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Von Willebrand factor is a major determinant of ADAMTS-13 decrease during mouse sepsis induced by cecum ligation and puncture

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Auteur	Lerolle, Nicolas [1], Dunois-Lardé, C. [2], Badirou, I. [3], Motto, D. G [4], Hill, Gary [5], Bruneval, Patrick [6], Diehl, Jean-Luc [7], Denis, C.V. [8], Baruch, D. [9]
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Mots-clés	ADAMTS-13 [10], Animal model [11], Sepsis [12], thrombosis [13], von Willebrand factor [14]
Résumé en anglais	Summary. Background: During sepsis, von Willebrand factor (VWF) is abundantly secreted; the main mechanism regulating its size involves specific proteolysis by the metalloprotease ADAMTS-13. Objectives: To determine whether ADAMTS-13 consumption due to its binding to, and/or cleavage, of VWF contributes to its decrease during sepsis and whether abrogating or enhancing ADAMTS-13 activity influences sepsis outcome. Methods: ADAMTS-13 activity was evaluated in a model of sepsis induced by cecum ligature and puncture (CLP) in wild-type and Vwf−/− mice. Sepsis outcome was studied in those mice and in Adamts-13−/− mice. Finally, survival was studied in wild-type mice injected hydrodynamically with the human ADAMTS-13 gene. Results: In wild-type mice, CLP-induced sepsis elicited a significant ADAMTS-13 decrease, and a strong negative correlation existed between VWF and ADAMTS-13. In Vwf−/− mice, CLP also induced severe sepsis, but ADAMTS-13 was not significantly diminished. Notably, Vwf−/− mice lived significantly longer than wild-type mice. In contrast, Adamts-13−/− mice and wild-type mice were comparable with regard to thrombocytopenia, VWF concentrations, absence of thrombi, and survival. Hydrodynamic hADAMTS-13 gene transfer with the pLIVE expression vector resulted in high and stable ADAMTS13 activity in CLP mice; however, no impact on survival was observed. Conclusions: VWF secretion is a major determinant of ADAMTS-13 decrease in the CLP model, and plays an important role in sepsis-induced mortality, but the complete absence of its regulating protease, ADAMTS-13, had no detectable impact in this sepsis model. Furthermore, increasing ADAMTS-13 activity had no impact on survival.

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