Novel digital pathology quantifies peripapillary fibrosis in mitral valve prolapse.

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1 Introduction
Mitral valve prolapse (MVP) is a common cardiac condition characterized by the improper closure of the mitral valve in the heart, often leading to mitral regurgitation. MVP risks progression to more severe cardiac complications, including arrhythmias and heart failure, and is thus a target for treatment via surgery to repair the valve.

2 Aim
Chronic valve prolapse, pre-surgery, causes mechanical stress on valve linked myocardial regions can lead to significant scarring of the papillary and peri-papillary region. Fibrosis in turn may underlie arrhythmias and postoperative LV dysfunction, which occurs in 20% of surgical MVP patients. Here, we use FibroNest™, a novel digital pathology platform to quantify the fibrosis in the peripapillary region to better understand the role of fibrosis in MVP.

3 Method
There were 6 patients involved in this study:
- From each patient 2 Endomyocardial Biopsies were collected:
  - 1 from the posterior myocardial wall adjacent to the posteromedial papillary muscle (Post-Pap)
  - 1 from a non-valve-linked area of the heart either LV septum or LV Apex

FFPE (~4 microns) sections for each sample was stained with Masson’s Trichrome and scanned at 40X.
- Each sample was then quantified using FibroNest™, a cloud-based image analysis platform, was used to quantify the fibrosis phenotype including 32 traits for collagen deposition, fiber morphometry, and architecture. Principal quantitative fibrosis traits (up to 315 qFTs) are automatically detected and combined into a Phenotypic Fibrosis Composite Score (Ph-FCS).

4 Representative Images

5 Results
- Our comparisons showed a significant increase in the severity of fibrosis in the post-pap region compared to the remote region when looking at the myocardium and endocardium separately, and close to significant difference when combined (Figure A,B,C).
- Each of these comparisons looks at traits that are significant for those regions. When analyzing traits that are significant across all these regions, we generated a co-model (Fig D) which shows higher fibrilic levels in the endocardium compared to the myocardium for both remote and post pap regions (mean myo = 2.70, endo=6.02). Furthermore, the gain seen in post-pap fibrosis is greater in the endo- than in the myocardium.

6 Conclusions
The findings from this study demonstrate prevalent regionalized myocardial fibrosis localized to valve-linked heart regions at the time of valve surgery and highlight this important and under-recognized pathology of Mitral Valve Prolapse. The use of FibroNest, has enabled a detailed and quantitative analysis of fibrosis, revealing a higher severity of fibrosis in the post-pap region compared to remote areas of the heart. Notably, the endocardium showed a greater fibrilic response than the myocardium, suggesting a differential impact of MVP on these cardiac layers. Further research pairing this data with post-surgery outcome data could show that post-pap scaring is an important indicator for the success of surgical interventions in MVP patients.