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*Special Article*

## *Research Development of Vascular Surgery in Thailand*

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### **Abstract**

Vascular surgery in Thailand has been developing the research in 5 clinical aspects: peripheral arterial occlusive diseases (PAOD), aneurysm, venous thromboembolism, varicose vein and vascular access for hemodialysis to improve surgical care of vascular diseases toward international standard. The present article summarizes the development of research on PAOD in the past 40 years.

Vascular surgery in Thailand in the past 40 years has been developing the research in 5 clinical aspects, peripheral arterial occlusive diseases (PAOD), aneurysm, venous thromboembolism, varicose vein and vascular access for hemodialysis to improve surgical care of vascular diseases toward international standard. The present article reviews the development of research on PAOD. Epidemiologic study of atherosclerosis obliterans in lower extremities in Thai patients was the original clinical research of PAOD in Thailand. Diabetes mellitus and cigarette smoking were announced as the major risk factors in this clinical problem, causing major limb loss and high mortality in our population. The most effective treatment during that time was arterial bypass surgery.

Major limb amputation with poor quality of life at post-operative period induced a higher mortality rate than revascularization procedure. The research has encouraged surgeons to attempt surgical revascularization for limb salvage rather than major amputation.<sup>1</sup>

Regarding diabetic mellitus being the major risk factor of PAOD, the comparative study in clinical aspects of PAOD in diabetic patients and non-diabetic patients were carried out. The arterial occlusions have been involved more distally and more multiple levels in diabetic patients. Limb infection were also found more frequently in diabetic patients causing major limb loss. This research provided the information for the strategy of arterial bypass surgery more extensively in the distal

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area of arterial occlusion particularly in diabetic patients. The composite vascular conduit has been created for the numerous extensive and innovative surgical procedures to achieve limb salvage. However, the clearance of foot infection was the priority to surgical revascularization in diabetic patients.<sup>2</sup>

Arterial embolism was the major cause of acute limb ischemia requiring emergency revascularization with substantial varieties of treatment outcome. The most important prognostic factor was the duration between the onset of disease and the timing of revascularization. The research clarified that the surgical treatment within 24 hours achieved more than 90% successful limb salvage whereas the revascularization procedure after 24 hours had only 40% success rate requiring more adjunct procedures for the better outcome. This research has created a strong policy to educate the surgical trainees and general practitioners for the early diagnosis of this disease from clinical criteria.<sup>3</sup>

The common causes of acute limb ischemia were acute arterial embolism and acute arterial thrombosis carrying the different types of revascularization procedure. Acute arterial embolism could be simply treated by surgical embolectomy whereas acute arterial thrombosis required the more complicated procedures for limb salvage such as arterial endarterectomy, arterial bypass surgery or endovascular therapy which were not available through the whole country. For general surgeons working in countryside without the facilities of angiography, surgical equipment for complex vascular procedure and endovascular devices, the differentiation of these diseases by clinical manifestations was essential for the decision making of treatment in their hospitals with limitation of facilities or referral to the medical center. The research of clinical differentiations of these diseases was conducted for this purpose and the results were in the followings. The progression of severity of acute limb ischemia due to arterial embolism was more rapidly worse than arterial thrombosis. History of intermittent claudication was found more commonly in arterial thrombosis. Normal peripheral ankle pulses in contralateral limbs were more detected in arterial embolism. The clinical risk factors such as atrial fibrillation was more associated in arterial embolism whereas diabetes mellitus and smoking were more commonly found in arterial thrombosis. This research provided clinical information useful for general surgeons in taking care of patients with acute limb ischemia.<sup>4</sup>

The clinical trial of stem cell therapy was originally conducted to avoid major amputation in patients with chronic limb threatened ischemia (CLTI) and poor distal arteries prohibiting revascularization procedure for limb salvage. With the cooperation of Ben-Gurion University in Israel, stem cells (angiogenic cell precursors) being cultivated and proliferated from peripheral blood were subsequently injected into calf muscles of patients with critically ischemic limbs and ischemic ulcer. The success rate of healing of ischemic ulcers was 80%. This was the first clinical trial of stem cell therapy for CLTI in Thailand.<sup>5</sup> Subsequently, the new generation of stem cells has been developed and cultivated in the same institute to clarify the possibility of their efficiency in vitro.<sup>6</sup> Then, a clinical pilot study of the effectiveness of this generation of stem cells has been conducted in CLTI patients with 87% successful outcome of limb salvage.<sup>7</sup>

In patients with foot ulcer particularly in diabetic patients, the possibility of complete healing could be determined by transcutaneous oxygen pressure measurement. This prediction was extremely important in clinical practice whether the revascularization was required. This research was originally conducted to determine the level of skin oxygen pressure required for successful healing of foot ulcer. The results of this study could clarify the clinical application of this laboratory test for the effective evaluation of this common problem in general practice.<sup>8</sup> The innovation of original treatment modality for the reperfusion injury of severely acute limb ischemia of bilateral lower extremities was to divert venous blood from leg veins through hemodialysis machine and subsequently to reinfuse into systemic circulation through neck vein during revascularization procedure. The venous blood containing high potassium and anaerobic metabolic acids were equilibrate in the hemodialysis process instead of entering into systemic circulation. This innovative model could save life and limb of patients suffering from the reperfusion injury in acute limb ischemia, a high mortality and morbidity condition.<sup>9</sup>

Poor distal artery run off prohibits successful revascularization procedures for chronic limb threatened ischemia (CLTI) either arterial bypass surgery or endovascular therapy. Major limb amputation is inevitable in this situation. A case series with innovative surgical procedure to revascularize ischemic foot through the deep vein at the ankle with the disruption of distal vein valve for limb salvage in CLTI with non-reconstructable distal arteries was announced in the publication.<sup>10</sup>

The surgical technique has been worldwide accepted for the achievement of limb salvage in the desperate situation and presented in the international vascular meeting for more than 10 years. Furthermore, endovascular procedure has currently created by using the same principle of this surgical technique.<sup>11</sup>

After developing the composite graft to be vascular conduit in arterial bypass surgery, multiple extensive surgical procedures have been created for successful revascularization in the highly complicated PAOD. A case of the most extensive arterial bypass from ascending thoracic aorta to bilateral popliteal arteries for the advanced arterial occlusive disease from aorto-iliac, ilio-femoral, and femoro-popliteal arteries and failure of multiple attempts of axillo-bifemoral bypasses has been reported. The long-term patency of this procedure was 9 years without reintervention procedure.<sup>12</sup>

Two epidemiologic studies of Buerger's disease were carried out in Thai patients. This disease was found mostly in young men with heavy smokers causing inflammatory occlusive disease of upper and lower extremity arteries. There was a seasonal variation of this disease in the Northern part of Thailand.<sup>13</sup> The highest prevalence of this disease was in winter followed by rainy and summer season. However, the incidence and recurrence of this disease were decreased in the Northern part of Thailand. This information may be due to the successful campaign of cigarette cessation in the community.<sup>14</sup>

A case series of necrotizing arteritis from *Pythium insidiosum* (vascular pythiosis) were reported.<sup>15,16</sup> This disease was found in Thalassemic patients working in the swamps with accidental minor injuries of their feet. This fungus mainly found in standing water and occasionally soil in the tropical countries could penetrate through small wounds and cause necrotizing inflammation in the surrounding arteries with rapid progression towards proximal arteries of lower extremities. The diagnostic modalities of this disease were identification of microorganism, immunological studies, computed tomographic angiography (CTA). Adequate surgical removal of microorganisms was only treatment option. Major limb amputation was most commonly carried out among these patients. The residual microorganisms would definitely cause recurrent disease and mortality. Therefore, when the disease has been involved the arteries above the groins, the mortality of these patients was 100%. A challenging case of supra-inguinial vascular

pythiosis successfully treated by aggressive surgical eradication has been reported.<sup>17</sup> A patient with infected aneurysm of external iliac artery and thrombosis of the whole lower extremity arteries was treated by above knee amputation and extensive surgical removals of all iliac arteries with surrounding tissues. This patient has survived after 3-year follow up with good condition. Furthermore, the factors influencing the outcomes of treatment of this disease were identified through a retrospective case record review of these patients.<sup>18</sup> Early detection of this disease combined with multidisciplinary approach to treatment including aggressive surgical removal, antifungal agents, and immunotherapy offered the best outcome of management.

Arterial embolism is the well known as the cause of acute limb ischemia whereas chronic arterial embolism has never been recognized in the arterial occlusive disease of lower extremities. The epidemiologic study of chronic arterial embolism was carried out to demonstrate that this disease could be one of the causes of chronic limb threatened ischemia carrying different types of treatment from atherosclerosis obliterans (peripheral atherosclerotic occlusive disease) and worst prognosis requiring major limb amputation in late stage of disease with fibrotic arteries.<sup>19</sup> The information of this study has encouraged the awareness of this disease in order to provide the treatment at early stage to improve limb salvage rate in surgical practice.

Arterial embolism could originally be treated by surgical embolectomy with balloon Fogarty catheter in immediately threatened acute limb ischemia. Later, chemical thrombolytic therapy was introduced to dissolve thrombus in the artery as another therapeutic option of this disease. With the delayed effect of successful treatment, the latter treatment modality has been applied in the lesser degree of acute limb ischemia. Subsequently, the clinical study of the effectiveness of catheter-directed thrombolytic therapy was carried out for the treatment of marginally threatened acute limb ischemia in Thailand.<sup>20</sup> Despite the successful outcomes, the awareness of this treatment modality was major bleeding requiring the intensive monitoring of coagulation study. Moreover, when arterial embolism occurred more than 24 hours, the thrombus induced an inflammatory reaction and adhesiveness at inner layer of arterial wall. At this stage, balloon Fogarty catheter could not completely remove thrombus from arterial lumen. The clinical study of the effectiveness of intraoperative thrombolytic therapy in

conjunction with surgical embolectomy of immediately threatened limb ischemia of lower extremities was carried out in Thailand.<sup>21</sup> The technique could improve the successful thrombus removal in the delayed treatment of acute arterial embolism.

The limited awareness of carotid artery stenosis, one of the common causes of ischemic stroke in general practice resulted in minimal prevalence of surgical correction for this disease in Thailand. With the improvement of duplex ultrasonography to demonstrate the pathology of carotid artery, the number of carotid endarterectomies has been substantially increased among several vascular surgery training centers. A case series of 100 patients undergoing carotid endarterectomy for symptomatic extracranial carotid artery stenosis with 10-year follow up has been reported from a university hospital with successful outcomes.<sup>22</sup>

With the improvement of vascular service in Thailand toward international standard, the invitations to participate in global clinical trials were sent to Thai Vascular Association and distributed to all vascular surgery training centers in Thailand with achievement of the awards of the clinical trials.<sup>23-25</sup>

## CONCLUSION

In conclusion, this summary of research development of peripheral arterial occlusive disease should provide the information as a history and basic knowledge of this clinical aspect in Thai population for the future research project to improve the management of this major problem of vascular surgery in Thailand.

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