

Novel Insights into the Effects of Insulin-Like Growth Factor 1 and Endothelin Signalling on Vascular Redox State in Patients with Type 2 Diabetes Mellitus

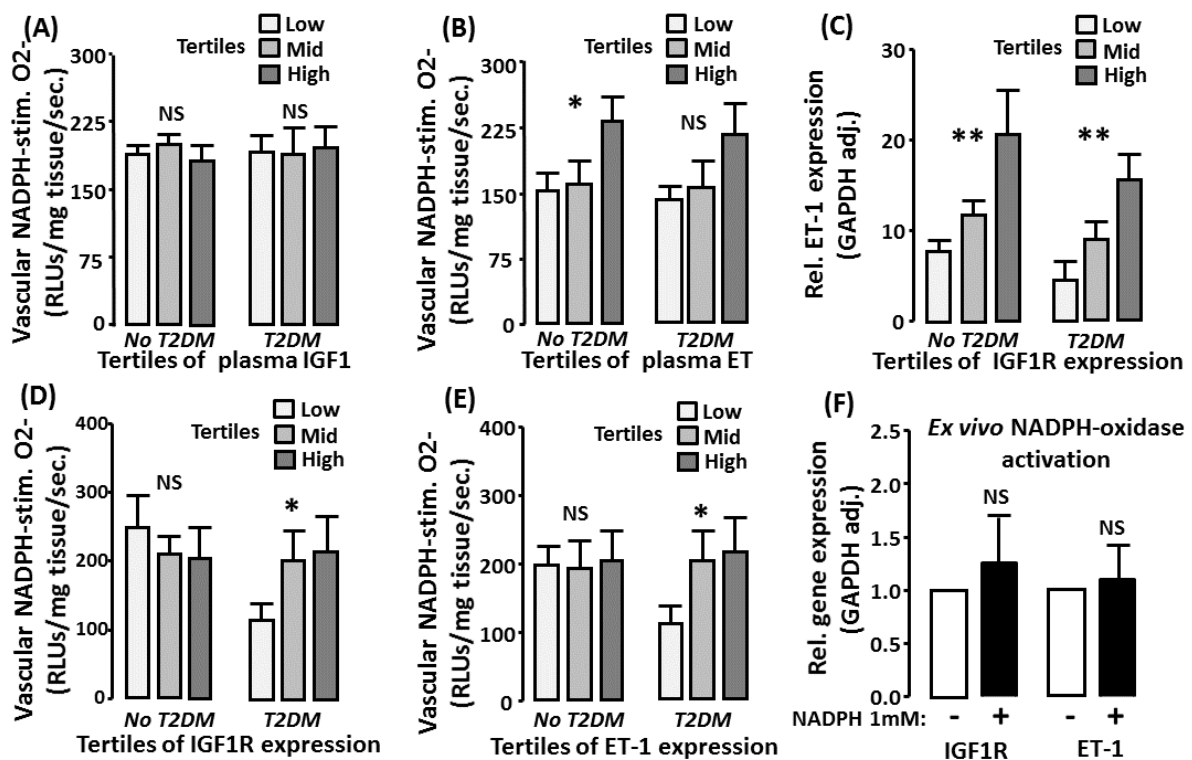
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Oxidative stress participates in the vascular complications of Type 2 Diabetes Mellitus (T2DM). Endothelin 1 (ET1) and insulin-like growth factor 1 (IGF1) affect redox hubs, but their effect on vascular redox state in T2DM patients is unknown. We explored the role of ET1 and IGF1 signalling on vascular redox regulation in T2DM patients with coronary atherosclerosis.

Internal mammary artery (IMA) segments were obtained from 486 patients undergoing coronary bypass surgery (146 T2DM) and used for superoxide (O_2^-) measurement *ex vivo*. Plasma ET1 and IGF1 were measured by ELISA.

High plasma ET1 (not IGF1) was associated with elevated vascular NADPH oxidase activity (A, B), while vascular IGF1R and ET1 expression were strongly correlated (C). Vessels with increased IGF1R and ET1 expression had higher NADPH oxidase activity only in T2DM patients (D, E). To test the direction of these associations, we induced O_2^- generation in IMAs by incubating with NADPH 1mM *ex vivo*, showing no effect on IGF1R or ET1 expression (F).

We demonstrate for the first time in humans that elevated vascular IGF1R expression and plasma or vascular ET1 may drive vascular NADPH oxidase activity selectively in T2DM patients. Our findings suggest dysregulation of vascular IGF1R and ET1 pathways in T2DM, identifying them as therapeutic targets to prevent vascular complications in such patients.



* P<0.05; ** P<0.001, NS=Non significant

Disclosures

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