CRITICAL CARE

LETTER

The 372 T/C genetic polymorphism of TIMP-1 as a biomarker of mortality in patients with sepsis

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See related commentary by Behnes *et al.*, http://ccforum.com/content/17/4/170 and related research by Lorente *et al.*, http://ccforum.com/content/17/3/R94

In the previous issue of *Critical Care*, Behnes and colleagues [1] provide an interesting commentary on our study showing that septic patients with the T-allele in 372 T/C (rs4898) genetic polymorphism of the tissue inhibitor of metalloproteinase-1 (TIMP-1) had higher mortality and higher TIMP-1 serum levels than those without it [2].

As the authors state in their commentary, our study had some limitations. One limitation was the relatively small sample size to establish prognostic implications by only one single-nucleotide polymorphism (SNP) challenge. However, the sample size was large enough to find an association between polymorphism and survival.

Another limitation was that we tested only the rs4898 SNP, a tag SNP, for the region of interest. However, it may be that this SNP, which is in strong linkage disequilibrium with other TIMP-1 polymorphisms, is linked to other SNPs associated with the same effect.

Another possibility is that this association represents only an epiphenomenon since, in our study, a cause-effect relationship between polymorphism and mortality was not established. However, we found that patients with the T-allele had higher TIMP-1 serum levels and that patients with higher TIMP-1 circulating levels showed higher mortality [3,4]. Besides, we found a positive association between TIMP-1 and plasminogen activator inhibitor-1 circulating levels, previously found in myocardial infarction patients [5], probably suggesting a prothrombotic state. In conclusion, we think that the determinations of 372 T/C genetic polymorphism and circulating levels of TIMP-1 could be used as mortality biomarkers in patients with sepsis.

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Abbreviations
SNP: Single-nucleotide polymorphism; TIMP: Tissue inhibitor of matrix metalloproteinase.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
LL drafted the manuscript and MMM reviewed it. Both authors read and approved the final manuscript.

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