Authors' Reply:

To the Editor:

We thank Dr. Madias for his interest in our study.¹ Our conclusion that hypotension in Takotsubo cardiomyopathy (TTC) is likely to be multifactorial in origin reflected the lack of any strong association on multivariate analysis. Indeed, Dr. Madias' comments raise the issue of an additional potential contribution to the overall mix of determinants of blood pressure response.

We agree that recent data from rat experiments suggest that epinephrine might induce regional negative inotropic effects via β_2 -Gi signaling.² However, it should not be suggested that this represents a complete reversal of the conventional pressor effects of catecholamine stimulation. In regard to inotropy, most patients with TTC exhibit only regional hypokinesis, and indeed basal hyperkinesis is sometimes seen. Furthermore, there is no reason to assume that the vasoconstrictor α -adrenoceptor-mediated effects of epinephrine are in any way diminished.

It is true, as Dr. Madias points out, that the majority of the literature has utilized ejection fraction as a measure of

the extent of left ventricular systolic dysfunction in TTC. We preferred to use the wall motion score as a more precise index of the extent of regional hypokinesis, bearing in mind that regional hyperkinesis might also be present. If ejection fraction were added to the model, that too would not be a (multivariate) determinant of hypotension.

Last, we agree that intraventricular gradient would be of potential importance in the study. Unfortunately, outflow tract obstruction was not routinely evaluated at admission and was only detected in 6 of our cohort of patients. Furthermore, severe mitral regurgitation, which has previously been shown to be associated with shock and often with outflow tract obstruction,^{3,4} was noted only in 1 case in our cohort. Ultimately, we recognize that the identification of correlates of hypotension in TTC represents only one step toward determining causation and subsequent development of appropriate modes of therapy for the condition.

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