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Frequent premature atrial complexes... truly a benign finding? Author reply

We thank Dr Sérgio Barra for his comments1 on our recent observation of the association between frequent premature atrial complexes (PACs) and new-onset atrial fibrillation (AF) and ischaemic stroke in symptomatic patients published in the Journal.2

We generally agree with Dr Barra’s comment that rapid runs of PACs at least mechanistically would be a better surrogate marker for AF than absolute number of PACs. While conceptually attractive, the use of rapid runs of PACs as a marker for AF could present clinical difficulty because of its heterogeneity and complexity. Specifically, the quantification of runs of PACs include parameters that include number of runs of PACs per day, number of PACs per runs, rate of runs and total duration of PACs. Inarguably all these parameters can reflect a different facet of atrial arrhythmogenic foci that potentially contribute to AF development. Nonetheless, direct comparison of these parameters remains complicated and challenging, thus lessening its clinical practicality. In stark contrast, the simplicity of the absolute number of PACs that can easily be obtained by most automatic systems may allow rapid clinical application: the prognostic performance of frequent PACs in predicting new AF and stroke in our cohort was reasonable with the C-statistics of 0.66 and 0.58, respectively.

In addition to frequent PACs, our study also demonstrated that increasing age and coronary artery disease were independently associated with new AF and ischaemic stroke. Increasing age and coronary artery disease are nevertheless not only risk factors for AF as previously reported,3,4 but also independently associated with increasing PACs as highlighted by Dr Barra. This raises consequent concerns on whether frequent PACs are truly independently associated with new AF or merely epiphenomenal. To clarify this, we further evaluated the relationship between frequent PACs and the occurrence of new AF in patients with and without coronary artery disease. Figure 1A depicts the Kaplan–Meier survival curves in patients with no coronary artery disease. Patients with PAC >100/day had a higher

Figure 1 Kaplan–Meier estimate of percentage of new-onset atrial fibrillation survival in relationship to the presence or absence of frequent premature atrial complexes in (A) patients with no coronary artery disease, (B) patients with coronary artery disease, (C) patients younger than 75 years, and (D) patients older than or equal to 75 years.
incidence of new AF with hazard ratio (HR) of 4.3 [95% confidence interval (CI): 3.1–14.3] and C-statistics of 0.66 (Figure 1A). Among patients with coronary artery disease, those with PAC \( >100/\) day also had a higher incidence of new AF with HR of 3.7 (95% CI: 2.0–17.3) and C-statistics of 0.65 (Figure 1B). It is worth noting that patients with coronary artery disease had a higher overall incidence of new AF than those with no coronary artery disease. Likewise, the association between frequent PACs and new AF was also observed in patients with age <75 or \( \geq 75 \) (Figure 1C and D). We hope these supplemental data lend further support to our suggestion that frequent PACs per se can predict new AF. Research incorporating frequent PACs into conventional AF risk stratification scheme will certainly help.

**Conflict of interest:** none declared.

**References**


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