Letters to the Editor

In Response to Estimating Creatinine in Ultramarathon Runners by Little et al

To the Editor:

Little et al presented a valuable study concerning the accuracy of estimated creatinine in healthy runners.¹ The authors present interesting results and analysis based on estimation of glomerular filtration rate (GFR) and the back-calculation of creatinine level. Nevertheless, although present estimation methods are widely accepted, this study exposes the limitations of this approach in the evaluation of kidney function.

There is a basic methodological problem with this estimation methodology. The excretory function of the kidney can be established on the basis of serum creatinine measurement and Modification of Diet in Renal Disease Study or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations; however, using these equations one has to assume that a patient has average muscle mass and a normal diet and that production of creatinine is stable. It is a *conditio sine qua non*. A low creatinine level can be a result of cachexia, and a high creatinine level is typical of bodybuilders without kidney disease.^{2,3} During exercise, the production of creatinine is increased,³ and creatinine is low in individuals on meat-free diet.⁴ In all these situations, estimation of GFR will be misleading. The Modification of Diet in Renal Disease and CKD-EPI equations are mainly used for patients with chronic kidney diseases. In healthy populations they underestimate normal GFR. The CKD-EPI has some advantages, but it also has limitations (eg, significantly underestimating normal to high GFR levels in individuals with diabetes).⁵

The diagnosis of acute kidney injury (AKI) is based on a relative increase in creatinine level and in some cases decrease in urine output. When serum creatinine level is changing, the GFR equation is imperfect. During exercise, when production of creatinine is increased, the creatinine level reflects not only kidney function but also muscle mass and exercise intensity. In this situation, creatinine can be measured in serum and urine to calculate creatinine clearance. Recently, we published a study showing that creatinine clearance remained unchanged after ultramarathon, although serum creatinine was significantly increased.⁶ Another method to diagnose early AKI is based on cystatin C (CysC) measurement.³ CysC has been recognized as a promising marker of GFR, and

controlled physiological studies have demonstrated that acute changes in CysC provide a better approximation of GFR than serum creatinine.⁷

It can be difficult to diagnose early kidney injury; as a result, some new markers of AKI, such as neutrophil gelatinase lipocalin (NGAL) and kidney injury molecule-1, have been proposed. Although not widely used in clinical practice, these markers were tested in experimental studies. Urinary NGAL was increased after long endurance exercises,⁸ whereas after short, intense exercise (treadmill test) urinary NGAL remained unchanged and urinary kidney injury molecule-1 was significantly increased.⁹ The significance of recurrent postexercise increases in creatinine and new markers of AKI has not been established. The increase in creatinine level can be a sign of severe dehydration (prerenal azotemia), which is a benign condition, but it is possible that recurrent episodes of dehydration and muscle injury may contribute to subsequent kidney function.¹⁰

In summary, the authors presented a very interesting study and showed that some calculations used in clinical practice should not be used for the evaluation of kidney function in healthy runners.

Wojciech Wołyniec, PhD

Renke Marcin, PhD

Department of Occupational, Metabolic and Internal Medicine, Institute of Maritime and Tropical Medicine, Medical University of Gdansk, Gdynia, Poland
Email address: wolyniecwojtek@gmail.com

Wojciech Ratkowski, PhD

Department of Athletics, Gdansk University of Physical Education and Sport, Gdansk, Poland

References

1. Little CE, Lipman GS, Migliaccio D, Young DS, Krabak BJ. Accuracy of estimated creatinine in multistage ultramarathon runners. *Wilderness Environ Med*. 2019;30(2):129–33.
2. Meamar R, Maracy M, Nematollahi S, Yeroshalmi S, Zamani-Moghaddam A, Ghazvini MR. Effect of taking dietary supplement on hematological and biochemical parameters in male bodybuilders an equation model. *Iran J Nurs Midwifery Res*. 2015;20(6):681–8.

3. Baxmann AC, Ahmed MS, Marques NC, Menon VB, Pereira B, Kirsztajn GB, et al. Influence of muscle mass and physical activity on serum and urinary creatinine and serum cystatin C. *Clin J Am Soc Nephrol*. 2008;3(2):348–54.
4. Gutierrez A, Alvestrand A, Qureshi GA, Bergström J. Influence of a meat-free diet on the urinary excretion of 3-methylhistidine and creatinine in chronic renal failure. *J Intern Med*. 1992;232(2):129–32.
5. MacIsaac RJ, Ekinci EI, Premaratne E, Lu ZX, Seah J, Li Y, et al. The Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation does not improve the underestimation of glomerular filtration rate (GFR) in people with diabetes and preserved renal function. *BMC Nephrol*. 2015;16:198.
6. Wołyniec W, Ratkowski W, Kasprowicz K, Jastrzębski Z, Małgorzewicz S, Witek K, et al. Glomerular filtration rate is unchanged by ultramarathon. *J Strength Cond Res*. 2018;32(11):3207–15.
7. Odutayo A, Cherney D. Cystatin C and acute changes in glomerular filtration rate. *Clin Nephrol*. 2012;78(1):64–75.
8. Machado JCQ, Volpe CMO, Vasconcellos LS, Nogueira-Machado JA. Quantification of NGAL in urine of endurance cycling athletes. *J Phys Act Health*. 2018;15(9):679–82.
9. Wołyniec W, Ratkowski W, Urbański R, Bartoszewicz M, Siluk D, Wołyniec Z, et al. Urinary kidney injury molecule-1 but not urinary neutrophil gelatinase associated lipocalin is increased after short maximal exercise. *Nephron*. 2018;138(1):29–34.
10. Sánchez-Lozada LG, García-Arroyo FE, Gonzaga G, Silverio O, Blas-Marron MG, Muñoz-Jimenez I, et al. Kidney injury from recurrent heat stress and rhabdomyolysis: protective role of allopurinol and sodium bicarbonate. *Am J Nephrol*. 2018;48(5):339–48.

Leaf-Cutter Ants in Wound Closure

To the Editor:

Adequate laceration management continues to challenge providers in resource-poor settings. Even minor lacerations in wilderness scenarios can rapidly lead to significant morbidity. Most noncontaminated lacerations, once appropriately irrigated, can be treated safely with acute primary closure.^{1,2} Multiple commercial options for wound closure are available, including tissue adhesives, surgical tapes, staples, and sutures. However, if wilderness providers do not have ready access to such supplies, they may need to depend on improvised techniques using resources found in the environment.

There may be value in a “natural” method of laceration closure that has not been previously mentioned in recent wilderness medicine literature. Leaf-cutting ants, members of 2 genera—*Atta* and *Acromyrmex* (subfamily: Myrmicinae; tribe: Attini)—have been used to close wounds in Central and South America for centuries.³ These ants are found in the tropics and subtropics approximately between

latitudes 33°N and 44°S, including regions of Texas and Louisiana.⁴ Leaf-cutting ants are usually red-brown in color with 11-segmented antennae, 3 pairs of thorax spines, and a 2-segmented petiole (narrow waist). Nests are made from soils and can extend up to 1200 m² in surface area and more than 7 m deep. These colonies are typically easily identified by their numerous surface-level, crescent-shaped mounds.⁵ Leaf-cutter ants, like many insects, are polymorphic, meaning that within each species there are a variety of body types, with each suited to a specific task necessary for colony survival. The soldier caste of a leaf-cutting colony is the largest of all castes and defends the colony against threats. Members of this caste are most suitable for the application of wound closure given their larger mandible size.

When primary closure is necessary, both sides of the leaf-cutting ant's head are held firmly between the first and second digits (Figure 1). Gentle pressure is applied, forcing the ant's oral cavity to open. The ant's head is placed perpendicularly to and transversely across the wound. On contact with a surface, such as the skin, the oral cavity quickly closes, bringing the 2 sides of the wound together in apposition. The thorax and abdomen of the ant are subsequently detached, leaving the head and mandible behind. The decapitated head reportedly stays in place for approximately 3 d³; however, there is no literature detailing such information or the rates of dehiscence.

Some anecdotal reports indicate that wounds closed with leaf-cutter mandibles are less prone to infection than untreated lacerations. This may be secondary to the leaf-cutter ant's natural chemical defenses against parasites. The metapleural glands of this type of ant secrete bioactive components that inhibit a range of microorganisms.^{6,7} When the metapleural glands of *Acromyrmex octospinosus* were artificially occluded, the ants experienced a subsequent increase in susceptibility to invading bacteria.⁸ Unfortunately, there are no studies available to determine whether the metapleural secretions of leaf-cutter ants are active against human skin pathogens.

Leaf-cutter colonies can contain millions of individuals, allowing ants to be a readily available and renewable resource. Although there is not enough evidence to recommend this means of wound closure over commercially available devices, in appropriate situations with limited supplies, this may be a worthwhile option. Additional investigation into this means of laceration repair is certainly warranted.

Acknowledgments: The author thanks Taylor Marks, BS, with assistance with photography used in Figure 1.