Letter to the Editor

The significance of acylcarnitine ratio indices in diagnosing carnitine-acylcarnitine translocase deficiency

Congcong Shi[1,2], Hu Hao[2,3], Sitao Li[2,3]

[1]Inborn Errors of Metabolism Laboratory, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [2]Biomedical Innovation Center, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [3]Department of Pediatrics, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Correspondence to: Sitao Li, MD. Department of Pediatrics, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; Biomedical Innovation Center, The Sixth Affiliated Hospital, Sun Yat-sen University, 19 Yuancun New Street, Tianhe District, Guangzhou 510655, China. Email: lisit@mail.sysu.edu.cn.

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We thank Tan *et al.* for his comments on the article "*Increased acylcarnitine ratio indices in newborn screening for carnitine-acylcarnitine translocase deficiency shows increased sensitivity and reduced false-positivity*" published in *Translational Pediatrics* (1,2). According to the suggestions of the authors, we provided the C2 and C3 levels of 15 patients with carnitine-acylcarnitine translocase (CACT) deficiency. The median concentration of C2 was 8.39 μmol/L (1.18–16.42 μmol/L), normal reference range was 4.50–44.50 μmol/L. The median concentration of C3 was 0.55 μmol/L (0.13–2.01 μmol/L), normal reference range was 0.45–4.10 μmol/L. The results showed that patients with CACT deficiency have low or borderline low levels of C2 and C3. CACT deficiency can result in a significant depletion of free carnitine, ultimately causing a reduction in the levels of both C2 and C3 as the concentration of free carnitine decreases.

To compare the false-positive rate of the acylcarnitines markers to that of marker ratios in newborn screening, these specific metabolic biomarkers of CACT deficiency were independently analyzed statistically in *Tab. 3*. We assert that employing indicators with lower rates of false positives as diagnostic markers can effectively decrease the false positive rate for CACT deficiency. To the best of our knowledge, various fatty acid oxidation disorders and organic acidemias can lead to decreased concentrations of plasma C0 and C2, thereby causing secondary carnitine deficiency (3). Although C0 and C2 can assist in the diagnosis of CACT deficiency, they are not specific metabolites of CACT deficiency, so they are not shown in *Tab. 3*.

Compared with the normal control group, the levels of (C16 + C18:1)/C2 and C16/C2 in heterozygous carriers significantly increase, demonstrating the high specificity and sensitivity of these two indicators. Nonetheless, the detection values of these two indicators fall within the normal reference range of newborn screening. As a result, we preliminarily believe that heterozygous carriers may not lead to false positive results, which is the purpose of our study. Based on suggestions, we will also explore the use of C16/(C0 + C2) and (C16 + C18:1)/(C0 + C2) as diagnostic indicators for CACT deficiency in the future work.

In *Tab. 4*, *t*-tests were used, we apologize for not clearly describing it in the article. As the number of heterozygous carriers is relatively limited and our research objective solely entails a preliminary investigation of potential variations in the concentration of indicators between carriers and the normal control group, thus *t*-tests were employed. In the statistical analysis of subsequent research, we will attempt to use receiver operating characteristic (ROC) curves analysis to better determine the sensitivity and specificity of these ratio indicators.

In order to ensure the scientific validity and rigor of the false-positive sample screening, C12 has been excluded from the inclusion criteria due to having the highest false positive rate (0.88%) as observed in our research results

(*Tab. 3*). *Fig. 1* was intended to visually demonstrate the discriminative ability of detection values for each indicator in distinguishing between the positive and false positive groups. Therefore, we did not provide detailed information such as means, standard deviations, and significance of differences. Thanks again to the authors for their valuable suggestions.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Shi C, Ao Z, Liu B, et al. Increased acylcarnitine ratio indices in newborn screening for carnitine-acylcarnitine translocase deficiency shows increased sensitivity and reduced false-positivity. Transl Pediatr 2023;12:871-81.
2. Tan Y, Wang L, Qi X, et al. Acylcarnitine ratio indices in diagnosing CACT deficiency in newborns. Transl Pediatr 2023. doi: 10.21037/tp-23-371.
3. McHugh D, Cameron CA, Abdenur JE, et al. Clinical validation of cutoff target ranges in newborn screening of metabolic disorders by tandem mass spectrometry: a worldwide collaborative project. Genet Med 2011;13:230-54.

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