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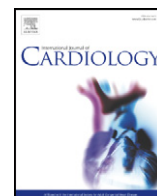
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Reply to “Circadian variation in acute myocardial infarction size: Likely involvement of the melatonin and suprachiasmatic nuclei”



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We read with great interest the letter by Dominguez-Rodriguez, Abreu-Gonzalez and Reiter regarding our article [1]. We thank the authors for pointing out that although the circadian “clock” genes are expressed by most tissues, the suprachiasmatic nuclei of the hypothalamus are predominantly responsible for their secretion and regulation in mammals and they also influence the expression of melatonin. Melatonin has numerous benefits as described in their letter but it is secreted in a circadian pattern. This may partly explain our findings of a circadian variation of myocardial infarction size, depending on the time of onset of symptoms. We admire their enthusiasm to champion melatonin as a promising cardioprotective agent against ischemia–reperfusion injury in the setting of ST-segment elevation myocardial infarction (STEMI) [2]. Although the MARIA trial [2] was neutral for infarct size reduction, a post-hoc analysis found that those presenting within 2.5 h of symptom onset showed a significant reduction in myocardial infarct size [3]. This highlights the fact that careful patient selection is crucial for optimizing the translation of promising cardioprotective therapies in the clinical setting [4]. Furthermore, around 50% of STEMI patients treated by primary percutaneous coronary intervention develop microvascular

obstruction [5] and therefore any cardioprotective therapy, even if administered via the intra-coronary route, would fail to reach the microcirculation in half of these patients [6]. An alternative approach, which has not yet been studied so far, may be to combine low dose thrombolysis (to regain flow in the microcirculation as currently being investigated in the T-TIME trial – NCT02257294) with a promising cardioprotective therapy (to reach the ischemic myocytes and protect against lethal myocardial injury), in order to minimize reperfusion injury and improve outcomes in these patients [6].

Conflicts of interest

The authors report no relationships that could be construed as a conflict of interest.

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