

Effects of rivaroxaban and dabigatran on global hemostasis in patients with atrial fibrillation

Anica Petkovic^{a,b}, Faris Al-Khalili^c, Aleksandra Antovic^d, Majeed Ammar^{e,f,g}, Iva Pruner^{b,h}, Aleksandra Vranic^a, Nida Soutari^{b,i}, Nebojsa Zdravkovic^j, Rickard E. Malmström^k, Vladimir Jakovljevic^{l,m} and Jovan P. Antovic^{b,i}

Background

- Unlike warfarin, routine laboratory monitoring of DOACs is not recommended; however, measurement of drug concentrations and/or intensity of anticoagulation are desirable in specific clinical conditions.
- Liquid chromatography–tandem mass spectrometry (LC–MS/MS) is the gold standard for measuring the plasma concentrations of DOACs. However, this type of assay is available only in highly specialized centers, and even only during working hours.

Aim of the study

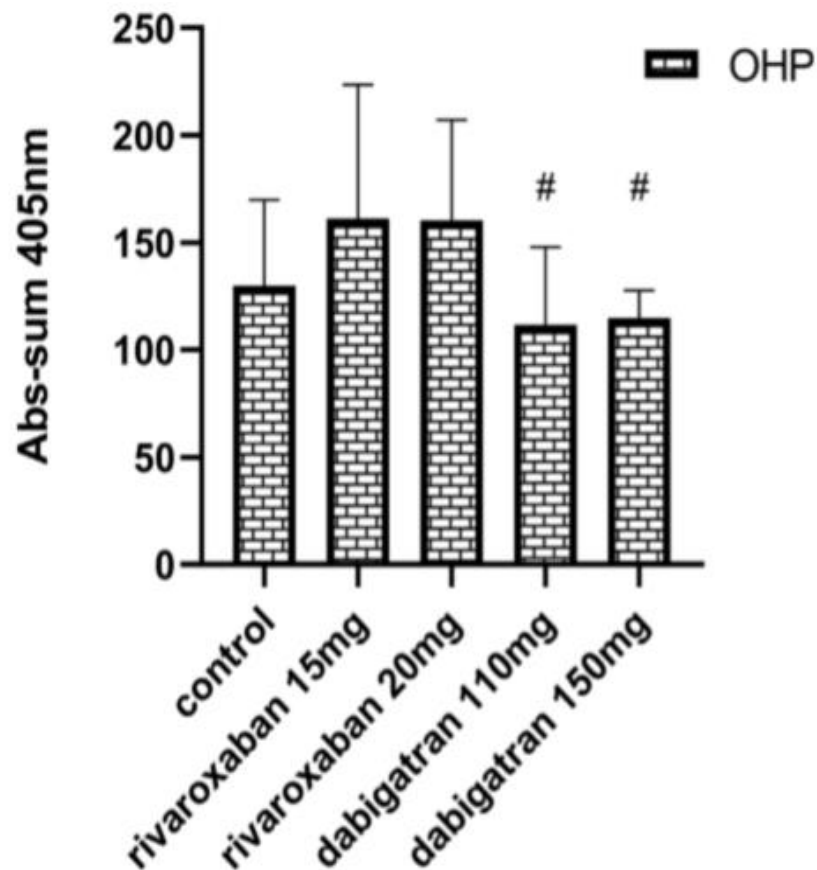
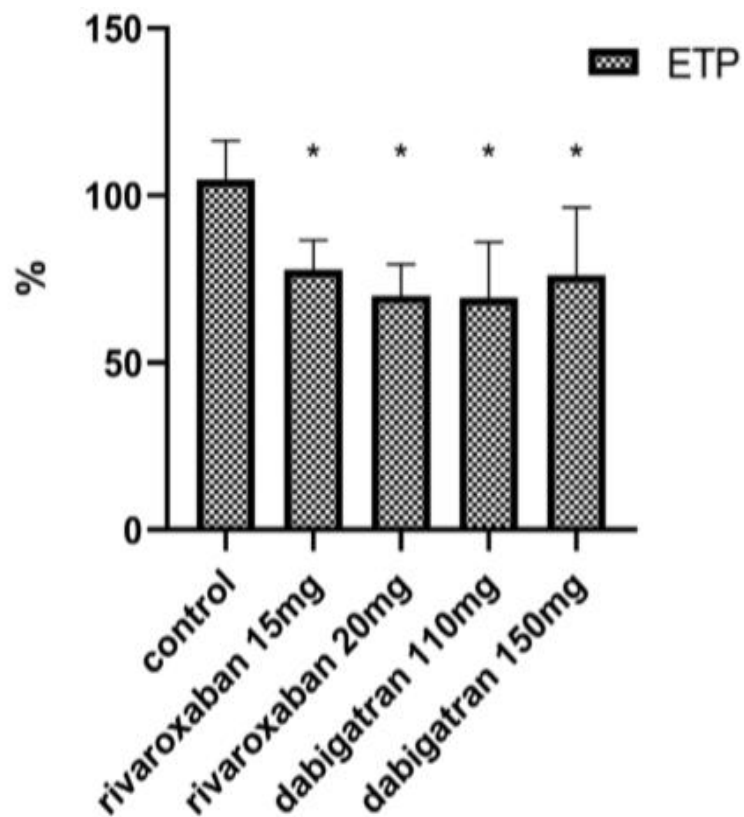
- The study was aimed to evaluate the effects of two standard doses of rivaroxaban and dabigatran on global hemostatic assays in patients with atrial fibrillation.

Methods

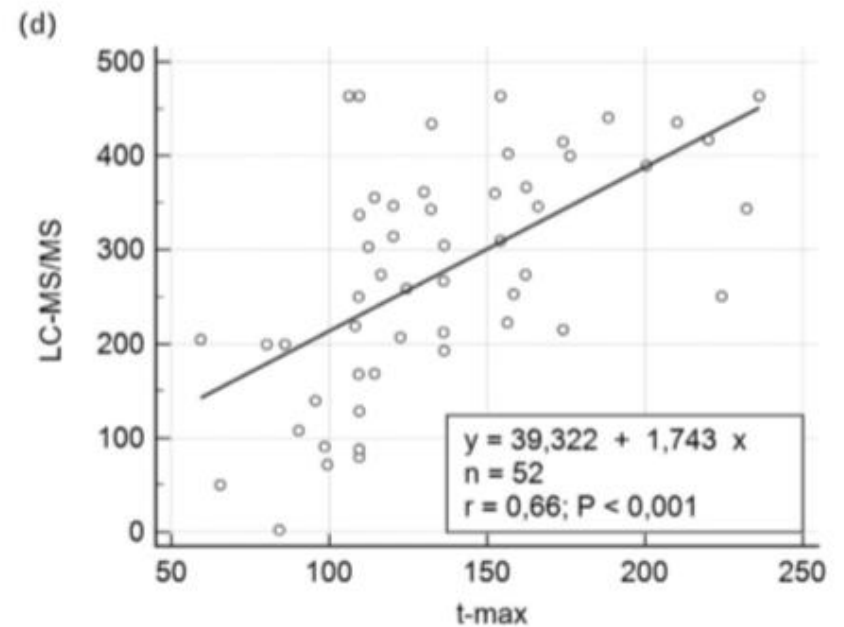
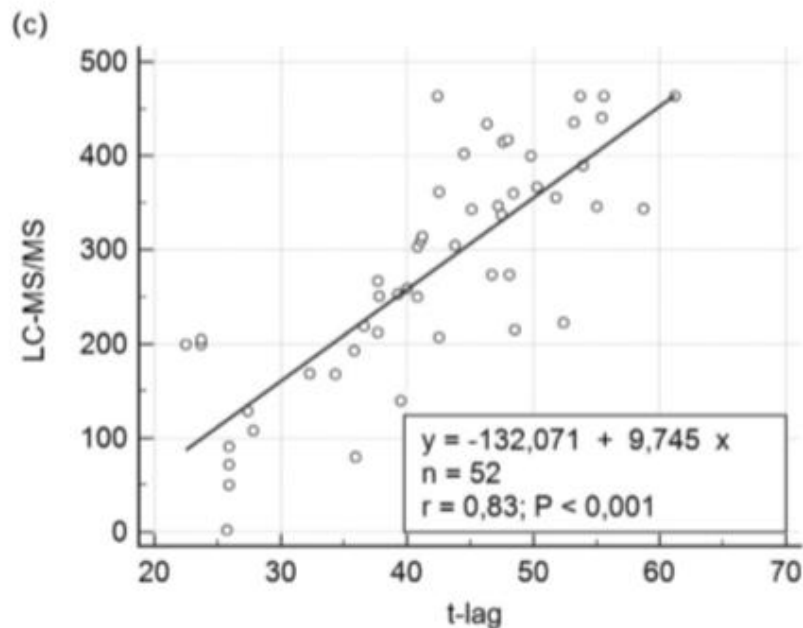
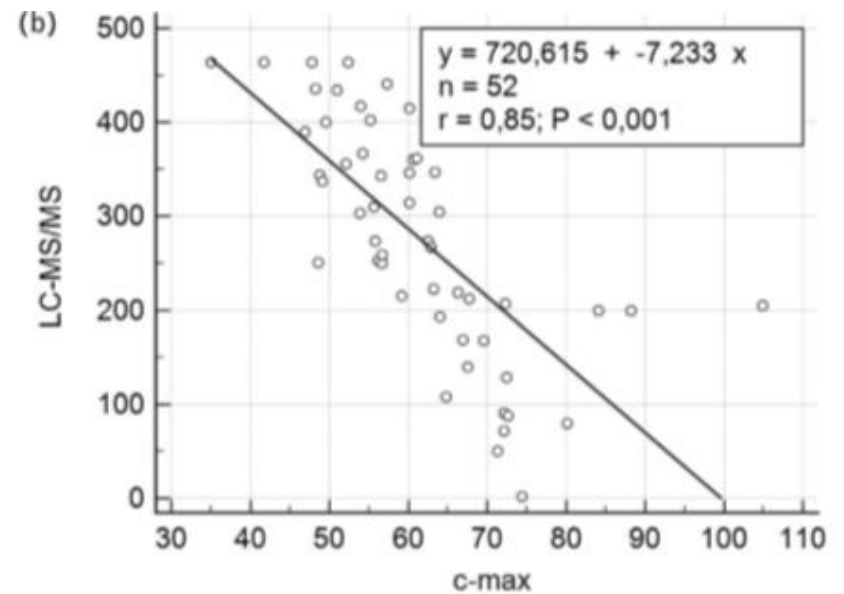
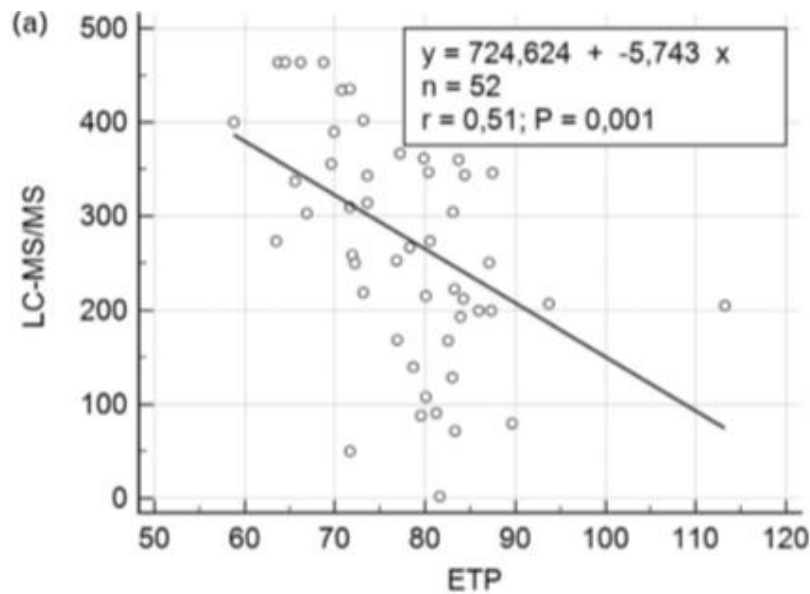
- The study included 52 patients treated with rivaroxaban (15/20mg), 50 on dabigatran (110/150mg) and 20 healthy individuals.
- Platelet-poor plasma was used for determination of three global hemostatic assays, namely endogenous thrombin potential (ETP), calibrated automated thrombogram (CAT) and overall hemostasis potential (OHP).

Results

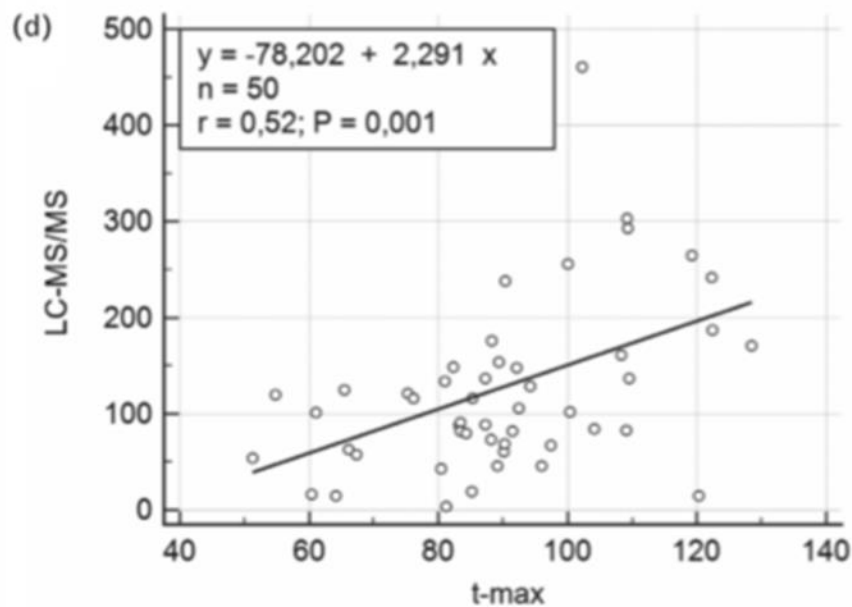
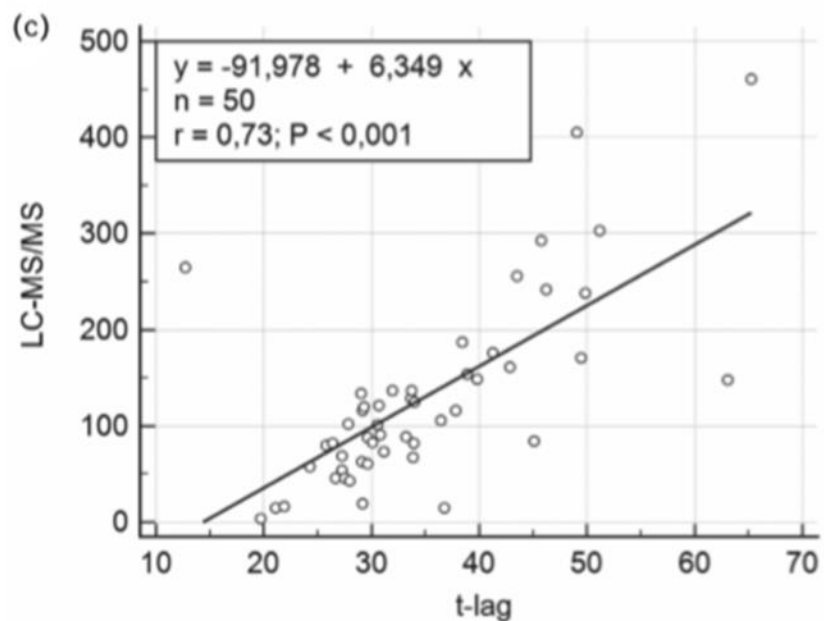
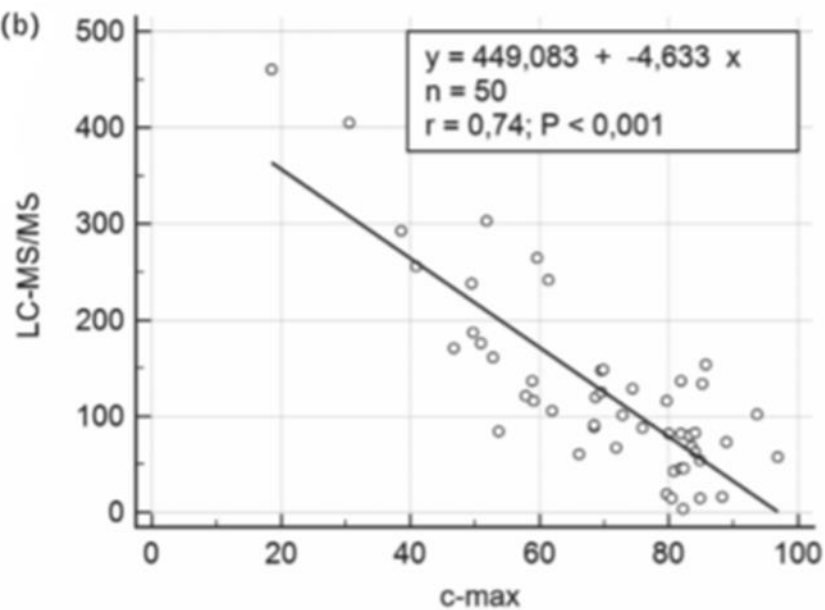
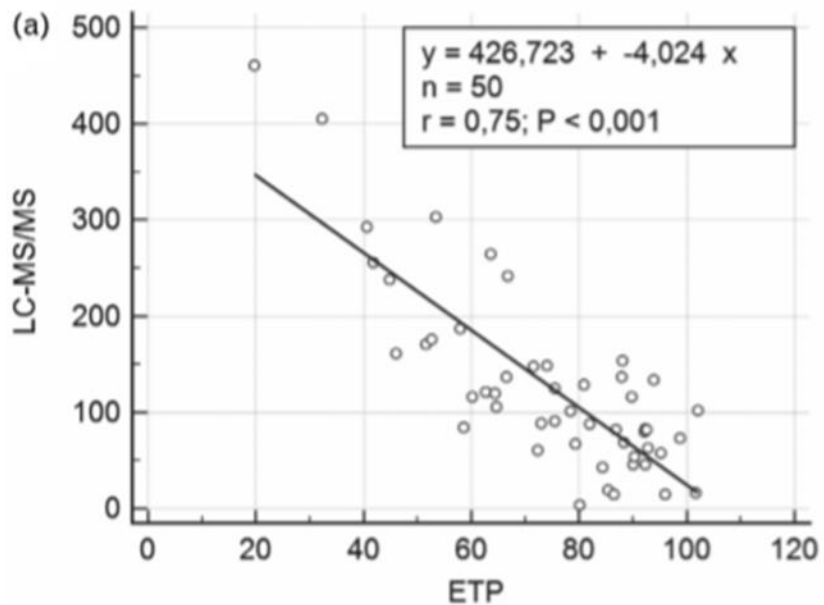
- Rivaroxaban and dabigatran reduced ETP ($P < 0.01$) although OHP ($P < 0.05$) was diminished only by dabigatran.
- Strong correlations were noticed between ETP parameters and the plasma concentrations of as well as with plasma concentration of dabigatran.
- However, significant correlation between CAT parameters and plasma concentration of both direct oral anticoagulants was not observed.



Endogenous thrombin potential and overall hemostatic potential in connection with both doses of direct oral anticoagulants; *statistically significant at $P < 0.05$; #highly statistically significant at $P < 0.01$.



Correlation between plasma concentration of rivaroxaban and endogenous thrombin potential assay parameters; LC-MS/MS, liquid chromatography-tandem mass spectrometry; (a) ETP, endogenous thrombin potential; (b) c-max, peak of thrombin generation; (c) t-lag, lag phase until initiation; (d) t-max, time to reaching peak of thrombin generation.



Correlation between plasma concentration of dabigatran and endogenous thrombin potential assay parameters; LC-MS/MS, liquid chromatography-tandem mass spectrometry; (a) ETP, endogenous thrombin potential; (b) *c*-max, peak of thrombin generation; (c) *t*-lag, lag phase until initiation; (d) *t*-max, time to reaching peak of thrombin generation.

Discussion

- The automated chromogenic assay measuring ETP is the most promising method for estimation of global hemostatic capacity of rivaroxaban and dabigatran.
- On the other hand, CAT assay is not fully sensitive as regards rivaroxaban and unsuitable for estimation of dabigatran effects although role of OHP needs to be certified in future investigations.