

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.

## 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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