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Global RAS regulation in HTx

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EFFECTS OF ANGIOTENSIN-CONVERTING ENZYME INHIBITOR THERAPY ON THE REGULATION OF PLASMA AND CARDIAC TISSUE RENIN-ANGIOTENSIN SYSTEM IN HEART TRANSPLANT PATIENTS

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Abstract

BACKGROUND: Angiotensin-converting enzyme (ACE) inhibitors (ACEis) are beneficial in patients with heart failure, yet their role after heart transplantation (HTx) remains ambiguous. Particularly, the effects of ACEis on plasma and cardiac metabolites of the `classical` and `alternative` renin-angiotensin-system (RAS) in HTx patients are unknown.

METHODS: This cross-sectional study used a novel mass spectrometry-based approach to analyze both plasma and tissue RAS regulation in heart biopsy homogenates of stable HTx patients without RAS blockade (n = 10) and with ACEi therapy (n = 15). Angiotensin (Ang) levels in plasma and Ang formation rates in biopsy homogenates were measured.

RESULTS: We demonstrate that plasma Ang II formation is exclusively ACE-dependent, while cardiac Ang II formation is primarily chymase-dependent in HTx patients. ACEi therapy substantially increased plasma Ang-(1-7), the key effector of the `alternative` RAS, leaving plasmatic Ang II largely

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