Clinical importance of left atrial infiltration in cardiac transthyretin amyloidosis

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Funding Acknowledgements: Type of funding sources: None.

INTRODUCTION: The clinical significance of left atrial (LA) involvement in ATTR amyloidosis cardiomyopathy (ATTR-CM) has not been characterized. The aims of this study were to characterize: (1)LA pathology in explanted ATTR-CM hearts; (2)LA mechanics using echocardiographic speckle-tracking in a large cohort of ATTR-CM patients; (3)to study the association with mortality.

METHODS AND RESULTS: Congo red staining and immunohistochemistry was performed to assess the presence, type and extent of amyloid and associated changes in 5 explanted ATTR-CM atria. Echo speckle-tracking was used to assess LA reservoir, conduit, contractile function and stiffness in 906 ATTR-CM patients (551 wt-ATTR-CM;93 T60A-ATTR-CM;241 V122I-ATTR-CM;21 other).

There was extensive ATTR amyloid infiltration in the 5 atria with loss of normal architecture, vessels remodelling, capillary disruption and subendocardial fibrosis. Echo speckle-tracking in 906 ATTR-CM patients demonstrated increased atrial stiffness [median(25th-75th quartile) 1.83(1.15-2.92)] that remained independently associated with prognosis, after adjusting for known predictors (lnLA stiff:HR = 1.26,CI 1.07-1.57;p = 0.009). There was substantial impairment of the three phasic functional atrial components [reservoir 8.86(5.94-12.97)%; conduit 6.5(4.53-9.28)%; contraction function 4.0(2.29-6.56)%]. Atrial contraction was absent in 21.6% of patients whose ECG showed sinus rhythm (SR)-"atrial electro-mechanical dissociation"(AEMD). AEMD was associated with poorer prognosis compared to SR patients with effective mechanical contraction (p < 0.0001). AEMD conferred a similar prognosis to patients in AF.

CONCLUSION: The phenotype of ATTR-CM includes significant infiltration of the atrial walls with progressive loss of atrial function and increased stiffness, which is a strong independent predictor of mortality. AEMD emerged as a distinctive phenotype identifying patients in SR with poor prognosis.

Abstract Figure.