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Growth and Risk Factors for Expansion of Dilated Popliteal Arteries

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Abstract *Objectives:* The aims of this study were to investigate the change in maximum diameter of ectatic popliteal arteries during ultrasound surveillance and assess clinical predictors of their expansion.
Methods: Over a ten year period 67 patients with ectasia affecting one ($n = 1$) or both ($n = 66$) popliteal arteries entered this surveillance study. Patients were followed for a median of 3.1 years, at a median scan interval of 7.6 months.
Results: Growth of ectatic popliteal arteries was typically slow (<1 mm/yr). Initial artery diameter at entry to the study was not found to be predictive of subsequent growth. Seven patients followed for a median of 2 years had an expansion in popliteal artery diameter to ≥20 mm during follow-up. All of these patients had undergone aneurysm repairs at other arterial sites and none of them had diabetes. These participants also had a significantly higher rate of previous intervention of the contralateral popliteal artery in comparison to those that did not reach the 20 mm threshold ($p < 0.001$). Growth profiles of arteries that underwent significant expansion during surveillance were frequently characterised by a staccato pattern.
Conclusions: Expansion of ectatic popliteal arteries is typically slow but difficult to predict. Trends observed in this study suggest that patients with extra-popliteal aneurysms, patients with previously treated contralateral popliteal artery ectasia and those who are not diabetics may be more prone to significant expansion. Further studies are required to validate these potential growth predictors.

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Introduction

Patients with popliteal aneurysms that are detected early and are treated electively have superior outcomes in terms of limb loss, graft patency and mortality than those who present emergently.[1,2] The risk of thromboembolic complications appears to increase with aneurysm size, however, small aneurysms may still result in clinically silent or symptomatic distal thromboembolism.[3,4] Based on this, it has been advocated that patients with favourable operative risk undergoing surveillance of asymptomatic popliteal aneurysms be considered for intervention once the aneurysm reaches 2 cm in maximum diameter.[5,6] Smaller aneurysms with mural thrombus and evidence of silent or symptomatic thromboembolism should also be considered for intervention.

Duplex examination is commonly used to monitor the growth of ectatic and aneurysmal (henceforward in this article referred to as ectatic) popliteal arteries. In determining appropriate surveillance intervals of ectatic popliteal arteries, an understanding of growth patterns and predictors is required. To date there has been very little data published on the natural history of ectatic popliteal arteries that are relatively small, ie $<$20 mm, with only a few small case series published.[7,8] In the absence of more rigorous data, surveillance intervals are therefore currently determined in an empirical and variable manner.

The aim of this study was to determine the growth rates and patterns of ectatic popliteal arteries, and to define clinical predictors of progressive growth. This information could potentially be applied to help identify those patients most at risk of progressive expansion and complications, and to help determine appropriate surveillance regimens.

Methods

Over a ten year period, patients with popliteal artery ectasia under the care of the Vascular Surgery Department at The Townsville Hospital and The Mater Misericordiae Hospital Townsville were entered into an ultrasound surveillance program. Most patients were recruited after being referred for assessment of an incidentally identified aortoiliac aneurysm ($n = 42$). Five patients were referred specifically with popliteal artery ectasia, of which four were symptomatic requiring immediate repair. The remaining 20 patients were referred to the Vascular Surgery service for consideration of other vascular pathology, and were incidentally found to have prominent popliteal arteries on routine examination.

Inclusion criteria included ectasia of one or both popliteal arteries, patient consent to surveillance, and consideration that the patient would be a potential candidate for intervention. Patients with arteries $>$20 mm in maximum diameter were only entered into surveillance if the vascular specialist considered that patient was at low risk of thromboembolic complications, if intervention was considered higher risk (due to patient co-morbidities or technical reasons) or if the patient declined intervention. Ectasia of the popliteal artery was defined as a maximum popliteal artery diameter greater than the predicted 95% confidence interval based on published nomograms according to gender, age and body surface area.[9] In this cohort, the threshold for considering an artery abnormally dilated varied from 9 to 12 mm according to the published nomograms.[9] Ectasia and aneurysm were not distinguished since no agreed distinction exists. The term ectatic or ectasia is used throughout to refer to popliteal arteries dilated above the predicted normal diameter. Approval from the relevant ethics committee and written patient consent to data collection was obtained.

At entry into the program, a detailed history and clinical examination was conducted by a vascular surgeon, and clinical risk factors and patient characteristics were recorded. Hypertension was defined by a history of diagnosis or treatment for high blood pressure. Diabetes mellitus was defined by a history of or treatment for hyperglycaemia. Dyslipidaemia was defined by a history of or treatment for high cholesterol. Smoking included both current and reformed smokers. Coronary heart disease (CHD) was defined by a history of angina, myocardial infarction or previous treatment by coronary medications or intervention. An arterial aneurysm at a distant site was defined by a history of diagnosis or treatment of an aneurysm at a site other than the popliteal artery.

Maximum popliteal artery diameters were measured by an experienced vascular sonographer on a Philips ATL HDI 5000 machine, with a 7—4 MHz linear array transducer. Surveillance intervals were prescribed by the treating surgeon at their discretion, typically at 6 or 12 month intervals. A total of 67 patients were entered into the program between January 1997 and May 2008.

We carried out a reproducibility study whereby the diameters of 24 popliteal arteries were assessed on two separate occasions by the same sonographer who also carried out the surveillance measurements. The 95% confidence interval of the difference between the readings was -0.74 to 0.49 mm. These findings supported looking for changes of 2 mm to be confident of a real change in diameter.

Statistical analysis was performed using SPSS Statistics Version 17.0 software (SPSS Inc., Chicago). Continuous variables were compared with the Mann—Whitney U test, and dichotomous variables were assessed with the Chi-squared test as appropriate. Differences were considered significant at a two-tailed probability of less than 0.05.

Results

Patient characteristics

Of the 67 patients entered into the program, 66 had bilateral and one had unilateral popliteal artery ectasia. Seven patients had one ectatic popliteal artery already previously treated. One patient had bilateral disease, however, data was only available for one side. Therefore, a total of 125 ectatic popliteal arteries underwent surveillance, of which 61 were left sided and 64 were right sided.

Median age at entry into surveillance was 72.6 years (Interquartile range (IQR): 65.7, 78.1). All but one patient was male. A history of hypertension ($n = 46$), dyslipidaemia ($n = 41$), coronary heart disease ($n = 32$) or smoking ($n = 45$) was more prevalent than the presence of diabetes mellitus ($n = 13$).

Aneurysms at locations other than the popliteal artery were present in 48 patients. Of these, 31 patients had an abdominal aortic aneurysm (AAA), 8 had an aortoiliac aneurysm, 4 had iliac aneurysms, 1 had both a thoracic aortic aneurysm and an AAA, 1 had a thoracoabdominal aneurysm, 1 had both an ascending aortic aneurysm and an AAA, 1 had a visceral aneurysm, and 1 had both an iliac and visceral aneurysm. 34 of these 48 patients underwent aneurysm repair prior to or during surveillance.

Changes in popliteal artery diameter during surveillance

Median initial popliteal artery diameter was 11 mm (IQR: 10, 13; range: 9, 27). Only one patient entered surveillance with a popliteal artery greater than 20 mm. This artery contained mural thrombus, but the patient was asymptomatic with palpable pedal pulses. The patient was followed for 12 months without change in symptoms or popliteal artery diameter, after which the patient elected to withdraw from surveillance.

Patients underwent a median of 4 scans (IQR: 3, 6), at a median scan interval of 7.6 months (IQR: 6, 12). The median duration of surveillance was 3.1 years (IQR: 2, 4.9). Eight patients died during follow-up. None of these deaths were due to complications of popliteal ectasia or related interventions. Three deaths were secondary to cardiac disease, two from malignancy, two from ruptured aortic aneurysms, and one from a stroke. Both of the patients that died from ruptured aortic aneurysms had previously identified aneurysms but declined elective repair.

The median final diameter of arteries at the end of surveillance was 13 mm (IQR: 11, 15). The annual growth rates of popliteal arteries were assessed by taking into account all diameters measured during follow-up and calculating time-weighted average growth rates for each artery. The median average growth rate was 0.3 mm/year (IQR -0.2, 0.9). The majority of arteries ($n = 75$, 60%) either remained static in size or had minimal growth (<2 mm). 44 (35.2%) arteries increased in diameter by >2 mm, and 6 (4.8%) arteries regressed >2 mm.

The diameters for the 12 (10%) arteries which remained under surveillance for the longest duration (all >6 years) are illustrated in Fig. 1. The observed pattern is quite variable, with predominant periods of stasis or slow growth, and occasional periods of more rapid growth and at times, regression.

Popliteal artery growth rate in relation to initial diameter

Arteries were divided into 2 groups based on initial diameter less than or greater than the median diameter (11 mm). Slightly larger average growth rates were observed in the arteries with initial diameter $\leq$ median ($p = 0.001$) (Table 1).

Mural thrombus and distal thromboembolism

At entry to surveillance, mural thrombus was identified in 4 popliteal arteries of 4 different patients on duplex examination (median diameter 15.5 mm, IQR: 14, 24). Two patients were asymptomatic and had normal pedal pulses. In the other two patients no pedal pulses were palpable in the relevant leg, but only one had symptoms of long distance claudication. These patients underwent surveillance for median of 12.5 months (IQR: 8, 23). None of these patients developed any new symptoms, new clinical

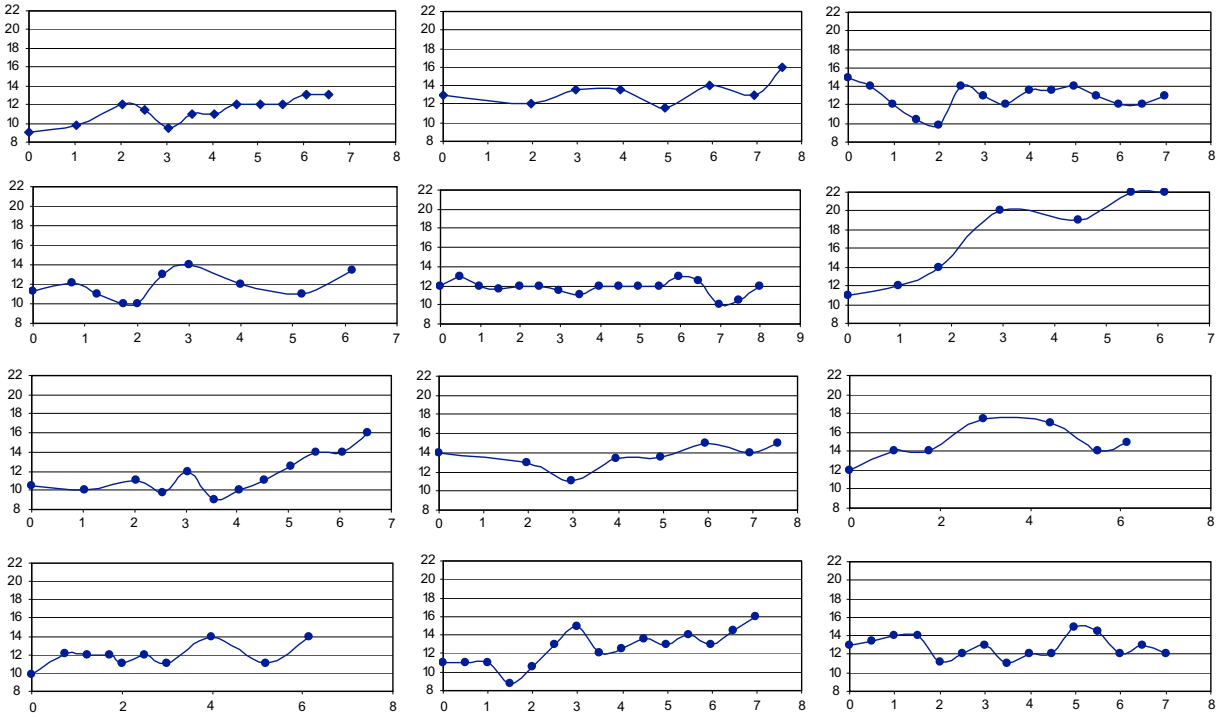

Figure 1 Growth profiles of popliteal arteries under surveillance for greater than 6 years.

Table 1 Average changes in popliteal artery diameter during surveillance in relation to initial diameter.

Initial diameter group	Initial diameter (mm) median (IQR)	Average weighted growth rate (mm/year)	
		Median (IQR)	Mean (95% CI)
≤Median ($n = 64$)	10 (9, 11)	0.56 (0.16, 1.01)	0.94 (0.43, 1.46)*
>Median ($n = 61$)	13 (12, 15)	0.00 (−0.54, 0.70)	0.59 (−0.30, 1.48)*

*$p = 0.001$.
IQR = interquartile range.

evidence of distal thromboemboli, or subsequently underwent intervention.

During the surveillance period, a further 5 patients developed ultrasound evidence of mural thrombus. The median size at which this was detected was 25 mm (IQR: 15, 43). Three of these patients went on to have elective surgical intervention without undergoing further surveillance, although only one of these had clinical evidence of distal thromboembolism (evidenced by a new absence of palpable pedal pulses), but was asymptomatic. Two patients underwent further surveillance after detection of mural thrombus. One of these patients was noted to have the new finding of no palpable pedal pulses at review 12 months later. The diameter of the patient's popliteal artery was also noted to increase from 16 mm to 33 mm in the 12 months. The patient underwent elective surgery. The remaining patient underwent a further 26 months of surveillance, with no increase in popliteal artery size (14 mm) or evidence of distal thromboembolism. The median averaged growth rate of arteries with evidence of mural thrombus that underwent further surveillance (including both those identified at entry and those identified during surveillance) was 1.9 mm/yr (IQR: −2.8, 4.8 mm), in comparison to 0 mm/yr (IQR: −1.0, 2.0 mm) in arteries with no evidence of mural thrombus ($p = 0.3$).

Patients in whom popliteal artery diameter reached 20 mm during surveillance

Of the 67 patients and 125 arteries that underwent surveillance, one patient had an initial artery diameter of >20 mm but did not receive an intervention at entry, leaving 124 arteries for analysis. Seven patients had a least one artery reach 20 mm in maximum dimension during the study period. Of these seven patients, one had both sides reach 20 mm during surveillance, and three had previously had the contralateral artery repaired.

The remaining 116 arteries in 60 patients did not reach 20 mm during the study period. None of these patients had any documented complications relating to popliteal artery ectasia.

There was no statistically significant association between the initial artery size, number of scans performed or scan intervals and a popliteal artery reaching 20 mm during surveillance (Table 2). The median surveillance duration was shorter in those limbs that reached the 20 mm threshold (1.3 vs 3.1 years, $p = 0.024$). The average change in artery size was significantly greater in the group that reached the 20 mm threshold (median 6.5 mm/year vs 0.3 mm/year for the group that did not reach threshold, $p < 0.001$).

The diameters of arteries that reached 20 mm in maximum dimension during surveillance are illustrated in Fig. 2.

Of the 7 patients that reached the 20 mm threshold during the study period, none had diabetes, but all had aneurysms diagnosed at other sites (Table 3). In comparison, 13 (21.7%) had diabetes and 41 (46.9%) had extra-popliteal aneurysms in the group that did not reach threshold, however, these trends did not reach statistical significance ($p = 0.17$, and 0.08 respectively). 4 (57.1%) of the group that reached threshold had had the contralateral artery previously treated, in comparison to 4 (6.7%) of the group that did not reach threshold ($p < 0.001$).

Discussion

The main finding of this study was that the average growth rate of ectatic popliteal arteries was slow, and below those

Table 2 Comparison between popliteal arteries that expanded and did not expand to 20 mm during surveillance.

	≥20 mm group[a] median (IQR)	<20 mm group median (IQR)	*P* value[b]
Initial size (mm)	13.5 (9.6, 14.3)	11.6 (10, 13)	0.23
Final size (mm)	23.5 (20, 30.4)	13 (11, 14)	<0.001
Surveillance duration (years)	1.33 (1.02, 2.73)	3.16 (1.98, 4.98)	0.02
Scans performed	3 (2.25, 4)	4 (3, 6)	0.15
Scan interval (years)	0.78 (0.52, 1.06)	0.62 (0.50, 1.00)	0.33
Average weighted change in artery size (mm/year)	6.5 (3.2, 16.6)	0.3 (−0.3, 0.8)	<0.001
Total limbs	8	116	

IQR = Interquartile range.
[a] For arteries in the ≥20 mm group, any size measurements recorded after the 20 mm threshold was reached were excluded from this analysis.
[b] Mann–Whitney U Test.

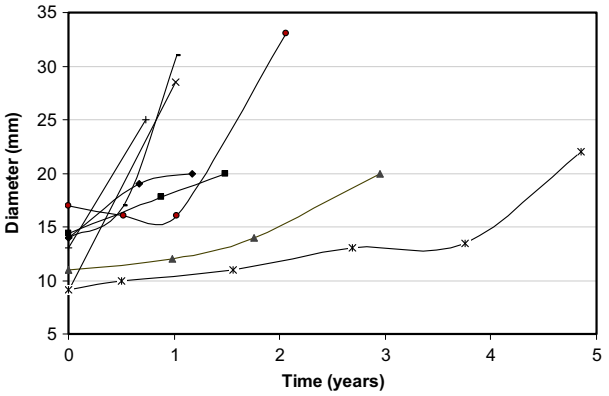

Figure 2 Growth profiles of popliteal arteries reaching 20 mm during surveillance.

previously published. Pittathankal *et al*. reported an average growth rate of 1.5 mm/year (95% CI −0.018, 3.018) for ectatic popliteal arteries measuring <20 mm. These investigators included only 12 ectatic popliteal arteries of which the mean initial diameter was higher than in the present study (16.75 mm).[8] Stiegler *et al*. conducted a prospective study of 36 patients with 46 ectatic popliteal arteries, of which 26 patients attended annual ultrasound surveillance. The mean growth rate was 0.7 mm/year for arteries measuring <20 mm in maximum diameter.[7]

In the current study we also found a much higher rate of bilateral ectasia than previously reported case series (typically reported to be 50%).[3–5] The likely explanation for the disparity is the inclusion of smaller arteries in the current study compared to previous studies, which have typically used a 15–20 mm size threshold for inclusion. In the current study we relied on published nomograms to define popliteal ectasia.[9]

An important finding of the current study was that the pattern of change in popliteal artery diameter observed during surveillance was variable. For the majority of arteries there was no significant change in diameter between surveillance scans, but occasional examples of rapid increase or even decrease in diameter were noted. A similar stacatto growth pattern has also been reported in AAAs.[10]

Table 3 Comparison of patients with at least one popliteal artery reaching 20 mm during surveillance compared to those that did not reach this diameter.

	≥20 mm Group		<20 mm Group		P^a
	n	%	n	%	
Age >70 years	5	71.4	32	53.3	0.74
Male gender	7	100	59	98.3	0.73
Hypertension	6	85.7	40	66.7	0.30
Dyslipidaemia	4	57.1	37	61.7	0.81
Diabetes mellitus	0	0	13	21.7	0.17
Tobacco use	4	57.1	42	70.0	0.80
Coronary heart disease	4	57.1	28	46.7	0.60
Extra-popliteal aneurysm	7	100	41	46.9	0.08
Contralateral intervention	4	57.1	4	6.7	<0.001
Total patients	7		60		

[a] *Pearson Chi-Squared Test*.

Initial artery size at entrance to surveillance was not found to be predictive of subsequent growth rate or progression to 20 mm in this study. This is in contrast to multiple studies on AAA growth rates, which have shown that initial size on entry to surveillance is predictive of subsequent growth and operative intervention.[11,12] The lack of association in this study may possibly reflect the relatively small diameters of the arteries enrolled in this surveillance program or the limited number of patients enrolled. A further limiting factor in the current study was that most patients had bilateral popliteal artery ectasia. Analysis of the results was therefore complicated by the need to assess both factors related to the patient, such as diabetes, and those related to the artery, such as initial diameter. Additional larger studies will therefore be required to assess the association of initial diameter with popliteal artery expansion.

Several studies on growth predictors of small AAAs have found that diabetes is associated with a slower rate of aneurysm expansion.[10–14] A similar trend was observed in this study of popliteal arteries, although further studies with larger cohorts will be required to assess whether there is a significant predictive effect of diabetes. A possible biological explanation for this observation may be the finding that diabetes is associated with decreased synthesis and activity of matrix metalloproteinases (MMPs), which have been implicated in aneurysm pathogenesis.[15] This effect may be secondary to aberrant monocyte–matrix interactions in the setting of abnormal matrix glycation.[14]

Hypertension has been associated with more rapid growth in AAAs.[11,16,17] Pittathankal *et al*. observed that patients with no history of hypertension were more likely to have stable ectatic popliteal arteries.[8] These trends were not confirmed by this study, with similar rates of hypertension in patients in whom their popliteal artery expanded to 20 mm or not.

In the current study, a history of a previous intervention on a contralateral ectatic popliteal artery was predictive for progression of the ipsilateral artery to 20 mm in maximum diameter. In addition, there was a trend to higher rates of extra-popliteal aneurysms in the group with artery expansion to ≥20 mm. A recent follow-up study of patients with popliteal artery ectasia demonstrated that 25% of patients with unilateral disease will develop contralateral disease during follow-up (where popliteal artery ectasia was defined as ≥15 mm).[18] The frequency of extra-popliteal aneurysms at the completion of this study by Ravn *et al*. was 68%. These findings suggest a more generalized aneurysm ''phenotype'' makes progressive artery dilatations more likely.

As with previously published reports the current study was limited by the relatively small sample size, meaning that more complex statistical analysis, such as multivariate analysis, was not feasible. Further larger studies will be needed to confirm the effect of these observed trends on ectatic popliteal artery growth.

Pittathankal *et al*. recommended a scanning interval of 12 months for ectatic popliteal arteries measuring <17 mm,

and 6 monthly for those >17 mm if a 20 mm operative threshold is used (based on the upper limit of the 95% CI for the mean annual growth rate of aneurysms <20 mm).[8] Based on the relatively slow median growth rates of ectatic popliteal arteries observed in this study, it is tempting to recommend scanning intervals of a more prolonged duration than those previously suggested, particularly when dealing with small arteries. However, as we found that growth patterns were unpredictable with occasional periods of rapid growth, and small ectatic popliteal arteries also occasionally developed mural thrombus and distal thromboemboli, a surveillance interval of greater than 12 months can not be recommended if intervention will be considered at 20 mm and the risk of complications during surveillance is to be minimized. Rather than recommending surveillance intervals based on diameter and threshold for intervention alone, intervals should ideally be customized to the individual patient after consideration of risk factors for growth such as diabetes, a previous contralateral ectatic popliteal artery repair, and aneurysmal disease elsewhere. More frequent surveillance intervals, for example 6 monthly, may be appropriate in patients with multiple risk factors for growth, or evidence of mural thrombus on imaging. Larger studies are ultimately required to confirm the observed trends and to guide clinical application.

Conflict of Interest

None.

Acknowledgements

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