

AS-amyloidosis. Dual pathology or novel disease? A multimodality, multi-centre assessment across health and disease

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Background: The coexistence of severe aortic stenosis (lone AS) and transthyretin cardiac amyloidosis (lone amyloidosis) is common, but the resultant AS-amyloidosis phenotype is unclear.

Purpose: We characterised AS-amyloidosis, hypothesizing that the dual insult of AS-amyloidosis results in a severe phenotype.

Methods: We compared four cohorts with deep phenotyping: 81 older age controls, 359 lone AS, 36 AS-amyloidosis (Perugini grade 2 and 3) and 107 lone amyloidosis (Perugini grade 2 and 3).

Results: AS-amyloidosis was similar to lone AS with respect to left ventricular mass and LVEF (57 (45, 64)%). It was similar to lone amyloidosis with respect to lateral S" (0.04 (0.03, 0.06) m/s), NT-proBNP (4149 (1449, 6459) ng/L) and troponin T (56 (34, 100) ng/L). Whilst, prevalence of carpal tunnel syndrome (CTS) (17%) and diastolic function (E/A ratio 1.1 (0.8, 2.8)) were intermediate.

Conclusion: AS-amyloidosis is not a double insult from AS and amyloidosis, but a mixed phenotype with features similar to lone amyloidosis (cardiac biomarkers), lone AS (remodelling and LVEF) or intermediate (diastology and CTS).

Characteristics across all 4 groups

Variable	Older age controls (n = 81)	Lone AS (n = 359)	AS-amyloidosis (n = 36)	Lone amyloidosis (n = 107)	P value
Age (years)	82 (80, 84)*†‡	85 (80, 88)§∞	88 (85, 92)#	80 (75, 84)	<0.005
Sex (% male)	69 *‡	49 ∞	61 #	94	<0.005
Carpal tunnel syndrome (%)	0	2 §	17 #	38	<0.005
Voltage/mass ratio	0.22 (0.14, 0.27)†‡	0.18 (0.13, 0.28)∞	0.18 (0.09, 0.21)#	0.07 (0.05, 0.10)	<0.005
NT-ProBNP (ng/L)	131 (66, 221)*†‡	1629 (639, 3941)§∞	4149 (1449, 6459)	2888 (1755, 5483)	<0.005
hsTnT (ng/L)	12 (8, 17)*†‡	24 (15, 40)§∞	56 (34, 100)	62 (41, 82)	<0.005
Inferolateral wall thickness (cm)	0.9 (0.8, 1.0)*†‡	1.1 (0.9, 1.3)∞	1.3 (1.1, 1.5)#	1.7 (1.6, 1.9)	<0.005
Anteroseptal wall thickness (cm)	1.0 (0.9, 1.2)*†‡	1.4 (1.2, 1.6)§∞	1.5 (1.3, 1.8)	1.7 (1.6, 1.9)	<0.005
Indexed LV mass (g/m ²)	79 (66, 102)*†‡	128 (99, 152)∞	126 (116, 140)#	174 (159, 200)	<0.005
LVEF (%)	59 (54, 63)†‡	59 (50, 65)∞	57 (45, 64)#	39 (31, 48)	<0.005
Lateral S" (m/s)	0.08 (0.07, 0.09)*†‡	0.07 (0.05, 0.08)§∞	0.05 (0.04, 0.07)	0.05 (0.04, 0.06)	<0.005
Septal S" (m/s)	0.06 (0.06, 0.08)*†‡	0.05 (0.04, 0.06)∞	0.04 (0.03, 0.06)	0.04 (0.03, 0.05)	<0.005
E/A	0.7 (0.6, 0.8)*†‡	0.8 (0.7, 1.3)§∞	1.1 (0.8, 2.8)#	2.4 (1.8, 3.3)	<0.005
RV Wall thickness (cm)	0.4 (0.3, 0.4)*†‡	0.4 (0.4, 0.6)∞	0.6 (0.4, 0.7)#	0.8 (0.7, 1.0)	<0.005
TAPSE (cm)	2.4 (2.0, 2.7)*†‡	2.1 (1.6, 2.5)∞	1.9 (1.5, 2.1)#	1.4 (1.2, 1.9)	<0.005
Classical LFLG AS (%)		9	13		0.472

* p < 0.05, Old age control vs Lone AS† p < 0.05, Old age control vs AS-amyloidosis‡ p < 0.05, Old age control vs Lone amyloidosis§ p < 0.05, Lone AS vs AS-amyloidosis∞ p < 0.05, Lone AS vs Lone amyloidosis# p < 0.05, AS-amyloidosis vs Lone amyloidosis

Abstract Figure. AS-amyloidosis compared to other cohorts

