

Figure 1 Coagulation cascade and coagulation tests. Activated partial thromboplastin time (APTT) measures the speed of coagulation by the intrinsic pathway, while prothrombin time (PT) evaluates the speed of clotting by the extrinsic pathway. Anti-Factor Xa activity (anti-FXa) shows how much the investigated drug inhibits the activated coagulation Factor X. ROTEM® delta analyzer (Instrumentation Laboratory, Werfen, Barcelona, Spain) enables a global assessment of hemostatic function in a timely manner. It gives information on the whole coagulation process in whole blood. Clotting time (CT) measures the time between the start of the analysis and the start of clot formation. Maximum clot firmness (MCF) gives information about the strength of the clot. Modified from Yada and Nogami, 2020; Hoffman, 2003.

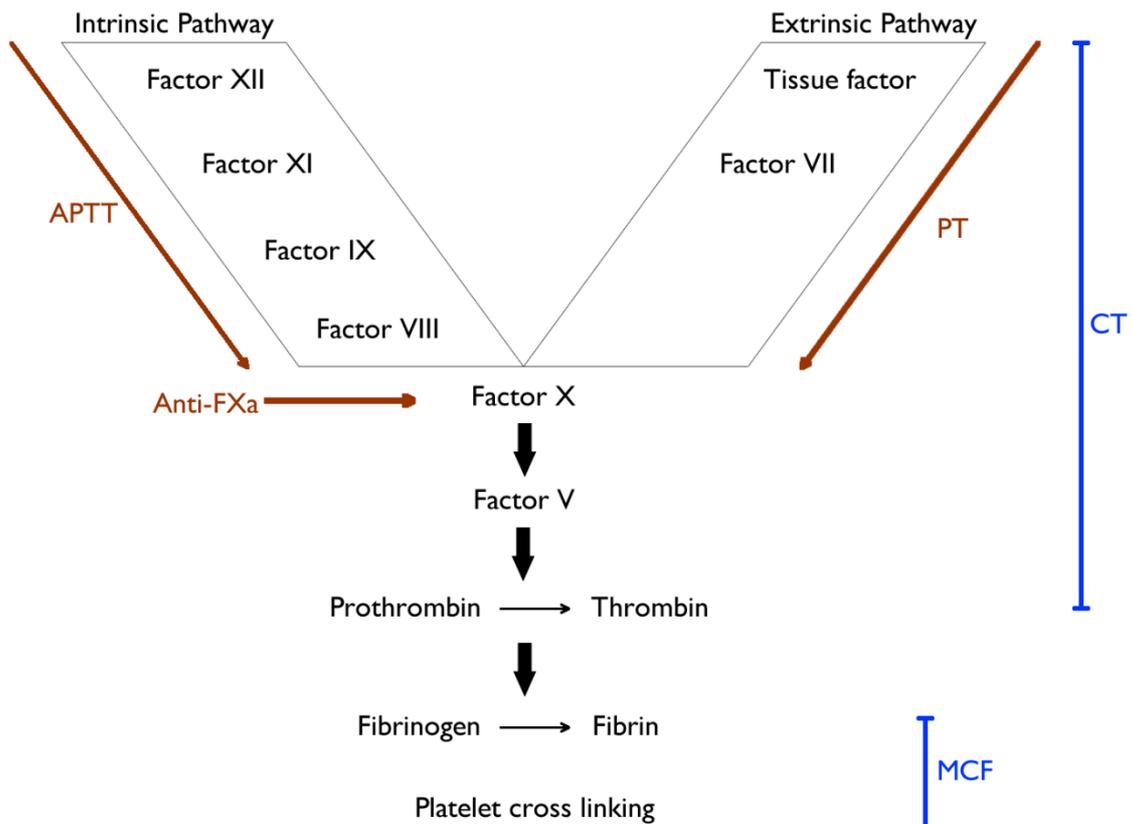


Figure 2 CT-ExTEM, CT-FibTEM, MCF-ExTEM and MCF-FibTEM at 2, 4, 6, 8 and 24 h after a single 60 mg dose of edoxaban. Each gray line represents an individual subject and the blue line represents the mean value.

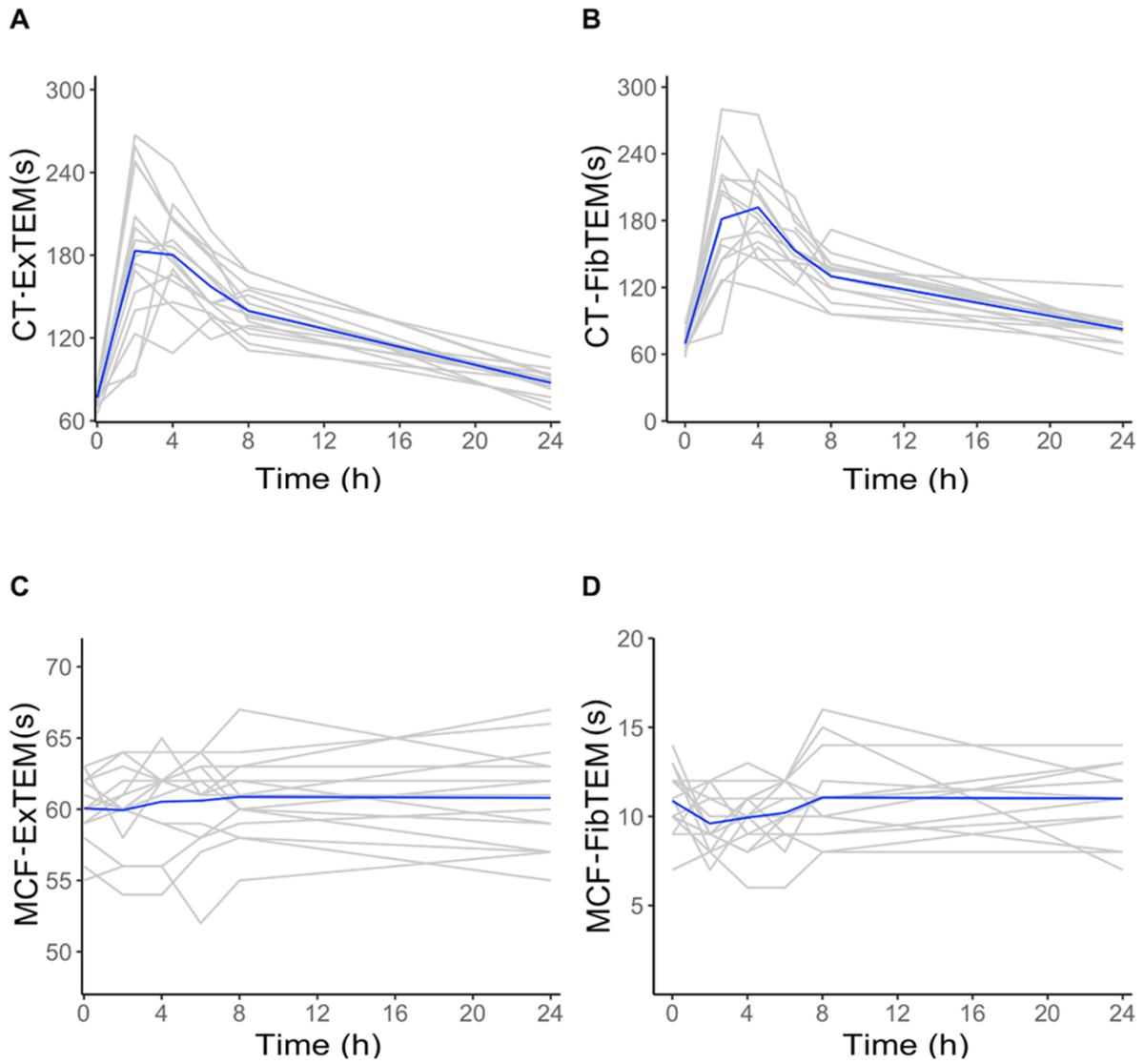


Figure 3 APTT, TT and anti-FXa at 2, 4, 6, 8 and 24 h after a single dose of 60 mg edoxaban. Each gray line represents an individual subject and the blue line represents the mean value. Anti-FXa measurement was not calibrated for the study drug edoxaban and values exceeding 2 IU/mL were reported as “> 2 IU/mL”.

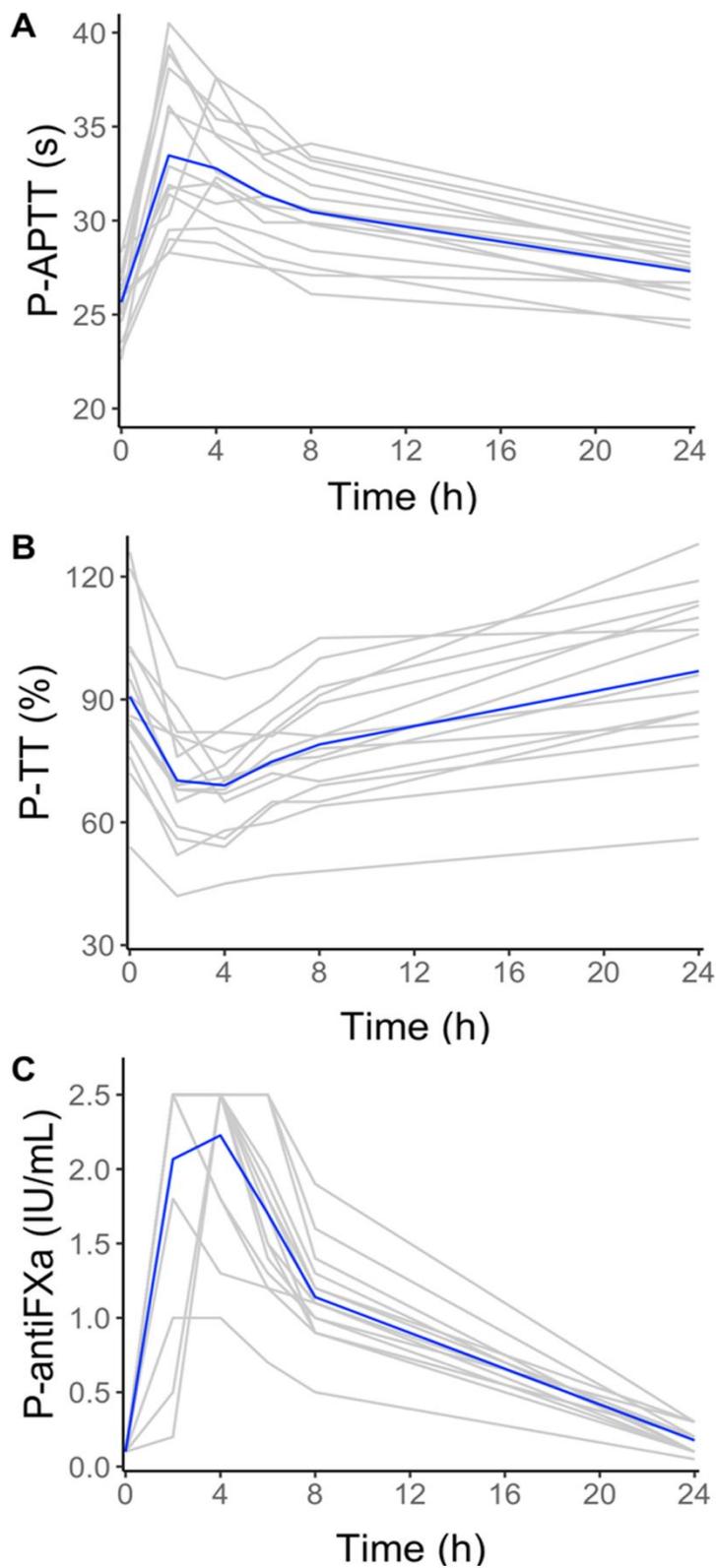


Figure 4 Edoxaban and metabolite M4 plasma concentrations at 2, 4, 6, 8 and 24 h after a single dose of 60 mg edoxaban. Each gray line represents an individual subject and the blue line represents the mean value.

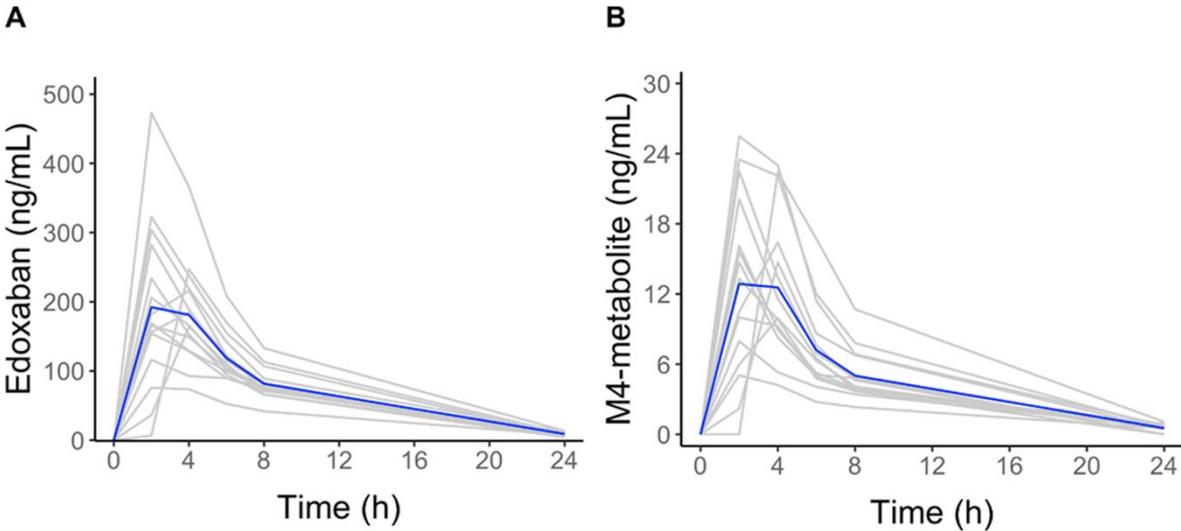


Figure 5 Correlations among plasma concentration of edoxaban and parameter values in ROTEM ExTEM® and FibTEM® and changes in standard coagulation tests, correlation of parameters in every time point are expressed in one plot.

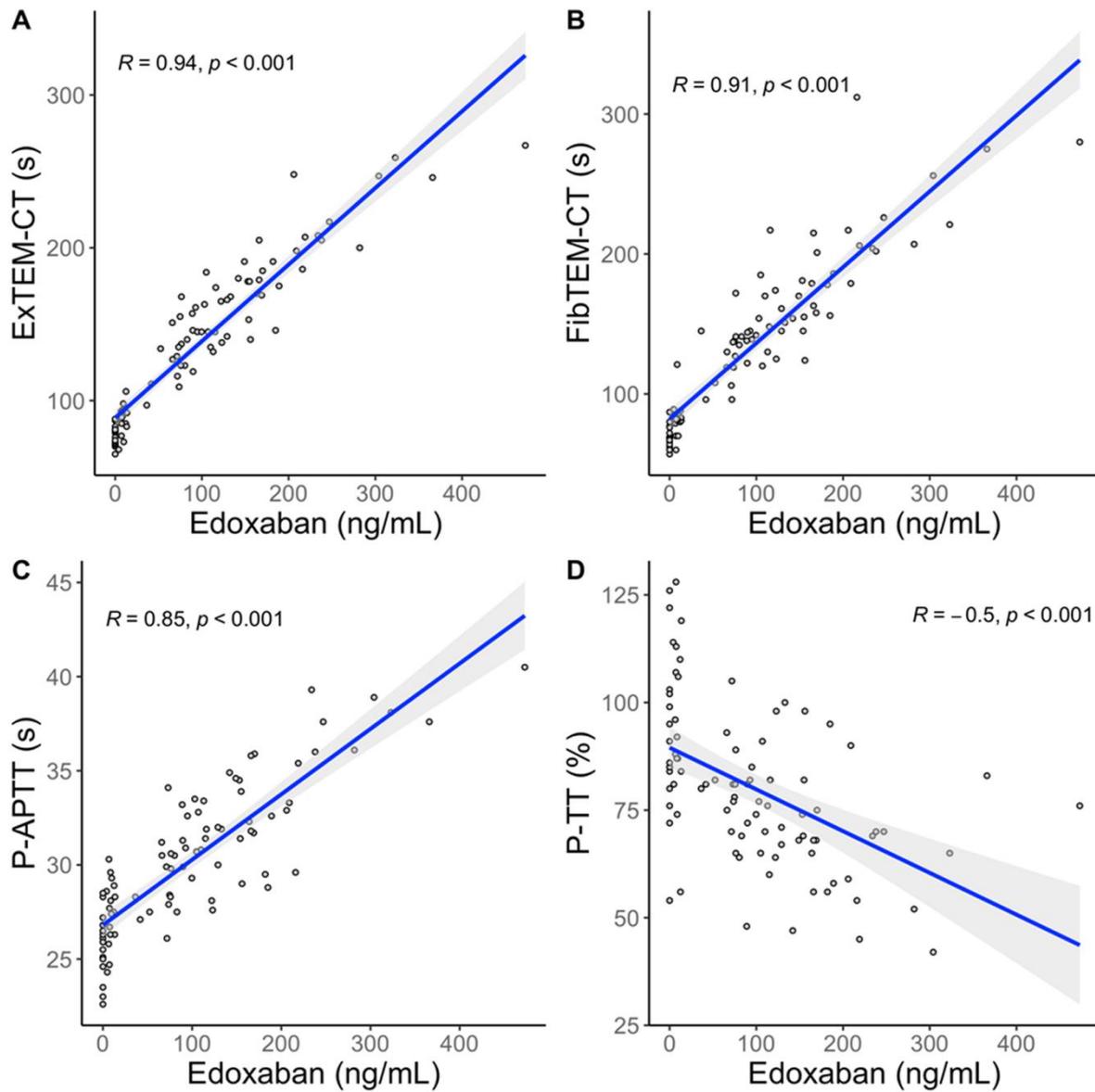


Figure 6 Correlation between edoxaban plasma concentrations and changes from baseline in coagulation measurements (CT-ExTEM, CT-FibTEM, anti-FXa and APTT) after a single dose of edoxaban in the course of the study. Broken line represents correlation of 0.50. Anti-FXa measurement was not calibrated for the study drug edoxaban and values exceeding 2 IU/mL were reported as “> 2 IU/mL”.

