VEDA: vascular ultrasound evaluation of different arterial beds

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Aims and objectives

Introduction:

Atherosclerotic Cardiovascular Disease (ASCVD) is a leading cause of morbidity and mortality among adults worldwide and its societal impact is even more acute in India where symptomatic ASCVD occurs at a much younger age compared to North America and Western Europe \cite{1}. There is considerable interest in the early diagnosis of ASCVD when patients are still asymptomatic. Exposure to certain risk factors can lead to slow progression of ASCVD, perhaps over decades, with minimal or no symptoms. The first clinical manifestation is often catastrophic: acute myocardial infarction (MI), unstable angina, ischemic stroke or sudden death. Use of imaging modalities has been advocated to better predict the risk of future atherothrombotic events \cite{2-4}.

The INTERHEART-South Asia study of around 2000 symptomatic individuals identified that eight established ASCVD risk factors—abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, low fruit and vegetable consumption, and lack of physical activity—accounted for 89% of the cases of acute myocardial infarction in the Indian population \cite{5}. However, not all individuals exposed to atherogenic risk factors go on to develop ASCVD events. In a retrospective study of 232,000 patients admitted to hospital with Coronary Artery Disease (CAD), almost half of the patients had LDL levels <100 mg/dL and less than 10% had HDL #60 mg/dL \cite{6}. In a large European study involving over 10,000 relatively young asymptomatic subjects with a 10 year follow-up, ultrasound examination of four arterial sites correctly identified 99% of future ASCVD events (MI, Stroke, Peripheral Arterial Disease and deaths) \cite{7}.

Atherosclerosis is a systemic process. Many clinical, epidemiological and pathological studies have shown that atherosclerosis develops simultaneously in the central and peripheral arterial system \cite{8-11}. Direct identification of plaque in easily accessible peripheral arterial sites, therefore, may be a better strategy to target those individuals who would benefit from medical intervention compared to traditional risk factor assessment for the prevention of ASCVD events. The rationale for early detection of ASCVD is that detection during the subclinical stages of disease might permit the reliable identification of subjects at increased risk of a major adverse cardiac event (MACE) and that appropriate therapy (e.g. lipid lowering) might improve the prognosis of those at high risk \cite{12, 13}.

Ultrasound is safe, portable and low-cost imaging modality. Considerable improvements in image quality over the past twenty years make it possible for it to be considered for deployment in routine clinical use. In an earlier study, we assessed the clinical utility of B-mode ultrasound examination of the extracranial carotid system in an asymptomatic population in northern India \cite{14}. The present study expands on this work by incorporating
examination of the iliofemoral arteries. We report atherosclerotic disease burden in four different arterial sites, which were bilateral common carotid arteries and bilateral common femoral arteries and their bifurcations.

Specific study aims were:

1. Determine the prevalence of atherosclerotic disease in relatively young asymptomatic individuals in India using B-mode ultrasound examination of the extracranial carotid system.
2. Assess whether addition of the bilateral iliofemoral B-mode ultrasound examination provides improved identification of atherosclerotic disease burden.
3. Assess the feasibility of routine clinical deployment of an ultrasound machine (Panasonic CardioHealth Station) that requires minimum expertise for image acquisition and interpretation with its unique automated functions.
Methods and materials

A free health check-up camp was organized in rural (Sirsa, Haryana) and urban (Jaipur, Rajasthan) parts of India and a total of 942 asymptomatic volunteers were recruited. Institutional Review Board (IRB) approvals were taken and all the participants provided written informed consent. Eight radiology residents received two hours of training prior to performing the ultrasound examination on dedicated automated vascular ultrasound equipment (Panasonic CardioHealth Station). Bilateral B-mode ultrasound was used to detect plaque and measure intima-media thickness (IMT) of the extracranial carotid system. This exam was extended to the iliofemoral region to include the common femoral artery and its bifurcation. Resting blood pressure was measured to identify any undetected hypertension and history of current medications was noted. The participants also completed a simple questionnaire about their lifestyles and exposure to atherogenic risk factors.

Carotid & Femoral Artery Examination: Participants were screened in the supine position. For carotids, the neck was oriented 45° using a custom pillow and B-mode ultrasound images were captured with a 9MHz linear transducer in accordance with the clinical protocol recommended by the American Society of Echocardiography (ASE) Consensus Statement [11]. Presence or absence of plaque in the carotids and femorals were first determined by acquiring short-axis (transversal view) and then it was reconfirmed in long-axis (longitudinal view). If a plaque was found, the ultrasound image was marked up with the help of on-board tools as illustrated in Figure 1(a). Plaque was defined as any focal wall thickening greater than 1.5 mm protruding into the lumen of the scanned vessel [12]. In the neck, the transducer was manually moved in the cranial direction from the proximal CCA (clavicle) to the highest segment above the carotid bifurcation that was accessible. The iliofemoral arteries were examined from just below the inguinal ligament with little compression maneuver to compress the adjacent common femoral vein. The transducer was moved downwards from the common femoral artery to approximately 2cm below the bifurcation.

Intima Media Thickness (IMT) was measured from a single scan angle, which showed the clearest visualization of IMT and the straightest artery segment. The ultrasound system used incorporates a sensor in the transducer that tracks the scanning angle in real time and records the transducer angle position at which the IMT is taken. The ultrasound system also tracks the arterial diameter change continuously and determines systole and diastole timing based on vessel lumen diameter changes without requiring an external electrocardiogram. Automated calculation of IMT was done over a 1-cm region of interest (ROI) based on raw radiofrequency data in the far wall of the vessel examined. Within the 1cm ROI, the system tracks 24 spatial measurements at 200 frames/s for a total of 4,800 measurements every second. Thus, the reported IMT values from the ultrasound
system are an average of 24 spatial measurements over a 1cm region at end diastole (Figure 1B).
**Fig. 1**: Figure 1 (a): Transversal image of atherosclerotic plaque found in a 25 year old subject Figure 1 (b): Longitudinal plane image showing the plaque and far wall IMT.

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Results

A total of 942 subjects participated in the carotid and femoral ultrasound exam evaluation (mean age, 44±14 years), 624 were men (44.5±14.5 years) and 318 women (43.6±12.1 years); age distribution by gender is illustrated in Fig 2. Participants in the rural community of Sirsa were primarily involved in active lifestyle practices like tilling fields or performing other labor-intensive work. All of them had undergone aggressive lifestyle modifications under the guidance of a local spiritual leader. Based on the responses to the questionnaire, 61 male enrollees (15%) identified themselves as former smokers, none were current smokers, 90 (19%) were on medication to control hypertension and 9 (2%) were on medication for Type II diabetes. The male urban enrollees from Jaipur on the whole led a more sedentary lifestyle, 64 (40%) were current or former smokers, 33 (21%) were on medication to control hypertension and 10 (6%) were on medication for Type II diabetes.

An analysis of the 942 subjects showed that 224 (23.8%) had atherosclerotic plaques in either the carotid or femoral arteries. In 107 (11.4%) subjects, only the carotids were involved and in 47 (5.0%) subjects, only the femoral arteries were involved. In 70 (7.6%) subjects, plaques were found both in the carotids and femoral arteries. A summary of plaque findings in different arterial sites is presented in Figure 3. Prevalence of plaque in the male cohort was higher (n= 190, 30%) compared to the female cohort (n= 34, 10%). Age distribution of subjects found to have plaques is shown in Figure 4. Older age and male gender was significantly associated with the presence of plaque both in urban (58±12, p < .0001) and rural populations (57±12, p < .0001). However, association with systolic blood pressure was not observed (140±30 vs. 135±18, p = NS) in either population. The number of male subjects in the rural population of Sirsa found to have plaques was 123 (27%) compared to 67 (41%) males from the urban population of Jaipur.

Focusing just on the male subjects, it is interesting to note that the percentage of subjects on medication to control hypertension were almost identical in the rural and urban communities (around 20%). Similarly, the percentage of males on medication to control Type II diabetes were also comparable (2% rural vs 6% urban). However, there was a stark difference in the number of smokers or former smokers (15% rural vs 40% urban). This difference alone may serve to explain the higher prevalence of plaque findings in the urban population. Another factor may be the small difference in average age (42±15 rural vs 49±12 urban).
Images for this section:

**Fig. 2:** Age distribution of study enrollees

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Fig. 3: Distribution of Plaques in Different Arterial Sites

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Fig. 4: Age Distribution of Subjects with Plaque
Conclusion

Prevalence of atherosclerotic plaques in a relatively young (49±12 years old) cohort of asymptomatic urban male population was very high (41%) compared to the prevalence overall (24%). Adding the bilateral iliofemoral examination identified an additional 5% of the cohort who would otherwise have been missed if only bilateral carotid examination was administered.

B-mode ultrasound is safe, quick, easy to perform, non-invasive and widely available imaging tool that may help in better identifying those individuals who would benefit from medical intervention for primary prevention of ASCVD related events. Even though the updated ACC/AHA guidelines recommend against "CIMT" testing\textsuperscript{17}, the panel drafting this document did not consider plaque findings in their recommendation. Clearly direct evidence of subclinical atherosclerotic plaques presented here provides motivation for aggressive medical intervention. In developing countries such as India where a much younger population is afflicted with the devastating consequences of ASCVD related events, an alternative strategy for identifying high-risk individuals is warranted.

Our study shows that rapid screening for subclinical atherosclerosis is feasible with automated ultrasound examination of carotids and iliofemoral arteries. Adding B-mode examination of the iliofemoral arterial sites identifies additional individuals who would benefit from prophylactic medical intervention for the prevention of ASCVD related events. Surely, such a simple approach merits adoption on a wide scale as a modern approach to a modern scourge of rapidly rising ASCVD related events in developing countries such as India.
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