The 9th Asian PAD Workshop builds on the progress and achievements made at the previous medical education workshops held across Asia. The latest edition focused on the challenges of managing patients with PAD (peripheral arterial disease) and diabetes mellitus (DM). PAD incidence and prevalence continue to grow at an alarming rate in Asia and DM is a critical factor in its onset. Five distinguished speakers invited from Thailand, Korea, China, and Japan provided an excellent opportunity for clinicians to discuss in detail and share their clinical experiences and treatment strategies. Case studies were presented along with the latest clinical study data supporting the use of individualized pharmacotherapeutic, surgical and endovascular approaches and how best to select the right treatment for the right patient. The role of beraprost sodium in the management of PAD with diabetes continues to evolve with new clinical evidence emerging. Raising awareness of PAD, its consequences and links with DM remains critical to encourage early diagnosis and intervention to prevent disease progression and achieve the best patient outcomes possible.

### Keynote Address: Management of PAD Patients with Diabetes

Dr. Hiroshi Shigematsu
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The first Asian PAD workshop was held in Jeju Island in 2009. At that time, we have discussed the prevalence, diagnostic approaches, and management of PAD, especially focusing on the PAD patients with diabetes mellitus, one of the most critical risk factors in the onset of PAD. Subsequent workshops focused on the diagnosis, management, treatment, complications and the risk of chronic kidney disease. The 9th workshop revisits the management of PAD patients with diabetes.

In 2010, the American Diabetes Association (ADA) included A1c for the first time among tests recommended for the diagnosis of diabetes mellitus. This recommendation has also been adopted by the European Association for the Study of Diabetes, the World Health Organization, among others. The ADA now state that an A1c value of ≥6.5% or previous criteria for fasting glucose (≥126 mg/dL) or 2-h glucose (≥200 mg/dL) can be used for the diagnosis of diabetes mellitus. In 2010, the ADA also added A1c to the tests used to identify people with prediabetes, who are at increased risk for type 2 diabetes mellitus. Along with fasting glucose of 100 to 125 mg/dL or 2-h glucose of 140 to 199 mg/dL, individuals with A1c in the range of 5.7% to 6.4% are classified as having an increased risk for diabetes mellitus.1)

Studies have identified consistent risk factors for PAD. In Asia, an association between PAD and diabetes has been seen mostly in Hong Kong, followed by Philippines and China.2) New data on the epidemiology of PAD are available, indicating that diabetes, smoking and aging are the most detrimental risk factors for its development in high income countries.3)
Studies have also identified five-year mortality rates to be highest in PAD patients stratified by age (≥75 years) and diabetes (i.e., those with diabetes vary considerably among patients with PAD. Predictors of death included presence of critical limb ischemia (CLI), high-sensitivity C-reactive protein (hs-CRP) and amino-terminal pro-B-type natriuretic peptide (NT-proBNP).\(^1\) Furthermore, in the ADVANCE-ON study, the cumulative incidence of all-cause mortality, major macrovascular events, cardiovascular death, and fatal or non-fatal myocardial infarction were higher in participants with history of major PAD at baseline compared to those without PAD (\(p<0.0001\) for all).\(^2\)

In 2015, the TASC II lesion classification was updated to reflect technological advances.\(^3\) Endovascular therapy is the treatment of choice for type A lesions and surgery is the treatment of choice for type D lesions; endovascular treatment (EVT) is preferred for type B and surgery is preferred for type C. The new infrapopliteal lesion classification (Fig. 1) incorporates several features that attempt to address the multivessel nature of possible infrapopliteal anatomies. Several recommendations were proposed in TASC II for the management of CLI. Most patients will ultimately need a revascularization procedure; therefore, referral to vascular specialists should not be delayed. Other components of CLI management include medical interventions to control pain and infection in the ischemic leg, prevention of progression of the systemic atherosclerosis, and optimization of cardiac and respiratory function. The natural history of CLI is such that intervention is indicated to salvage a useful and pain-free extremity. After revascularization, ulcer healing may require adjunctive treatments that may be best achieved in collaboration between the vascular specialist and specialists in foot care. Angioplasty is regarded as important and is becoming the first-choice strategy.

![Fig. 1 TASC classification of infrapopliteal lesions.](image)

A significant overlap is apparent in the respective incidence of coronary artery disease, cerebrovascular disease and PAD.\(^4\) Based on the findings of the REACH (REduction of Atherothrombosis for Continued Health) registry, approximately 61% of patients with PAD also have evidence of concomitant coronary and/or cerebrovascular disease. This indicates the need for a common approach to reduce the risk of major adverse cardiovascular events and limb vascular events and improve symptoms in patients with PAD.\(^5\)

Beraprost sodium was the world’s first orally active prostacyclin analogue preparation. It is very stable to gastric pH and has been widely used in Japan over the last 25 years for patients with ischemic limb symptoms. Beraprost has several therapeutic properties including vascular endothelial protection, antiplatelet and anti-inflammatory effects, and vasodilatory activity. These properties contribute to improved pathological process in the lower extremities and reduction in the incidence of systemic vascular events. Beraprost contributes to an overall systemic vascular protective action and is expected to have dual effects on improving ischemic symptoms due to PAD and on preventing cardiovascular (CV) events due to polyvascular disease (Fig. 2).\(^6–11\) A meta-analysis of clinical data in PAD has shown beraprost to achieve a highly significant 39% reduction (\(p=0.012\) vs. placebo) in the risk of systemic vascular events (defined as the events of cardio/cerebrovascular events and exacerbation of leg symptoms).\(^5\)

![Fig. 2 Proposed dual effects of beraprost to improve PAD ischemic symptoms and prevent CV events.](image)

Patients with PAD typically have multiple cardiovascular risk factors, which puts them at markedly increased risk for CV events. According to TASC II, all PAD patients should have their low-density lipoprotein (LDL)-cholesterol lowered to <100 mg/dL and patients with PAD and a history of acute coronary syndrome should have their LDL cholesterol lowered to <70 mg/dL.\(^6\) All patients with PAD should be strongly and repeatedly advised to stop smoking. PAD patients with hypertension should have blood pressure controlled to <140/90 mmHg or <130/80 mmHg if they also have diabetes or renal insufficiency. Patients with diabetes and PAD should have aggressive control and normalization of blood sugar. Hemoglobin A1c levels <7% should be obtained.

Finally, although the prevalence of PAD in patients with diabetes mellitus is estimated to be 29%, it is unknown whether aggressive treatment to optimize serum glucose levels decreases the likelihood of adverse CV events in these patients. However, atherosclerosis tends to be more aggressive, and amputation rates in diabetic patients with atherosclerosis of the lower extremity are five to 10 times higher than in nondiabetic counterparts. Sensory neuropathy and increased susceptibility to infection contribute to an elevated amputation rate.

**REFERENCES**

Critical limb ischemia (CLI) leads to limb loss and therefore requires urgent intervention. According to TASC II, one-year outcomes in patients with CLI currently indicate alive with two limbs in 45%, amputation required in 30% and death in 25%. The five-year mortality rate is now higher (at almost 70%) than for many cancers. The primary goals for the treatment of CLI are therefore to prevent amputation, relieve rest pain and to minimize the risk of death, stroke, myocardial infarction (MI), and this is best done via a multidisciplinary team approach.

Identifying which foot is most likely to heal can be helpful. Non-invasive arterial testing values (including macrocirculation: ankle-brachial index [ABI] <0.4 and ankle systolic pressure <50 mmHg and various microcirculation values) suggest an inability to heal. Factors influencing amputation risk in CLI patients include limb status (wound, ischemia and foot infection), patient status (risk factors and comorbidities) and anatomy (including occlusion vs. stenosis, lesion length, multiplicity of lesion, disease pattern etc.). The WIfI classification can also be useful. It is based on three major factors that impact amputation risk and clinical management: Wound, Ischemia, and foot Infection.

A three-pronged approach for ischemic leg ulcers has been proposed: noninvasive assessment of the arterial circulation; revascularization when clinically able based on anatomy and surgical risk; and aggressive local wound care before/after revascularization. Perfusion assessment is simply done by ABI, with values 0.00–0.39 indicative of severe disease. The physiologic criteria for CLI are as follows: an ankle pressure <70 mmHg and toe pressure <50 mmHg if or an unhealed ulcer; while an ankle pressure <50 mmHg and toe pressure <30 mmHg for ischemic rest pain. The ABI can also give a good indication of the risk for cardiovascular (CV) events, with the odds ratio for MI, stroke or CV death rising sharply with an ABI <0.6. Unfortunately, it should be considered that around 30% of CLI patients have near-normal or normal ABI. In diabetes (DM) and end stage renal disease (ESRD) patients, the assessment of toe-brachial index (TBI) may help for diagnosis of CLI due to the ABI is artificially increased (>1.40) or may be falsely read as normal. Transcutaneous oxygen tension (TcPO2) is also a useful predictor of ulcer healing in CLI (Fig. 1). Fluorescence angiography is a new technology that is beginning to be introduced in some centers. Although not yet validated, it is considered comparable to TcPO2.

Management of Ischemic Leg Ulcer
Dr. Wuttichai Saengprakai
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Critical limb ischemia (CLI) leads to limb loss and therefore requires urgent intervention. According to TASC II, one-year outcomes in patients with CLI currently indicate alive with two limbs in 45%, amputation required in 30% and death in 25%. The five-year mortality rate is now higher (at almost 70%) than for many cancers. The primary goals for the treatment of CLI are therefore to prevent amputation, relieve rest pain and to minimize the risk of death, stroke, myocardial infarction (MI), and this is best done via a multidisciplinary team approach.

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Fig. 1 TcPO2 and management interventions in CLI.

The second step for the treatment of CLI is revascularization; even limb salvage can be achieved in some patients with arterial insufficiency and uncomplicated chronic nonhealing limb ulcers using a program of wound management without revascularization. Healing proceeds slowly and requires nearly a year in many cases. The following are important current concepts in treating CLI:

- CLI is due to multi-segment disease
- Treat both inflow and outflow if there is tissue loss
- Shift the focus from in-line flow to ulcer related flow ("angiosome concept")
- Long-term patency in not essential for limb salvage (studies show that primary patency does not reflect limb patency and that secondary patency is more reflective of limb salvage)
- Although we have a choice between bypass and endovascu-
lar surgery, recent data indicate that, in patients presenting with severe limb ischaemia due to infra-inguinal disease and who are suitable for surgery and angioplasty, a bypass-surgery-first and a balloon-angioplasty-first strategy are associated with broadly similar outcomes in terms of amputation-free survival. Moreover, in the short-term, surgery is more expensive than angioplasty.\(^{11}\)

Although there is a paucity of high-quality data available to guide clinical decision making, the available literature suggests that there is no difference in clinical outcomes for patients with CLI treated with endovascular or surgical revascularization, with no difference in all-cause mortality, amputation and amputation-free survival.\(^{12}\)

The usual approach at the Vajira Hospital (Thailand) most of the CLI patients underwent an endovascular surgery first and trying to perform angiosome-directed revascularization whenever possible. Follow-up and wound care are very important steps, including infection control, debridement and local wound care. Figure 2 details a management algorithm to help optimise outcomes.

**Fig. 2** Management of CLI at the Vajira Hospital (Thailand).

### Discussion points (Panel discussions)

- The importance of a patient's nutritional status to help improve outcomes in CLI. The nutrition team will assess the patient and take care of their nutritional status.
- In CLI, the ABI does not always provide an accurate assessment in some cases, so we may also need to use pulse volume recording and the TBI.

### REFERENCES


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**Management of PAD Patients with Diabetes**

Dr. Jae Hyuk Lee (Korea)
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Patients with type 2 diabetes (T2D) are at increased risk of CV mortality compared with those without diabetes.\(^{1}\) Indeed, cardiovascular disease (CVD) is the primary cause of death among patients with type 2 diabetes; approximately 40% of deaths are due to ischemic heart disease, about 15% are due to other heart disease, principally congestive heart failure, and about 10% are due to stroke.\(^{2}\) The more cardiometabolic comorbidities a patient has (diabetes, stroke, MI), the greater their risk for death.\(^{3}\) Overall, these observations suggest that therapies to treat diabetes should be evaluated, at least in part, by their effects on CVD.

The situation with PAD is similar as it is an independent predictor of cardiovascular and cerebrovascular ischemic events, affecting both the quality and expectancy of life.\(^{4}\) Multiple
metabolic aberrations in DM, such as advanced glycation end-products, low-density lipoprotein cholesterol, and abnormal oxidative stress, have been shown to worsen PAD (Fig. 1). PAD also increases the risk of lower extremity amputation. In a recent meta-analysis, diabetes in PAD was associated with a statistically significant increased risk of all-cause mortality (odds ratio: 1.89, 95% confidence interval [CI]: 1.51–2.35, p < 0.001), and the effect was even more pronounced in patients with CLI (odds ratio: 2.38, 95% CI: 1.22–4.63, p < 0.001). Although factors such as poverty, industrialization and infection might influence the development of PAD, the ageing of the population and increase in traditional cardiovascular risk factors, such as smoking, diabetes mellitus, and hypertension, are likely to be the main driving forces. When risk factors coexist (smoking, diabetes, high blood pressure, high blood cholesterol, age > 40 years, family history), the mortality risk increases several-fold.

![Fig. 1 Pathophysiology of PAD in diabetes mellitus.](Adapted from Yang et al. (2017).)

The mainstay of PAD screening for diagnosis remains history taking and the measurement of ABI and brachial-ankle pulse wave velocity (baPWV). For the ABI, a value above 0.90 is normal, 0.71–0.90 indicates mild impairment, 0.41–0.70 moderate impairment 0.00–0.40 and severe impairment. The management of PAD in diabetes (e.g., as per the 2016 AHA/ACC Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease) involves controlling modifiable risk factors, notably hypertension, dyslipidemia, intervention of antiplatelet agents, smoking cessation and glucose control. More strict blood pressure control is required in PAD patients with diabetes. For dyslipidemia, treatment with a statin medication is indicated for all patients with PAD (it is established that for every reduction of LDL-C by 1 mmol/L, there is a 36% risk reduction of coronary artery disease). Plasma lipid levels of diabetic patients must be more strictly controlled than non-diabetic population in order to avoid an increased risk for coronary heart disease. All guidelines currently recommend more aggressive lipid management for T2D patients. Antiplatelet treatment (i.e., aspirin or clopidogrel) is recommended in symptomatic and asymptomatic (as a reasonable approach) PAD patients with diabetes to reduce the risk of MI, stroke and vascular death. However, in asymptomatic patients with borderline ABI (0.91–0.99), the usefulness of antiplatelet therapy to reduce these risks is uncertain. While increased platelet aggregability and adheresiveness is observed in patients with diabetes, such patients also show reduced sensitivity of platelets to aspirin and this may affect metabolic control.

Beraprost sodium is a further option for consideration. Its multiple mechanisms of action involve antiplatelet, vasodilation and endothelial hypotrophy inhibitory activity and it acts to restore the balance of PGI$_2$ and thromboxane A$_2$ (TXA$_2$) (Fig. 2), which helps to maintain optimal levels of platelet aggregation and vasoconstriction/vasodilation.

![Fig. 2 Beraprost acts to restore the balance of PGI$_2$ and TXA$_2$.](Present in cell membranes
- Arachidonic acid
- COX1
- Thromboxane A$_2$
- COX2
- Prostacyclin
- Promotes platelet aggregation and vasoconstriction
- Inhibits platelet aggregation and vasodilation
- Homeostatic balance maintained

The benefits of beraprost in diabetes have been investigated. In a series of 11 patients with cold intolerance 6 to 24 months after digital revascularization/replantation, beraprost treatment daily for 2 weeks was found to reduce pain 9/11 cases and digital thermography showed significantly increased surface temperature after the 2-week course of beraprost. These findings support the use of beraprost to relieve symptoms of cold intolerance under these clinical conditions. The long-term effects of beraprost on arteriosclerosis obliterans (ASO) were investigated in a single-center retrospective study of Japanese patients. Beraprost significantly reduced lower limb ischemic symptoms vs. baseline and significantly reduced carotid intima/media thickness at 12 months (p < 0.001) vs. baseline. In addition, 120 µg beraprost was significantly more effective than < 120 µg beraprost in maintaining the cumulative CV event-free rate at 10-years (85.7% vs. 43.8%, p < 0.001).

![Fig. 3 Long-term improvement in ASO symptoms in Japanese patients (all patients and those with diabetes) treated with beraprost.](Adapted from Arai (2013). The visual analog scale scores were rated on a scale of 0–10 by patients with each symptom at baseline and after 3, 6 and 12 months of treatment. Values are mean±standard deviation. **p<0.001 versus baseline.

**p<0.001 versus baseline.

The metabolic abnormalities caused by diabetes induce vascu-
lar dysfunction that predisposes these patients to atherosclerosis. Since most patients with diabetes die from complications of atherosclerosis, they should receive intensive preventive interventions to reduce their cardiovascular risk. Blood pressure control, lipid-lowering therapy, angiotensin-converting enzyme inhibition, and antiplatelet drugs significantly reduce the risk of cardiovascular events.

**Discussion points**

- Primary prevention for PAD patients with diabetes involves an individualized pharmacotherapeutic approach which may involve aspirin, clopidogrel and beraprost. Secondary prevention may involve a combination of aspirin and antiplatelet agent.
- High dose statin therapy can be important in the management of atherosclerosis in patients with PAD and diabetes.

**REFERENCES**


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**Endovascular and Medical Treatment of Lower Extremity Ischemia**

Dr. Kun Fang  
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Although it is frequently undiagnosed, it has been estimated that 4.3% of the US population ≥40 years has PAD, and a similar prevalence has been found in Western Europe, with population studies estimating the prevalence between 4–8%. A survey of PAD in the Chinese natural population showed that the overall prevalence was 3.08% (2.52% in males and 3.66% in females), and prevalence significantly increased with age in population (p<0.01). Moreover, the prevalence of lower extremity arterial disease (LEAD) in the natural population was 6.2%; among the population with diabetes and metabolic syndrome, the incidence was up to 38.7% and 45.1%, respectively. Correlative analysis based showed a significantly positive correlation between the occurrence and the severity of LEAD with risk factors, including age, smoking, diabetes, high systolic blood pressure and high low-density lipoprotein cholesterol. ABI >1.3 was also found to be an independent predictor for CVD and PAD.

TASC II recommends that aspirin and clopidogrel effectively reduce risks of cardiovascular events for PAD patient. For the improvement of claudication, a 3- to 6-month course to determine efficacy of cilostazol should be first-line pharmacotherapy to relieve claudication symptoms, improvement in treadmill exercise performance and in quality of life. The randomised, blinded, CAPRIE (clopidogrel versus aspirin in patients at risk of ischaemic events) study, found a modest reduction in the combined risk of ischaemic stroke, myocardial infarction or vascular death with long-term clopidogrel vs. aspirin (8.7%, p=0.043). The overall safety profile of clopidogrel was at least as good as that of medium-dose aspirin (with better gastric tolerance, p<0.05). Meanwhile, a subsequent study found that the combined use of aspirin and clopidogrel is not better than aspirin alone and, more recently, ticagrelor was not found to be significantly better than clopidogrel. Regarding the combination of an oral anti-coagulation plus anti-platelet, this combination was not more effective than antiplatelet therapy alone in preventing major cardiovascular complications and was associated with an increase in life-threatening bleeding.

For antihypertension, the TASC II recommends a target of <140/89 and lower (<130/80) in patients with diabetes and renal insufficiency. Thiazides and ACEI/ARB are the initial recommended blood-pressure lowering drugs. TASC II also recommends that patients with diabetes and PAD should have aggressive control of blood glucose levels with a hemoglobin A1 goal of <7.0% or as close to 6% as possible. Regarding lipid-lowering therapies, all PAD patients should have a target of LDL <2.59 mmol/L (<100 mg/dL), with statins the mainstay of therapy. Finally, TASC II recommend that patients be strongly and repeatedly advised to stop smoking and that supervised exercise therapy should always be considered as part of the initial treat-
ment for patients with claudication and PAD.3)

TASC was a true attempt to collaborate across nations and specialties to develop guidelines for the diagnosis and management of PAD. TASC III, which seeks to achieve transatlantic and interdisciplinary consensus, aims to establish new standards for regulatory approval and reimbursement of new therapies. For CLI, it would expand on amputation-free survival to include healing of ischemic ulcers, relief of ischemic pain, avoidance of additional procedures and improvement in functional status.

Recently, a TASC systematic review and consensus was published on the prioritization of treatments for lower extremity peripheral artery disease in low- and middle-income countries.5) Pharmacotherapy for intermittent claudication was found to be expensive and improve walking distance by a modest amount. Exercise and endovascular therapies were more effective and exercise the most cost-effective. For CLI, bypass surgery and endovascular therapy, which are both resource intensive, resulted in similar rates of amputation-free survival. Substantial reductions in cardiovascular events occurred with use of low cost drugs (statins, ACE inhibitors, anti-platelets) and smoking cessation. The panel concluded that, in low- and middle-income countries, cardiovascular prevention is a top priority, whereas a lower priority should be given to pharmacotherapy for leg symptoms and revascularization, except in countries with established vascular units.

Various techniques are available as first-line strategies for endovascular repair in PAD, these include stent implantation, covered stent, drug-eluting stents, drug-coated balloon (DCB), cutting balloon angioplasty (CBA), directional atherectomy (debulking). A hybrid procedure can be used for patients with complicated pathology (including multilevel lesions, disappointing long-term patency after percutaneous transluminal angioplasty [PTA] and poor PTA access). In a study involving DES, 228 implantations were performed with no procedural deaths; 96% of patients were discharged within 24 h. The 3-year cumulative incidence of amputation was 6 ± 2%, survival was 71 ± 5%, and amputation-free-survival was 68 ± 5%.9) DCB is the current preferred approach in China with many DCBs available commercially. One study involved 476 patients with symptomatic intermittent claudication or ischemic pain. At 12 months, the rate of primary patency among patients, drug-coated balloon vs. conventional angioplasty (65.2% vs. 52.6%, p = 0.02). The incidence of freedom from primary safety events was 83.9% with the DCB and 79.0% with standard angioplasty (p = 0.005).10) In a study involving CBA, 73 patients with symptomatic lower limb ischemia underwent the procedure, 20% adjunctive stenting because severe intimal dissection or inadequate hemodynamic result. Overall, 89.5% of threatened limbs were salvaged after mean follow-up of 1 year.11) Below the knee lesions can be treated successfully and safely with directional atherectomy and midterm clinical results are encouraging.

Discussion points

• Regarding TASC III, it is difficult to say what is the discipline of the main person governing the consensus procedure as so many society leaders have joined the process from many different regions of the world. Collectively they represent vascular surgeons, cardiologists, endocrinologists. For the different aspects of the process, different specialties tend to take the lead in guiding the process and recommendations.

• It should also be noted that we may have to wait 4–5 years for the publication of TASC III.

• It was pointed out that most of the data informing TASC to date has come from registry studies and trials conducted in higher income countries; there is a paucity of data from low and middle-income countries for which TASC next aims to make better recommendations. More studies on Asian PAD populations and with the hindsight of improved study designs than many conducted to date are therefore called for. These should also take into account the heterogeneous Asian populations, climates, diets, and lifestyles.

• For managing lower extremities symptoms for patients with PAD, it is important to consider the presence of inflammation and autoimmunity factors within the wall of the vessels in your selection of treatment. Conservative treatment may therefore be the best approach in this situation.

REFERENCES


Day 1, Session 2: Special Lecture

Chairperson:
Dr. Hiroshi Shigematsu
Executive Director of Vascular Surgery, Sanno Medical Center, Professor of Clinical Research Center for Medicine, International University of Health and Welfare, Tokyo, Japan

Trends in Japanese Patients with Critical Limb Ischemia

Dr. Nobuyoshi Azuma
Professor and Chairman, Vascular Surgery, Asahikawa Medical University, Asahikawa, Japan

The features of CLI have recently been changing in Japan. The combination of an increasing proportion of the population aged >65 years and an increasing prevalence of diabetes, means that longer exposure to diabetes is enhancing vascular disease including PAD and renal disease. Table 1 details some key differences emerging between populations of patients with CLI included in trials over the past 12 years, notably the higher proportion of patients with diabetes and end stage renal disease (ESRD) in Japan than elsewhere.

Table 1 Key demographic differences between CLI patient populations

<table>
<thead>
<tr>
<th>Study Name</th>
<th>BASIL trial</th>
<th>PREVENT III</th>
<th>OLIVE registry</th>
<th>SPINACH study</th>
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<td>Multicenter RCT</td>
<td>Multicenter registry</td>
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<td>CLI</td>
</tr>
<tr>
<td>No of patients</td>
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<td>559</td>
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<td>Comorbidities</td>
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The tissue loss involved in an infrapopliteal arterial lesion with microcirculation disorder occurs easily in Japanese CLI patients. Consequently, we need evidence on how to select the best revascularization procedure for infrapopliteal arterial lesions with tissue loss. The key features of CLI in dialysis-dependent patient are long diffuse infrapopliteal arterial disease with severe calcium concomitant with below-the-ankle arterial disease. They have a high prevalence of cardiovascular comorbidities and poor life prognosis. Their lesions easily develop into advanced gangrene and deep infection. As dialysis-dependent patients are too sick to perform major surgery, we believe that these patients group should be managed with EVT first. However, long diffuse infrapopliteal arterial disease with severe calcium sometimes increases the risk for EVT failure.

The options for revascularization for infrapopliteal arterial disease include distal bypass or balloon angioplasty.

How should we decide the adequate procedure for each patient or each lesion? It is important to consider both the extent of arterial lesion (by TASC guideline; however, there is no description regarding infrapopliteal lesion in TASC II), the life expectancy of the patient (based on the BASIL trial; however, only 42% of enrolled patients were diabetic and 31% of bypasses were infrapopliteal, including only 1.7% of pedal bypass) and the wound status (possibility for healing) and the potential for walking.5)

Heterogeneity is the main reason why it has been so difficult to establish a clinically relevant guideline for CLI. Factors affecting decision making process of CLI treatment include vascular factors (i.e., focal or diffuse lesion, heavy calcification, etiology, quality of vein conduit) systemic factors (i.e., cardiac risk, renal function, walking ability, life expectancy, wound healing ability), ulcer status (i.e., Rutherford 5 or 6, heal gangrene, infection) and social factors (device differences, knowledge and skill of the vascular team). We must also add the patient’s background, the goals of treatment (Fig. 1) and the clinical circumstances (including devices and players) to this mix.

Fig. 1 Heterogeneity of treatment goal for the CLI patient.

The SPINACH registry is a clinical study designed and carried out by both vascular surgeons and interventional cardiologists collaboratively to investigate current treatment for CLI in Japan.4) The registry aimed to recruit approximately 450 patients with CLI, including approximately 150 patients who underwent bypass surgery and approximately 300 patients who underwent endovascular treatment in 23 institutions (Fig. 2). The primary endpoint is amputation-free survival at 36 months (chosen because this endpoint can more easily be compared to historical data). Secondary endpoints include freedom from MALE (major adverse limb event) + POD (perioperative death), initial success rate, hemodynamic status of revascularized limb, freedom from major amputation at 36 months, freedom from MACE (major adverse cardiovascular event) at 36 months, cardiovascular events, re-intervention, survival at 36 months, patency rate at 36 months, ulcer healing, and their composite outcomes.6) Figure 3 shows the number of registered patients. To date, more than 500 CLI patients have been registered, and 3 year follow-up has been completed. Overall, SPINACH aims to provide a suitable patient model for each revascularization procedure, bypass and endovascular treatment, and will expound on the role of each approach for critical limb ischemia treatment.

The aim of the SPINACH study is not to determine which treatment (EVT or surgical revascularization) is better for CLI. The study findings are expected to help clinicians choose an appropriate revascularization procedure according to the patient’s general condition and foot lesions severity evaluated by WIfI classification system.6)
An increasing incidence of diabetic and dialysis-dependent patients as well as an aging population, have led to an acceleration in the number of older CLI patients with tissue loss in Japan. Therefore, a reduction of invasiveness of distal bypass technique for CLI is needed in order to encourage wider use of this procedure. Techniques being investigated include small skin incision, in situ grafting, hybrid revascularization and use of nerve block anesthesia. For infrainguinal bypass surgery the lower extremity nerves to be blocked are the femoral nerve and the sciatic nerve. The nerve block technique is very useful not only for infrainguinal bypass surgery but also minor amputation and plastic surgeries for salvaging foot.

Discussion points

- Importance of taking the patient’s history before surgery including cardiac and lung function and also their nutritional status.
- The assessment of patients’ general condition and of their lower extremity lesions are highly important in determining the most suitable treatment strategy for CLI.
- Considering that CLI patients with lower extremity arterial lesions will rapidly increase in number in Asia, a system that can provide both EVT and bypass surgery in a well-balanced manner is needed.

REFERENCES


Day 2, Session 3

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Management of PAD in Korea, a Vascular Surgeon’s Perspective

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In the 21st century, PAD has become a global problem. The worldwide prevalence of lower extremity PAD is between 3–12%. In 2010, 202 million people around the world were living with PAD; there are 55 million individuals in southeast Asia and 46 million in the western pacific region living with PAD. The number of individuals with PAD increased by 29% in low/middle income regions and 13% in high income regions from 2000 to 2010 compared with the preceding decade. 1) In specific countries, 4.3% of the Singaporean population had an abnormal ABI result (higher in Malay, Indian patients), 2) and in Korea, 3.2% showed an abnormal ABI result amongst 2,002 T2D patients. 3)

Undoubtedly, endovascular interventions have gained increased acceptance as a first-line treatment strategy to vascular surgeon for PAD patients. In Korea, while leg artery bypass surgery rates have remained relatively stable at approximately 1,300 performed per year, leg artery EVT–PTA is increasing (from around 6,500 in 2010 to almost 13,000 in 2014), with a
similar trend for leg artery EVT-stent. Surgery has numbered consistently less than 1,500 between 2010–2014, while EVT overall has increased from, 11,144 in 2010 to almost 20,000 in 2014. **Figure 1** shows the types of treatment patients receive in different regions of the world for PAD, with EVT and medical therapy dominating in all areas; **Fig. 2** shows PAD treatment approach by anatomy. For the iliac artery, stenting is typically the first treatment (>80%); infrapopliteal, balloon angioplasty most common; and femoropopliteal, stenting and angioplasty used equally.

**Fig. 1** Global treatment of PAD.

**Fig. 2** PAD treatment by anatomy.

The big question in leg artery EVT is how can we keep it open? Paclitaxel balloon vs. drug eluting stents (DES). This is being investigated in the IN.PACT global study de novo in-stent restenosis imaging cohort, a study of drug-coated balloon treatment for femoropopliteal artery disease. A total of 131 subjects with 149 in-stent restenosis (ISR) lesions were included for analysis. The mean age of the cohort was 67.8 years and mean lesion length was 17.17 ± 10.47 cm, including 34.0% total occlusions and 59.1% calcified lesions. The 12-month Kaplan–Meier estimate of primary patency was 88.7%. The rate of clinically driven target lesion revascularization (CD TLR) at 12 months was 7.3%. The primary safety outcome, a composite of freedom from device- and procedure-related mortality through 30 days and freedom from major target limb amputation and CD TLR within 12 months, was 92.7%. There were no major target limb amputations, no deaths, and a low (0.8%) thrombosis rate. Moreover, the 12-month outcomes showed a very low incidence of CD-TLR in the Asian population.

A retrospective, multicenter analysis from Japan investigated angiographic dissection patterns after balloon angioplasty for superficial femoral artery (SFA) lesions. A total of 621 patients (mean age 72.8 ± 9.5 years) were examined with 748 symptomatic de novo SFA lesions treated with endovascular therapy. No dissection was found in 16% (120/748) of lesions, and types A and B dissections were seen in 19% (142/748) and 23% (172/748), respectively. Severe dissection was found in 42% of cases after PTA. A small vessel diameter and/or TASC II C/D lesions were related to a high incidence of dissection. These findings indicate that severe dissection during procedures employing balloon angioplasty only could affect long-term patency.

However, is this strategy carrying over into clinical studies and real-world use? Provisional stenting in DCB studies ranges from 2–50%. Reimbursing DCB and DES in Korea will change the physician’s choice regarding extension of vessel patency results. However, surgery still offers robust outcomes in complicated cases where hybrid procedures (e.g., combinations of endarterectomy or bypass + thrombectomy + PTA or stent) may be considered. Even with wound related complications, the merit of surgery is in offering long term patency compared to less invasive endovascular treatment. It is consequently recommended as 1st therapy for the young, healthy patient.

**Discussion point**

- For reasons of cost and reimbursement, we have to very carefully select the device for each segment of a procedure.

**REFERENCES**


**Closing Remarks**

Dr. Jung Kee Chung closed the 9th PAD Workshop by summarising the key points of each international expert and thanking the organisers and participants. Delegates attended from across Asia, notably from China, Indonesia, Korea, Thailand and Japan.