Letter to the Editor

Beneficiality of levosimendan for Takotsubo syndrome remains uncertain

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With interest we read the article by Guo *et al.* about a study of levosimendan as an adjunctive treatment of 100 patients with Takotsubo syndrome (TTS) (1). The authors concluded that levosimendan "showed reliable efficacy and safety in Chinese elderly patients with TTS, supporting the idea that levosimendan has the potential to be an essential drug applied for patients with TTS" (1). We have the following comments and concerns.

An inclusion criterion of the study not mentioned in the method section was NYHA stage IV, since all patients in both groups were in NYHA stage IV according to Table 1 (1). This criterion should be explicitly mentioned although it is implausible that all TTS patients were truly in the NYHA stage IV at onset.

A further curiosity of the study is that mean ejection fraction (EF) values were the same in both groups at baseline (29%), at the 30-day follow up (47%), and at the 180-day follow-up (49%) (1). It is also curious that these values were significantly different at the 30- and 180-day follow-up but not at baseline. Significant differences of the 30- and 180-day values are surprising with regard to the similar ranges of values in both groups. Since proBNP values were higher in the control group at baseline, we can expect that the EF was also lower in controls at baseline.

More patients in the levosimendan group than among controls received angiotensin-converting enzyme inhibitors (AECI) at baseline (29 *vs.* 23). Is it conceivable that the outcome was better in the levosimendan group because these patients received heart failure treatment already at baseline more frequently than controls?

Outcome of TTS may strongly depend on the triggering event, such as physical triggers, medical conditions (fear, pain, uncertainty), or procedures (2,3). Thus, we should be informed about differences regarding the triggering events in both groups.

A further shortcoming of the study is that comorbidities of the included patients were only marginally reported. Death associated with TTS may not only be attributable to TTS itself but also to other causes. Thus, we should be informed if patients of the control group had a higher number of comorbidities or more severe stages of comorbidities than patients in the levosimendan group.

There is no mentioning of the non-cardiac drugs patient in both groups were regularly taking. Possibly, patients in the control group were taking drugs with more severe side effects than patients in the levosimendan group.

Missing is the differentiation between the different types of TTS. Outcome of global TTS type is less favorable than that of the apical or mid-ventricular type of TTS and atypical TTS types may have a better outcome than classical types (4). Thus we should be informed if patients of the control group had TTS types which per se are associated with a worse outcome compared to the TTS types with a more favorable outcome in the levosimendan group.

Missing in this report is also any mentioning of side effects of levosimendan or any other drug administered. We should be informed if any of the 200 patients developed an adverse reaction to levosimendan or any other cardiac drug administered for the treatment of TTS.

Overall, data presented in this study are highly questionable and do not allow the conclusion that levosimendan improves the outcome of TTS patients. It is crucial that readers are informed about comorbidities, TTS

types, and co-medication in both groups. Since the majority of TTS patients recovers without treatment, assessment of the effect of levosimendan not only requires homogenous groups but also a control group, which did not receive cardiac treatment at all.

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Footnote

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