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Stroke Risk Prediction beyond Classical Risk Factors: The Role of the Ankle-Brachial Index

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Major cardio- and cerebrovascular events often occur in individuals without known preexisting cardiovascular disease. The prevention of such events, including the accurate identification of those at risk, remains a serious public health challenge [1]. Scoring equations to predict those at increased risk have been developed using cardiovascular risk factors, but they tend to overestimate the risk in low-risk populations and underestimate it in high-risk populations [2].

Peripheral arterial disease (PAD) is increasingly recognized as a clinically important marker of atherosclerotic disease due to its association with cardiovascular disease incidence and mortality. Determination of the ankle-brachial index (ABI), which is the ratio of systolic pressure at the ankle to that in the arm, is quick, easy to measure and a noninvasive method used to establish the presence of PAD. A reduced ABI has been shown to identify patients at risk for cardiovascular events [3]. Patients with stroke or transient ischemic attack often had PAD. However, it is still unclear whether PAD is also a good predictor for future cerebrovascular disease. A recent meta-analysis demonstrated a pooled multivariate adjusted relative risk of 1.35 (95% confidence interval, CI, 1.10–1.65) for stroke in patients with an ABI <0.9 [3].

In this issue of *Cerebrovascular Diseases,* Meves et al. [4] report intriguing findings from the German Epidemiological Trial on Ankle-Brachial Index (getABI), a large and prospective cohort study of a typical primary care sample of unselected elderly patients. The authors quantified the association between PAD, either symptomatic or asymptomatic (defined as an ABI <0.9), and the future stroke risk in 6,880 patients. During the 5-year follow-up period, 183 patients had a stroke. In patients with PAD (n = 1,429) compared to those without PAD (n = 5,392), the incidence of all stroke types, with the exception of hemorrhagic stroke, was about doubled (for fatal stroke tripled). The corresponding adjusted hazard ratios were 1.6 (95% CI 1.1–2.2) for total stroke, 1.7 (95% CI 1.2–2.5) for ischemic stroke, 0.7 (95% CI 0.2–2.2) for hemorrhagic stroke, 2.5 (95% CI 1.2–5.2) for fatal stroke and 1.4 (95% CI 0.9–2.1) for nonfatal stroke. Lower ABI categories were associated with higher stroke rates. Besides high age, previous stroke and diabetes mellitus, PAD was a significant independent predictor for ischemic stroke. The stroke risk was similar in patients with symptomatic (n = 593) as compared to asymptomatic (n = 836) PAD. The authors concluded that the risk of stroke is substantially increased in PAD patients and that PAD is a strong independent predictor for stroke.

Interestingly, recent studies that analyzed the prognostic impact of low ABI values (<0.9) on stroke recurrence and cardiovascular events in acute stroke patients revealed comparable results. Purroy et al. [5] observed an increased stroke recurrence rate (32.1 vs. 13.6%, $p < 0.001$) and more vascular events (50 vs. 70%, $p < 0.001$) in patients with low ABI values. Similar results were seen in the SCALA trial [6] that examined 852 patients from 85 neurological stroke units throughout Germany as well as the PATHOS study [7] from Italy with 755 acute stroke patients. Busch et al. [8] described an increased risk for stroke, myocardial infarction or death in acute stroke patients with a low ABI <0.9 (relative risk 2.2; 95% CI 1.1–4.5).

Summarizing these data, asymptomatic PAD as defined as an ABI <0.9 is a clear predictor of increased stroke risk in primary care patients as well as of stroke recurrence in acute stroke.

An important prerequisite for the use of surrogate parameters for risk prediction particularly in the primary care setting is that these parameters add substantial incremental value in risk prediction beyond the traditional Framingham-type risk scores. A recent meta-analysis [9] clearly demonstrated that the ABI provided additional risk information compared with the Framingham risk score. A low ABI (<0.9) approximately doubled the risk of total mortality and cardiovascular risk across all Framingham risk categories. These changes of risk classification would likely have an effect on decisions to commence preventive treatment, e.g. lipid-lowering treatment [9]. In addition, the ABI can be easily measured in the primary care physician's office and in community settings. The equipment is inexpensive – a handheld Doppler sonograph costs less than 400 EUR. The procedure is simple, taking less than 10–15 min, and can be performed by a suitably trained nurse or health care professional.

The findings of the getABI study may have implications for risk evaluation in the primary care setting:

- the detection of PAD defined as an ABI <0.9 identifies high-risk patients for further vascular events; the vascular risk including stroke is clearly increased even in subjects with asymptomatic PAD;
- elderly patients in the primary care setting should be screened for (asymptomatic) PAD to enable consequent treatment of modifiable cardiovascular risk factors to reduce the risk of ischemic stroke and other vascular events; however, whether this screening is cost-effective remains to be established.

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