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Distribution of Peripheral Arterial Disease in Patients Undergoing Endovascular Revascularization for Chronic Limb Threatening Ischaemia: Insights from the Vascular Quality Initiative in Singapore

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This study aimed to examine the distribution of lower limb atherosclerotic lesions in a multi-ethnic Asian cohort with chronic limb threatening ischemia (CLTI) from Singapore. The Society for Vascular Surgery Vascular Quality Initiative registry database was used to identify 265 CLTI patients who underwent percutaneous angioplasty between June 2019 and December 2019, of whom 171 (64.5%) were male, and the mean age was 67.9±11.0 years. The majority were diabetic (84.5%) and 145 (54.7%) had chronic kidney disease (CKD). The majority of the lower limb atherosclerotic lesions were de novo lesions (598/797, 75.0%), predominantly TransAtlantic Inter-Society Consensus II C/D (451/797, 56.6%), and were moderately to severely calcified (76.3%). The anterior tibial artery and femoral-popliteal artery were the most commonly affected vessels. The mean length of the treated lesions was 14.5±13.7 cm. There was a tendency, albeit insignificant, of multi-level disease in those who were diabetic or had CKD.

Key Words: Angioplasty, Peripheral arterial disease, Lower extremity, Ischemia, Singapore

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INTRODUCTION

Chronic limb-threatening ischemia (CLTI), the most severe stage of peripheral arterial disease (PAD), is characterized by atherosclerotic occlusion of the lower extremity arteries with pain at rest, gangrene, and ulceration for more than two weeks. When left untreated, it can lead to major lower extremity amputation (LEA), reduced quality of life, and increased mortality. A 2019 systematic review found that the global estimates of individuals with PAD above the age of 25 years were 236 million in 2015 [1]. Advanced age, smoking, hypertension, and cardiovascular diseases were also associated with a higher risk of PAD. The majority of the included studies consisted mainly of Caucasian cohorts, indicating a lack of data on PAD in the Asian population.

The prevalence of PAD in Asian cohorts is reported to be 6%-10% [2]. The Singapore Reduction of Atherothrombosis for Continued Health (REACH) registry estimated that PAD affected 8.1% of the local population in 2008, with a mean age of 64.4±9.8 [3]. The PAD cohort in Singapore is frailer than its Western counterparts, with a high proportion of patients with concomitant comorbidities, such as diabetes mellitus, chronic kidney disease (CKD), and congestive heart failure [2]. These comorbidities may contribute to the late diagnosis and treatment of PAD, increased healthcare costs, and a higher incidence of adverse outcomes. PAD prevalence also increases with age (20% at 40 years of age to 29% in those aged over 50 years). Hence, PAD contributes to frailty in the growing local population.

The Society for Vascular Surgery (SVS) Vascular Quality Initiative (VQI) is an ongoing prospective international registry consisting of detailed clinical data on common vascular procedures. The VQI was designed to improve patient care through the dissemination of information, streamlining variations in practices, and international benchmarking guidelines for vascular surgical practices. Centers enrolled in the VQI were reported to receive biannual "Center Opportunity Profiles for Improvement" reports, which consolidate procedural outcomes into actionable center-level data to improve patient care. As of January 2021, more than 360 peer-reviewed publications have been published from the SVS VQI documenting regional demographic variations and outcomes for quality improvement in vascular surgery. Consisting of 750 participating institutions, including academic medical centers, teaching hospitals, and individual clinics across the United States and Canada, our local vascular center joined this collaboration 18 months ago and is the first and only Asian-based vascular center to contribute to this growing United States-based vascular registry.

This study aimed to highlight the demographics and distribution of lower limb anatomical arterial occlusive lesions in patients with localized PAD who are undergoing endovascular revascularization.

METHODS

This was a retrospective observational study of the SVS-VQI registry. Modeled after the Vascular Study Group of New England (www.vqi.org), the goal of VQI is to utilize aggregated data to recognize variations in procedures and outcomes through the collaboration of regional quality groups. It is a web-based data collection platform that captures a range of variables, such as patient demographics and clinical, perioperative, and postoperative details. Between January 2018 and December 2020, there were a total of 108,960 percutaneous vascular interventions registered in the VQI registry across 793 participating centers. This study was approved by the SingHealth Centralised Institutional Review Board (CIRB number: 2018/2995). Patient consent was waived, given the deidentified nature of the data.

The VQI database was used to identify CLTI patients who underwent lower limb angioplasty for limb salvage between June 2019 and December 2019 at our local hospital, a tertiary vascular center located in central Singapore. We perform over 900 lower limb salvage procedures annually. Of these, 95% are for CLTI (Rutherford 5-6). The institution has adopted an endovascular-first approach since 2005 and has performed approximately 10-15 surgical bypasses per year for failed endovascular revascularization. All patients who underwent elective, urgent, or emergency percutaneous transluminal angioplasty (PTA) were included (Elective, planned; Urgent, required within 72 hours after 12 hours of admission; Emergency, required within 12 hours of admission). We reviewed patient demographics, comorbidities, clinical history, symptoms, lesions, and perioperative details. Data forms, the definitions of comorbidities, and procedural details within the VQI are available online at www.vqi.org.

The variables were summarized using descriptive statistics. Categorical data are reported as numbers and percentages. Continuous variables are reported as means and standard deviations. Univariate analysis for categorical and continuous variables was performed using the chi-squared test and Mann–Whitney U-test, respectively. Statistical significance was set at $P<0.05$. All statistical analyses were performed using R version 1.3.1 (R Development Core Team, 2013; http://www.r-project.org/).

RESULTS

A total of 291 procedures were identified, and 265 patients (294 limbs) were included, of whom 171 (64.5%) were males, and the mean age was 67.9±11.0 years. The majority of the patients were Chinese (175, 66.0%), diabetic (224/265, 84.5%), hypertensive (240, 90.6%), and had a history of coronary artery disease (156/265, 58.9%) and CKD (145/265, 54.7%). Baseline demographics are shown in Table 1.

The majority of wounds were Rutherford 6 (192/294, 65.3%), followed by 40/294 (13.6%) Rutherford 5 (non-healing amputation wounds), and 26/294 (8.8%) with ischemic pain at rest (Table 2) [4]. The mean Wound, Ischemia, and foot Infection (WIfI) score was 3.02±1.98, and the mean toe pressure was 43.5±26.9 mmHg. Risk stratification based on WIfI scores showed that 115/294 (39.1%) limbs were at moderate to high risk of amputation (majority>wound 1, ischemia 2, foot infection 2).

A total of 797 lesions were treated. The majority were de novo lesions (598/797, 75.0%). The majority of lesions were TransAtlantic Inter-Society Consensus II (TASC II) C and D (25.2% and 31.4%, respectively). Most were moderately to severely calcified (608/797, 76.3%) (Table 3). The anterior tibial artery and the femoral-popliteal artery were the most commonly treated vessels (168/797, 21.1% and 103/797, 12.9%, respectively). The mean length of the treated lesions was 14.5±13.7 cm. The majority of lesions were multi-level

Table 1. Patient demographics

Characteristic	Patient (n=265)
Age, years	67.9±11.0
Body mass index, kg/m^2	20.2±4.0
Sex	
Male	171 (64.5)
Female	94 (35.5)
Ethnic group	
Chinese	175 (66.0)
Malay	39 (14.7)
Indian	45 (17.0)
Eurasian	3 (1.1)
Indonesian	1 (0.4)
Caucasian	1 (0.4)
Myanmar	1 (0.4)
Smoking status	
Non-smoker	162 (61.1)
Smoker	57 (21.5)
Ex-smoker	46 (17.4)
Comorbidities	
Diabetes	224 (84.5)
Hypertension	240 (90.6)
Coronary artery disease	156 (58.9)
Chronic kidney disease	145 (54.7)
On dialysis	87 (32.8)
Cerebrovascular disease	68 (25.7)
Dysrhythmia	53 (20.0)
Congestive heart failure	46 (17.4)
Chronic obstructive pulmonary disease	11 (4.2)
Chronic medications	
Pre ACE-inhibitor/ARB	264 (99.6)
Statin	234 (88.3)
Antiplatelets	216 (81.5)
Prior interventions	
Leg arterial bypass/endarterectomy/PVI	131 (49.4)
Percutaneous coronary intervention	64 (24.2)
Coronary artery bypass graft	58 (21.9)

Values are presented as mean±standard deviation or number (%).
ACE, angiotensin-converting enzyme; ARB, angiotension receptor blocker; PVI, peripheral vascular intervention.

Table 2. Indications for intervention

Reason for intervention	Limb (n=294)
Side	
Right	153 (52.0)
Left	141 (48.0)
Prior interventions	
Angioplasty (ipsilateral)	111 (37.8)
Amputations	
Minor (leg, foot, toe)	66 (22.4)
Major contralateral (AKA, BKA)	23 (7.8)
Femoral endarterectomy	6 (2.0)
Urgency	
Urgent	209 (71.1)
Elective	75 (25.5)
Emergency	10 (3.4)
Rutherford classification	
6 (necrotic ulcer)	192 (65.3)
5 (non-healing amputation)	40 (13.6)
4 (ischemic rest pain)	26 (8.8)
3 (claudication)	32 (10.9)
0 (asymptomatic)	4 (1.4)
Wound, Ischemia, and foot Infection score	3.02±1.98
Toe pressure, mmHg	43.5±26.9
Risk of amputation[a]	
1 (very low risk)	104 (35.4)
2 (low risk)	75 (25.5)
3 (moderate risk)	46 (15.6)
4 (high risk)	69 (23.5)
Multi-level disease	194 (66.0)
FP+tibial	172 (58.5)
Iliac+FP	14 (4.8)
Iliac+FP+tibial	8 (2.7)

Values are presented as number (%) or mean±standard deviation.
AKA, above-the-knee; BKA, below-the-knee; FP, femoral-popliteal.
[a]Risk of amputation according to Wound, Ischemia, and foot Infection category derived from the article of Mills et al. (J Vasc Surg 2014;59:220-234.e1-2) [4].

(194/294 limbs, 66.0%) and distributed amongst the femoropopliteal and tibial regions (172/294 limbs, 58.5%). There were also 68/797 (8.5%) lesions that were inframalleolar.

Subgroup comparisons between diabetics and non-diabetics showed a higher distribution of severely calcified, multi-level, TASC II C lesions among diabetics (severely calcified 39.5% vs. 29.4%, P=0.046; multi-level 59.8% vs. 52.1%, P=0.408; TASC II C 27.4% vs. 12.6%, P<0.001). Interestingly, there was a significantly higher proportion of TASC II D and iliac artery lesions among patients who were non-diabetic (TASC II D, non-diabetes mellitus (DM) 42.9% vs. DM 29.4%, P=0.005; iliac artery, non-DM 9.2% vs. DM 2.8%, P=0.002). There was also a higher proportion of diseased multi-level femoropopliteal-tibial lesions among patients with diabetes and patients with CKD, though this difference was non-significant (DM 59.8% vs. non-DM 52.1%, P=0.408; CKD 62.5% vs. non-CKD 53.7%, P=0.161) (Fig. 1).

Table 3. Distribution of lesions between diabetics and non-diabetic subgroups

Characteristic	Total (n=797)	Diabetic (n=678)	Non-diabetic (n=119)	P-value
Technical success				
Successful (stenosis≤30%)	733 (92.0)	630 (92.9)	103 (86.6)	0.053
Technical failure	42 (5.3)	32 (4.7)	10 (8.4)	
Stenosis>30%	22 (2.8)	16 (2.4)	6 (5.0)	
Lesion length, cm	14.5±13.7	14.5±13.9	14.9±12.6	0.446
De novo lesion	598 (75.0)	506 (74.6)	92 (77.3)	0.611
Re-stenotic				
Prior angioplasty	167 (21.0)	151 (22.3)	16 (13.4)	
Prior stenting	32 (4.0)	21 (3.1)	11 (9.2)	
TASC II				
A	133 (16.7)	114 (16.8)	19 (16.0)	0.924
B	213 (26.7)	179 (26.4)	34 (28.6)	0.703
C	201 (25.2)	186 (27.4)	15 (12.6)	<0.001
D	250 (31.4)	199 (29.4)	51 (42.9)	0.005
Calcification				
Severe	303 (38.0)	268 (39.5)	35 (29.4)	0.046
Moderate	305 (38.3)	266 (39.2)	39 (32.8)	0.217
Mild	122 (15.3)	105 (15.5)	17 (14.3)	0.843
Focal	52 (6.5)	29 (4.3)	23 (19.3)	<0.001
None	15 (1.9)	10 (1.5)	5 (4.2)	0.076
Lesion location				
Anterior tibial artery	168 (21.1)	148 (21.8)	20 (16.8)	0.264
SFA+popliteal	103 (12.9)	84 (12.4)	19 (16.0)	0.355
SFA	98 (12.3)	82 (12.1)	16 (13.4)	0.793
Posterior tibial artery	93 (11.7)	78 (11.5)	15 (12.6)	0.849
Tibioperoneal trunk	75 (9.4)	64 (9.4)	11 (9.2)	>0.999
Popliteal	70 (8.8)	62 (9.1)	8 (6.7)	0.484
Peroneal	69 (8.7)	60 (8.8)	9 (7.6)	0.777
Dorsalis pedis artery	47 (5.9)	43 (6.3)	4 (3.4)	0.288
Iliac artery	30 (3.8)	19 (2.8)	11 (9.2)	0.002
Common plantar artery	21 (2.6)	20 (2.9)	1 (0.8)	0.346
Common femoral artery	18 (2.3)	14 (2.1)	4 (3.4)	0.328
Profunda artery	5 (0.6)	4 (0.6)	1 (0.8)	0.555

Values are presented as number (%) or mean±standard deviation.
TASC II, TransAtlantic Inter-Society Consensus II; SFA, superficial femoral artery.

DISCUSSION

Within the vascular field, the VQI is a useful tool for understanding regional cohort outcomes and quality improvement. Thus far, studies reporting outcomes from the VQI database largely examine vascular procedures such as carotid endarterectomy, lower extremity bypass, and aortic aneurysms. The outcomes of endovascular treatments are also largely targeted to the Western populations, leaving a gap in our understanding of the Asian endovascular cohorts. This study demonstrated the distribution of demographics and diseased lesions in Asian patients undergoing endovascular revascularization for PAD. Comparing to the endovascular Western cohorts from the SVS VQI registry [5], the Asian CLTI patient population was more complex, presenting with a higher incidence of comorbidities (84.5% vs. 56.2% diabetics, 54.7% vs. 8.2% CKD, respectively), a higher proportion of severely diseased lesions (78.9% vs. 22.5% TASC C-D, respectively), along with a higher proportion of patients with tissue loss (78.9% vs. 27.6%, respectively). The Singaporean (SG) cohort also appeared to have more comorbidities at baseline than their Asian counterparts in

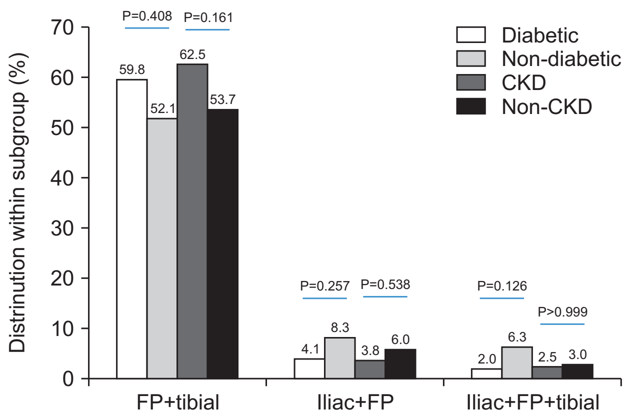

Fig. 1. Distribution of multi-level lesions across subgroups. CKD, chronic kidney disease; FP, femoral-popliteal.

Taiwan (TW) and Japan (JP) (diabetes: SG 84.5%, TW 81%, JP 68%; hypertension: SG 90.6%, TW 85%, JP 81%) [6]. Comparing to data from the 2008 REACH registry, it is also evident that PAD is presenting later within the local population (mean age in 2008: 64.4±9.8 years vs. mean age in 2019: 67.9±11.0 years) [3]. This has impacted clinical practice, as physicians have shifted to an endovascular approach instead of the more invasive open surgical bypass option since older patients are generally frailer and more adverse to procedures involving larger incisions and greater trauma [2].

Despite varying demographics and comorbidities, and consistent with our findings, published evidence supports the hypothesis that patients with diabetes are significantly less likely to have disease in the aortoiliac segment, and more likely to have multi-level diseases and atherosclerotic disease in the tibial vessels [7]. These findings can be attributed to several metabolic consequences of diabetes, such as advanced glycation, changes in low-density lipoprotein cholesterol, abnormal oxidative stress, and platelet activation. Diabetes and its influence on the distribution of atherosclerotic disease are related to poorer outcomes following revascularization procedures. Park et al. [8] demonstrated that patients with diabetes had higher proportions of femoral and below-the-knee lesions and displayed a higher rate of major adverse limb events, especially below the ankle amputations. Furthermore, patients with PAD and diabetes are also more susceptible to microvascular diseases (neuropathy, retinopathy, nephropathy) that cannot be treated by angioplasties as PTA would only restore macrocirculation, resulting in poorer outcomes, such as failure of wound healing post-intervention. The majority of the diabetic lesions treated were also multi-level and extremely severe (65.4% multi-level, 56.8% TASC II C-D). Such occluded distal vessels are often too small to bypass onto, resulting in the need for a larger bypass conduit, further revascularization, or major LEAs.

The clinical benefits of understanding the demographic and anatomical distribution of these lesions are twofold. First, it allows for more streamlined preoperative risk stratification and multidisciplinary optimization to improve periprocedural outcomes. A retrospective analysis of risk factors for immediate technical failure, such as the inability of the guidewire to cross a chronic occlusion, followed patients who had endovascular treatment for femoral-popliteal occlusive lesions and showed that ostial occlusion and heavy calcification of the superior femoral artery and popliteal artery were negative predictors [9]. Predictive models based on these findings may aid physicians in performing an adequate endovascular revascularization procedure in a realistic timeframe. Second, preoperative knowledge of the anatomical distribution of lesions allows for better management of patient and caregiver expectations on wound healing and functional outcomes. TASC II C/D infrapopliteal lesions are associated with higher major LEA and lower primary patency than are TASC A/B infrapopliteal lesions [10]. Thus, early recognition of the potential loss of ambulation status among these complex patients could aid in decision making, including whether the revascularization or major amputation-first policy should be instituted, thereby allowing for better management of postoperative functional outcomes.

CONCLUSIONS

This local Asian CLTI cohort presented with multi-level atherosclerotic disease with long, highly calcified stenotic segments, contrary to our western counterparts [5]. Understanding the underlying chronic comorbidities, such as diabetes and CKD, that contribute to varying PAD severity at presentation may impact decision making for a revascularization- or amputation-first policy and assist in the prediction of realistic postoperative outcomes.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHOR CONTRIBUTIONS

Concept and design: TYT. Analysis and interpretation: TYT, SXYS. Data collection: SXYS, AP, TTC, CJQY, HTT, KHT, CS. Writing the article: TYT, SXYS. Critical revision of the article: TYT. Final approval of the article: TYT. Statistical analysis: SXYS. Obtained funding: none. Overall responsibility: TYT.

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