Update on the Management of Peripheral Arterial Disease (PAD)

N C Liew, FRCS*, K Moissinac, FRCS, Limi Lee, MD*, Tikfu Gee, MS*, R B H Raja Zezeman, FRCS***

*Department of Surgery, University Putra Malaysia, **Department of Surgery, Penang medical College, Penang

SUMMARY

There has been much progress made in the management of peripheral arterial disease (PAD) in the past two decades. Progress in the understanding of the endothelial-platelet interaction during health and disease state have resulted in better antiplatelet drugs that can prevent platelet aggregation, activation and thrombosis during angioplasty and stenting. Collaborative effort by different international societies has resulted in a consensus guideline that recommends the modality of intervention in certain disease states. Progress in perioperative care has reduced the morbidity and mortality associated with peripheral vascular reconstruction surgery. Nevertheless, the advances in percutaneous peripheral intervention (PPI) have made a paradigm shift in the current management of patients. The procedure is safe and effective and is emerging as the first choice revascularization procedure.

KEY WORDS:
Antiplatelet, Angioplasty, Stenting

INTRODUCTION

Progress in the management of peripheral arterial diseases (PAD) from the 1950s to the 1990s had been largely confined to the newer techniques in peripheral bypasses and the development of newer conduits to replace the vein. In the past two decades, improvement in perioperative care has reduced the mortality and morbidity of patients with peripheral bypass. Parallel to that progress, experiences gained in percutaneous coronary intervention (PCI) and newer antithrombotic drugs have resulted in a paradigm shift in the management of patients with PAD. More data have emerged that affirms the role of percutaneous peripheral intervention (PPI). In tandem with endovascular therapy, consensus evidence- based guidelines have been published to help in the understanding, interpretation and application of these techniques.

There are four areas which have made an impact on the management of patients with PAD:

1. Newer antiplatelet drugs
2. Trans Atlantic Inter-Society Consensus (TASC-II)
3. Improvement in perioperative care
4. Endovascular techniques and technology

NEWER ANTIPLATELET DRUGS

At the cellular level, the interaction of platelet and endothelium in health and disease has been unraveled. When an area of endothelium is breached, the exposed collagen, fibronectin, laminin and von Willebrand factor (vWF) are highly thrombogenic and promotes platelet adhesion. The adhesion requires binding of vWF to platelet receptor glycoprotein (Gp) Ib. The platelets then expose and assemble membrane GP IIb/IIIa, which then bind fibrinogen and vWF, causing more platelet recruitment and aggregation. The activated platelets secrete granules which further increases the aggregation of platelets. The platelet membrane becomes available for adsorption and concentration of clotting factors and resulting in a fibrin network[1].

Antiplatelet drugs have made an impact not only in reducing cardiovascular risk of PAD patients but improving claudication and patency of balloon angioplasties[2]. COX-1 inhibitor Aspirin, ADP receptor antagonists like Ticlopidine and Clopidogrel have proven their worth in ATC trial and CAPRIE studies, reducing the adverse vascular events[3,4]. Cyclic AMP phosphodiesterace III inhibitor like Cilostazol is recommended for improving claudication[5]. Newer antiplatelet drugs targeting glycoprotein receptors like abciximab have found their role in PCI and would perhaps find their role in PAD in the future[6].

TRANS-ATLANTIC INTER-SOCIETY CONSENSUS –II

The TASC[7] was published in January 2000 as a result of cooperation between fourteen medical and surgical vascular, cardiovascular, vascular radiology and cardiology societies in Europe and North America. TASC II was initiated in 2004 and has included societies from Asia, Africa and Australia.

While TASC is not really advancement in PAD, it provides a comprehensive, evidence-based consensus that forms a robust base for vascular practice. It covers epidemiology, management of cardiovascular risk and other existing risk factors, intermittent claudication, chronic critical limb ischaemia and acute ischaemia, revascularization, non-invasive vascular laboratory and imaging.

It provides recommendations and selected statements based on guidance as advocated by the Agency for Health Care Research and Quality. The grade of recommendations is based on level of available evidence. It provides 43 recommendations beginning with recommendation 1 on

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Corresponding Author: Liew Ngoh Chin, Universiti Putra Malaysia, Department of Surgery, Faculty of Medicine & Health Sciences, 10B Floor, Grand Seasons Avenue, Jalan Pahang, 53000 Kuala Lumpur, Malaysia Email: liewnc@yahoo.com

smoking cessation in PAD to recommendation 43 on indications on methods to localize arterial disease.

TASC has made the selection of pharmacotherapy for intermittent claudication simple. It has classified drugs into those with evidence of clinical utility, with supporting evidence of clinical utility and with insufficient evidence of clinical utility for claudication. An example of which is Recommendation 15 on pharmacotherapy for intermittent claudication which states that: A 3 to 6 months course of Cilostazol should be the first-line pharmacotherapy for the relief of claudication symptoms, as evidence shows both an improvement in treadmill exercise performance and in quality of life. [A]

One major contribution of TASC is its classification of aorto-iliac and femoro-popliteal lesions into type A to D. Lesion A being short segment stenosis and D being long segment or multiple segment occlusions. This has facilitated management decisions whereby endovascular technique is recommended for the former and surgical bypass is recommended for the latter. This also allows for comparison of patency results of the two modalities and of different centres around the world.

TASC classification of atherosclerotic lesions is probably comparable to the TNM classification of tumours where in a systematic classification of disease is agreed upon and management decision made uniform. It should form a basis for current vascular practice.

IMPROVEMENTS IN PERIOPERATIVE CARE

Patients undergoing major vascular surgery experience a 30-day operative mortality of 5% to 6%, which arises principally from cardiac events[8]. Although the pathophysiology is not entirely clear, evidence shows that coronary plaque rupture, which leads to thrombus formation and subsequent vessel occlusion is the dominant causative mechanism[9].

Measures to decrease perioperative cardiac mortality would include preoperative risk assessment. The goal is to identify serious cardiac conditions like recent myocardial infarction, heart failure, unstable angina, significant arrhythmias and valvular heart disease. Other conditions like diabetes, stroke, renal insufficiency and lung diseases should also be identified. These conditions must be corrected or improved and if necessary, surgery is to be postponed if it is non-emergent. TASC recommendation 7 pertains to patients with coronary artery diease (CAD) and PAD. It states that patients with PAD considered for vascular surgery should undergo further risk stratification and those found to be at very high risk managed according to current guidelines for coronary revascularization. [C]

Beta-blockers have been shown in several studies to reduce the perioperative cardiac risk. Poldermans et al evaluated Bisoprolol in a group of high risk patients and have demonstrated a 91% reduction in perioperative risk of MI or death from cardiac causes[10]. However, recent trials in the UK have shown no benefit of perioperative beta blockade in reducing the cardiac mortality in vascular surgery and the article by Devereaux et al have generated intense debate on the strength of evidence on beta-blockade[11].

Non randomized studies have shown that statins confer benefit in reducing perioperative cardiac risk but recently this has been doubted by a systemic review[12]. Kapoor et al have questioned the strength of evidence for perioperative usage of statins to reduce cardiovascular risk[13]. More evidence is needed before recommendations can be made.

ENDOVASCULAR TECHNIQUES AND TECHNOLOGY

Endovascular procedures were started way back in the 1960s by Dotter but did not emerge as a therapeutic maneuver until 1974 when Gruntzig reported the usefulness of percutaneous transluminal angioplasty in different vascular beds, including coronary, renal, iliac and femoral. Metallic stents was introduced by Julio Palmaz in 1985. This is followed by the great advance of endovascular abdominal aortic aneurysm repair by Juan Parodi, reported in 1991.

Endovascular therapy's initial slow acceptance by the vascular community is no doubt due to its poor patency rates compared to the better results from decades of established open repair. However, in the past two decades, endovascular techniques and devices have improved leaps and bounds.

Peter Schneider wrote that 'the most important endovascular consideration is that endovascular techniques are replacing open surgery'[14]. This is due to better imaging systems, improved guide wire and catheters and better stent technology. More importantly, endovascular technique owes its great advantage to its 'minimally invasiveness' with decreased perioperative morbidity and mortality and promises a better quality of life as compared to open surgery. In this era of information technology, patients are better informed and their preference would increase and hasten the development of endovascular procedure.

Alternative techniques have evolved to manage areas unattainable with open surgery, like poor runoffs in the leg arteries and areas inaccessible to current intraluminal techniques like long segment occlusions. Amman Bolia introduced the technique of subintimal angioplasty (SIA) in 1990 as percutaneous intentional extraluminal recanalization (PIER)[15]. While the initial patency rates were inferior to established transluminal angioplasties, SIA have recently regained popularity with reasonable initial technical success and intermediate term patency. The advantage of the technique is that failure to achieve revascularization does not preclude open revascularization.

Intravascular stents have become an important tool in peripheral angioplasty to treat lesions with flow limiting lesions and lesions significant elastic recoils. The introduction of nitinol (nickel-titanium alloy) stents in the femoro-popliteal segment have improved patency and allowed easier delivery device with smaller introductory sheath[16]. The improvement in patency however, is not comparable to that achieved with bypasses. Lesion restenosis and stent fractures are issues that have not been resolved.

Recently, covered stents or stent grafts have been added to the repertoire of endovascular therapy and the results have been encouraging. Saxon et al reported a 79% primary patency rate and 93% secondary patency rate at 4 year follow up using Hemobahn or Viabahn stent grafts in the femoral and popliteal arteries[17]. This is almost comparable to that using achieved with prosthetic bypasses.

Drug eluting stents (DES) have not established their realm in PAD; unlike in PCI. In the SIROCCO 1 and II trials, DES were applied to the Superficial Femoral Artery, hoping to improve the long term patency following stenting[18,19]. At 24 months follow up, the outcomes were similar in both groups; with restenosis rate of 25% and 24% for bare stent and DES respectively[20]. Perhaps the peripheral arteries behave differently due to its length, mobility and remodeling behaviour. More studies are needed before their acceptance in PPI.

Atherectomy devices have been introduced to salvage lesions not amenable to PTA, stenting or SIA. Mechanical devises like Silverhawk and excimer laser help to remove dense eccentric plaques[21,22]. They are investigational and the outcomes are generally unsatisfactory for its widespread usage.

CONCLUSION

We live in an interesting time where the frontiers of open surgery are slowly closing in and the horizon of endovascular surgery expanding. From being skilled technicians in performing anastomosis, vascular surgeons have now learn to reestablish themselves as good physicians, haematologist, imaging specialist and surgeons. With further elucidation of atherosclerosis pathophysilogy, endothelium-platelet interaction and further refinement of guidewire-catheter techniques, bypass surgery might be reduced to a salvage procedure before amputations.

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MCQ (TRUE/FALSE)

1. When an atherosclerotic plaque ruptures, thrombus forms due to:
A. Exposed collagen promotes platelet adhesion
B. RBC becoming tethered to the von Willebrand factor
C. Platelets expresses Glycoprotein that causes aggregation
D. Plasma becomes hypercoagulable
E. Endothelium expresses adhesion molecules

2. Cilostazol is:
A. Anti-platelet
B. Anti-coagulant
C. Effective in improving claudication distance
D. Inhibitor of Phosphodiaesterase III
E. Contraindicated in patients with heart failure

3. The following agents have been shown to decrease perioperative cardiac complications in patients undergoing vascular surgery:
A. Anti-lipids
B. Beta-Blockers
C. Pre-operative risk stratification
D. Cessation of smoking
E. Regional anaesthesia

4. Percutaneous peripheral intervention is recommended in:
A. Patients with intermittent claudication
B. Patients with TASC D arterial pathology
C. High risk patients
D. Younger patients
E. Patients with non-atherosclerotic arterial occlusions

5. Antiplatelets:
A. Has reduced cardiac mortality in PAD patients
B. Impedes progression of atherosclerosis
C. Prolongs the patency of vascular stents
D. Is used in claudicants to improve collateral circulation
E. Acts only on the phospholipid pathway