Reply: “Possible Takotsubo Syndrome” – A Refreshing Start toward the Path to Detect the True Prevalence of Takotsubo Syndrome

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We would like to thank Dr. Madias for his interest in our recent publication showing that, in real-world clinical experience, coronary evaluation for strict diagnosis of Takotsubo syndrome (TTS) is not frequently feasible [1, 2]. We also appreciate his insightful comments on the disadvantages of implementation of strict diagnostic criteria or protocols in TTS [3] and potential issues of expanding the spectrum of TTS. Actually, his innovative proposal of “new criteria” for TTS diagnosis was well cited in our original manuscript [4]. In our clinical study, we tried to convince the readers to accept the idea that clinicians should accept the paradigm shift for appropriate positioning of TTS from differential diagnosis of “acute coronary syndrome” (ACS) to differential diagnosis of “acute heart failure syndrome” (Table 1).

Dr. Madias raised important issues and questions in this letter, which deserve full attention of the readers. A rapid recovery of wall motion abnormality in TTS within hours to less than 1 day (question #1) is an interesting idea, which seems to be in line with mild cases of TTS (question #4) and the role of hand-held echocardiographic service for expedited diagnosis of TTS (question #9). We excluded patients who developed typical ballooning after open heart surgery or in association with pheochromocytoma (question #2), as we sought to keep a relatively stringent definition of TTS in this study. Open heart surgery is characterized by reversible ventricular dysfunction due to myocardial stunning associated with extracor-

poreal circulation by artificial pump and thus many patients after open heart surgery show transient left ventricular dysfunction. We believe that inclusion of these patients may make our message weaker; however, we included patients who developed TTS after non-cardiac surgery. In patients with pheochromocytoma, sudden catecholamine surge can trigger development of typical ballooning, but we believe this condition should be differentiated from typical TTS without pheochromocytoma. The presence of coronary artery disease does not necessarily mean that coronary artery disease is a cause of development of wall motion abnormalities. However, in the typical clinical setting of ACS or ST-segment elevation myocardial infarction (STEMI), we are reluctant to accept the idea of “TTS component” in conjunction with an ACS or STEMI (question #3), as these conditions were characterized by acute plaque rupture resulting in near total occlusion of an epicardial coronary artery. In addition, ACS or STEMI needs acute revascularization for better clinical outcome, whereas supportive care is a main management strategy for patients with TTS. We do not have right answers or data regarding the questions #5, #6, #7, and #8. Our responses to important questions raised by Dr. Madias in this letter may represent personal bias based on limited clinical experience, which should be cleared by further investigations.

Table 1. Paradigm shift and evolution of TTS from ACS to acute heart failure syndrome

	Old	New
Frequency	Rare	Relatively common
Main trigger	Emotional	Physical illness
Type	Primary Takotsubo	Secondary Takotsubo
Clinical presentation	Chest pain	Dyspnea or hypoxia
ECG change	ST-segment elevation	Nonspecific changes
Echocardiography	Apical ballooning	Nonapical ballooning
Clinical course	Benign	High complication rates
Differential diagnosis	ACS	Acute heart failure syndrome
Primary role	Emergency physicians or cardiologists	General physicians or surgeons

As mentioned above, TTS should not be considered anymore as a rare disease entity with typical clinical presentation of chest pain syndrome and ST-segment elevation on electrocardiogram triggered by emotional stress, for which emergency physicians and/or cardiologists are doing a main role. The cumulative clinical experience tells us that vigilance of general physicians or surgeons is necessary to have more favorable clinical outcomes of TTS, a relatively common disease entity, which is characterized by higher frequency of physical trigger, secondary TTS, nonspecific ECG changes, dyspnea, and high complication rates representing acute heart failure syndrome (Table 1).

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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Author Contributions

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