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CE - LETTER TO THE EDITOR

Foamy urine and stiffened blood vessels

Chia-Ter Chao

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To the editor,

I am quite interested in the article entitled "The PANDORA study: peripheral artery disease in patients with non-high cardiovascular risk" by Cimminiello et al. [1] published early online on February 5, 2011 of the *Journal*. The article describes the multi-national effort to identify the percentage of asymptomatic peripheral artery disease (PAD) within a low- to moderate-risk population. Excluding diabetes patients, Cimminiello et al find a prevalence of 17.8%, a higher prevalence to which they ascribe to different screening strategy, statin use, and psychosocial factors. However, I think there might be several other reasons to explain this:

First, renal dysfunction and more specifically, albuminuria, may play a significant role in the high prevalence. Albuminuria and chronic kidney disease (CKD) both have significant impacts on various cardiovascular diseases, and among them, PAD is a more important one owing to its usual silent nature. Previously, urine albumin excretion and renal function impairment have been shown to correlate with the ankle brachial index (ABI) and PAD. Tseng et al, in their study on the urine albumin creatinine excretion ratio (ACR) and ABI, demonstrate that for every one unit increment of ACR using a natural logarithm, the odds ratio for PAD is 2.1–3.86 [2]. Similarly, Mostaza et al also indicate that albuminuria is associated with a 60% increased risk of developing PAD [3]. In the same study, patients with CKD, defined as an estimated glomerular filtration rate <60 ml/min per 1.73 m^2, are also found to have a 50% higher risk of developing PAD. In a population of non-dialyzed CKD, de Vinuesa et al [4] clearly show that 32% of these patients have an ABI value less than 0.9, while these PAD patients have worse renal function than those without. Thus I wonder what the creatinine level and urine dipstick test result of Cimminiello et al.'s population would be. For comparison, it is helpful to look at the exact prevalence of albuminuria and CKD in the European countries. In the MARPLE study from Germany, Schrader et al. [5] find a 32% prevalence of microalbuminuria in a hypertensive cohort without diabetes. Another study from Norway also finds a similar 33% prevalence in a non-diabetic population without cardiovascular disease. As for renal function, it is estimated that long-term community dwelling hypertensive patients have about 50% risk of developing CKD if they have hypertension. From these surveys, we can presume that around one-fourth to one-third of patients in the PANDORA study might have albuminuria present, and about 10% of the patients might already have CKD. I think this can partially explain the higher prevalence of PAD in this seemingly low- to moderate-risk population. By excluding occult albuminuric and CKD patients, the exact prevalence would be more akin to the real percentage. However, it is a pity that none of these parameters were collected during the survey.

Second, medication use is another issue that merits consideration. As Cimminiello et al discuss in the content, statin use is lower in groups with PAD. Here I am curious about the percentage of angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) use. These medications have been reported to possess anti-inflammatory ability and reduce the oxidative stress of endothelial cells, thus improving endothelial function while

C.-T. Chao (✉)
Division of Nephrology, Department of Internal Medicine, National Taiwan University Hospital, College of Medicine, National Taiwan University, No. 7, Chung-Shan South Road, Taipei 100, Taiwan, Republic of China
e-mail: b88401084@ntu.edu.tw

attenuating vascular remodeling. ACEI/ARB may also curb or even halt the progression of peripheral vascular disease through a reduction of albuminuria [2]. It is tempting to guess that the use of ACEI/ARB is also restricted in Cimminiello's population, so that the prevalence may be somewhat higher. Similar imbalance of medication use between the PAD and the non-PAD group may also be present, skewing the study result.

In summary, I believe there is still more information that should be gathered for a better estimation of exact PAD prevalence, especially in such a specific population. Risk factors such as albuminuria and renal impairment could easily be excluded with a urine dipstick test or addition of a creatinine level determination to the battery of tests already included. It would be better to adjust for these factors next time before we start further analysis.

Conflict of interest None.

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