

Hypertrophic Epicardial Adipose Tissue is a Source of EPAC Proteins Directly Associate to ST2 Production and Heart Dilatation and may be Potential Index of Heart Remodeling in CVDs Patients

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Introduction: Epicardial adipose tissue (EAT) is a myocardial fat from which released molecules can directly reach the heart. In pathological conditions, the ubiquitously tissue hypertrophy mediators are the exchange proteins directly activated by cAMP (EPACs), named EPAC1 and EPAC2. In the heart the main protective signalling against detrimental remodelling is the ST2 and IL33 molecules. ST2 exists both as transmembrane receptor (ST2L) and soluble (sST2) form and in case of physiological stretch ST2L bind IL33 promoting anti-fibrotic signals. Contrarily in CVDs, sST2 is up regulated functioning as scavenger of IL33 and promoting heart dilatation. Interesting is that ST2 can be also produced by adipose tissue in normal condition. Due to EPACs properties to induce hyperplasia, our hypothesis is that larger EAT cells may also produce sST2 that can local amplify its detrimental role on myocardium. For these reasons we want to verified in CVDs patients first if larger EAT cells are able to up regulate EPAC proteins and second if EPACs may be associate to sST2 EAT production and heart dilatation. **Methods:** 50 CVD patients are enrolled and stratified according to EAT median thickness (8mm). plasma and EAT biopsies are collected during surgery. Indexed left ventricular mass (hLVM), end-diastolic posterior wall (EDPW), relative wall thickness (RWT), left ventricular mass (LVM) values are used as cardiac dilatation indexes commonly approved in clinical practice. Gene expression and protein assays are performed to investigate EPACs, ST2, IL33 mRNA and protein production. **Results:** Our data demonstrated that CVDs patients with EAT >8mm have significantly positive correlation with RWT and they also presented higher EPAC1 and ST2 mRNA and protein levels than CVDs patients <8mm; contrarily IL33 protein is down regulated in CVDs >8mm and up-regulated in CVDs patients < 8mm. CVDs patients with hypertrophic EAT both EPAC1 and EPAC2 presented positive correlation with hLVM, EDPW, LVM indexes and ST2 mRNA levels. **Conclusion:** Our results demonstrated that EPACs are directly associate to EAT hyperplasia and sST2 local production suggesting their implication in detrimental heart hyperplasia. From these results we can suggest that EAT thickness can be a potential newer parameter of detrimental heart remodelling in the prevention of CVDs complications.