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The Evolution of PCI and CABG

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Executive Summary

Coronary artery bypass grafting (CABG) remains the gold standard for the treatment of multivessel coronary artery disease. While CABG has continued to evolve, percutaneous coronary intervention (PCI) has also had major advancements in recent years, particularly with drug-eluting stents (DES) and techniques for treating chronic total occlusions, elevating it to a viable alternative to surgery in patients with multivessel disease. Still, data comparing these two modalities in modern times is lacking. The non-randomized ARTS II (Arterial Revascularization Therapy Study II) suggests similar rates of survival from major adverse coronary and cerebrovascular events with DES compared to CABG out to three years follow-up. In addition, rates of repeat revascularization with DES are approaching those of CABG, even in high-risk subsets such as diabetics. When the coronary anatomy is equally suitable for either PCI or CABG, the decision of which modality to use for multivessel disease should consider practice guidelines, emerging risks such as stent thrombosis, and the preferences of the fully informed patient.

Introduction

In the past three decades the treatment of patients with multivessel coronary artery disease (CAD) has undergone significant positive changes due to advances in both percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). PCI has evolved from balloon angioplasty of a single coronary stenosis to multivessel stenting with drug-eluting stents (DES) and treatment of chronic total occlusions (CTOs) with advanced techniques and devices. Likewise, CABG has progressed from using solely saphenous vein grafts (SVGs) to the use of multiple arterial grafts, and from a median sternotomy to minimally invasive techniques and off-pump approaches (1). While both PCI and CABG have become more elegant and sophisticated, the evolution of PCI has put it in a position to be considered as an alternative to CABG, the gold standard for achieving complete revascularization of multivessel disease.

Multivessel Coronary Artery Disease

Choice of Revascularization

With either PCI or CABG, the goals of revascularization are that it be complete, that it improve symptoms, that it decrease the incidence of future nonfatal events such as congestive heart failure (CHF), myocardial infarction (MI), and arrhythmia, and that it improve overall survival. The extent to which either revascularization modality achieves these goals with minimal adverse outcomes is dictated by a myriad of patient and technical factors. Specific clinical factors associated with increased adverse events after PCI include advanced age, female sex, congestive heart failure, unstable angina, diabetes mellitus, and multivessel CAD [(2)]. Similarly, seven core preoperative variables found to be predictive of early mortality after CABG include urgency of the operation, age, prior heart surgery, female sex, left ventricular (LV) dysfunction, percent stenosis of the left main coronary artery, and the number of major coronary arteries with more than a 70% stenosis [(3)].

PCI is less invasive than CABG, has a lower in-hospital mortality rate, and requires a shorter hospitalization and recovery time with an earlier return to work (4). However, PCI has a higher rate of early restenosis and a lesser ability to fully revascularize patients with multivessel disease when compared to CABG [(2)]. Other considerations in deciding whether to choose PCI or CABG include the number of vessels involved, the particular location of the stenoses, the complexity of the lesions for a percutaneous approach, and the distal targets for a surgical approach. Currently, PCI with DES is the preferred approach for single or two vessel CAD, while CABG remains the procedure of choice in patients with unprotected left main CAD and diffuse multivessel CAD, especially in diabetics and patients with LV dysfunction [(2,5)]. It has been demonstrated that patients with two or more diseased coronary arteries have a higher adjusted rate of long-term survival with CABG compared to PCI [(6)]. Similarly, a meta-analysis of 13 randomized, controlled trials comparing CABG with PCI for multivessel disease showed that CABG provided a statistically significant survival advantage at five years and at eight years [(7)]. Notably, neither of these studies had drug-eluting stents and off-pump CABG was underrepresented. True comparison of the two modalities remains difficult with the rapid rate of change in the fields.

Early Clinical Trials Comparing PCI and CABG

There were several randomized trials published in the 1990s that compared balloon angioplasty to CABG. These included RITA (Randomized Intervention Treatment of Angina), EAST (Emory Angioplasty versus Surgery Trial), GABI (German Angioplasty Bypass Surgery Investigation), CABRI (Coronary Angioplasty Bypass Revascularization Investigation), ERACI (Estudio Randomizado Argetino de Angioplastia versus Cirugia), BARI (Bypass Angioplasty Revascularization Investigation), and Tolouse (Table 1- PTCA Trials [(8-14)]).

In general, the PTCA trials showed similar survival with balloon angioplasty compared to CABG, but significantly increased rates of repeat revascularization with balloon angioplasty. Follow-up for most of these trials was less than five years but an observational follow-up of almost 2000 patients from these trials showed no differences in adjusted survival at 10 and 20 years [(20)]. Also, while repeat intervention was significantly higher in the first year after balloon angioplasty, after 7-8 years, re-intervention was greater in patients who initially had CABG.

An exception to the relative safety of balloon angioplasty seen in these trials was uncovered in the BARI trial [(13)]. The BARI trial showed that the five-year survival rate in treated diabetics was significantly reduced in patients treated with balloon angioplasty compared with CABG (66% vs. 81%, $p<0.003$). A similar trend was seen at seven years. The improved outcome with CABG was limited to patients with drug-requiring diabetes who received at least one internal mammary artery graft. Long-term internal mammary artery graft patency is thought to have contributed to this benefit by reducing the mortality from late myocardial infarctions by providing a better alternative source of perfusion in hypoperfused areas [(21)].

While of historical interest, these early trials clearly

Table 1 **Summary of Randomized Trials of PTCA and Stents versus CABG for Multivessel Disease***
Adapted from ACC/AHA/SCAI Practice Guidelines' 2005* ***Update of the 2001 Guidelines for Percutaneous Coronary Intervention* [(2)]

Trial	Years	Location	# of pts.	Follow-Up (y)	End Point	Comments
PTCA Trials						
RITA (8)	1989-1991	UK Multicenter	1011	2.5	Death or MI	45% of patients had SVD
EAST (9)	1987-1990	Emory University	392	3	Death, Q-wave MI, or large ischemic defect on Thallium	Repeat revascularization in 5.4% of PTCA group versus 13% of CABG patients.
GABI (10)	1986-1991	German Multicenter	359	1	Freedom from Angina	IMA used in only 37% of CABG patients; more than 80% of patients had 2-vessel disease
CABRI (11)	1988-1993	Europe Multicenter	1054	1	Mortality, symptom status	Complete revascularization with PTCA was not required
ERACI (12)	1988-1990	Argentina	127	3.8	Event-free survival (MI, Angina, and RR)	Similar in-hospital and 1-year survival and freedom from MI; less angina and fewer repeat procedures after CABG
BARI (13)	1988-1991	North American Multicenter	1829	7	Death	Overall survival similar with PTCA and CABG, but late survival of treated diabetic patients better with CABG when IMA grafts were used
Toulouse (14)	1989-1993	France	152	2.8	Freedom from angina 1 year after revascularization	Similar survival with PTCA and CABG at 5 years, but better event-free survival with CABG (fewer repeat procedures)
Stent Trials						
ARTS (15)	1997-1998	Europe Multicenter	1205	3	Freedom from major adverse cardiac and CV events	No significant difference between PCI and CABG in terms of death, stroke, or MI; PCI was associated with greater need for RR
AWESOME (16)	1995-2000	Veterans Affairs Multicenter	454	3	Death	Comparable survival between PCI and CABG in patients with medically refractory myocardial ischemia, with higher RR in PCI group
ERACI II (17)	1996-1998	Argentina	450	1.5	MACE (death, Q-wave MI, stroke, RR)	Better survival and freedom from MI with PCI than with CABG; RR higher in PCI group
SoS (18)	1996-1999	Europe, Canada Multicenter	988	1	RR	Significantly higher number of RRs with PCI; no difference in composite measure of death and Q-wave MI; fewer deaths in the CABG group
MASS II (19)	1995-2000	Brazil, single center	611	1	Cardiac death, nonfatal acute MI, and unstable angina	Included medical therapy arm; no difference in cardiac death or MI among patients in the CABG, PCI, or medical therapy groups; significantly greater need for RR procedures in patients who underwent PCI

CABG indicates coronary artery bypass graft surgery; CV, cerebrovascular; IMA, internal mammary artery; MACE, major adverse cardiac events; MI, myocardial infarction; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; RR, repeat revascularization; SVD, single-vessel disease; and y, year.

do not represent current practice patterns. The patients were relatively low risk with only 10% having LV dysfunction and 70% having only 1 or 2 vessel disease. The first year mortality rate was 2.6%, and 1.9% per year thereafter. Predominately SVGs were used in the CABG cohort and simple balloon angioplasty is rarely used today [22].

Contemporary Clinical Trial Comparing PCI and CABG

Of more current interest are trials utilizing stents in PCI as well as more modern surgical techniques. Contemporary randomized trials include ARTS I & II (Arterial Revascularization Therapy Study), AWESOME (Angina With Extremely Serious Operative Mortality Evaluation), ERACI II (Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients With Multiple Vessel Disease), SoS (Stent or Surgery), and MASS II (Medicine, Angioplasty, or Surgery Study) (Table 1- Stent Trials [15-19]).

The ARTS I and SoS randomized trials [15,18] compared PCI with bare metal stent implantation to CABG using mostly arterial grafts in patients with multivessel disease. The two approaches produced similar outcomes except for a much higher rate of target vessel revascularization (TVR) with PCI (17% vs. 4% and 21% vs. 6%, respectively). Still, restenosis rates with stenting were about 50% lower than that seen in BARI. In ARTS I at five years follow-up, the incidence of repeat revascularization continued to be significantly higher in the stent group (30.3%) compared to the CABG group (8.8%) ($p < 0.001$), but overall freedom from death, stroke, or myocardial infarction did not significantly differ between the groups (18.2% in the stent group vs. 14.9% in the surgical group, $p = 0.14$) [23].

With the current predominant use of drug-eluting stents (DES) which reduce the rates of both angiographic restenosis and TVR by about 70% compared to BMS, the findings of ARTS I and SoS have limited applicability. ARTS II [24] was a non-randomized comparison of 607 patients receiving sirolimus-eluting stents (SES) for multivessel disease with 1202 historical controls from the ARTS 1 trial who received either CABG (n=602) or bare metal stents (n=600). Attempts at complete revascularization were done in ARTS II with an average of 3.7 stents deployed. One year outcomes revealed similar major adverse cardiac and cerebrovascular events (MACCE) between the SES group and the ARTS 1 CABG group (10.4% vs. 11.6%, p=0.46). After adjustment for risk factors, MACCE was lower in the SES group compared with the ARTS1 CABG group (8.1% vs 13.1%), and the rate of repeat revascularization was 8.5% in ARTS II, 4.1% in ARTS I CABG, and 21.3% in ARTS I BMS. At three years, the ARTS II trial continues to show similar rates of survival from MACCE between the SES and ARTS1 CABG groups (80.6% vs. 83.8%, p=NS) [25]. Survival from MACCE in the ARTS1 BMS group is significantly lower at 66%.

Emerging risks with multivessel DES stenting include the increased 30-day MI rates (predominately periprocedural NQWMI) seen in the TAXUS V trial when multiple overlapping DES were used [26], and the small, but significant risk of subacute and late stent thrombosis [27-29].

Emerging Clinical Trials Comparing PCI and CABG

Anticipated trials comparing DES in a randomized fashion to CABG in complex lesion subsets including CTOs, left main CAD, and diabetics include SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) and FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease). These trials will investigate the extent to which DES will reduce MACCE, target lesion revascularization (TLR), and TVR compared to CABG in complex lesion/high-risk patient subsets. SYNTAX is a randomized trial of paclitaxel-eluting stents (PES) versus CABG in 1800 patients with multivessel and left main CAD. Enrollment started in March 2005. The primary end point is to show non-inferiority of MACCE at twelve months. In the FREEDOM trial, 2400 patients with diabetes and multivessel CAD randomized to SES or PES versus CABG will be followed for five years (a minimum of three years) and the primary end point is the composite of death from any cause, nonfatal myocardial infarction, or stroke.

Patients with Multivessel CAD in whom CABG may be preferred

For treatment of multivessel disease, CABG is still recommended in 1) patients with severe angina and left ventricular dysfunction, and in whom complete revascularization cannot be accomplished by PCI, 2) patients who have a large amount of myocardium at risk due to significant unprotected left main disease, diffuse triple vessel disease, or two vessel disease with significant involvement of the LAD coronary artery, especially if the left ventricular ejection fraction is reduced, and 3) patients with diabetes mellitus [2, 30]. Both the BARI trial and ARTS I trial showed improved mortality outcomes for diabetics with CABG. In addition, ARTS I demonstrated a significantly lower rate of repeat revascularization after CABG compared with PCI using BMS (3% vs. 22%, $p<0.001$) [31]. However, there is increasing evidence

of both safety and much lower rates of restenosis and TVR with DES in diabetics with multivessel disease, even to levels that may be comparable with CABG. For example, the rate of TVR in diabetics has fallen from 22% with bare metal stents in ARTS I to 7% with sirolimus-eluting stents in ARTS II.

Patients with Multivessel CAD in whom PCI may be Preferred

PCI for multivessel disease may be preferred in 1) patients with focal coronary disease and preserved left ventricular function, 2) patients who refuse surgery, or in those with significant comorbidities who may have a prohibitively high operative risk or short life expectancy, and 3) younger patients who may otherwise be expected to require one or more bypass operations in their lifetime due to progression of coronary disease and to saphenous vein graft degeneration. Reoperation is associated with higher perioperative mortality and is less often fully successful [32].

Conclusion

Restenosis and the need for repeat revascularization has been the main difference between PCI and CABG in the majority of patients undergoing revascularization for chronic multivessel CAD. The best indication for revascularization is to improve patient symptomatology. Survival can only be prolonged in high-risk subsets, and only if patients survive long enough to derive a net survival benefit. Because of the risk of periprocedural events, neither CABG nor PCI prevent MI on the aggregate. Only medical therapy as an adjunct seems to be able to do that.

When the coronary anatomy is equally suitable for either PCI or CABG, attention must be paid to the patient's expectations and willingness to undergo repeat procedures, if necessary. Some patients are reluctant to undergo CABG because of concerns about increased periprocedural morbidity and mortality, as well as the ensuing prolonged convalescence. On the other hand, some patients are less interested in PCI because of the potential need to undergo repeat interventions and the fear surrounding stent thrombosis. The final decision of PCI or CABG should be individualized, keeping these factors in mind. The importance of clinical decision making and an open dialogue between the interventionalist and cardiothoracic surgeon should not be underestimated, particularly in an era when the technology is outpacing the science.

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