

## Correspondence

## Reply

To the Editor:

We thank Alvarez-Twose et al<sup>1</sup> for their valuable comments on our recent study<sup>2</sup> investigating clinical signs and parameters of severe Hymenoptera venom-induced anaphylaxis. Alvarez-Twose et al<sup>1</sup> refer to their previous articles implementing the Spanish Network on Mastocytosis (REMA) score as a clinical tool to individually predict the risk of mast cell clonality in patients with symptoms of systemic mast cell activation,<sup>3</sup> pointing out that they have likewise defined the absence of urticaria/angioedema during episodes of anaphylaxis as an indicator of systemic mastocytosis. As specified in our Results section, screening for underlying mast cell disease was performed in a defined subgroup of patients with a history of moderate to severe sting-related anaphylaxis (n = 384), using the baseline serum tryptase (BST) as a surrogate marker as suggested in international guidelines on Hymenoptera venom allergy.<sup>4,5</sup> A BST level exceeding 11.4 µg/L (95th percentile of the general population) was found in 46 patients (that is 7% of the total study group). In cases of suspected mastocytosis, patients were transferred for hematologic workup.

Our data demonstrate that the absence of urticaria/angioedema during the anaphylactic episode is indicative of both, severe sting-related anaphylaxis ( $P < .001$ ) and—indirectly—an elevated BST level ( $P = .02$ ). This observation is not a proof of causality and we do, of course, fully agree with Alvarez-Twose et al that the severity of anaphylaxis is not a *result* of the lack of urticaria/angioedema. There is need to point out, however, that the absence of skin symptoms during anaphylactic sting reactions is not necessarily a direct consequence of underlying mast-cell clonality either: In a subgroup of 167 patients with

a history of severe anaphylactic reactions (grade III, according to a modified version of the system proposed by Muraro et al<sup>6</sup>), elevation of the BST level was related to a history of hypotensive shock or cardiac arrest ( $P = .001$ , Fig 1), thereby confirming an association between underlying mast cell disease and the most severe cardiovascular manifestations of anaphylaxis. The association of BST level elevation and an absence of skin symptoms as observed in the total study group, however, was no longer significant if assessed in this subgroup of patients with grade III reactions ( $P = .45$ ). We and other authors hypothesize that in venom-allergic patients with mastocytosis as well as in those without underlying mast cell disease, the absence of urticaria/angioedema is an epiphenomenon of severe anaphylaxis, possibly resulting from counterregulatory release of endogenous epinephrine with consecutive peripheral vasoconstriction.<sup>7</sup>

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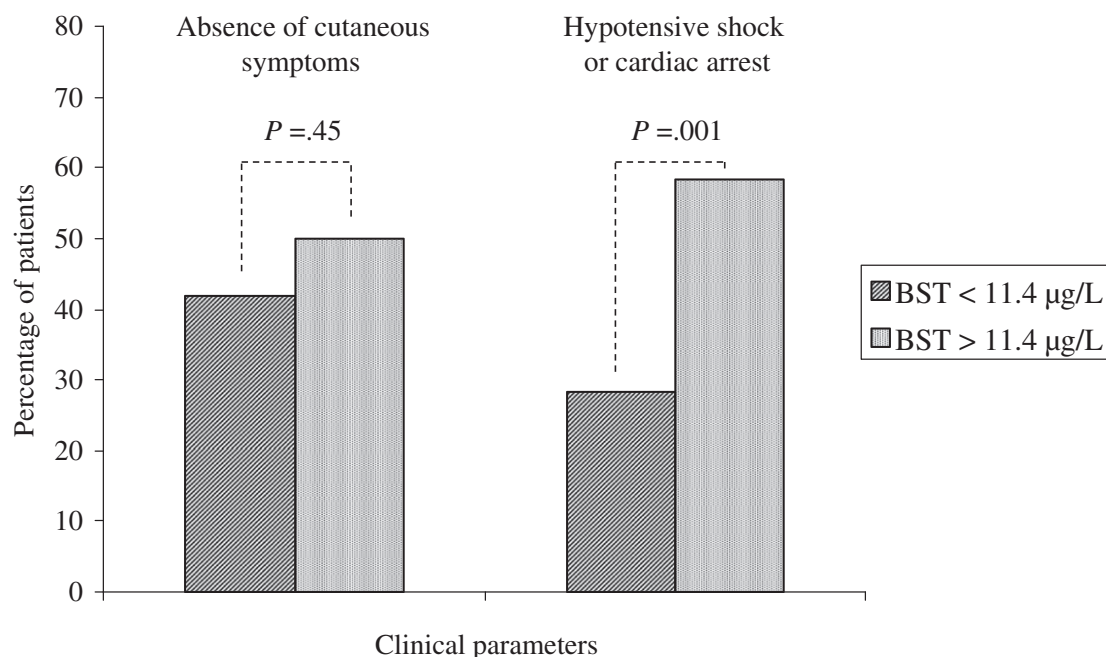


**FIG 1.** Frequency of clinical parameters during severe (grade III<sup>6</sup>) sting-related anaphylaxis in 167 patients with (n = 36) and without (n = 131) BST elevation.

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