

Infrapatellar fat pad in reconstruction of anterior cruciate ligament *versus* infrapatellar fat pad in osteoarthritis: comparative characterization study by molecular biology

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The infrapatellar fat pad (IFP) was recently recognized as an emerging player in knee osteoarthritis (OA), actively contributing to disease development. However, there is consensus in claiming the lack of an adequate control group to fully describe/understand the IFP role in OA. In fact, the different biomechanical and physiological functions of subcutaneous adipose tissue make it inadequate to effectively embody this role. Thus, the aim of this study was to compare the molecular features of OA-IFPs from patients undergoing total knee replacement (TKR) (n=8) *vs* the IFPs (i.e. biopsies) of patients undergoing reconstruction of anterior cruciate ligament (ACL) (n=8) and regarded as healthy control group.

The demographic data were recorded; then, the IFPs were processed for gene expression analysis. In particular, qRT-PCR analysis were performed to evaluate the mRNA expression levels of growth factors (*VEGF*, *TGF-β*), adipokines (*leptin*, *adiponectin*, *PPARγ*, *FABP4*), cytokines (*IL-6*, *TNF-α*, *MCP-1*) and genes involved in extracellular matrix (ECM) remodelling (*COLI*, *COLIII*, *COLVI*, *GPNMB*, *ITH5*, *SERPIN2*).

Compared to ACL patients, OA subjects were demographically elder (median age 71.50, [IQR=75-62.5] *vs* 22.00 [IQR=38.5-21.25]; $p<0.0001$) and with higher BMI (27.84 [IQR=29.97-25.16] *vs* 23.74 [IQR=25.77-22.32]; $p=0.010$). Higher lymphocytic infiltration (*IL-6*) and vascularization (*VEGF*) occurred in the OA-IFP. Regarding the adipokines, mRNA expression levels were higher for *leptin*, *adiponectin* and *FABP4* in OA-IFP than ACL-IFP; while no differences were observed for *PPARγ* as well as for *TNF-α* and *MCP-1* between the two groups. Finally, analysis of ECM-remodelling genes, showed higher expression levels for *ITH5*; no difference for *COLVI* and *SERPIN2* and a decreased expression level for *COLI*, *COLIII* and *GPNMB*. A slight decrease in *TGF-β* gene expression level was found in end-stage OA-IFP compared to ACL-IFP. All gathered results confirm the inflammatory profile of OA-IFP, suggesting ACL-IFP as an adequate healthy control. Differences in ECM-related genes expression levels should be furtherly investigated in the future.