

## Serum Calcium and Risk of Sudden Cardiac Arrest in the General Population

**To the Editor:** We were pleased to read the article by Yarmohammadi et al<sup>1</sup> in the October 2017 issue of *Mayo Clinic Proceedings*, in which they reported an independent association between low calcium levels and an increased risk of sudden cardiac arrest (SCA). We applaud their methodology and focused exploration of possible causal mechanisms of cardiac arrest. However, we are concerned about the weak physiologic basis for their findings, the range of calcium values discussed in the article, and the potential harm to the general population if calcium levels become a target for intervention.

The physiologic basis for calcium being a major or direct cause of lethal arrhythmia is controversial, whereas other electrolytes, specifically magnesium and potassium, are closely associated with calcium levels and have a much stronger and consistent relationship with lethal arrhythmias. Moreover, although hypocalcemia alters the cardiac action potential and lengthens the QTc interval, these effects are rarely present near the generally accepted ranges reported by Yarmohammadi et al. In addition, the reported QT intervals do not support that hypocalcemia induced the observed arrhythmias. Although the difference in QT intervals between the cases and controls was statistically significant, the difference between calcium levels in these groups was clinically negligible, implying that calcium may not have been the only factor responsible for the observed QT difference. Even so, the observed QT difference was not likely clinically significant given the overall inaccuracy of measuring clinical QT intervals. Lastly, despite a 2.3-fold increase in

the risk of SCA, there was no difference in QT intervals between the highest and lowest quartiles of calcium, suggesting that some unaccounted factor may have been responsible for the relationship.

Several factors associated with SCA and QT prolongation could be considered in this analysis, including a history of thyroid disease, elevated parathyroid hormone levels due to the high prevalence of chronic kidney disease, myocardial infarction, and the use of QT prolonging medications.<sup>2,3</sup> A major consideration would be magnesium levels, which were not available in this study.<sup>4,5</sup>

We applaud the skilled work the authors have conducted in this very important area. However, because of the concerns we outlined, the extrapolation of their findings to SCA prevention is premature. As the authors stated, evidence regarding the association between calcium and cardiac events is equivocal, and the evidence at present does not support a change in our understanding of the relationship between electrolyte abnormalities and SCA.

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**Potential Competing Interests:** The authors report no competing interests.

1. Yarmohammadi H, Uy-Evanado A, Reinier K, et al. Serum calcium and risk of sudden cardiac arrest in the general population. *Mayo Clin Proc.* 2017; 92(10):1479-1485.
2. Lee H. Serum calcium: a sudden cardiac arrest risk factor [editorial]. *Mayo Clin Proc.* 2017;92(10): 1466-1468.
3. Benoit SR, Mendelsohn AB, Nourjah P, Staffa JA, Graham DJ. Risk factors for prolonged QTc among US adults: Third National Health and Nutrition Examination Survey. *Eur J Cardiovasc Prev Rehabil.* 2005;12(4):363-368.
4. Peacock JM, Ohira T, Post W, Sotoodehnia N, Rosamond W, Folsom AR. Serum magnesium and risk of sudden cardiac death in the Atherosclerosis Risk in Communities (ARIC) study. *Am Heart J.* 2010;160(3):464-470.

5. Kieboom BC, Niemeijer MN, Leening MJ, et al. Serum magnesium and the risk of death from coronary heart disease and sudden cardiac death. *J Am Heart Assoc.* 2016;5:e002707.

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## In Reply—Serum Calcium and Risk of Sudden Cardiac Arrest in the General Population

We appreciate the interest from Husain and colleagues in our recent article, in which we reported an association between lower levels of serum calcium and increased risk of sudden cardiac arrest (SCA). We will respond to each of their comments and also refer readers to the editorial by Lee<sup>1</sup> in the same issue, which we believe provides a balanced perspective on our findings.

To our knowledge, our work remains the first community-based study to report the association of lower serum calcium level with SCA. It is also important to recognize that measurement of serum calcium within 90 days of the SCA event is a unique aspect of our study. All of the previously published associations between serum electrolytes were performed using measurements in samples collected at baseline, ranging between approximately 5 and 15 years in advance of the SCA event.<sup>2-4</sup> It is difficult to know how relevant these remote measurements may have been to the distant SCA event. Because our case-control study design does not allow for direct causal inferences, we were careful not to make any. Given the complexity of the SCA phenotype, we agree that prolongation of the QTc is likely to be multifactorial and is a consistent finding in multiple populations including ours.