

Review

# Role of prosthetic conduits in coronary artery bypass grafting

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## Summary

Prosthetic grafts are required for coronary artery bypass grafting (CABG) when the availability of suitable autologous conduits is limited. The ideal cardiovascular bypass graft requires a broad range of characteristics including strength, viscoelasticity, biocompatibility, blood compatibility and biostability. Many alternative conduits have been developed and used in the past, but most of them have failed, except in rare instances. This review aims to analyse the current status of their use and prospects for the future. We performed a literature search on PubMed using the generic terms 'conduits for coronary artery bypass grafting'; 'reoperative coronary artery bypass grafting'; 'redo coronary artery bypass grafting'; 'PTFE'; 'Dacron or PET'; 'gastroepiploic artery'; 'inferior epigastric artery'; 'biological grafts'; 'tissue-engineered grafts'; 'synthetic grafts'; 'prosthetic grafts'; 'polyurethane grafts'; 'cephalic veins'; 'short saphenous vein'; and 'alternative conduits'. In addition, we searched through related citations and references from selected articles. A total of 1253 references and 110 full-text articles were reviewed, and they were further selected based on available information. This review concludes that, over the past three to four decades, achieving the goal of a prosthetic graft with equivalent function and durability to the internal mammary artery or long saphenous vein has proved to be elusive.

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## 1. Introduction

Coronary artery bypass grafting (CABG) remains the mainstay of revascularisation for multivessel coronary artery disease (CAD). The most widely used conduits are autologous internal thoracic arteries, radial arteries and saphenous veins, which provide excellent mechanical stability and natural anti-thrombogenicity [1,2]. However, expanded indications for the procedure, shift to elderly population and increased number of re-operations may limit the availability of suitable autologous grafts for CABG [3]. It is estimated that approximately 20% of all patients who require coronary bypass fall into this category [4]. About one-third of patients do not have veins suitable for grafting owing to pre-existing vascular disease, vein stripping or vein harvesting for prior vascular procedures [5].

Likewise, the increasing frequency of re-operations restricts the availability of the left internal mammary artery (IMA). In addition, because of concerns of sternal infection, dehiscence and mediastinitis, the right IMA is avoided in elderly, obese or insulin-dependent diabetic patients [6]. The radial artery is avoided in patients with a positive Allen test, diffuse arteriosclerosis and medial calcification, renal dysfunction, trauma to upper limbs, Raynaud disease and

recent transradial coronary angiography [7]. Potential insufficient flow in the presence of coronary flow competition and vasospasm are major concerns in the use of the gastroepiploic artery. Harvest of the gastroepiploic artery requires a laparotomy, and several abdominal complications have been reported. An upper abdominal malignancy represents an absolute contraindication to gastroepiploic artery harvesting, and intra-abdominal adhesion owing to previous abdominal operation could result in prolonged harvesting time and accidental graft injury [8].

Despite the evolution of myocardial revascularisation techniques and the progressive ageing of the surgical population, complete revascularisation remains a fundamental principle of CABG, increasing the quality of life and long-term survival [9]. Complete revascularisation is the goal, unless the target coronary arteries are small, severely diseased, or both. To realise complete revascularisation, the use of additional autologous arterial grafts has steadily increased. Nevertheless, their use could be either limited or contraindicated. Lacking autologous grafts, prosthetic conduits have been proposed in CABG.

## 2. Alternative conduits for CABG

There is a widely recognised need for a readily available, functional, small-diameter vascular graft. The ideal cardi-

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Table 1. Published case series of alternative conduits (last 20 years).

Author	Year	Conduit	Patient number	%Patency	Follow-up (years)
Englberger et al. [49]	2008	The No-React bovine internal mammary artery	17	23	<1
Reddy et al. [50]	2004	The No-React bovine internal mammary artery	7	57	5
Laube et al. [40]	2000	Endothelial cell-seeded PTFE graft	14	90.5	27.7 months
Mitchell et al. [24]	1993	Bovine internal mammary artery	18	16	2
Laub et al. [51]	1992	Cryopreserved veins	19	41	<1
Suma et al. [23]	1991	Bovine internal thoracic artery	2	100	20 days and 10 days

ovascular graft requires a broad range of characteristics including strength, viscoelasticity, biocompatibility, blood compatibility and biostability [10]. It also needs to adapt to the prevailing haemodynamic conditions, both immediately and in the long term. The main synthetic graft materials used in peripheral vascular reconstructions are expanded polytetrafluoroethylene (ePTFE) and woven polyethylene terephthalate (PET), commonly known as Dacron. Table 1 gives an overview of published case series of the use of biological or prosthetic conduits in the past 20 years.

### 2.1. ePTFE

PTFE is an inert fluorocarbon polymer and subsequently made more microporous by extrusion and sintering to form expanded PTFE (ePTFE). This polymer is non-biodegradable with an electronegative luminal surface that is anti-thrombotic and is now widely used for lower-limb bypass grafts (7–9 mm) with excellent results. Cardiac surgeons have used ePTFE grafts, though reluctantly, in many centres. These grafts are rigid compared with the elastic host artery [11]. The poor mechanical characteristics (compliance) and the lack of endothelial cells (ECs) lining the lumen of such graft materials are the significant factors contributing to their poor patency [12,13].

### 2.2. Dacron

Dacron is a type of polyester in the form of multiple filaments either woven or knitted into vascular grafts [14]. Dacron has been used as an alternative to autologous grafts, but it has shown poor patency rates when used in small-diameter sizes or in low-flow locations [15]. In 1976, Sauvage reported a successful adult case with a knitted Dacron vascular graft (4 cm long and 3.5 mm in diameter) between the aorta and right coronary artery [16]. The graft was angiographically patent up to 16 months after surgery. At that time, the literature showed only two other successful uses of aortocoronary Dacron prostheses, both of which were placed in children with coronary anomalies [17,18]. These three successful prostheses were short and used as interposition grafts between the ascending aorta and the proximal end of the coronary artery with high flow.

### 2.3. Biologic prosthesis

Some biologic vascular grafts have been applied in the coronary artery position; however, most of them have failed because of thrombogenicity and degenerative changes. Like some other artificial small-diameter vascular grafts showing excellent anti-thrombogenicity in *in vitro* studies, no long-term results or patencies have been reported so far for their

use in CABG. A human umbilical vein (HUV) graft (Biograft, Meadox Medicals, Oakland, NJ, USA; 4 mm internal diameter) demonstrated angiographic graft patency rates of 46% (6/13) at 3–13 months [19]. In another report, treated bovine IMA graft (Biocor BIMA Biograft, Biocor laboratory, 4 and 5 mm of internal diameter) was implanted in the coronary artery position of 20 patients [20]. Graft patency was confirmed in only two patients at 6 months. However, no long-term results or other patient information has been reported so far. Perloff et al. implanted two glutaraldehyde-tanned polyester mesh-supported sheep connective tissue tubes (6 mm diameter) for left and right main coronary artery bypasses in one patient [21]. They confirmed patency angiographically at 19 months.

Dialdehyde starch-treated bovine artery grafts (Bioflow, Bio-Vascular Inc., St. Paul, MN, USA) were used over the past few years outside of the USA [22], including in Japan [23]. Only one long-term follow-up clinical report was available, and it revealed graft patency rates of 16% (3/19) at 3–23 months [24]. This is much lower than the reported patency rates for PTFE grafts. Furthermore, the graft has a tendency for dilatation due to degenerative changes, as has been reported in a coronary artery position in a canine study [25].

### 2.4. Tissue-engineered grafts

Attempts to improve synthetic grafts have included embedding them with anti-thrombotic drugs, seeding with ECs or developing new biomaterials. Although heparin-coated grafts have had better results than standard prostheses, improvements have, in general, been marginal and heparin is rapidly lost to plasma [26]. Extensions of this approach have included embedding grafts with dipyridamole, hirudin, tissue factor pathway inhibitor or non-thrombogenic phospholipid polymer. The surface texture of prostheses has also been altered in an attempt to increase patency and promote endothelialisation [27].

However, the challenges faced by the approach of tissue engineering for replacing blood vessels are substantial. They include providing an elastic vessel wall that can withstand cyclic loading, matching the compliance of the graft with the adjacent host vessel, and a lining for the lumen that is anti-thrombotic [5].

### 2.5. Synthetic biomaterials and polyurethanes

Traditional synthetic material technologies have not been able to fulfil the requirements of an ideal prosthetic conduit despite a larger volume of material research in this arena [12]. Polyurethanes have been investigated as alternative graft material because they are more compliant than Dacron and PTFE, and, thus, their mechanical and flow parameters are better matched to those of the native vasculature. Early

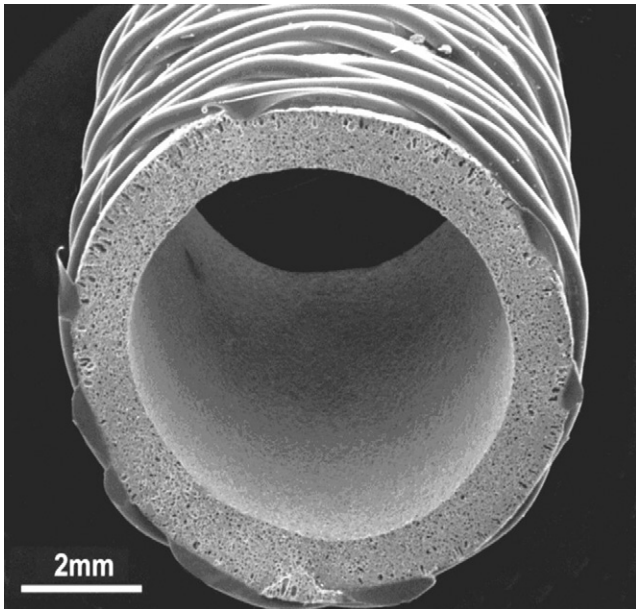


Fig. 1. Compliant polyurethane graft with external support; the sponge-like structure of the wall allows pulsatile elastic recoil even with external support and after perigraft tissue incorporation has taken place.

attempts using polyurethane led to high rates of aneurysm formation and thrombosis compared with conventional prosthetic grafts [28]. However, there has been renewed interest in using modified forms of polyurethane grafts that are biostable [29], and retain seeded ECs [30].

The development of a compliant, small-bore, vascular graft has been a major goal of our unit. We have developed a small-diameter bypass graft for CABG based on our nanocomposite polymer (UCL-Nano™ consisting of polyhedral oligomeric silsesquioxane and poly(carbonate-urea) urethane). This graft is undergoing *in vivo* studies in a carotid interposition sheep model, and we are in the process of obtaining Food and Drug Administration (FDA) approval. In addition, a bio-resistant compliant polyurethane graft (MyoLink) (Fig. 1) has undergone pilot clinical studies both for dialysis access and in lower-limb bypass grafting. In over 100 implantations with a follow-up of up to 18 months, no aneurysmal change or significant dilatation of the graft has been found. The graft, therefore, appears to be resistant to biodegradation. There is insufficient follow-up to properly assess its clinical performance in terms of patency rates, and the results of phase one clinical studies are awaited.

### 3. Discussion

EC coverage or non-antigenicity has not eliminated the problems of autologous arterial and venous conduits in the coronary artery position. Viable grafts do not always have perfect characteristics for CABG, and homologous venous conduits, including fresh and cryopreserved, have been used with unsatisfactory results [31]. Synthetic grafts have been used for revascularisation in patients, who have limited autologous graft materials available. In the past decade, numerous studies have been conducted to develop novel

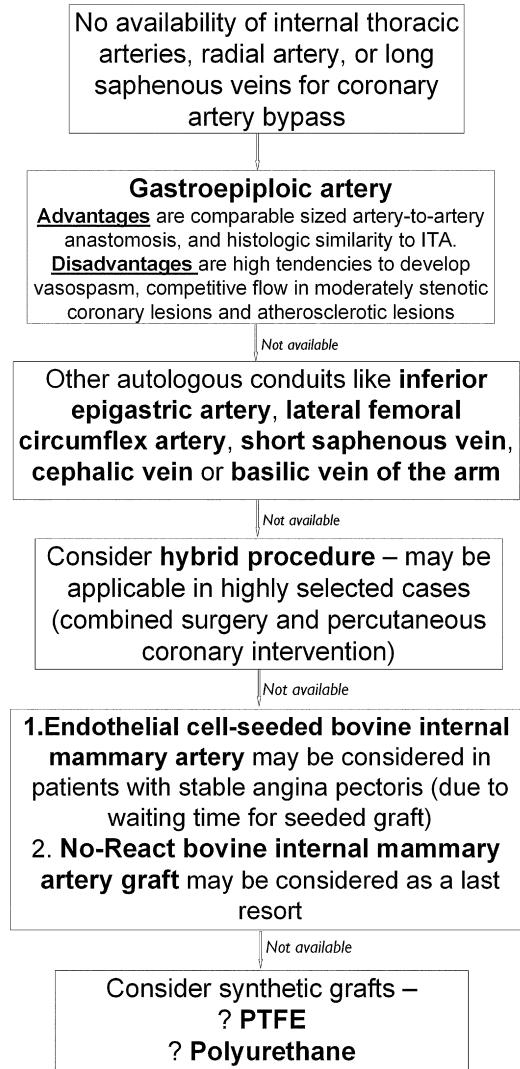


Fig. 2. Algorithm of decision-making when no conduits are available for CABG [42–48]. ITA: internal thoracic artery.

small-calibre prostheses for potential use in aortocoronary vascular reconstruction. Fig. 2 gives a flow chart for use of alternative conduits, based on current evidence.

Satisfactory synthetic materials have not been successful for CABG so far because of their poor long-term patency rates. Although Dacron and ePTFE grafts have been used successfully in peripheral revascularisation cases, these small-calibre vascular grafts have failed for coronary revascularisation [32]. Dacron grafts suffer from thrombosis and neo-intimal proliferation. ePTFE grafts also have had poor patency rates because of surface thrombogenicity [33]. In general, patency rates have varied widely between 60% at 1 year and 14% at approximately 3 years [31,34–36]. Reports of long-term follow-up have been sporadic in the form of case reports [37,38]. It has been described that EC-seeded grafts could decrease thrombogenicity and intimal hyperplasia [39–41]. However, cell-seeded grafts are not practical for CABG cases because of the complex, time-consuming and costly manufacturing process.

#### 4. Conclusions

We have seen so far that the patency of synthetic small-calibre grafts has been poor and they have not been practical for CABG. The major causes of graft failure have been thrombosis and intimal hyperplasia of the graft. If a synthetic small-calibre graft were resistant to thrombosis in addition to being biocompatible, it would have several advantages over traditional autologous grafts. A synthetic graft would have unlimited availability and consistent quality and patency. Moreover, the biomechanical uniformity of a synthetic graft could enable the development of an effective anastomotic device for minimally invasive surgery. The requirement of a prosthetic graft with a non-thrombogenic surface, sufficient mechanical strength, similar compliance to native vessels, spontaneous endothelialisation, resistance to intimal hyperplasia and compatibility with the host tissue remains a major challenge for vascular tissue engineering.

#### 5. Future prospects

New graft development to match as closely as possible the mechanical characteristics and functions of normal human arteries will remain a major priority for cardiovascular surgeons for at least the next decade. Over the next 5 years, improved prosthetic grafts will become available with the introduction of biodurable and compliant polyurethane grafts. Indeed, such grafts are already available for vascular access in renal dialysis patients. Lumen modulation by anticoagulant molecules, cell ligands and growth factors will further enhance performance. EC seeding of standard ePTFE grafts brings improved patency and resistance to infection. Seeding protocols are already under pilot clinical study and promise to be widely clinically applicable within the next 5 years. Similarly, the development of totally autologous tissue-engineered grafts is in its infancy, but is progressing rapidly with the potential for clinical application within the next 5–10 years.

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