Index for recognition of early vascular disease

To the Editor: We read Reffelmann’s article concerning urinary albumin excretion as a predicting marker for the subsequently increased left ventricular mass with great interest. Under present common practice, the recognition of underlying vascular disease either macro or micro is underestimated and much late. We would strongly support your view of considering urinary albumin excretion reflecting underlying vascular disease and predicting future heart disease. In this regard, we as well as others consider microalbuminuria as a reflection of vascular disease. In this article, we have noted that 53-81% of cases had hypertension as well as impaired renal function (chronic kidney disease stage 2), which implies that vascular disease has already been present. We have recently demonstrated that the mechanism of vascular repair has already been mildly defective in this stage of renal impairment. Altered angiogenic factors, such as vascular endothelial growth factor, angiopoietin-1 in conjunction with antiangiogenic factor angiopoietin-2 and reduction in renal perfusion were noted. However, an effective preventive strategy to restore renal perfusion and function can be accomplished at this early stage, but would be ineffective if treatment is deferred to a later stage. To clarify this issue further, it is noted that only a quarter of cases have been treated with vasodilators, which is considered to be inappropriate. To serve the above purpose for early or primary preventive strategy, a search for other sensitive diagnostic marker for early vascular disease is a must, and treatment should be early implemented.

ACKNOWLEDGMENTS

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1. Reffelmann T, Dör M, Volzke H et al. Urinary albumin excretion, even within the normal range, predicts an increase in left ventricular mass over the following five years. Kidney Int 2010; 77: 1115–1122.

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The Authors Reply: We highly appreciate the interest that Futrakul and Futrakul take in our article. They emphasize two main aspects that are of general interest: first, identification of markers indicating very early stages of vascular and renal disease is of outstanding interest, as they could guide treatment or preventive strategies initiated very early in the disease process, which is presumed to be most effective. Second, microalbuminuria, or, as suggested in our article, even lower levels of urinary albumin excretion within the normal range (albumin-to-creatinine ratio > ~0.5 mg mmol⁻¹), may present such an early marker of vascular disease. Moreover, Futrakul and Futrakul set forth that early stages of renal disease are associated with reduced renal perfusion and mildly defective mechanisms of vascular repair, involving altered angiogenic and antiangiogenic factors. In various population-based investigations, a close association of early stages of kidney disease and altered vascular functioning, such as reduced flow-mediated vasodilation, was observed, which may support the concept of a pathophysiological linkage between early stages of vascular disease and renal impairment. Whether these observations reflect that vascular dysfunction may promote early stages of renal disease or mildly reduced kidney function results in altered vascular functioning or both, remains to be determined.

2. Reffelmann T, Dör M, Volzke H et al. Urinary albumin excretion, even within the normal range, predicts an increase in left ventricular mass over the following five years. Kidney Int 2010; 77: 1115–1122.

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Comments on ‘A young man with acute kidney injury after exercise’

To the Editor: I read with great interest the ‘make your diagnosis’ article describing a young man with acute kidney injury after exercise by Yan et al.1

My diagnosis is acute renal failure with severe loin pain and patchy renal ischemia after aerobic exercise (ALPE)\(^2,3\) in a patient with renal hypouricemia instead of exercise-induced acute kidney injury in hereditary renal hypouricemia. The cause of acute kidney injury in this case is unknown, although a few hypotheses may be proposed.\(^2\)

There are two types of exercise-induced acute kidney injury, myoglobinuric and nonmyoglobinuric acute renal failure.\(^2\) The latter was first described as acute renal failure with severe loin pain and patchy renal vasoconstriction in 1982\(^1\) and reviewed as ALPE in 2002.\(^2\)

In ALPE, patients complain of severe loin pain several hours after anaerobic exercise such as the 200-m dash and present at the emergency room.\(^2\) Acute kidney injury with normal or mild elevation of creatine phosphokinase develops not due to rhabdomyolysis. In 1990, 3 of 13 injury with normal or mild elevation of creatine phosphokinase.

ALPE in a patient with renal hypouricemia, showing patient with renal hypouricemia, but a more specific disease, is not merely exercise-induced acute kidney injury in renal hypouricemia. However, it is appropriate from the above review that this case is unknown, although a few hypotheses may be high frequency. Only acute renal injury that develops in renal hypouricemia is ALPE.

Yan \textit{et al.}\(^1\) described this case as exercise-induced acute kidney injury in renal hypouricemia. However, it is not merely exercise-induced acute kidney injury in a patient with renal hypouricemia, but a more specific disease, ALPE in a patient with renal hypouricemia, showing specific symptoms such as bilateral groin pain after a 400-m dash, and specific laboratory data such as normal creatine phosphokinase.


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\textbf{The Authors Reply:} We fully appreciate the comments from Dr Ishikawa\(^1\) on this case of exercise-induced acute nonmyoglobinuric renal failure in hereditary renal hypouricemia. Patients with renal hypouricemia are now well known to carry a higher risk of acute kidney injury, primarily acute tubular necrosis after strenuous anaerobic exercise. Several proposed mechanisms for acute renal failure in this setting include exercise-induced excessive oxidative stress production, acceleration of adenosine triphosphate degradation, renal vasoconstriction (spasm), and acute uric acid nephropathy.\(^2\) ALPE characterized by acute renal failure with severe loin pain after anaerobic exercise is an uncommon syndrome consisting of diverse underlying disorders including renal hypouricemia. The pathogenesis of ALPE, albeit incompletely understood, was considered to be a severe arterial vasoconstriction in the kidney as patchy wedge-shaped defects by contrast media-enhanced computed tomography, color Doppler imaging, and magnetic resonance imaging.\(^3,4\) Given the potential nephrotoxicity of contrast media, we did not perform the contrast-enhanced computed tomography in this patient to unveil the presence of renal patchy ischemia despite a similar feature with ALPE. Of note, loin pain presumably due to renal vasoconstriction or ischemia may be a nonspecific symptom and not exclusively present in patients with renal hypouricemia suffering from exercise-induced acute kidney injury. In terms of clinical manifestation, ALPE is still an important variant feature of exercise-induced acute renal failure in renal hypouricemia.


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