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## Can platelets facilitate adhesion of Staphylococcus aureus to cardiac graft tissue, used in RVOT revalvulation, and lead to increased risk of infective endocarditis (IE)?

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Introduction and Objectives: RVOT reconstruction in congenital heart disease can be surgically done using cryopreserved pulmonary homograft (CH) and alternatively xenografts such as the bovine jugular vein (BJV) valved conduit. Despite this good therapeutic alternative recent clinical studies report an increased risk of IE in BJV. This raises the question of why such valves are more prone to IE than homografts. We investigate whether different tissues promote interactions with blood components and therefore enhance the risk for S. aureus adhesion to valve tissue.

Methods: Grafts were incubated with fluorescently labeled plasma fibrinogen (Fg). Then, S. aureus adhesion to the tissues was assessed under flow conditions using a flow chamber system after tissue preincubation with human plasma, albumin or serum. Moreover, tissue susceptibility for platelet interaction was evaluated upon blood perfusion using a colorimetric assay. To document a contribution of Fg-mediated pathway to the interplay bacteria-tissue-platelets, bacterial mutants and anti-platelet drugs were employed. Fg binding to tissues was quantified with fluorescence microscopy and bacterial adhesion was evaluated by CFU counting on blood agar. Bacteria and platelets were visualized on the tissues with confocal or electron microscopy.

Results: Bovine pericardium presented higher protein binding ($P < 0.05$) compared to BJV and CH. Although
not significant, there is a trend towards higher Fg interaction with BJV than CH. After incubation with plasma S. aureus adhesion to BJV increased significantly under flow compared to control conditions (serum $P < 0.05$ and albumin $P < 0.001$). Both bacterial and platelet adhesions to BJV were greater in relation to CH ($P < 0.01$). Moreover, deletion of clfA hampered bacterial adhesion to BJV ($P<0,05$) as well as eptifibatide significantly reduced ($P < 0.001$) platelet reactivity towards BJV.

Conclusions: Our results indicate that the role of Fg-mediated pathway is important for both bacterial and platelet recruitment to endovascular tissues. The grafts differ in susceptibility to bind platelets what might promote bacterial adhesion, where the interaction Fg-integrin αIIbβ3 receptor takes a part. Future studies will focus on endothelialization of grafted valves and how this affects lesion formation and development of infection. Moreover, anti-platelet treatment will be addressed to study its effect on bacterial recruitment.