We agree with Drs. Palazzuoli and Ruocco that several other parameters determine prognosis in patients with pulmonary arterial hypertension (PAH). As summarized in Figure 1, these factors include, although not limited to, parameters of right ventricular (RV) function, pulmonary resistance, functional class as well as the etiology of PAH. Stability of function over time is also emerging as an important prognostic factor in PAH (1). In addition, risk prediction models must be tailored to their context, i.e., prevalent (as in our study) versus incident cases and chronic versus acute decompenated right heart failure. In our study, we were not suggesting that “the right heart score” should replace well-validated risk prediction formulas or scores but that quantitative measures of right heart structure or function could simplify risk prediction. Moreover, because of our small sample size, it is difficult to account for the complexity of risk stratification without overfitting the data. In the future, these risk scores could help tailor therapy or improve stratified randomization for clinical trials.

We agree with the authors that right heart adaptation is a key determinant of survival in PAH (2). A ventricle that is able to hypertrophy or better increase its contractility in response to the increased afterload is more likely to have improved survival. In this regard, the concept of mass-to-volume ratio is interesting; for example, patients with a higher RV mass-to-volume ratio for a given pulmonary vascular resistance (PVR) are likely to have a better prognosis. Interpretation of RV mass-to-volume ratios should, however, take into account PVR and the acuity of the disease. For example, a lower mass-to-volume ratio would not necessarily indicate worst adaptation but may also be reflective of lower PVR. In contrast to the mass-to-volume ratio, metrics of RV function such as right ventricular ejection fraction (RVEF) or RV global longitudinal strain have been more validated and appear to be more robust metrics (2). Another concept related to ventricular function is the concept of proportionality of ventricular adaptation; for example, although a slight decrease in RVEF is expected in patients with a slight increase in PVR (e.g., 5 Wood units), a moderate to severe decrease in RVEF would be disproportional. Future studies are needed to identify a simple metric for the proportionality of ventricular adaptation and to determine its role in outcome analysis. In conclusion, risk prediction in patients with PAH can be simplified using quantitative measures of right heart size and function, but, as the authors highlight in their letter, a simple score is unlikely to capture the complexity of risk stratification.

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REFERENCES

LA Size in Former Elite Athletes

A recent meta-analysis by Iskandar et al. (1) nicely showed that endurance athletes have larger left atrial (LA) diameters compared with control subjects. Yet

DLCO = diffusing capacity of the lungs for carbon monoxide; PAH = pulmonary arterial hypertension.
only 9 of 54 studies included in their analysis reported LA volume values corrected for body surface area (BSA). In fact, few studies have determined LA volume in young athletes, and, to the best of our knowledge, no study has reported this variable in older athletes. This is an important question given the growing debate about the potential deleterious effects of long-term strenuous endurance exercise on the human heart, notably the higher risk of atrial fibrillation (AF), a condition for which both atrial dilation and the normal aging process are thought to be potential causative mechanisms (2). Thus, we aimed to assess the long-term consequences of endurance exercise on LA volume in athletes who were highly competitive at younger ages and are still active. To this end, we compared BSA-corrected LA volumes determined with late gadolinium enhancement magnetic resonance imaging (LGE-MRI) in former elite endurance athletes and sedentary control subjects.

After institutional review board approval, 5 healthy individuals (control subjects) and 10 former elite endurance athletes (all men; ages 57.0 ± 4.3 years and 52.4 ± 6.3 years; body mass index, 25.8 ± 2.7 kg/m² and 22.6 ± 1.3 kg/m², respectively) provided written informed consent and were studied. Control subjects had never participated in regular exercise, whereas the athlete group included former professional road cyclists (n = 6) and runners (n = 4, 1 of whom was a 2-time marathon world champion). Their mean experience in professional sports competition (including, for some of them, participation in the Olympic Games) was 24.3 ± 4.2 years. All but 1 of them are still training and competing regularly in Master categories. The only nonactive athlete had been retired from competition for 24 years.

Evaluations were performed with a Signa HDx 3.0-T instrument (GE Healthcare, Buckinghamshire, United Kingdom). Approximately 10 to 15 min after injection of 0.2 mmol/kg gadolinium-chelate contrast, high-resolution late gadolinium enhancement images of the left atrium were acquired in the 3 cardiac planes. LA volumes were evaluated using the software Report Card 4.3 (GE Healthcare) by a single blinded, experienced researcher.

The values of LA volumes corrected for BSA followed a normal distribution and were significantly higher in athletes compared with control subjects (58 ± 14 ml/m² vs. 39 ± 14 ml/m², respectively; p = 0.026). In the former, the lowest LA volume was found in the only inactive subject (individual values are shown in Figure 1).

This is the first attempt to evaluate LA volumes with LGE-MRI in former elite athletes. Although our results are preliminary and more research is needed with larger cohorts, in accordance with Iskandar et al. (1), our data suggest that long-term participation in regular endurance exercise increases LA volume. Interestingly, LA dimensions are also larger in former highly trained athletes compared with their younger peers (as shown in Figure 2 of the Iskandar et al. [1]paper), probably due to the combined effects of long-term strenuous endurance exercise together with age-related physiological changes. It seems, however, that LA enlargement in endurance-trained athletes is an overall benign adaptation coupled with the left ventricular (LV) enlargement and volume overload induced by long-term exercise (3,4); indeed, endurance training preserves ventricular compliance, thereby preventing heart failure in later life, whereas sedentary aging is associated with decreased LV compliance and diastolic performance. Further, LA enlargement associated with sedentary aging is due to LV dilation owing to increased LV mass and eccentric hypertrophy (e.g., caused by obesity) and/or a concentric increase in LV mass (e.g., caused by essential hypertension), and eventually leads to impaired ventricular filling and diastolic dysfunction (5). However, although the association between increased LA diameter/volume and higher risk of AF is well documented, no athlete studied here has ever received a diagnosis of persistent or paroxysmal AF.

In conclusion, clinicians should be aware of the fact that highly trained endurance athletes usually have larger LA diameters compared with the general population, a phenomenon especially remarkable in
veteran athletes. Future research might elucidate the clinical implications (if they exist) of such morphological changes.

**THE AUTHORS REPLY:**

We appreciate the kind comments of Dr. Sanchez-Gomar and colleagues about our meta-analysis of left atrial (LA) size in athletes (1) as well as their novel use of cardiac magnetic resonance to assess LA volume more accurately in older former elite endurance athletes. Their results suggest that LA size adjusted for body surface area is almost 50% (58 ± 14 ml/m² vs. 39 ± 14 ml/m²) greater in their athletes than control subjects, a percentage difference much greater than the 30% (30.9 ± 1.4 ml/m² vs. 24.1 ± 1.0 ml/m²) that we observed in our meta-analysis, probably because the athletes in the study by Dr. Sanchez-Gomar and colleagues were older (age 57.0 ± 4.3 years) than those in our study (age 27 ± 4 years) (1), and all were formerly elite endurance competitors. Sanchez-Gomar et al. consider the increase in LA size noted in both of our studies as “an overall benign adaptation.” This may be true, but the risk of atrial fibrillation (AF) increases with LA size, and it is not clear that an increase in LA size from endurance training presents less risk of AF than other causes of LA enlargement. Indeed, increased LA size may be an explanation for the possible increase in AF noted in endurance athletes (2).

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