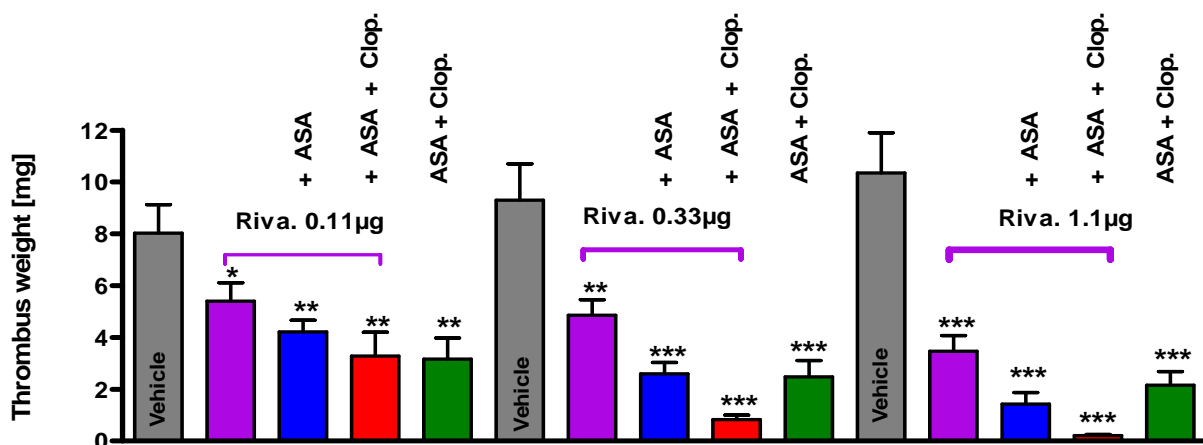


Effects of rivaroxaban, ASA and clopidogrel alone and in combination in a porcine model of stent thrombosis

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Purpose: Stent thrombosis incidence with standard dual antiplatelet therapy with acetylsalicylic acid (ASA) and clopidogrel, remains at 1.4% after stent placement for acute coronary syndrome (ACS). New oral anticoagulants are in late stage clinical studies for secondary prevention after acute coronary syndrome and may be beneficial for prevention of stent thrombosis. The aim of this study is to evaluate the efficacy of rivaroxaban, a novel oral Factor Xa inhibitor, alone and in combination with ASA and clopidogrel in inhibiting high-shear induced stent thrombosis in a porcine ex vivo model.

Methods: Stents (Cordis) (12 stents, 3 per treatment) were continuously deployed in a porcine ex vivo arteriovenous shunt and exposed to flowing arterial blood at a shear rate of $1,500 \text{ s}^{-1}$. Stent thrombus formation was analysed under different treatments: vehicle (n=7); rivaroxaban 0.11, 0.33 and $1.1 \mu\text{g}/\text{kg}/\text{h}$ i.v. (n=8); rivaroxaban + ASA (1 mg/kg i.v.) (n=6); rivaroxaban + ASA (1 mg/kg i.v.) + clopidogrel (0.5 mg/kg i.v.) (n=7); and ASA (1 mg/kg i.v.) + clopidogrel (0.5 mg/kg i.v.). Thrombus weight is displayed as mean \pm SEM.



Vehicle Control n=7, Rivaroxaban n=8, Riva.+ ASA n=6, Riva. + ASA + Clop. n=7, ASA + Clop. n=6
 *, **, *** unpaired ttest vs. representative Vehicle group

Results: Rivaroxaban alone dose-dependently reduced stent thrombus by 33, 48 and 66%, respectively. Dual antiplatelet therapy with ASA + clopidogrel decreased thrombus weight by 79%. Rivaroxaban in combination with ASA was similar or even more effective in inhibiting stent thrombosis (48, 72 and 86%). Finally, the combination of rivaroxaban with ASA + clopidogrel inhibited stent thrombus formation under these experimental conditions to a nearly undetectable limit of 98%.

Conclusions: Rivaroxaban, alone or in combination with antiplatelets, effectively inhibits stent thrombosis in an *ex vivo* model. These data provide additional support for further clinical studies.