Amyloid deposits and fibrosis on left ventricular endomyocardial biopsy correlate with extracellular volume in cardiac amyloidosis

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Background: The relative contribution of amyloid and fibrosis to extracellular volume expansion in cardiac amyloidosis (CA) has never been defined.
Methods: We included all patients diagnosed with amyloid light-chain or transthyretin (AL/ATTR) CA at a tertiary referral center between 2014 to 2020 and undergoing a left ventricular (LV) endomyocardial biopsy (EMB).
Results: Patients (n=37) were more often male (92%), with a median age of 72 years (68–81). Lambda+ AL was found in 14/19 AL cases (38%) and kappa+ AL in 5/19 (14%), while TTR was detected in the other 18 cases (48%). Amyloid deposits accounted for 15% of tissue sample area (10–30%), without significant differences between AL and ATTR. All patients displayed myocardial fibrosis, with a median extent of 15% of tissue samples (10–23%, range 5–60%), in the absence of spatial overlap with amyloid deposits. Interstitial fibrosis was often associated with mild and focal subendocardial fibrosis. The extent of fibrosis or the combination of amyloidosis and fibrosis did not differ significantly between ATTR and AL subgroups. In 20 patients with myocardial T1 mapping at cardiac magnetic resonance (CMR), the combined amyloid and fibrosis extent displayed a modest correlation with extracellular volume (ECV; r=0.661, p=0.001). The combined amyloid and fibrosis extent correlated with high-sensitivity troponin T (p=0.035) and N-terminal pro-B-type natriuretic peptide (p=0.002) serum levels.
Conclusions: Extracellular spaces in CA are enlarged to a similar extent by amyloid deposits and fibrotic tissue. Their combination can better explain the increased ECV at CMR and circulating biomarkers than amyloid extent alone.