

Changes in Platelet Transcriptome and Function Following Transcatheter Mitral Valve Intervention

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Background

Transcatheter mitral valve intervention (TMVI) has emerged as a less invasive FDA-approved treatment option for patients with severe mitral valve disease who have high surgical risk. Recent studies have demonstrated inflammation mediated platelet dysfunction among patients undergoing TMVI which were associated with worse clinical outcomes.

Objective

This objective of this study was to investigate the mechanism of platelet dysfunction at the level of platelet transcriptome following transcatheter mitral valve intervention (TMVI).

Methods

We enrolled 21 patients undergoing transcatheter mitral valve repair (Mitraclip) or replacement (TMVR) at the University of Cincinnati Medical Center. Flow cytometry and microscopy were used to analyze platelet function. Platelets were isolated from whole blood using magnetic beads and analyzed with RNA sequencing.

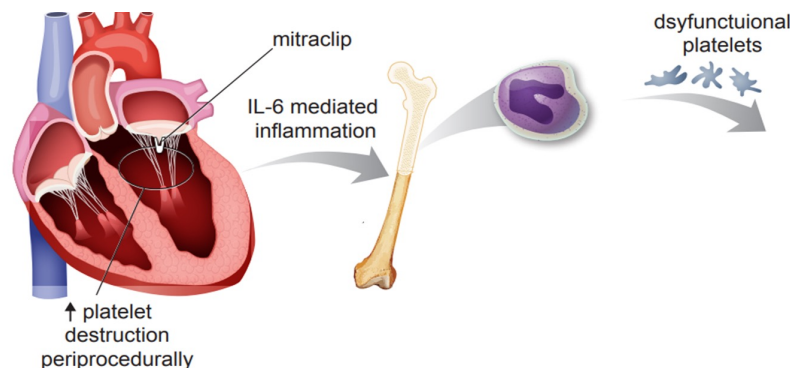


Figure 1: Mitraclip and other TMVI result in release of inflammatory mediators, including IL-6, which lead to inflammatory changes in circulating platelets and megakaryocytes leading to platelet loss and dysfunction

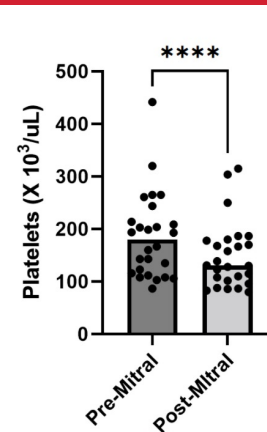


Figure 2: There was a significant decrease in platelet count following Mitraclip.

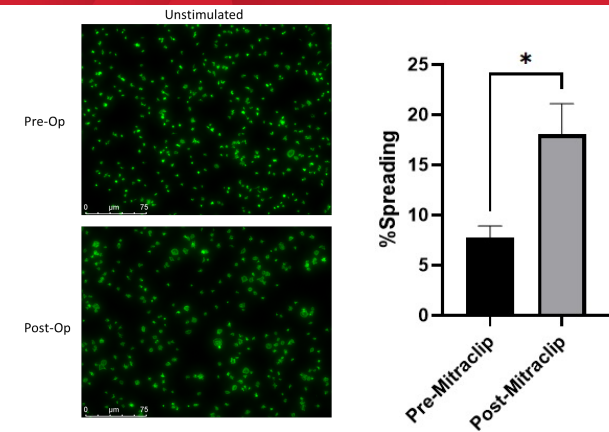


Figure 3: There was a significant increase in spreading of isolated platelets on fibrinogen (100ug/mL) following Mitraclip indicating activation of integrin signaling

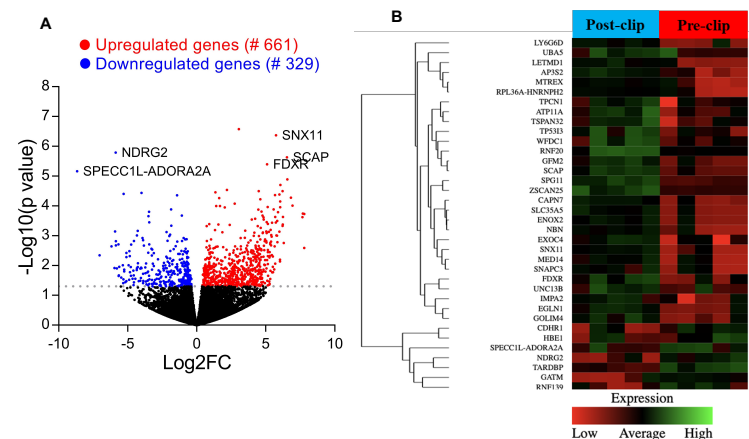


Figure 4: RNA-seq was performed on RNA isolated from purified platelets of 5 patients prior to and following Mitraclip. (A) Volcano plot demonstrating mRNAs which were significantly increased (red) or decreased (blue). (B) Heat map of significantly differentially expressed platelet transcripts with red indicating decreased relative expression and green indicating increased relative expression.

Results

There was a significant decrease in platelet count and increase in platelet activation following Mitraclip. We report the first description of dynamic changes in the platelet transcriptome following Mitraclip. Analysis of platelet RNA demonstrated upregulation genes involved in platelet endosomal trafficking.

Disclosures:
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