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Title: Letter to the editor regarding article “*Cardiac Abnormalities in Patients With Hutchinson-Gilford Progeria Syndrome*”

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To the Editor:

We have read with great interest the study of Prakash *et al*(1), aimed at describing the prevalence and natural history of cardiac abnormalities in patients with Hutchinson-Gilford progeria syndrome (HGPS). They conducted a cross-sectional study to describe several cardiovascular parameters in the largest-to-date cohort of HGPS patients. They reported that electrocardiographic abnormalities were rare (7%), and only present during the second decade of life. The latter is in sharp contrast with our recent report(2), demonstrating overt repolarization abnormalities in 7 out of 15 HGPS patients at advanced disease stages. In our study HGPS patients exhibited significant T-wave flattening, which was exacerbated as the disease progressed. More specifically, we analyzed the T-wave alterations rigorously using a newly developed, rate independent T-flattening score that enabled us to quantify T-wave flatness using lead II and precordial V5 tracings(3). Importantly, similar to HGPS patients, progeroid mice showed age-dependent repolarization abnormalities manifested as significant T-wave flattening compared with controls (2).

Therefore, we respectfully challenge the assertion by Prakash *et al*.(1) that we could have overestimated the degree of T-wave inversion on the right precordial leads, potentially misclassifying normal ECG findings in our series. We did not use right precordial leads to quantify T-wave alterations. Moreover, despite being retrospective, our analysis was not limited to a cross-sectional ECG evaluation, but included 51 ECGs from 15 patients at different ages and disease stages. We also included a control group with 13 gender- and age-matched healthy control volunteers, who did not present any T-wave abnormalities. Detailed description of every single ECG was also provided in the supplemental material, although such a qualitative description was not used for comparisons to avoid interpretation bias. From the foregoing, it is clear that, rather than a misclassification, our data provided strong evidence of T-wave abnormalities in HGPS patients, without the limitations of a cross-sectional ECG evaluation.

Other repolarization abnormalities like mild QT interval prolongation were previously reported by Merideth *et al*(4). QT interval analysis in this new series by Prakash *et al*.(1) also supports the evidence that QT prolongation is not a common finding in HGPS patients. In this regard, our series was in agreement with these two studies. Moreover, similar to HGPS patients, corrected QT intervals in progeroid mice were also normal during our sequential follow-up (2).

Therefore, it is important to clarify to the scientific community that repolarization abnormalities are a robust finding in HGPS patients as they age.

References

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