**HEMODYNAMIC MODULATION OF NON-PLATELET THROMBOXANE GENERATION**

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Thromboxane A2 (TXA2) is a signal-activated eicosanoid generated from the metabolism of arachidonic acid by the cyclooxygenase (COX) and thromboxane synthase enzymes. In healthy individuals, TXA2 is predominantly produced in platelets where it mediates platelet activation and local vasoconstriction. Aspirin (ASA) exerts its principle cardioprotective effect by suppressing platelet TXA2synthesis via irreversible inhibition of platelet COX-1. In patients with cardiovascular disease, substantial TXA2 generation emanates from non-platelet sources not effectively suppressed by ASA and predicts future risk of atherothrombosis and death. This is especially true in patients with heart failure, where non-platelet TXA2 generation potentiates the mortality risk associated with reduced ejection fraction. In a study of subjects undergoing right heart catheterization, the degree of non-platelet TXA2 generation directly correlated with cardiac filling pressures, suggesting that pressure-induced stretch may be a stimulus for TXA2 generation by vascular and endocardial endothelium. The mechanism by which non-platelet TXA2 generation increases mortality in patients with heart failure not appear to be due to increased platelet reactivity but may be related to its vasoconstrictive effect son the vasculature. As standard ASA therapy is incapable of suppressing non-platelet TXA2 formation, alternative strategies will need to be identified to modify this novel cardiovascular risk factor and improve outcome.