different mean rates, as several indices have been previously proposed to analyse the dynamics of ventricular response to AF. Moreover, it should be taken into account that in patients with AF most of these indices show a positive association with mean ventricular cycle length. From this point of view, in order to better analyse the effect of heart rate on the differences in cardiac function between regular and irregular ventricular pacing, it may be appropriate to generate sequences of RR intervals with different mean rate but similar rate-adjusted parameters of both variability and irregularity. However, it might also be interesting to evaluate the haemodynamic effect of sequences characterized by variable degrees of RR variability and irregularity, in order to explore the relative role of each index, and its interaction with mean heart rate, in affecting cardiac function. We believe that future analyses investigating these issues may further reinforce the message of this study, and clarify intriguing aspects of LV haemodynamic response to AF.

References

Impact of ventricular response irregularity in patients with atrial fibrillation and heart failure: reply

We appreciate the interest of Ballo et al. in our study and their thoughtful comments. Their major concern was that the observed haemodynamic differences between regular and irregular pacing at two different levels of heart rate might have been confounded by differences in R–R interval variability at the two rates. We appreciate how this concern might arise given the lack of full details regarding the pacing sequence we used to simulate atrial fibrillation. However, as explained in detail here, we believe this concern is not warranted.

We used a random number generator to derive an R–R interval sequence at a mean rate of 80, which yielded an event histogram following a Poisson distribution. As noted, this is typical of R–R interval histograms that approximate naturally occurring atrial fibrillation. Therefore, for studies at the faster rate, we used the identical random sequence of R–R intervals, but shortened each interval by one-third, taking into account dependency of heart-rate variability on prevailing mean heart rate. Thus, the coefficient of variation (COV = SD/mean × 100) was identical at both mean rates (25.6%). This mirrors measured data from patients with atrial fibrillation in whom adrenergic or anticholinergic medications were used to vary heart rate (48, 60, and 90 b.p.m.), yet the COV of the R–R intervals remained essentially constant at ~23% for each rate. In addition, we used the identical ‘random’ time-sequence of R–R intervals at both rates, so the temporal course of intervals was reproduced in each patient at each rate. We regret that these details were not provided in the manuscript.

We agree that it would be interesting to investigate the haemodynamic consequences of different degrees of R–R variability and irregularity (entropy), particularly in the setting of an animal model. However, in an invasive study of severely ill human subjects, we limited our efforts to the most contrasting conditions—the categorical comparison between completely regular and irregular pacing sequences with a distribution that resembles real-life atrial fibrillation.

References