Invited paper

Status of percutaneous coronary intervention and coronary artery bypass

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Summary

At present a rapid and profound change in myocardial revascularization has evolved from the work of Gruentzig. The recent technological advances have been so fast paced that there has not been ample time to fully assess each new facet of technology and pharmaceutics before another arrives. The interface between percutaneous intervention (PCI) and coronary artery bypass (CAB) is not well defined as previously so that continental, national and regional differences exist. The progress in PCI from balloon angioplasty to drug eluting stents has seen a progressive decline in restenosis and reintervention but relief of symptoms has not equaled that attained with CAB. Survival benefit for CAB over PCI has not been demonstrated in the many randomized clinical trials which are limited by selection of only 5—12% of potential patients so that higher risk patients and those with more extensive and complex coronary disease are excluded. These excluded patients are included in the registries where survival benefit for CAB over PCI is clearly evident. Situations less amenable to PCI include: left main disease; three vessel disease; vessels that are smaller, diffusely diseased or with distal lesions which are frequently associated with diabetes; ostial and bifurcation lesions; and coronary arteries that are tortuous, calcified or with very long lesions. It is in these situations that PCI does not provide revascularization equivalent to CAB. Surgeons must appreciate the success of PCI, acknowledge their reduced role in revascularization and strive to provide the best operation possible when the clinical situation demands it.

Keywords: Coronary artery disease; Coronary artery bypass; Percutaneous coronary intervention; Coronary stenting

1. Introduction

In his Honored Guest Lecture Loop reviewed the initial three decades of myocardial revascularization [1]. We are now well into the fourth decade which has witnessed the successful evolution of percutaneous coronary intervention (PCI) from balloon angioplasty (BA), to bare-metal stents (BMS), and now drug-eluting stents (DES), and the concurrent decline in the need for surgical revascularization. It is the purpose of this report to briefly review these trends and evidence supporting them.

2. Coronary artery bypass and medical therapy

In the first decade three randomized controlled trials (RCT) were initiated to compare coronary artery bypass (CAB) with medical treatment. The Veterans Administration Coronary Artery Bypass Surgery Cooperative Study (VA study), included only males and demonstrated improved 5-year survival for left main stenosis treated with CAB as did the other two RCT’s [2]. The European Coronary Surgery Study (ECSS), was the only one to show a significant overall survival advantage for surgery at 5 years, which persisted 12 years, although the other two showed similar trends [3]. The Coronary Artery Surgery Study (CASS), along with the other two, showed greater freedom from angina with surgery at 5 years, but this was lost at 10 years in CASS [4], but not in ECSS. Meta-analysis of these three trials and several smaller ones showed surgical survival benefit for patients with two-and three-vessel disease and even single-vessel disease that included a proximal left anterior descending (LAD) stenosis, with or without abnormal left ventricular function [5].

3. Coronary artery bypass and balloon angioplasty

Coronary balloon angioplasty was introduced by Gruentzig et al. [6] in 1977 and led to 13 RCT’s comparing CAB with BA [7]. Meta-analysis revealed survival at 1 and 3 years was better, but not significantly so, with CAB. Repeat revascularization was more frequent after BA. Neither CAB nor BA
provided significant advantage for preventing nonfatal myocardial infarction (MI). These trials of CAB versus medical therapy and BA are primarily of historical interest, but nevertheless pertinent because the debate over the value of stenting versus medical therapy is ongoing (vide infra).

4. Medical therapy and balloon angioplasty

Meta-analysis of four RCT’s from 1979 to 1998 comparing medical therapy and BA revealed that the only outcome measure favoring BA was angina relief while the endpoints of death, MI and the need for repeat PCI were not significantly affected [8]. The need for subsequent CAB was nearly 60% less likely in medically treated patients. Seven-year results of the Second Randomized Intervention Treatment of Angina (RITA-II) trial comparing BA with medical therapy in 1018 patients suitable for either strategy revealed BA did not influence the risk of death or MI but improved angina and exercise tolerance [9].

5. Coronary artery bypass and bare-metal stents

Meta-analysis of RCT’s with patients having multivessel disease found similar survival for CAB and BMS at 3 years despite a reduction in operative mortality from 5.2% in trials without stents to 3.5% in stent trials [7]. Stenting provided a significant reduction in nonfatal MI compared to CAB. Although subsequent revascularization was more frequent after stenting, it was almost 50% less than observed in RCT’s of BA and CAB [7]. Meta-analysis of individual patient data from four RCT’s, which provides more reliable treatment effect estimates, gave similar results [10].

A large observational study from New York cardiac registry analyzed 59,000 patients with multivessel disease receiving CAB or BMS [11]. Risk-adjusted survival was greater for CAB than for stent placement in all anatomic subgroups studied at 3 years. Revascularization was required in 35.1% after stenting and 4.9% after CAB with the former being nearly twice that reported in the RCT’s above [7,10].

Eight-year follow-up of CAB or PCI with BMS in a single center, propensity-matched, controlled cohort study revealed significantly better survival, event-free survival and freedom from revascularization with CAB [12]. However, almost all of the survival benefit for CAB was due to patients with left main (LM) disease who received BMS. Propensity analysis of 6033 patients having CAB (5161) or PCI (872 with 70% receiving BMS) revealed 1- and 5-year unadjusted mortality of 5% and 16% for PCI and 4% and 14% for CAB; PCI was associated with an increased risk of death (propensity-adjusted hazard ratio, 2.3; \( p < 0.001 \)) [13]. Perioperative mortality was 1.1% despite 50% of CAB patients having diabetes or an ejection fraction of 30% or less.

6. Medical therapy, bare-metal stenting and coronary bypass

In the current era of improved medical treatment over that of the 1970s, ongoing trials are needed. In a single institutional study (MASS II), 611 patients with stable angina and multivessel disease were randomized to medical therapy, PCI or CAB [14]. One-year mortality was significantly lower in the medical therapy group (1.5%) versus PCI (4.5%) and CAB (4.0%). Q-wave MI rates at 1 year were higher after PCI (8.3%), lowest after CAB (2.0%) and intermediate in the medical therapy group (5.0%). Rates of event-free survival (freedom from cardiac death, MI or refractory angina requiring revascularization) were significantly different (\( p < 0.0001 \)) among the three groups: CAB, 93%, medical therapy, 88% and PCI, 76%. Freedom from angina at 1 year was significantly greater after CAB (61%) compared with medical therapy (36%), but was not different from PCI (55%). The need for subsequent revascularization was significantly greater after PCI than for the other modalities.

In a single institution 15-year registry of patients with CAD survival advantage was provided by PCI or CAB over medical therapy and following the introduction of stenting (1996) CAB gave a significant and increasing survival advantage for high-severity CAD [15].

7. Bare-metal and drug-eluting stents

Coating stents with antimitotic drugs will inhibit intimal hyperplasia, which is the principal cause of restenosis. Sirolimus and paclitaxel are the two commonly used agents; the latter is used directly on metal or bound to a polymer coating of the stent which acts as a reservoir for sustained release. Meta-analysis of 11 randomized trials of 5103 patients compared paclitaxel (PES) or sirolimus (SES) eluting stents to BMS with clinical follow-up of 6–12 months [16]. Mortality and MI rates were low and similar for DES and BMS. The rate of major adverse cardiac events (MACE) of death, MI or target vessel revascularization was 7.8% with DES and 16.4% with BMS and the angiographic restenosis rate was also lower for DES (8.9% and 29.3%). DES were not associated with higher rates of edge restenosis, stent thrombosis or late incomplete stent apposition. However, registry rates of restenosis, which reflect real practice in contrast to highly selective RCT’s containing low-risk patients, are 10—20% in more complex lesions [17,18] and as high as 28% in bifurcation lesions [19].

Stent thrombosis in a meta-analysis of 10 randomized studies comparing DES and BMS occurred at a rate of about 0.6%, which did not differ between sirolimus and paclitaxel DES [20]. A single institution study of 2006 patients equally divided between PES and SES and followed a mean of 1.5 years revealed a 0.35% incidence of stent thrombosis with 3/8 occurring while on no antiplatelet therapy and 5/8 after cessation of clopidogrel, but with continuation of aspirin [21]. Not only is there risk of late thrombosis of DES when clopidogrel is stopped but we are aware of early thrombosis for the same reason when patient noncompliance, non-comprehension or economic circumstances precluded this therapy. It is apparent that before DES implantation these issues must be resolved.

Despite the reduction in restenosis by DES there has been no associated survival advantage at this early interval. This is not a total surprise since post-procedure angiographic studies have shown that coronary events after stenting are often unrelated to stent restenosis but represent disease
progression elsewhere in stented vessels or in nonstented coronaries [22].

8. Drug-eluting stents and coronary artery bypass

One small case matched study of 113 pairs compared SES and CAB in multivessel disease patients [23]. All LAD lesions received SES in the PCI group as well as 32/63 right coronary lesions and 53/78 circumflex lesions. BMS were used in 25 right coronary and 16 circumflex arteries which were tortuous or calcified and BA was used in four and nine respectively for arteries smaller than 2.25 mm or in patients with focal in-stent restenosis. CAB patients received bilateral ITA grafts to the left coronary circulation. One-year reintervention free survival in the CAB group was significantly better in the PCI group (96% vs. 86.6%, \( p = 0.005 \) log-rank test).

9. Revascularization in diabetes

In diabetics CAB was associated with improved survival and reduced revascularization rates compared to BA in the Bypass Angioplasty Revascularization Investigation (BARI) trial at 7 years [24] and in the EAST trial at 8 years [25]. Similar results were obtained from a large observational database [26]. Use of BMS in the ARTS trial achieved survival equal to CAB in diabetics, but the revascularization rate remained significantly higher (22.3% vs 3.1%, \( p < 0.001 \)) at 1 year [27]. In BARI diabetic patients who sustained an MI in follow-up had a much lower mortality if initial treatment was CAB [28].

Randomized comparison of SES with BMS (SIRIUS) in 279 diabetics revealed a reduction in target lesion revascularization from 22.3% with BMS to 6.9% with SES (\( p = 0.001 \)) and a reduction in MACE from 25% to 9.2% [29]. Randomized comparison of PES and BMS (TAXUS) in 250 diabetic patients identified reduced restenosis with PES which was unrelated to diabetes whereas diabetes was a risk factor for restenosis with BMS [30].

However, SIRIUS [29] and also TAXUS [30] have been criticized as being under-powered to establish superiority of DES over BMS and both studies used thick-strut stents, known to have high restenosis rates, as controls [31]. At this time, although DES appear promising, it is not established that they lead to better outcomes than well-designed thin-strut BMS in diabetic patients. Further studies are needed to demonstrate any advantage of medicated stents over CAB in the diabetic with multivessel disease [32,33].

10. Completeness of revascularization

Complete revascularization was achieved in 84.1% of patients assigned to surgery and 70.5% of those assigned to PCI in the ARTS trial despite enrollment based on equivalent revascularization with either strategy [34]. Incomplete revascularization was associated with a five-fold increase in surgical revascularization at 1 year in the PCI patients, but in those initially treated with CAB there was no increase in revascularization [34]. In BARI and Coronary Angioplasty versus Bypass Revascularization Investigation (CABRI), similar 1-year outcomes were obtained when equivalent revascularization was not a condition of enrollment [35,36].

Analysis of the surgical arm (both randomized and registry) of BARI, using four definitions of complete revascularization, revealed no survival advantage at 7 years for traditional or functional complete revascularization compared to incomplete revascularization [37]. Thus, PCI is more frequently associated with incomplete revascularization than is CAB and the latter is effective when one graft is placed to each major diseased artery system. Placement of more than one anastomosis to any system other than the LAD confers no long-term advantage and may be deleterious [37].

11. Left anterior descending artery disease

Although PCI has been frequently used for left anterior descending (LAD) disease for many years, some have continued to believe that success of bypass with the in situ left internal thoracic artery (ITA) with a 97.2% patency at 15 years, remains a compelling alternative [38]. Two randomized trials indicate similar results with either strategy, but with greater target vessel revascularization after PCI with BMS at 6 months and more angina and the need for antianginal medication at 3 years [39,40].

In the SIRIUS trial 138 patients with proximal LAD stenosis were randomized to receive SES or BMS and had 1-year clinical and 8-month angiographic follow-up [41]. In-stent restenosis did not occur with SES and was 38% in BMS and MACE was 10.4% and 20.6%, respectively.

12. Left main disease

Long considered to be only a surgical disease there has been increasing use of PCI, usually with DES, for management of left main (LM) disease and particularly for isolated LM where greater than 50% of patients are now receiving PCI [42]. Comparison of SES and BMS for LM disease in two successive patient groups revealed that the DES group received more direct stenting, had fewer debulking atherectomies, had more stents placed, more segments stented, and more bifurcation stenting [43]. There was no death, stent thrombosis, Q-wave MI, or emergency CAB in either group. SES had less late lumen loss (\( p < 0.0001 \)) and a lower 6-month restenosis rate versus BMS. At 12 months freedom from death, MI, and target lesion revascularization was 98.0% in the DES group and 81.4% in the BMS group (\( p < 0.0003 \)) [43].

13. The view today

The snapshot of current practice in myocardial revascularization provided by run-in phase data from the SYNTAX study reveals that 60% (274/459) of patients with isolated LM disease and 9% (153/1645) of those with left LM and three-vessel disease received PCI and the others CAB [42]. The success of PCI for LM disease, despite the long-standing fear
of approaching this critical vessel segment, unless protected, is not surprising considering the greater size, short lesion length and high flow. There were important differences between European and North American sites with PCI more prevalent in Europe for three-vessel disease (30% vs 17%) and LM disease (26% vs 21%) [42]. Within Europe there are differences between countries: CAB for LM disease is lowest in the Netherlands (59%) and highest in Belgium (87%); for three-vessel disease CAB is lowest in France (42%) and highest in the United Kingdom (90%) [42].

This evolution of myocardial revascularization on two continents reveals acceleration of the pendulum toward PCI in Europe. Surgeons’ concern that longer (71-year or 10) follow-up is requisite to assess new techniques is moot in the face of a continuous stream of technological advances, each apparently superseding the previous. The many RCT’s of PCI versus medical therapy and CAB do not provide evidence of benefit from stenting in terms of the hard endpoints of death, MI and reintervention which is recognized by cardiologists [8,31,33,44–50] and surgeons [51]. Furthermore, RCT’s represent only 5–12% of all patients under going revascularization at participating centers [52,53] whereas large registries (59,000 patients) are not under powered and demonstrate survival advantage after only three years for CAB over BMS in all anatomic subgroups of two or three vessel disease after risk adjustment [11]. However, it is common to hear that the next iteration (DES) will provide this, which has not yet been proven despite a reduction in in-stent restenosis [16]. Perhaps the multinational SYNTAX [42] trial in more than 100 centers, the COMBAT trial in Seoul which will compare PES and CAB and the National Institutes of Health sponsored FREEDOM trial which will compare SES and CAB in diabetics will provide further guidelines to optimal revascularization.

14. The surgical position

Although the surgeon’s role in the management of CAB has declined there will be a continued need for CAB, which could as well be greater than at present, based on the information presented. It is critically important that we strive to provide the best possible operation in terms of safety, outcome and cost effectiveness. We are advantaged by vast experience in coronary surgery that exists today with declining operative mortality and morbidity [13]. Most importantly, we have more than a 20-year follow-up of patients having many of the bypass procedures currently used. Thus, we now know which techniques work best and how conduits behave. We have developed small incisions, off-pump procedures, port access and robotic techniques, which will continue to be refined to reduce the invasiveness of CAB.

15. The best operation

It is proven that the left ITA grafted to the LAD is the most important maneuver in CAB surgery [1]. It is likely that survival to 20 years is improved by using both ITA’s rather than one, but not supported by RCT’s [54–56]. Placing both ITA’s to the left side of the heart is advantageous over placing the right to the right side in most patients [55,57].

It may be that lack of evidence from RCT’s comparing one and two ITA grafts deters some surgeons from the bilateral strategy as in the United Kingdom [56]. Lacking that evidence, there is strong support from the third of the three principles of the survival impact of CAB from the first generation RCT’s (VA Study, ECS, CASS): (1) the amount of potential survival benefit was roughly proportional to the patient’s risk of death from the next coronary event, whether estimated using clinical, angiographic or physiologic variables; (2) revascularization is not a treatment for atherosclerosis, but a means of reducing the impact of later disease progression; (3) and benefit lasts only as long as the grafts (and stents) remain open [58].

There is a mountain of evidence documenting the vastly superior patency of the ITA (both right and left) over vein grafts [38,55,59,60]. What is lacking is our determination to use both ITA’s more frequently.

Beyond bilateral ITA grafting lies all arterial revascularization which can be achieved with three in situ grafts (by adding the gastroepiploic artery) or by using two in situ conduits and the radial artery (RA) which can be attached to the aorta or to an in situ arterial conduit. Also using only two conduits is feasible with one in situ and one as a T-graft [61,62]; although this is technically more demanding and flow capacity has been questioned [63–65]. All arterial grafting is intuitively appropriate because of the success of one and two ITA’s but survival benefit has not been proven and it will be difficult to do so. However, conduit performance is the greatest prognostic predictor following CAB and continued patency will favorably impact on MI and revascularization [1,58].

Arguments against using both ITA’s include operating time and sternal infection. Skeletonization of both ITA’s, or at least the right, probably reduces sternal wound complications and provides a longer conduit [66]. The GEA is not so predictable regarding size and freedom from arteriosclerosis but is favored by some despite patency which is similar to vein [67]. The RA is more consistently available in 90% of patients, longer and easier to handle than other conduits and will reach any site but must be used in the presence of more than 70–80% stenosis to achieve acceptable patency [68]. When so used patency was nearly 87% at 10 years [69]. All arterial revascularization can be achieved with an operative mortality of 0.8–3.0% in selected patients [61,62,70–74]. Why have we failed to use bilateral ITA grafts in more than 12% of patients [42]? Is this surgical inertia (laziness) or lack of conviction? In France bilateral ITA use is 39% which is impressive but not enough [42]. Does this reflect surgical desire to do a better job in the face of increasing competition or is it the realization cited above, that conduit patency is the bottom line, or both? When given the baton of CAB we must run with the best operation available. It is defined by using conduits which will perform the best in an operation of low mortality, morbidity and cost. It is in our best interest and that of the patient to safely provide the most durable grafts to all appropriate targets. Let’s not be slackers!

References


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