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## REPLY

We are well aware of the previous publications on the various applications of real-time 3D echocardiography (RT3DE), including those published by your group and obviously by ours. We greatly respect your work and your opinions, even when you disagree with us. We also are aware that some of the findings from our recent study might be interpreted as controversial and have anticipated a debate after its publication. In our view, such a healthy debate is a legitimate part of the work of scientists, and it is what differentiates science from nonscientific theories that cannot be disputed, proved, or disproved.

We believe that it is important to report findings, even when they do not fall within the common tenets and may thus warrant controversy. Generally speaking, we believe that publishing only noncontroversial findings while withholding findings contradicting previous publications is a dangerous approach that risks endorsing and perpetuating what may at times be only partial truths. There are many claims in your letter that we would like to briefly dispute, one by one, within the limited space allocated for this response.

Regarding the claim that our report contradicts our own previous publications, the unexpected findings of our study were as follows: 1) the normal range of the systolic dyssynchrony index (SDI) was half the magnitude of that previously established in smaller groups of normal subjects when a slightly different segmentation scheme was used; and 2) as a result, all patients with dilated cardiomyopathy (DCM) had abnormally high left ventricular (LV) dyssynchrony irrespective of QRS duration. These findings have important clinical implications for the selection of patients for cardiac resynchronization therapy and may partially explain the difficulties encountered by other investigators (1) and more notably in several recent multicenter studies.

Your claim that this study contradicts our own work was supported by a statement that we chose to cite only publications by others while "hiding" our own. The list of our publications you provided to prove this point consisted of 4 abstracts (references 9 to 12 in Monaghan et al. [2]). Two of these abstracts described our initial results in small groups of patients that led us to design the study by Sonne et al (3). The other 2 abstracts focused on epicardial pacing in patients with single ventricles, which are not relevant to this discussion. Of note, all 4 abstracts should not have been cited because they were published before 2006, i.e., more than 2 years earlier, and thus citing them is not allowed according to the *iJACC* instructions for authors.

Importantly, your list of our "undisclosed" publications contained no peer-reviewed articles, which would endorse the use of RT3DE-derived SDI in patients with severe LV dysfunction, simply because such articles do not exist. In fact, one article you mentioned (reference 7 in Monaghan et al. [2]) focused on LV dyssynchrony and compared RT3DE and tissue Doppler imaging measurements of dyssynchrony in a group of 122 patients with a wide range of ejection fraction. The results of this study showed

that the vast majority of patients (23 of 25) with ejection fraction <30% had abnormally high LV dyssynchrony, a finding that is in complete concordance with the results reported in our article in *iJACC*.

Finally, to answer your rhetorical question "how could the prevalence of dyssynchrony have changed so dramatically in such a short time?" The determination of what is abnormal depends on the abnormality threshold, which in our large group of normal subjects was significantly lower, as recently confirmed by other investigators (4), than in several previous publications. This deemed SDI in all patients with DCM in the study abnormally high, as quickly as images obtained in 135 normal subjects could be analyzed to derive these data.

Regarding your claim that our study was not done properly, the idea that our analysis technique might not have been optimal may have some merit. You mentioned technical details, such as the use of inappropriate temporal and spatial smoothing settings. Is it not always true that when one uses software with multiple settings, the optimal combination is not necessarily known a priori? This point is potentially a very important one. Have optimal smoothing settings for this particular software been established and are they uniform across studies? This issue likely deserves further research. You also mentioned that in your collective experience, "noisy curves are rare." Indeed, they are, except in patients with severely compromised LV function, which was the focus of our article. In these patients, the combination of frequently noisy curves coupled with the use of standard deviation as the index of dyssynchrony, which is prone to being strongly affected by single outliers caused by imperfect endocardial tracking, is a pitfall to be aware of and to seek ways to avoid.

Because we have previously validated regional volume curves, you were surprised that we chose to criticize this technique. The 2 articles you mentioned (references 8 and 9 in Monaghan et al. [2]) focused on validation of global and regional LV volumes and had virtually nothing to do with dyssynchrony because intertechnique agreement in volume values has nothing to do with the timing of regional end-ejection. It is important to understand that the aim of our article was not to negate RT3DE evaluation of regional LV function as a technique altogether but to highlight its current limitations in the context of dyssynchrony in patients with severe LV dysfunction.

Regarding your claim that our Figure 3 (3) showed examples that are not representative, indeed, those 2 patients had greater levels of dyssynchrony than the average of their respective groups and were chosen to demonstrate what we perceived to be a pitfall of SDI in patients with DCM because it could potentially mask the differences we were trying to detect. This is a very common approach used to depict findings, and it is difficult to understand why you found it so objectionable.

Regarding your claim that the use of proportional rather than absolute volume curves would be more appropriate, the notion that the use of proportional curves, where regional volume in each segment is normalized to 100% of its own maximum, is baseless because the choice of scale for the y-axis cannot change the timing of the detected nadir and therefore would have absolutely no effect on the calculated index of dyssynchrony.

We believe that future studies will determine whether we were right or wrong in our assessment that the current RT3DE methodology used for the evaluation of LV dyssynchrony is not quite ready for clinical use in patients with severe LV dysfunction and that further methodological improvements are needed.

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