BMI Is a Potential Confounder of Postpartum Relaxin-2 and Short-Term Left Ventricular Function Following Peripartum Cardiomyopathy

In their recent publication, Damp et al. (1), reported that early postpartum levels of relaxin-2 are associated with better short-term left ventricular function in women with peripartum cardiomyopathy (PPCM). This is of potential interest given our incomplete understanding of the pathophysiology of PPCM. However, it is important to note that the investigators have not taken the women’s weight or body mass index (BMI) into account in their analyses. Relaxin-2 levels during pregnancy are inversely associated with maternal BMI from pre-pregnancy (2) and early gestation (3), whereas there are previous reports indicating that maternal BMI (non-obese vs. obese (4) and linearly (5), respectively) is inversely associated with left ventricular ejection fraction at 12 months following PPCM. Notably, the latter observations are based on the same clinical dataset as Damp et al. have based their analyses on (the IPAC [Investigations of Pregnancy-Associated Cardiomyopathy] study). As there is a large variation in the increase of relaxin-2 levels during pregnancy, it is plausible that the early post-partum levels of relaxin-2 reported by Damp et al. are correlated with the levels produced in late pregnancy. Maternal BMI could thus be an important confounder in the presented analyses on relaxin-2 and short-term left ventricular outcomes following PPCM. Preferably, maternal BMI as a potential confounder should be addressed in future investigations on the topic.

*Simon Timpka, MD, PhD
*Brigham and Women’s Hospital and Harvard Medical School Division of Women’s Health
One Brigham Circle

1620 Tremont Street
Boston, Massachusetts 02120
E-mail: simon.timpka@med.lu.se
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Please note: Dr. Timpka has reported that he has no relationships relevant to the contents of this paper to disclose.

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REPLY: BMI Is a Potential Confounder of Post-Partum Relaxin-2 and Short-Term Left Ventricular Function Following Peripartum Cardiomyopathy

We read with appreciation Dr. Timpka’s comments on our paper (1). Dr. Timpka points out the important concept of an association of body mass index (BMI) with levels of Relaxin-2 during pregnancy and with left ventricular ejection fraction at 12 months in peripartum cardiomyopathy (PPCM). In our study population of patients with PPCM, there was not a clear correlation between BMI and Relaxin-2 levels, although this may have been caused, in part, by the relatively small number of patients. As Dr. Timpka points out, our investigator group is currently exploring the relationship further between BMI and recovery in this cohort of patients with PPCM. We acknowledge BMI as a potential confounder in our reported analysis in the relationship between Relaxin-2 and recovery and agree that this warrants further study. Future study would most ideally be done in larger cohorts and with BMI data before pregnancy, during pregnancy, and during follow-up.

*Julie Damp, MD
Dennis M. McNamara, MD, MS
We have read with interest the work by Murugiah et al. (1) exploring the trends of diagnosis and outcomes of patients with principal and secondary diagnoses of Takotsubo cardiomyopathy (TTC) using Medicare fee-for-service database. The current study illustrated an increase in the trend of TTC diagnosis coinciding with enhanced awareness of this condition. The authors showed that the incidences of inhospital, 30-day, and 1-year mortality in patients with TTC were less compared with patients with acute coronary syndrome. However, these incidences might be underestimated given how the authors defined patients with TTC in their cohort. The authors attempted to ensure an accurate diagnosis of TTC by ascertaining that all the patients who received the International Classification of Diseases-9 code of TTC had also received a procedure code of coronary angiography during the same hospitalization. Although this approach would be helpful in the accurate estimation of primary (principal) TTC trends, the same does not hold true for patients with secondary TTC and such an approach might be a source of unintentional selection bias in the current study. Secondary TTC usually occurs following a physical stressor that might be neurologic in nature (e.g., subarachnoid hemorrhage, intracranial hemorrhage, or acute ischemic stroke) (2,3). Multiple studies had shown that patients with secondary TTC carry different characteristics and worse outcomes compared with patients with primary TTC (3,4). Thus, such group of patients with TTC, by default, would have a lower chance of receiving a coronary angiography during their hospital stay, either because of the presence of a contraindication (e.g., subarachnoid hemorrhage or intracranial hemorrhage) or simply because they are clinically in unstable condition and at higher risk of complications to undergo any invasive procedure.

The effect of such selection methodology was clearly translated into a significant discrepancy in the mortality between the patients who received coronary angiography and those who did not, with an incidence of in-hospital mortality of 3% versus 7% and 1-year incidence of 11.4% versus 24.5%, respectively, for the patients with secondary TTC. Although other reasons, such as misdiagnosis of patients with acute coronary syndrome as TTC, might partially explain such discrepancy, such misdiagnoses are usually an individual random error and cannot explain the large number of patients with secondary TTC who did not receive coronary angiography during their hospital stay (54% of the total secondary TTC population).

On the basis of this limitation in the selection methodology, the mortality incidences presented in the current study probably lean toward more conservative estimates especially for the secondary TTC cohort of patients, who intrinsically have lower chances of receiving a coronary angiography during their hospital stay and higher chances of worse short- and long-term outcomes.

*Ahmed N. Mahmoud, MD
Marwan Saad, MD, PhD
Islam Y. Elgendy, MD
*Department of Medicine
University of Florida
1600 SW Archer Road
Gainesville, Florida, 32610
E-mail: ahmed.mahmoud@medicine.ufl.edu

Please note: All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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