Coronary Artery Revascularisation : Past, Present and Future

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Abstract

The high prevalence of coronary artery disease has inspired the development of technologies and techniques for coronary revascularisation, including coronary artery bypass grafting (CABG) and percutaneous coronary interventions (PCI). PCI have witnessed the impact of innovation with newer hardware and drug eluting stents (DES). DES have indisputably reduced restenosis, however there is an emerging concern over the risk of late stent thrombosis associated with their use. We discuss the limitations of the current generation DES and review advances in the stent technology. The technology used in CABG has improved, resulting in off-pump coronary artery bypass (OPCAB), endoscopic, video-assisted, and robot-assisted CABG with automated one-shot distal anastomotic devices being used increasingly. The difference in adverse outcomes between CABG and PCI continues to decline and the future may witness a close collaboration between the two.

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Introduction

Coronary artery bypass surgery (CABG) and percutaneous coronary intervention (PCI) are based on the principle that the myocardial ischemia related to the coronary artery obstructions can be corrected resulting in relief of the underlying ischemia. 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 pharmaceuticals before another arrives. 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 at par with CABG. In this review we highlight the developments in the field of coronary artery revascularization and the future modalities.

History of PCI and CABG

Coronary revascularisation is built on three centuries of research. Stephen Hales performed the first cardiac catheterization in 1711. The modern techniques have evolved from the works of Drs. Werner Forssmann, Andre Cournard and Dickinson Richards. Dr. Mason Sones discovered selective coronary angiography accidentally in 1958. Dr. Grüntzig performed the first percutaneous transluminal coronary balloon angioplasty (PTCA) in 1977, initiating the modern era of PCI [1]. In 1986 Jacques Puel and Ulrich Sigwart inserted the first stent into a human coronary artery [2].

CABG is the most common surgical procedure performed on the heart. In 1910, Alexis Carrel described the principles of CABG for which he was awarded the Nobel Prize in Medicine in 1912 [3]. In 1953, Dr. John Gibbon performed the first heart-lung bypass and in 1968 Dr. Rene Favaloro first used a saphenous vein graft for coronary artery disease [4]. The internal mammary artery was used for the first time in 1951 when Vineberg reported an experimental technique to revascularize the cardiac muscle using the internal mammary artery (IMA) directly implanted in the myocardium [5]. The first CABG in humans using IMA was done by Longmire in 1958 [6].

Coronary Artery Bypass Graft

The advent of the cardio-pulmonary bypass (CPB) machine permitted cardiac surgeons to perform complex operations on the defective heart. With the refinement of perfusion science, the impact of the pump run on the postoperative recovery of a patient has been lessened considerably since the pioneering days. The drive to reduce the well documented, if somewhat historical, adverse effects of CPB has resulted in attempts to perform coronary artery grafting off-bypass (OPCAB). Kolessov reported the first experience with coronary artery surgery on the beating heart in 1967, but the technique was soon abandoned [7]. However OPCAB experienced a revival beginning in the early 1990s with the work of Benetti [8]. The benefits of OPCAB in terms of less neurocognitive dysfunction and reduced

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incidence of multi-organ failure are controversial. More grafts are usually placed with ONCAB than the OPCAB technique, and some data suggests that OPCAB graft patency may be compromised and that revascularisation in some cases incomplete [9]. At present, the benefits of ONCAB and OPCAB revascularisation remain debatable and the outcome differential is likely to be trivial.

The Evolution of Grafts used in CABG

All surgically constructed grafts not only treat the target lesion but also protect against the subsequent development of new lesions in the portions of the target vessel proximal to the anastomosis for the entire life of the graft. No similar claim can be made of any currently available PCI. Saphenous vein grafts (SVGs) remain the most frequently used conduits in CABG. Historically, during the first year after bypass surgery, 10–15% of vein grafts fail and by 10 years 40–50% close, and of those remaining patent, half have significant obstructive disease [10]. For reasons that are unclear, the LIMA graft is surprisingly immune to atherosclerosis. If a LIMA-to-LAD graft is successfully constructed, there is a 95% chance the graft will be patent and functioning after 15 years or more. Moreover, a patent LIMA-to-LAD graft is associated with a significant survival advantage. The general superiority of the IMA as a bypass conduit is probably due to inherent vascular biological properties of the conduit itself and to the quality of the anterior coronary artery flow and resistances (LIMA anastomosed to the circumflex or right coronary artery provides worse results) [11]. As a consequence, the LIMA to the left anterior descending coronary artery anastomosis is considered the standard of care in coronary surgery.

The right internal mammary artery (RIMA) has superior long term patency as compared to the venous grafts. It is used either as a pedicled in-situ graft or as a composite Y graft anastomosed to the LIMA. The radial artery, which is less demanding to dissect than the RIMA is a popular arterial graft for CABG. So far, early and intermediate-term results indicated a superiority of the radial artery against the saphenous vein in term of graft patency (radial artery patency is between 90 and 95% after one or two years) but, unfortunately, long term results are not known [12]. The GEA (Gastroepiploic artery) has been used as an in-situ graft to revascularise the lower part of the heart and long-term clinical results have been similar to those of SVG (68% patency at 10 years) [11]. Its use has generally been discontinued. Furthermore an arterial conduit to the right coronary artery does not have better long term patency than an SVG, therefore SVG remains the conduit of choice to the right side.

Coronary Artery Stenting

Percutaneous coronary intervention (angioplasty) using stents is a common procedure in which two basic stent types are used: bare-metal stents (BMS) and drug-eluting stents (DES). Introduced to prevent abrupt closure, BMS were initially used exclusively for failed balloon angioplasty cases. BMS went through an initial phase of slow acceptance by physicians on account of stent thrombosis, the occurrence of which was overcome by the combined strategy of high pressure deployments and dual anti-platelet regimens. The pendulum then swung to the other extreme. Within a couple of years in the early 90's, stenting became the default procedure heralding the era of '*stent-o-mania*'.

DES were introduced in 2001 [13]. Until recently, two types of drug-eluting stents have been available: sirolimus- or paclitaxel-eluting stents. Both these drugs have a potent anti-proliferative action and are embedded in a non-reabsorbable polymer matrix completely covering the stent struts, thus allowing slow release of the drug in high concentrations to the local surrounding tissue. The net result is the inhibition of the neointimal hyperplastic response to vessel injury, which is the predominant cause of restenosis with the use of BMS. The Achilles Heel of stenting i.e restenosis seemed to be conquered with the unbelievable initial results of DES.

DES - The Myth of Sisyphus-Subacute Stent Thrombosis

After the initial widespread use of DES the potential downside in the use of DES-stent thrombosis emerged. Stent thrombosis is a serious complication that causes major myocardial infarction in more than 70% of cases and carries a mortality rate of 31-45% [14]. The drugs in the DES markedly inhibit or delay endothelialisation of the stent struts, thus making the stent more susceptible to thrombosis, particularly if dual antiplatelet therapy with aspirin and clopidogrel is interrupted after implantation.

A furore was generated when media highlighted that the incidence of late stent thrombosis (i.e more than 30 days post-implantation) was higher with DES as compared to BMS much to the dismay of the patients and the implanting cardiologists. Pooled analysis of the initial randomized studies comparing DES with BMS showed a substantial (three- to four fold) reduction in restenosis at 12 months with DES sans any apparent increased risk of stent thrombosis with DES [15]. However, four year follow-up data recently released now indicates a higher rate of stent thrombosis with DES as compared with BMS (1.3% v 0.8% for the paclitaxel-eluting stent, and 1.2% v 0.6% for the sirolimus-eluting stent) [16]. To allay considerable

anxiety this analysis also showed that critical end points of myocardial infarction and death were not altered on account of stent thrombosis. The increased risk due to late stent thrombosis is balanced by a corresponding reduction in the reduced rate of restenosis and re-intervention. Restenosis is not as innocuous as is perceived, though a far less serious complication than stent thrombosis, it nevertheless carries approximately a 10% risk of causing myocardial infarction [17].

DES - What went wrong?

The trials which heralded the use of DES generally had simple coronary lesions, whereas, in the “real world”, DES are frequently used for more complex coronary lesions which were not included in these trials. It is estimated that this “off-label” use accounts for at least 60% of DES usage. The likelihood of stent thrombosis is undoubtedly higher in more complex coronary lesions and therefore any increased tendency towards stent thrombosis with use of DES is likely to be accentuated. Based on this evidence, cardiologists now recommend that patients with DES continue on aspirin and clopidogrel for at least 12 months after implantation [18].

DES and Surgery

The prolonged prescription for the use of dual antiplatelet therapy has its problems. The treatment is expensive, exposes patients to a 1–2% per annum increased risk of major bleeding, and presents problems if non-cardiac surgery is subsequently required. Indeed many surgeons are reluctant to operate on patients using aspirin therapy, let alone dual antiplatelet therapy. Furthermore, antiplatelet therapy may be inadvertently ceased prior to dental or minor surgical procedures because the attending physician is unaware of the risks associated with its cessation. In patients who have DES, non-cardiac surgery should be delayed, if possible, for at least 12 months after implantation. Where non-cardiac surgery is required within 12 months of implantation, it should preferably be performed with the patient taking at least one antiplatelet agent and, if possible, both. The increased risk of bleeding needs to be balanced against the risk of the extremely serious complication of stent thrombosis. Furthermore, such surgery should be performed in a hospital with 24-hour facilities for emergency coronary angioplasty, which is the optimal treatment should stent thrombosis occur. Therefore, DES implantation imposes significant limitations on patients.

New Technology for Coronary Revascularisation

In the past decade, the face of surgical coronary revascularisation has been changed by a number of advances, most notably the development of minimally invasive techniques, including minimally invasive direct

coronary artery bypass (MIDCAB) and totally endoscopic, robot-assisted coronary artery bypass grafting (TECAB).

Robotic Surgical Systems and Totally Endoscopic Robot assisted CABG

Robotic surgical systems have permitted the manipulation of surgical instruments through limited thoracic incisions. The Da Vinci Surgical System consists of two primary components: the surgeon's viewing and control console and the surgical arm unit that positions and maneuvers detachable surgical EndoWrist instruments. Shortly after its clinical introduction in 1998, the Da Vinci system was first used for endoscopic internal mammary artery (IMA) harvesting. Success with endoscopic IMA harvest paved the way for the development of a TECAB operation, while initially restricted to single-vessel, LIMA-LAD revascularisation, cases of alternative vessel and multiple bypasses have now been reported. A number of technical issues related to TECAB have prevented its widespread acceptance and deployment. The learning curve is significant, which has translated into long operating room and CPB times. In addition, conversion rates to conventional sternotomy remain high and are often related to difficulty with remote-access perfusion or inadequate intra-thoracic working space.

Minimally Invasive Direct Coronary Artery Bypass (MIDCAB)

The IMA is harvested either under direct vision or with robotic assistance and a small anterior thoracotomy is made in the fourth intercostals space (ICS) and an OPCAB, hand-sewn LIMA-LAD anastomosis is performed under direct vision. This eliminates the need for femoral cannulation and cardiopulmonary bypass, thus reducing procedural times as compared to TECAB.

Anastomotic Devices

Another area of technological innovation has been the development of anastomotic devices for both the proximal and distal anastomosis. A few such systems are currently available which include the St. Jude Symmetry Aortic Connector and the Cardica C-Por, PAS-Port Anastomotic Systems with the Converge Anastomotic Coupler) [19].

New Stent Technology

The various constituent of DES include the stent platform, polymers used for drug delivery and the pharmacological agent which inhibits inflammation and neointimal growth and subsequently ISR (In-Stent restenosis). Development in DES addresses each of these components with new stent designs, better polymers and more effective drugs. The polymer matrix

used for coating the drug is bioresorbable within six months in the Conor Stent. DES with bio-degradable stent struts (Igaki Tamai stent) is an exciting innovation. DES are also designed as vehicles for drug delivery which promote vascular healing through cell and gene based therapies. The Genous Capture R Stent has a matrix with a layer of CD34+ antibody which captures the patient's endothelial progenitor cells (EPCs), accelerating the natural healing process. Once attached, EPCs rapidly form a protective endothelial layer over the stent, which is intended to protect against thrombus and minimise restenosis. A new stent coated with stem cell derived endovascular cells which promote vascular healing has recently been launched (Axordia) [20].

Conclusion

The goal of coronary revascularization should always be complete revascularisation whether the treatment choice is surgery or PCI. Completeness of revascularisation is not a competition between these two treatment strategies. Rather, it is an important factor in the decision-making process that requires careful thought before a patient is recommended for either treatment option. With the increased use of arterial grafts, increased experience with drug-eluting stents and other new devices in interventional cardiology, coupled with the widespread adoption of better secondary-prevention measures such as use of statins, the results that have been described previously are important but may not be as pertinent today. Minimally invasive and robotic CABG is paving the way for near out-patient coronary surgery. The future is likely to see a multi faceted approach to complete and sustained coronary revascularisation with increasing cooperation between the surgeon and the interventional cardiologist.

Conflicts of Interest

None identified

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