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## Elevation of Troponins in Rhabdomyolysis

To the Editor:

In their excellent comprehensive clinical review on rhabdomyolysis in *CHEST* (September 2013), Zimmerman and Shen,<sup>1</sup> to our surprise, did not mention that levels of troponin I and troponin T may be elevated. As clinicians, we realized that this can cause some difficulty in the interpretation of these specific biomarkers of cardiac injury, especially since rhabdomyolysis may occur with medications prescribed for patients with a history of heart disease, namely, statins, fibrates, and amiodarone. Up to 17% of patients may have elevated troponin levels, according to a study performed in the ED.<sup>2</sup>

The causes of the elevation are debated, but it is important to emphasize that with hydration, the cornerstone of the treatment of rhabdomyolysis, troponin levels revert to normal.<sup>3</sup> It is important at this stage not to subject the patient to either conventional or multidetector CT coronary angiography, to prevent contrast nephropathy. In our clinical experience, these patients can be reassessed for coronary artery disease after the episode of rhabdomyolysis with noninvasive imaging for significant ischemia and subsequent management determined accordingly. The etiology of the rhabdomyolysis can alert the physician to what may not be a case of a false-positive elevation, as is the case with

cocaine, which can cause both rhabdomyolysis and acute coronary syndrome.

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## Rhabdomyolysis

### Some Extra Clues to Diagnosis

To the Editor:

We read the recently published article in *CHEST* (September 2013) by Zimmerman and Shen<sup>1</sup> with interest. The authors prepared a high-quality review on the topic of rhabdomyolysis. It is essential to keep in mind that a considerable number of patients with rhabdomyolysis may lack clinical signs and symptoms.<sup>2</sup> So what other clues can be helpful in detecting cases of skeletal muscle injury?

Some laboratory parameters can be of assistance that were not mentioned in the review article.<sup>1</sup> Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) concentrations are laboratory tests typically included in a comprehensive metabolic panel. It is important to mention that both AST and ALT are present in skeletal muscle, with ALT being more specific to the liver.<sup>3</sup> Patients with rhabdomyolysis tend to have abnormal aminotransferase in the absence of liver disease.<sup>3</sup> In such cases, AST concentration tends to be higher than ALT concentration, and the AST to ALT ratio may be  $\geq 2:1$ , similar to alcoholic liver disease.<sup>3</sup>

In supporting this notion, one of us (A. E. M.) recently took care of two patients with clinically asymptomatic rhabdomyolysis. Both patients had an AST to ALT ratio of 2:1, with no evidence or risk factors for liver disease. Neither patient had any muscle weakness or muscle tenderness. Creatine kinase level was elevated 15-fold in the first and 13-fold in the second patient. IV hydration was started. Therefore, it is essential to keep a high index of suspicion for rhabdomyolysis in an appropriate clinical setting with an elevated AST to ALT ratio.

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## Response

To the Editor:

We thank Drs A. E. Mirrakhimov and E. M. Mirrakhimov and Drs Nobre and Thomas for their letters in response to our review article on rhabdomyolysis.<sup>1</sup> We agree that elevations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) concentrations can be excellent clues for the astute clinician to recognize the possibility of inapparent rhabdomyolysis and to order additional testing.<sup>2</sup> Of note, the AST to ALT ratio > 2:1 usually seen in acute rhabdomyolysis may not be present with more indolent forms of muscle breakdown, such as in inflammatory myositis.<sup>3</sup> Unexpected elevations of lactate dehydrogenase concentrations may also be another nonspecific clue suggesting rhabdomyolysis.<sup>2</sup>

Measurement of cardiac-specific troponins is useful for cardiac injury screening, but as Drs Nobre and Thomas point out, there are still limitations of these biomarkers to diagnose acute coronary syndrome. An early study found that troponin I and troponin T levels may be elevated in patients with rhabdomyolysis.<sup>4</sup> Other studies have suggested that troponin T level is more commonly elevated than troponin I in rhabdomyolysis due to several different etiologies.<sup>2,5</sup> Interpretation of an elevated troponin concentration in patients with rhabdomyolysis may be difficult because of limitations of the assay itself<sup>5</sup> or concomitant risk factors that could predispose to cardiac muscle injury. Further evaluation for acute coronary syndrome in patients with rhabdomyolysis and an elevated troponin concentration is best left to the judgment of the clinician caring for the patient. We strongly agree that exposure to contrast agents for diagnostic testing should be avoided if at all possible in patients with rhabdomyolysis.

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## Interobserver Variability in Grading Acute Rejection After Lung Transplantation

To the Editor:

We read with great interest the article by Bhorade et al<sup>1</sup> in *CHEST* (June 2013) about the interobserver agreement of grading acute rejection after lung transplantation. They indicated that the overall concordance rates for grade A and grade B biopsy specimens were 74% and 89%, respectively, and interobserver discrepancies for acute rejection were lower when pulmonary biopsies were performed earlier ( $\leq 6$  weeks) compared with later time points. However, we would like to add more information after deeper analysis of the data and address some important concerns.

In the Bhorade et al<sup>1</sup> study, the interobserver agreement for grade A and grade B readings were presented as the overall concordance rate, as well as that determined by treatment arm and clinical symptoms. The overall concordance rate ranged from 62% to 91%, according to the data from the tables in the article<sup>1</sup>; however, it should be noted that the interobserver agreement provided by the authors was ambiguous and requires further analysis. Therefore, we conducted  $\kappa$  analysis to reevaluate the concordance of interpretations for acute rejection between site pathologist and central pathologist (based on the data presented in tables in the article). The score of Cohen  $\kappa$  coefficients ranged from 0 to 1, where  $\kappa$  scores  $\geq 0.75$  represent fair agreement, scores  $< 0.4$  represent poor agreement, and the scale of 0.4 to 0.75 was considered moderate agreement. The McNemar-Bowker test was performed to estimate the diagnostic differences between site pathologist and central pathologist. After thorough statistical analysis of the data from Tables 2 and 3 in the Bhorade et al<sup>1</sup> article, we found that