Quantitative assessment of myocardial fibrosis by digital image analysis: an adjunctive tool for pathologist ground truth

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Funding Acknowledgements: None.

Aims: Myocardial fibrosis (MF) is a common pathological process in a wide range of cardiovascular diseases. Its quantity renders both current myocardial condition and previous accumulated damage. We aimed to assess if the use of an automated artificial intelligence software for the quantification of MF on endomyocardial biopsies (EMB) might improve individual pathologist’s semi-quantification and agreement, in terms of precision.

Methods and Results: EMB samples were studied from intraoperative biopsies of the interventricular septum of 30 patients with severe aortic stenosis submitted to surgical aortic valve replacement. Tissue sections were stained with Masson’s trichrome for collagen/fibrosis and whole slide images (WSI) from the experimental glass slides were obtained at a resolution of 0.5mm using a digital microscopic scanner. Three experienced pathologists made a first quantification of MF excluding the subendocardium. An automatic algorithm, developed on QuPath software for Masson’s trichrome brightfield WSI, was applied and MF quantification ensued (Figure 1), being revealed to the pathologists. A new blinded quantification was performed by each of the pathologists after two weeks. The agreement of MF quantification and the impact of the automatic quantification were tested with Bland-Altman type methodology.

Median values of MF on EMB were 8.33% [IQR 5.00-12.08%] and 13.60% [IQR 7.32-21.2%], respectively for the first pathologist’s and automatic algorithm quantification, being highly correlated (R²: 0.79; p<0.001) (Figure 2). Inter-observer discordance increased at first observation for higher percentages of MF, but the knowledge of the automatic quantification improved the overall pathologist’s agreement, which became unbiased for distinct grades of MF (Figure 3).

Conclusions: The use of an automatic digital pathology algorithm for the quantification of MF on EMB samples significantly improves the reproducibility of measurements by experienced pathologists. This may prove to be a useful adjunctive tool to both improve the reliability of the quantification of myocardial tissue components and imaging-pathology correlation studies.