as well as the predicted drop in share prices of the major stent manufacturers.

As clinicians we seem to have lost our clinical judgment, let alone our ability to view data and evidence...the whole field of angioplasty has been led astray by a preoccupation with re-stenosis, which study after study has shown no prognostic value. We are chasing problems that are iatrogenic that naturally would not exist in people. It is time to stop and re-evaluate...an epidemic of madness over the misuse of PCI for stable angina in general and drug eluting stents specifically. (Salim Yusuf, personal communication)

PCI reality

Current literature provides evidence that PCI applied to patients in current practice has results and implications considerably different than those actually presented to patients or derived from the many RCTs. At present, more than 75% of patients receive a DES due to evidence supporting its efficacy over bare metal stents, but "consistent with a recurring theme in interventional cardiology...the off-label indications out-paced the supporting evidence" (19,20). Some concerns are summarized in Table 2 (7,12,19-25).

No rational person can deny the beneficial effects of PCI nor the future for stent technology with the potential for new drug-eluting capacity-containing genes, anticoagulants or antibodies, with biodegradable or flexible stents and new polymers emerging. Certainly new data will emerge from the Synergy Between PCI and TAXUS and Cardiac Surgery (SYNTAX), Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) and other trials of PCI in left main and MVD and in patients with diabetes mellitus. The issues are those of appropriateness, communication and collaboration.

What can cardiac surgeons do?

It is essential that the cardiac surgical community promotes the worth of the modern coronary bypass procedure. Despite the increasing risk profile and comorbidities, the overall unadjusted risk for coronary surgery remains less than 2% in both the Society of Thoracic Surgeons database and in Ontario (26). Nonetheless, to be competitive, CABG must be less traumatic, more efficient, less costly, more durable and require fewer reinterventions. It is necessary to challenge our cardiology colleagues at every opportunity regarding the benefits of complete revascularization, the potential for aggressive endarterectomy in diffusely diseased vessels, the impact of total arterial conduits on graft patency and the predictable, consistent results of the coronary bypass operation over many years.

Is off-pump CABG (OPCAB) the answer? Does it satisfy the three most important questions: is it truly a minimally invasive option for surgical revascularization? Does it have better outcomes than conventional on-pump CABG? And can it be performed equally well by most cardiac surgeons? OPCAB numbers remain stable in Canada – at approximately 20% of cases – performed in greater numbers by a small cohort (less than 10%) of Canadian surgeons (unpublished data). There is still reluctance, resistance, skepticism and concern regarding anesthesia support, incomplete revascularization and graft patency. There is uncertainty regarding the true value of OPCAB versus its public (ie, market) appeal. Without greater numbers of OPCAB procedures being performed, there is no direct mentorship or teaching of young surgeons. In the hands of committed and experienced surgeons, OPCAB provides results equal to those of conventional surgery, and perhaps the beneficial sequelae of a less traumatic procedure, ie, less transfusion, early extubation and shorter hospital stay (27,28). Nonetheless, a meta-analysis of 37 randomized trials did not show significant differences for 30-day mortality or myocardial infarction, having inconclusive results regarding patency and cognitive disorders (29). In a recent propensity-matched cohort of conventional CABG versus OPCAB in octogenarians, Nagpal et al (30), from two experienced OPCAB centres in Canada, showed only a benefit in neurological dysfunction (2.3% versus 10.5%, $P=0.01$) and shorter intubation time (5.3% versus 13.3%, $P=0.04$). However, just as stent technology will certainly improve, there are many centres in Canada at the leading edge of less invasive coronary surgery through a traditional minimally invasive direct CABG, or small thoracotomy, for single- or multivessel disease, or endoscopic coronary bypass and a totally endoscopic coronary artery bypass. Whether these unique procedures will become commonplace and emerge as part of a hybrid procedure in a mixed-use cardiac catheterization laboratory is uncertain. In an ideal world, a stent applied to a type A lesion in the proximal right coronary artery or circumflex artery accompanied by a left ITA-LAD bypass remains the optimal scenario for patients with MVD.

CONCLUSIONS

Until such time as the most appropriate procedures for MVD are defined, it is incumbent on the leaders in cardiac surgery, that is, the Canadian Society of Cardiac Surgeons, to reverse the negativity and pessimism in our field, and revitalize the image of cardiac surgery in our hospitals and university residency programs. It is necessary to redefine the parameters of cardiac surgery training and practice by incorporating catheter-based and endovascular techniques, thereby changing the nature of our efforts to less invasive modalities. We should encourage the development of mixed-use cardiac catheterization laboratories in our hospitals. We should also insist on an institutional revascularization strategy based on a collaborative understanding of the RCTs and the results of real-world registries – a revascularization strategy that is communicated to patients, families and referring physicians. Cardiac surgeons should challenge cardiology, not just at combined rounds, but in continued medical education, as well as at major meetings, and sponsor open debates on PCI versus CABG. The Canadian Society of Cardiac Surgeons should, through the Canadian Cardiovascular Society, promote a large, accessible and transparent CABG and PCI database that is available to all physicians. Finally, we should publish guidelines in the public domain for appropriate revascularization techniques for the different presentations and extent of CAD to assist patients and families in reaching an informed decision.

ACKNOWLEDGEMENTS: The author expresses his appreciation to Dr David Taggart (Oxford, United Kingdom) for permission to use material from his superb Ferguson Lecture at the 42nd Annual Meeting of the Society for Thoracic Surgeons in Chicago, USA, in January 2006 and to Dr Salim Yusuf (Hamilton, Ontario) for his generosity in providing material from his 2006 Barcelona (Spain) and other presentations. This paper is The Wilfred Gordon Bigelow Lecture, which was presented at the Canadian Society of Cardiac Surgeons, Canadian Cardiovascular Congress, October 24, 2006, in Vancouver, British Columbia.

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