

Heading circulatory disease off at the pass

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Researchers at Oregon Health & Science University have devised an ultrasound imaging technique that picks up subtle early evidence of peripheral arterial disease (PAD) that current conventional tests miss.

The test, if approved for clinical use, could lead to early treatments that would head off the serious complications that can result from the disease. PAD, a condition in which atherosclerosis of the blood vessels in the legs limits blood flow, affects about 8 million Americans, particularly those older than 65 (American Heart Association statistics). Its presence raises the risk of a heart attack or stroke to four to five times that of the general population.

The disease poses particular dangers for diabetics because of the risk of infections and gangrene that can lead to amputations and death. PAD frequently goes undiagnosed in its early to mid stages. One of the reasons for this is the lack of cost-effective diagnostic tools capable of detecting PAD before it has grown serious. By contrast, cardiologists can noninvasively detect early signs of heart disease by imaging blood flows during exercise stress tests. No equivalent stress test has been available for PAD.

Lead investigator Jonathan R. Lindner, M.D., professor of medicine (cardiovascular medicine) at the OHSU School of Medicine, and his associates devised such a test for use in a study involving 26 control subjects with no history of coronary disease, hypertension or diabetes, and 39 patients with symptomatic PAD, of whom 19 had type 2 diabetes. Lipid-shelled microbubbles were injected intravenously as an

ultrasound contrast agent to evaluate microvascular blood flow in the calf muscles of subjects' legs at rest and during exercise. These microbubbles behave and circulate in much the way red blood vessels do and they "ring" in an ultrasound field giving off a strong signal. The results from blood flow imaging were compared with those from the most commonly used non-invasive diagnostic tests.

"We found that contrast-enhanced ultrasound imaging outperformed most conventional forms of diagnostics in measuring and evaluating impairment in a patient's ability to recruit blood flow in the legs during modest exercise," said Lindner. Specifically, the study found that patients with PAD had lower microvascular blood flow in their calf muscles than control subjects did after two minutes of plantar-flexion exercise in which the foot is flexed as when depressing the accelerator pedal of a car.

"Peripheral arterial disease is becoming a huge problem because of the aging of the population and the increasing incidence of diabetes," said Lindner. "But we don't have good diagnostics for it, partly because a lot of the methods we have are based on measuring what's going on in the big vessels, the arteries and veins. PAD is a complex, very diffuse disease, which often involves functional abnormalities in the microcirculation system, the tiniest small vessels that go into muscle, bone, skin and connective tissues. How well the microcirculation system is functioning is what determines how well tissue is getting fed, which is the critical issue."

Today diagnosing PAD relies mainly on detection of abnormal pulse volumes in the lower limbs, or blood pressure differences between separate readings at the ankle and the arm (the ankle-brachial index), but these are only effective in detecting moderate-to-severe cases and do not always detect disease in the small vessels.

"The real benefit of a test like this – which only takes about five minutes to do and doesn't require anything beyond the equipment and capabilities already in place in most vascular laboratories – is their value for selecting the right therapies," said Lindner. "There are new drugs in clinical trials at OHSU and elsewhere that involve gene and stem cell therapies aimed at improving the circulation by promoting new blood vessel growth. But the symptomatic benefits you get from these therapies generally can't be evaluated by conventional tests because they don't really test tissue perfusion. If you want to look at the improvement in perfusion, why not look at perfusion?"

Further studies are needed on subjects for whom no diagnosis has yet been made. The microbubbles used in the test already are approved for human use, although the PAD test is currently an off-label application. The technique does require additional training in how to receive the microbubble signals, said Lindner, but otherwise there are few significant hurdles yet to be cleared for the test to be used in vascular clinics everywhere.

Source: Oregon Health & Science University

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