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ORIGINAL RESEARCH

Atherosclerotic Burden and Remodeling Patterns of the Popliteal Artery as Detected in the Magnetic Resonance Imaging Osteoarthritis Initiative Data Set

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BACKGROUND: An artificial intelligence vessel segmentation tool, Fully Automated and Robust Analysis Technique for Popliteal Artery Evaluation (FRAPPE), was used to analyze a large databank of popliteal arteries imaged through the OAI (Osteoarthritis Initiative) to study the impact of atherosclerosis risk factors on vessel dimensions and characterize remodeling patterns.

METHODS AND RESULTS: Magnetic resonance images from 4668 subjects contributing 9189 popliteal arteries were analyzed using FRAPPE. Age ranged from 45 to 79 years (median, 61), and 58% were women. Mean lumen diameter, mean outer wall diameter, and mean wall thickness (MWT) were measured per artery. Their median values were 5.8 mm (interquartile range, 5.2–6.5 mm), 7.3 mm (interquartile range, 6.7–8.1 mm), and 0.78 mm (interquartile range, 0.73–0.84 mm) respectively. MWT was associated with multiple cardiovascular risk factors, with age (4.2% increase in MWT per 10-year increase in age; 95% CI, 3.9%–4.5%) and sex (8.6% higher MWT in men than women; 95% CI, 7.7%–9.3%) being predominant. On average, lumen and outer wall diameters increased with increasing MWT until the thickness was 0.92 mm for men and 0.84 mm for women. After this point, lumen diameter decreased steadily, more rapidly in men than women (–7.9% versus –6.1% per 25% increase in MWT; $P<0.001$), with little change in outer wall diameter.

CONCLUSIONS: FRAPPE has enabled the analysis of the large OAI knee magnetic resonance imaging data set, successfully showing that popliteal atherosclerosis is predominantly associated with age and sex. The average vessel remodeling pattern consisted of an early phase of compensatory enlargement, followed by a negative remodeling, which is more pronounced in men.

Key Words: artificial intelligence ■ magnetic resonance ■ popliteal atherosclerosis ■ remodeling patterns

See Editorial by Bluemke and Kawel-Boehm

Subclinical atherosclerosis is highly prevalent in the iliofemoral arteries, which are more frequently affected, compared with the carotid, abdominal, and coronary arteries.[1] In addition, plaque burden in the femoral territory is strongly associated with cardiovascular risk factors, as shown in the PESA (Progression of Early Subclinical Atherosclerosis) study.[2] Several studies have demonstrated the association between intima-media thickness of the popliteal artery and atherosclerosis and clinically manifest cardiovascular disease.[3,4] All these findings suggest that peripheral arteries, in general, and popliteal artery, in particular, are good models for studying atherosclerosis.

The OAI (Osteoarthritis Initiative; URL: https://www.clinicaltrials.gov. Unique identifier: NCT00080171)[5] provides a unique opportunity to study the remodeling process of popliteal atherosclerosis, since it has collected high-resolution magnetic resonance imaging

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CLINICAL PERSPECTIVE

What Is New?

- Using an automated artificial intelligence magnetic resonance image analysis tool, Fully Automated and Robust Analysis Technique for Popliteal Artery Evaluation, quantitative measures of the popliteal artery were obtained from 4668 subjects contributing 9189 popliteal arteries and over 500 000 cross-sectional images.
- Our study has shown that routine knee magnetic resonance imaging using a 3-dimensional double-echo steady-state sequence on patients with osteoarthritis can be used to rapidly detect popliteal artery vessel wall disease, from atherosclerosis to ectasia, and assess the association between demographic and clinical factors on patterns of peripheral artery remodeling in large cohorts.

What Are the Clinical Implications?

- We have shown the great potential that Fully Automated and Robust Analysis Technique for Popliteal Artery Evaluation offers to perform epidemiologic studies focused on the popliteal artery.
- These studies will advance the understanding of subclinical popliteal vascular diseases such atherosclerosis, identifying patients at risk of cardiovascular disease progression or ischemic events.
- Additionally, considering that in the United States, Medicare reported >806 000 magnetic resonance examinations to evaluate leg joints in 2017, the automatic arterial segmentation performed by Fully Automated and Robust Analysis Technique for Popliteal Artery Evaluation may also have direct clinical applications, such as for incidental detection of peripheral atherosclerosis and popliteal aneurysms on routine knee magnetic resonance imaging.

Nonstandard Abbreviations and Acronyms

DESS	double-echo steady-state
FRAPPE	Fully Automated and Robust Analysis Technique for Popliteal Artery Evaluation
MWT	mean wall thickness
OAI	Osteoarthritis Initiative
PESA	Progression of Early Subclinical Atherosclerosis

(MRI) data of the knee and thigh on a large and diverse population. MRI has emerged as a reliable noninvasive modality to detect atherosclerosis and quantify atherosclerotic plaque burden, allowing for a comprehensive characterization of artery morphology and plaque composition, which are both associated with cardiovascular disease and incidence.[6–9] Because of its highly reproducible morphologic measurements,[10–12] MRI has been used to analyze atherosclerotic lesions in peripheral vessels, including the femoral arteries.[10,11,13] An additional advantage of using the OAI population relies on the number of shared risk factors between osteoarthritis and atherosclerosis, such as age and obesity, and the added risk factors to atherosclerosis from osteoarthritis, such as impaired mobility and use of nonsteroidal anti-inflammatory drugs.[14] However, the challenge of analyzing this large data set lies on the time required for accurate manual delineation of the luminal and wall boundaries on the magnetic resonance (MR) images. To overcome this, we propose to use an artificial intelligence-based, fully automated vessel wall segmentation tool, Fully Automated and Robust Analysis Technique for Popliteal Artery Evaluation (FRAPPE), able to efficiently analyze population-based MR data sets.[15]

Our purpose was to characterize atherosclerotic remodeling patterns in the popliteal artery using FRAPPE.[15] In particular, we have analyzed the baseline MRI data collected through the OAI, assessing the impact of atherosclerosis risk factors on vessel wall thickness and the remodeling patterns in the popliteal artery.

METHODS

All data used in this study were collected by the OAI.[5] Study procedures were approved by the local institutional review boards, and all participants provided informed consent. The study was originally designed for knee osteoarthritis research as a multicenter, longitudinal, prospective observational cohort study. The baseline assessment collected data on imaging biomarkers (MRI and radiography), as well as on the clinical and joint status of subjects, and on risk factors for the progression and development of knee osteoarthritis (details can be found on https://nda.nih.gov/oai/). All subjects' data have been made publicly available and can be accessed at https://nda.nih.gov/oai/. The results of the segmentation performed by FRAPPE will be uploaded at https://github.com/clatfd/Frappe upon publication.

Study Cohorts

The original OAI cohort consisted of a total of 4796 subjects aged 45 to 79 years. Of these subjects, 4674 either had osteoarthritis at baseline (progression subcohort; n=1390) or were at risk of developing osteoarthritis over the study period (incidence subcohort; n=3284). The inclusion criteria for the incidence subcohort included an age-dependent mix of knee symptoms and other factors including being overweight, history of knee injury, history of knee surgery, family history, Heberden's nodes, repetitive knee bending, and advanced age (70–79). Refer to https://nda.nih.gov/oai/ for more details.

Cardiovascular Risk Factor Collection

Cardiovascular risk factors were collected among other demographic data during screening, the enrollment visit, or the baseline visit using standardized questionnaires and procedures. A physical exam was performed at baseline, which included measuring weight, height, and sitting blood pressure. Subjects were asked to bring in all medications used in the past 30 days for inventory. Additional risk factors were collected using a validated self-administered questionnaire modeled on the Charlson index. Smoking status was ascertained through self-report. Hypertension was defined as either systolic blood pressure ≥130 mm Hg, diastolic blood pressure ≥80 mm Hg, or the use of antihypertension medications within the past 30 days. History of diabetes mellitus was determined through self-report or the use of antidiabetic medications within the past 30 days. Use of statins within the past 30 days was also treated as a risk factor. History of major cardiovascular events was ascertained from the self-administered questionnaire.

Magnetic Resonance Imaging

Subjects underwent bilateral knee MRI with 1 of 4 identical Siemens 3T MRI scanners, which used standardized acquisition protocols across all sites. Vessel wall analysis was performed using 3-dimensional double-echo steady-state (DESS) sequence acquired in the sagittal orientation,[14] with the following imaging parameters: repetition time/echo time: 16.32/4.7 ms, field of view: 140×140 mm, 0.7 mm slice thickness, and 0.37×0.46 mm in-plane resolution. Coverage was 10 cm above and below the knee, including proximal and distal segments of the popliteal artery. The DESS sequence used in the OAI study has inherent blood suppression capability and enables the vessel luminal boundary to be identified. Additionally, it has fat suppression, enabling the vessel outer wall boundary to be identified. DESS has been demonstrated to provide good vessel wall delineation of lower-limb arteries.[14,16] Detailed imaging parameters for the OAI 3-dimensional DESS sequences can be found in the work by Peterfy et al.[17]

MR Image Processing

The 3-dimensional DESS volume was reformatted axially with in-plane resolution of 0.36 mm×0.36 mm and a slice thickness of 1.5 mm. We processed the MR images using FRAPPE, a fully automated and robust vessel wall segmentation tool, specifically designed for the popliteal artery, developed by our group using machine learning techniques.[15] Briefly, in FRAPPE, an artery centerline is generated from refinement on popliteal artery detection from each MR slice by a deep neural network model.[15] Vessel wall regions around the centerline are then segmented using another neural network model for segmentation in a polar coordinate system[15] (Figure 1). Contours from vessel wall segmentations are used for vascular feature calculation, such as mean wall thickness (MWT) and wall area. In a prior evaluation, FRAPPE achieved high accuracy for vessel wall segmentation compared with expert human readers (intraclass correlation coefficient of 0.73 for MWT, based on 25 subjects with 1391 images interpreted), a low segmentation error rate (only 1.2% of images had noticeable major errors based on review of 14 055 images from 225 subjects) and repeatability (intraclass correlation coefficient of 0.95 for MWT based on 50 subjects with 2 scans performed 6 months apart).[15]

Statistical Analysis

Vessel wall dimensions in the primary and normal cohorts were summarized as mean±SD and median (interquartile range [IQR]). Lumen diameter and outer wall diameter were estimated from the corresponding cross-sectional areas used for circles: $\text{diameter}=\sqrt{(4/\pi\times\text{area})}$. Associations between risk factors and MWT were evaluated using generalized estimating equation–based linear regression models to account for correlation between measurements of the left and right sides. MWT was log-transformed before modeling to reduce right-skewness.

Remodeling patterns were studied at the slice level by fitting nonlinear curves relating MWT to mean lumen diameter and mean outer wall diameter while adjusting for sex, age, height, and atherosclerosis risk factors using generalized additive models. This is similar to the methodologies used in prior studies of remodeling in coronary and carotid arteries.[18–21] Thin-plate regression splines were used to estimate nonlinear relationships. This flexible technique can capture a variety of functional shapes without specifying any a priori assumptions and, unlike many other spline techniques, is not dependent on specifying the number and location of knots.[22] The nonparametric bootstrap with resampling by subject (1000 resamples) was used to calculate 95% confidence bands for the spline curves.

All analyses were weighted using weights derived from the FRAPPE algorithm representing its level of confidence in measurements at the slice level

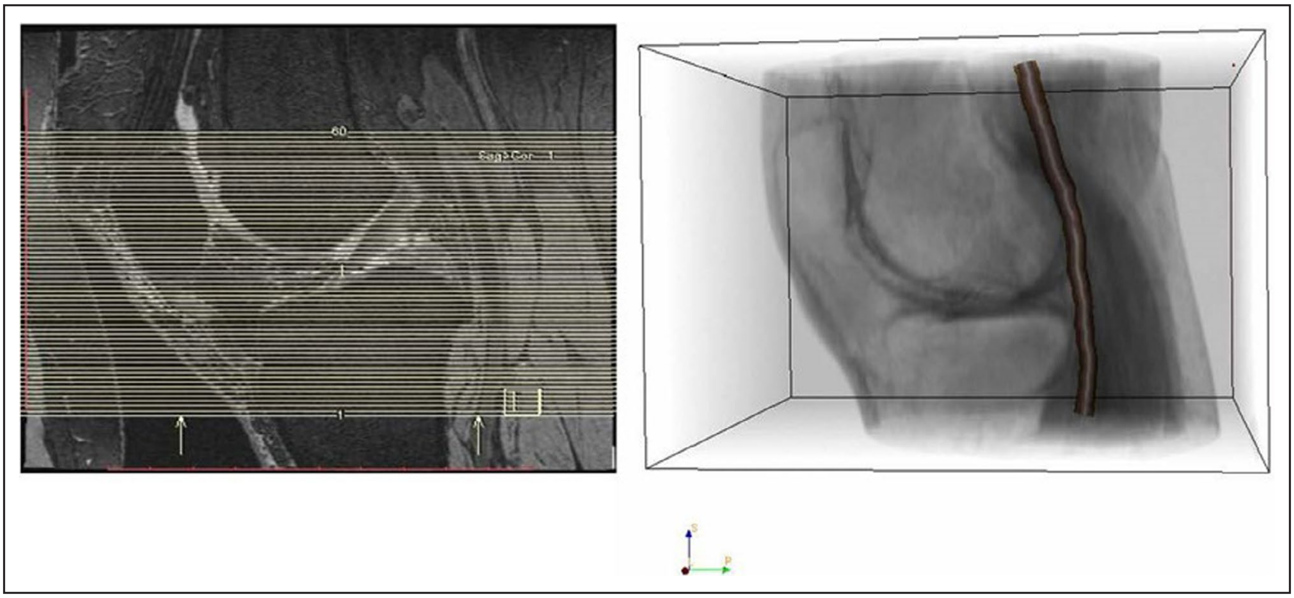

Figure 1. Three-dimensional display of segmented artery wall overlaid with original magnetic resonance (MR) image.

(side-specific), previously shown to improve the repeatability of the measurements.[23] All statistical calculations were conducted with the statistical computing language R (version 3.6.1; R Foundation for Statistical Computing, Vienna, Austria). The *mgcv* (version 1.8-31; Wood SN), *geepack* (version 1.2-1; Højsgaard S, Halekoh U, Yan J), and *boot* (version 1.3-25; Canty A and Ripley B) packages were used.

RESULTS

Of the 4674 subjects with osteoarthritis or at risk of developing osteoarthritis, 4668 (>99%) had analyzable knee MRI at baseline (Figure 2). A total of 9189 popliteal arteries (4521 subjects provided bilateral arteries) and 556 061 cross-sectional images were processed by the FRAPPE segmentation algorithm, of which all 9189 arteries and 555 105 images (>99%) were segmented. The median number of imaging slices per artery was 63 (IQR, 56–65), corresponding to imaging coverage 9.4 cm (IQR, 8.4–9.8 cm).

Demographics and risk factors are summarized in Table 1. Of 4668 subjects, 42% were male, 79% were White, mean age was 61±9 years, and 30% had osteoarthritis at baseline. Body mass index ranged from 17 to 49 kg/m^2 (median, 28 kg/m^2), 8% had diabetes mellitus, 9% were current smokers, and 6% had cardiovascular disease. Sixty-nine percent had hypertension, of which 63% were taking antihypertensive medications and 26% were taking statins. Among the 9189 popliteal arteries in the study cohort, median MWT, mean lumen diameter, and mean outer wall diameter were 0.78 mm (IQR, 0.73–0.84 mm), 5.8 mm (IQR, 5.2–6.5 mm), and 7.3 mm (IQR, 6.7–8.1 mm), respectively.

Associations Between Atherosclerosis Risk Factors and Vessel Dimensions

Univariable and multivariable associations of each risk factor and medication with MWT is summarized in Table 2. After multivariable adjustment, all potential risk factors were significantly associated with MWT except for race (P=0.23) and statin use (P=0.15). MWT was 8.6% thicker in men compared with women, increased 4.2% per 10-year increase in age, was 2.7% higher in people with diabetes mellitus than people without diabetes mellitus, and 2.6% higher in subjects with cardiovascular disease compared with those without. When age trends were evaluated separately by sex, men had larger increases in MWT with age (5.2% per 10-year increase; 95% CI, 4.8%–5.6%) compared with women (3.4% per 10-year increase; 95% CI, 3.0%–3.7%; P<0.001 for the difference with males). The trends in MWT with age, sex, and risk factors are also displayed in Figure 3.

The overall estimated R^2 of the full multivariable model was 42% (95% CI, 40%–44%) while a model including only age and sex produced R^2=37% (95% CI, 35%–39%). Age was the single strongest factor correlated with MWT, which produced an independent increase in R^2 (ΔR^2) after adjusting for all other factors of 10% (95% CI, 8.5–11%), followed by sex (ΔR^2, 6.2%; 95% CI, 5.1%–7.3%; P<0.001 for the difference with age). The other atherosclerosis risk factors and medications (body mass index, hypertension, antihypertensive medications, statins, diabetes mellitus, smoking, and cardiovascular disease) contributed ΔR^2=2.6% (95% CI, 2.0%–3.5%), while the remaining factors (race, height, and osteoarthritis) contributed ΔR^2=1.5% (95% CI, 1.0%–2.1%), both of which were significantly

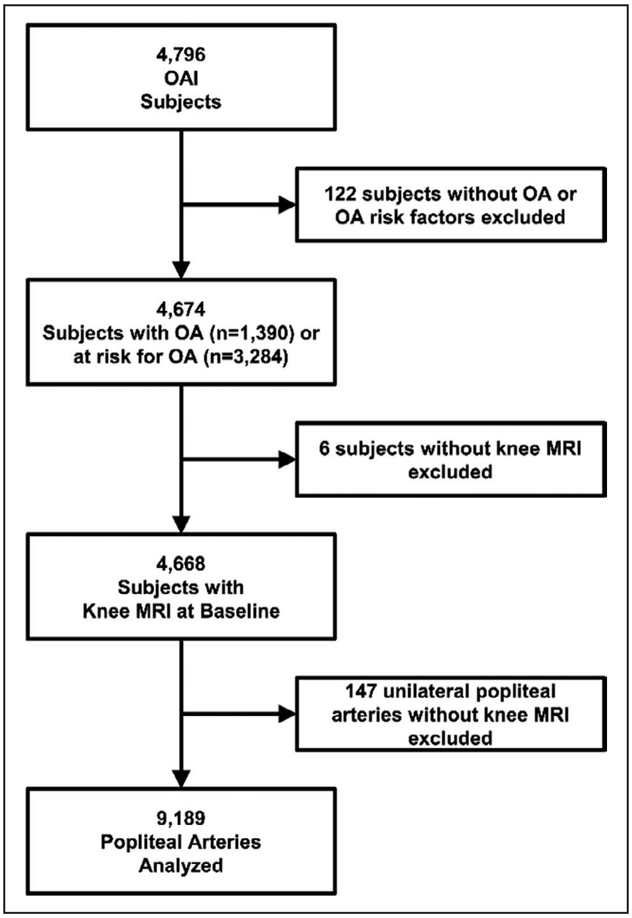

Figure 2. Subject flowchart.
Of the 4668 subjects with knee magnetic resonance imaging (MRI), 4521 had bilateral popliteal arteries imaged (9042 arteries) and 147 had 1 popliteal artery imaged, for a total of 9189 arteries. OA indicates osteoarthritis; and OAI, osteoarthritis initiative.

smaller than the contributions from age (P<0.001) or sex (P<0.001).

Vessel Remodeling Patterns

Spline-smoothed relationships of MWT with lumen and outer wall diameters across 235 152 cross-sectional images in men and 319 953 images in women are shown in Figure 4 after adjusting for risk factors. When MWT increased starting from <0.5 mm, both lumen and outer wall diameter also increased on average. When MWT exceeded 0.92 mm (95% CI, 0.91–0.93 mm) on average for men and 0.84 mm (95% CI, 0.83–0.85 mm) on average for women, the mean lumen diameter began to steadily decrease with further increases in MWT. Over the range 0.92 to 1.84 in men and 0.84 to 1.68 in women, the average lumen diameter decrease was more rapid in men (–7.9% per 25% increase in MWT; 95% CI, −8.8 to −7.1%) than women (–6.1% per 25% increase in MWT; 95% CI, −6.7 to −5.5%; P<0.001 for the difference with men).

Table 1. Demographics and Risk Factor Profile*

Variable	Value
Male sex	1944 (41.6)
Race	
White	3674 (78.8)
Black	864 (18.5)
Other[‡]	125 (2.7)
Age, y	61 (45–79)
Body mass index, kg/m^2	28.4 (16.9–48.7)
Using statins	1223 (26.3)
Hypertension	3204 (68.7)
No	1459 (31.3)
Yes and using medication	2019 (43.4)
Yes and not using medication	1177 (25.3)
Diabetes mellitus	372 (8.2)
Current smoker	429 (9.3)
Prior major cardiovascular disease event[†]	251 (5.6)
Osteoarthritis	1388 (29.7)

*Values are n (%) or median (range); subjects missing values were excluded from the corresponding summary: race (n=5), body mass index (n=4), hypertension (n=13), diabetes mellitus (n=117), current smoker (n=77), prior major cardiovascular event (n=151).

†Prior heart attack, stroke/transient ischemic attack, or bypass/angioplasty of leg vessels.

‡Other category includes Asian and Other non-White.

In contrast, over those same ranges, there was no significant increase in the outer wall diameter in men on average (–0.5% per 25% increase in MWT; 95% CI, –1.2 to 0.1%; P=0.12 compared with 0), while there was a small but statistically significant increase in outer wall diameter in women (1.2% per 25% increase in MWT; 95% CI, 0.8%–1.7%; P<0.001 compared with men). Figures 5 through 7 show samples of a normal artery, as well as 2 arteries with atherosclerotic lesions with different degrees of wall thickening and luminal narrowing. Figure 7 includes the lumen and outer wall segmentation performed by FRAPPE for the particular shown axial image.

DISCUSSION

In this study we used vessel wall MRI to perform a 3-dimensional assessment of the popliteal artery morphology in a large cohort. We examined vessel wall thickening, measured from the MRI baseline data collected in the OAI, with demographic and clinical risk factors and characterized the overall remodeling patterns across a wide range of atherosclerotic disease burden. The analysis of over 500 000 images from 9189 arteries was made technically feasible by an artificial intelligence-based, automated vessel wall segmentation tool, FRAPPE, recently developed for the popliteal artery.[15]

Table 2. Associations of Mean Wall Thickness With Risk Factors

Variable	Univariable Models			Multivariable Model		
	β*	(95% CI)	*P* Value	β*	(95% CI)	*P* Value
Male sex	11.8	(11.2 to 12.3)	<0.001	8.6	(7.7 to 9.3)	<0.001
Black race	−0.5	(−1.3 to 0.3)	0.19	0.4	(−0.3 to 1.1)	0.23
Age, per 10-y increase	3.8	(3.5 to 4.1)	<0.001	4.2	(3.9 to 4.5)	<0.001
Body mass index, per 1-SD increase	1.2	(0.9 to 1.5)	<0.001	1.2	(0.9 to 1.4)	<0.001
Using statins	2.9	(2.2 to 3.6)	<0.001	−0.4	(−1.0 to 0.2)	0.15
Hypertension			<0.001			0.002
No	(ref)			(ref)		
Yes and using medication	5.3	(4.6 to 6.0)		1.0	(0.4 to 1.6)	
Yes and not using medication	3.2	(2.5 to 4.0)		0.6	(0.1 to 1.2)	
Diabetes mellitus	5.7	(4.4 to 7.1)	<0.001	2.7	(1.6 to 3.9)	<0.001
Current smoker	2.5	(1.4 to 3.6)	<0.001	1.8	(0.9 to 2.7)	<0.001
Prior major cardiovascular disease event†	6.5	(4.8 to 8.2)	<0.001	2.6	(1.2 to 4.0)	<0.001
Height, per 1-SD increase	4.4	(4.1 to 4.7)	<0.001	1.8	(1.5 to 2.2)	<0.001
Osteoarthritis	2.1	(1.5 to 2.8)	<0.001	1.0	(0.5 to 1.5)	<0.001

*The regression coefficient corresponds to the estimate percent change in mean wall thickness per change in variable.
†Composite of prior stroke/transient ischemic attack, heart attack, or leg artery bypass/angioplasty.

While atherosclerotic risk factors were independently associated with MWT, as expected on the basis of studies of aorta, carotid, and femoral arteries,[24–28] their independent contributions were relatively small, while sex and age were the predominant factors. Age was the single strongest factor, with consistent increases in MWT with increasing age in men and women, improving the linear model R^2 from 32% to 42% after accounting for all other factors. The observation that age is a stronger factor than sex is consistent with an earlier study of the popliteal using ultrasound of 108 healthy subjects.[29]

Regarding the remodeling patterns of the popliteal artery, this OAI population-averaged analysis indicated a strong increasing relationship between wall thickness and mean lumen and outer wall diameters up to a wall thickness of 0.92 mm for men and 0.84 mm for women (Figure 4). These wall thickness values may indicate a threshold for a physiological natural variation with different arterial size depending on sex, or

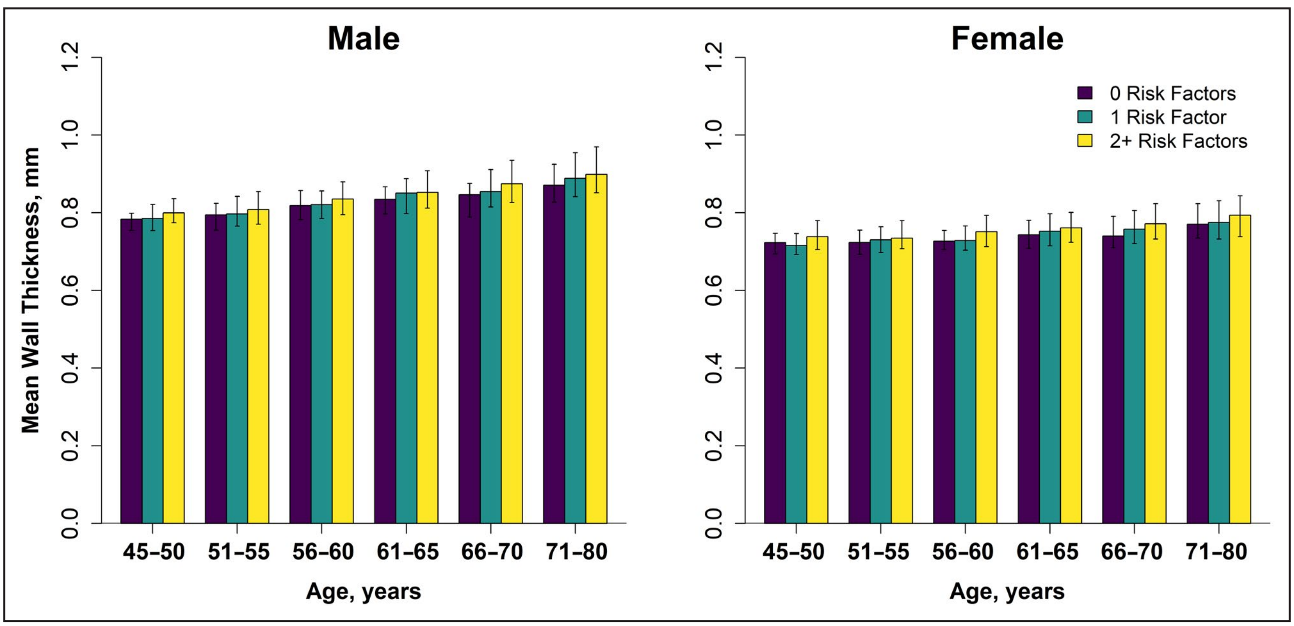

Figure 3. Mean wall thickness across age groups, stratified by sex and risk factors.
Bar heights indicate the median value and error bars indicate the lower and upper quartiles. The risk factors counted were body mass index ≥30 kg/m^2, hypertension, diabetes mellitus, prior cardiovascular event, and current smoker.

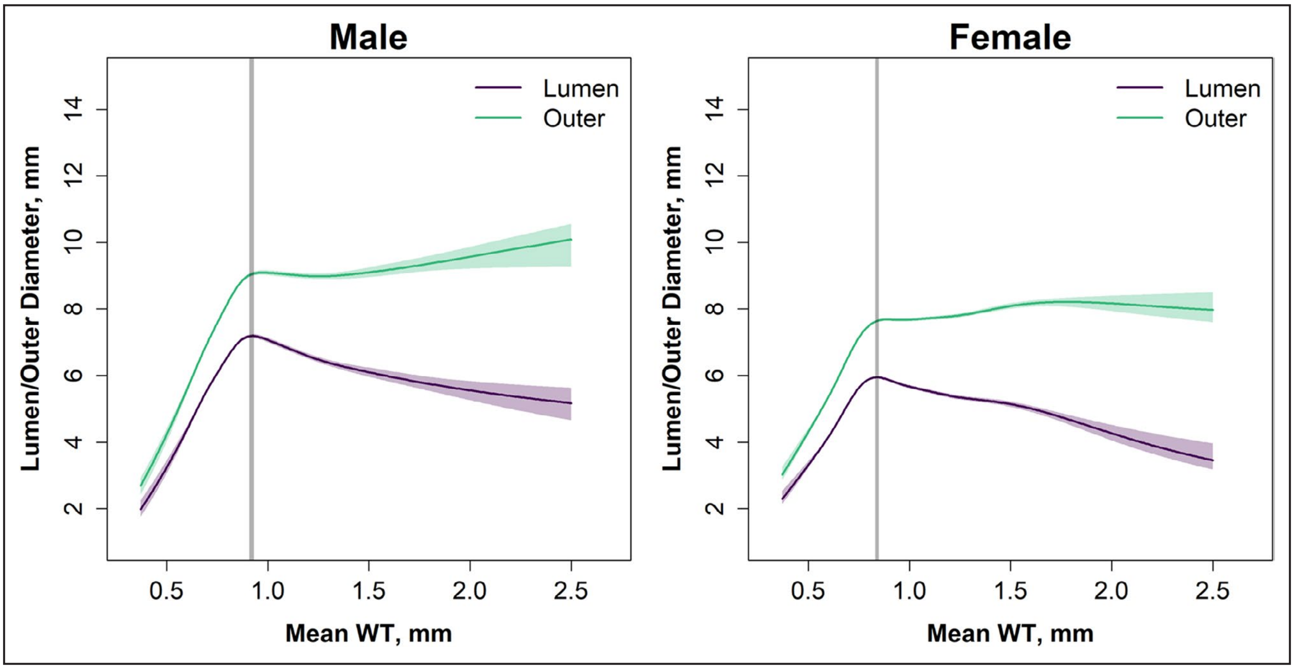

Figure 4. Popliteal artery remodeling patterns in men and women.
Spline-smoothed relationships of mean wall thickness with lumen diameter and outer diameter are shown, based on 235 152 and 319 953 cross-sectional images of men and women, respectively. The shaded regions represent 95% pointwise confidence bands. The vertical regions indicate the thickness where on average the mean lumen diameter tends to decrease with increasing thickness (0.92 mm in men and 0.84 mm in women). WT indicates wall thickness.

an early phase of disease with outward remodeling, as observed by Labropoulos and collaborators.[30] They studied the popliteal remodeling pattern in early atherosclerosis by measuring the intima-media thickness of 23 popliteal arteries and found an increase in both lumen and outer wall diameters when a small but detectable focal increase in intima-media thickness was measured. A similar compensatory enlargement paired

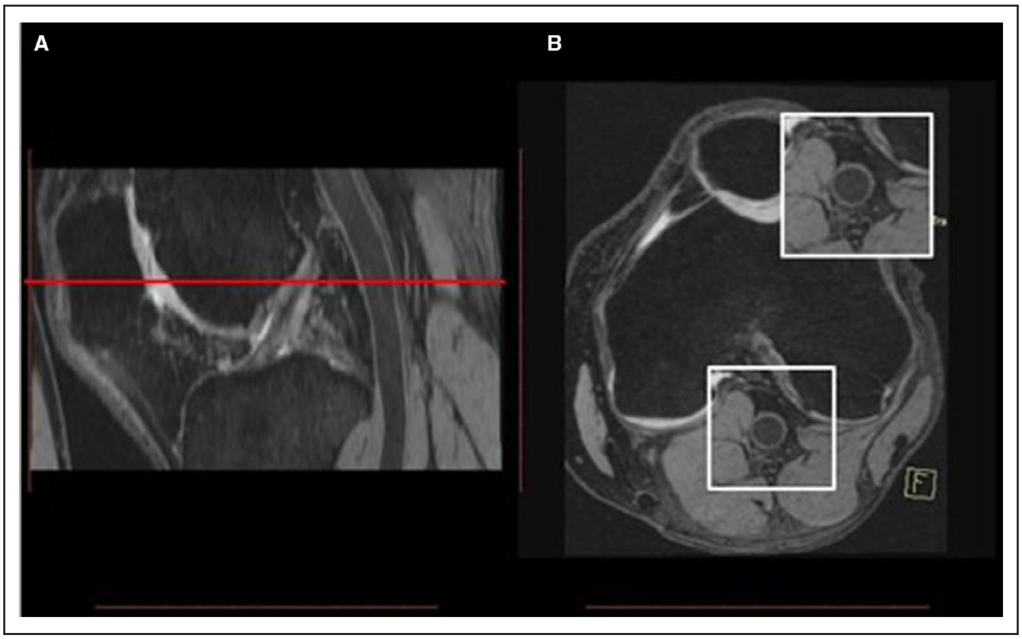

Figure 5. Example of a nonatherosclerotic popliteal artery.
Osteoarthritis Initiative (OAI) Case 9000296, left side, baseline (male, 69 years old). **A**, Magnetic resonance (MR) sagittal view of a knee showing this normal popliteal artery. **B**, MR axial knee image corresponding to the location marked with a red line on panel A; no wall thickening is observed in this artery.

Figure 6. Example of a diseased, atherosclerotic popliteal artery: OAI (Osteoarthritis Initiative) Case 9894047, right side, baseline (male, 68 years old).
A, Magnetic resonance (MR) sagittal view of a knee showing the thickened vessel wall of this atherosclerotic popliteal artery. **B**, MR axial knee image corresponding to the location marked with a red line on panel A; the atherosclerotic plaque is clearly seen on the insert. Arrowheads indicate the location of the diseased wall.

with early stage of the disease has been seen in other vessels. Both the common and internal carotid arteries have an early phase of remodeling with increased outer diameter with vessel wall thickness without compromising the lumen, with the common carotid having a greater ability to accommodate increased wall

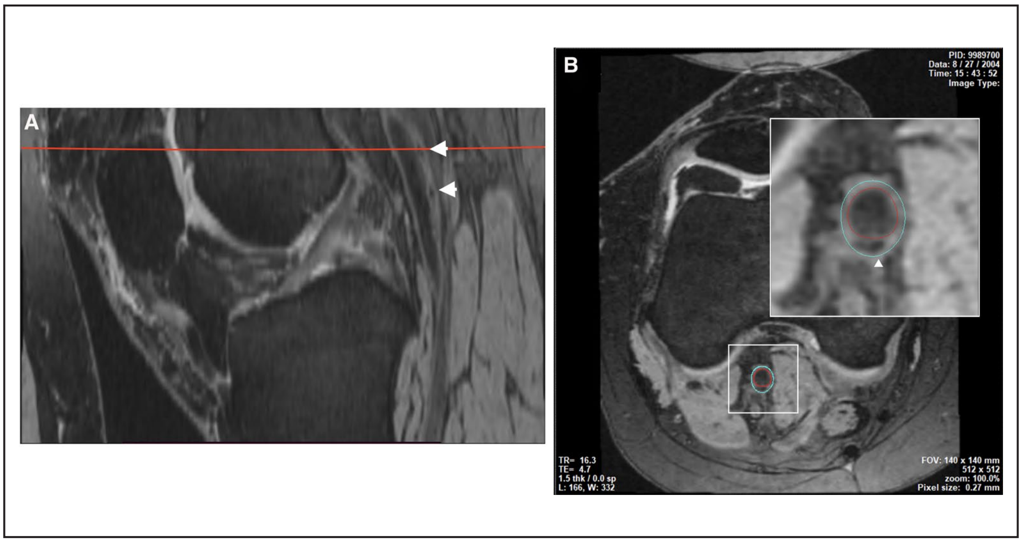

Figure 7. The baseline scan of the right side knee of OAI Case 9989700 (female, 74 years old) is used to illustrate the automatic vessel wall segmentation performed by Fully Automated and Robust Analysis Technique for Popliteal Artery Evaluation (FRAPPE).
A, Magnetic resonance (MR) sagittal view of this case that presents a calcified thickened wall. Note that there is more than one piece of calcification in this artery (see arrowheads). **B**, MR axial knee image corresponding to the location marked with a red line on panel A. Lumen (red) and outer wall (cyan) boundaries are automatically detected by FRAPPE.

thickness before compromising the lumen compared with the internal carotid artery.[19,20] However, these studies did not capture a parallel increase in carotid lumen and wall diameters as seen in the popliteal. The coronary artery, on the other hand, has followed a more similar compensatory enlargement to the popliteal with slight increase in lumen diameter and increased wall diameter as the wall thickness increases.[18]

After the early stage of remodeling, a distinctly different pattern followed. On average, lumen diameter decreased with further thickening, with a more rapid decrease in men. There was also a marked difference in behavior of the outer diameter with sex. The more rapid decrease in lumen diameter in men coincided with a slight decrease in outer wall diameter, followed by a less pronounced decrease in lumen and an increase in outer diameter, as if the arterial wall compensated the increase in wall thickness by increasing the outer diameter, avoiding further encroaching of the lumen. This inward remodeling pattern has also been reported in the femoral artery with advanced atherosclerotic disease,[31] though there was no specific analysis of the effect of sex on the remodeling pattern. In the female OAI population, we found that the lumen had a less pronounced decrease with wall thickness, while the outer diameter slightly increased, suggesting that the popliteal artery in women has a greater ability to compensate for increasing disease burden than in men. This sex-dependent wall behavior might be explained by the sex difference in wall layer architecture and corresponding mechanical properties proposed by Debasso and colleagues.[29] In their ultrasound study, they suggested that the increased popliteal vessel stiffness found in men compared with women could be attributable to their higher arterial thickness. Studies in other vessels have not been able to differentiate patterns according to sex either. The common and internal carotid[20] and the coronary[32] arteries have shown an inward remodeling with a decrease in lumen with increased wall thickness after the initial compensatory enlargement phase.

The success of FRAPPE in automatically segmenting 9189 popliteal arteries proves its potential to efficiently analyze population-based MR images and provides further support for its use as a tool for large-scale epidemiologic studies on subclinical popliteal atherosclerotic disease. Considering that in the United States, Medicare reported that 806 164 MR examinations were performed to evaluate leg joints in 2017, the automatic arterial segmentation performed by FRAPPE may also have clinical applications, such as for incidental detection of peripheral artery disease and popliteal aneurysms on routine knee MRI. Peripheral artery disease is the underlying condition for critical limb ischemia, which is often underdiagnosed and untreated, posing a risk for limb or life loss to patients. Patients diagnosed with critical limb ischemia have a poor long-term prognosis and lower survival rates than patients diagnosed with heart failure, stroke, and most cancers.[33] Popliteal artery aneurysms and pseudoaneurysms also pose a risk of developing critical limb ischemia. FRAPPE can detect these vascular anomalies and be used to assess the risk of thromboembolic complications linked not only to increased aneurysmal size but also to small aneurysms with mural thrombosis.

Our findings on the popliteal remodeling patterns are limited by the cross-sectional nature of the analysis, and they would need to be confirmed with the serial MRI from the OAI data set, though image registration, a critical and nontrivial step, will be required. This longitudinal analysis might allow determining the nature of the early phase of remodeling found in the popliteal artery, that is, whether it is a natural physiological behavior, an early phase of outward remodeling, or a combination of both. On the other hand, an advantage of our cross-sectional data analysis is the inclusion of a broad range of lesion sizes and ability to analyze at the slice level without substantial noise introduced once >1 time point is analyzed, with the potential of measurement, registration, and alignment errors. Finally, we have not performed any compositional analysis that may provide additional information to understand the remodeling patterns. Further technical development will be needed to perform such analysis automatically. Though the OAI data set includes only 1 MRI sequence suitable for vessel wall imaging, 3-dimensional DESS, it can provide information on the amount of necrotic core, or calcification, as these components can be clearly identified as illustrated in Figures 6 and 7.

CONCLUSIONS

Using a robust, artificial intelligence-based, automated vessel wall segmentation tool (FRAPPE), we have shown that atherosclerosis in the popliteal artery is markedly dependent on age and sex, compared with other factors known to affect atherosclerosis in other arterial vessels. The popliteal artery follows 2 very distinct remodeling patterns in response to atherosclerosis. An early phase of compensatory enlargement, where both the lumen and wall diameter increase with vessel wall thickening, is followed by a negative remodeling, which is more pronounced in men.

ARTICLE INFORMATION

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