Cardiac sympathetic denervation in wild-type transthyretin amyloidosis

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Topic(s):
Myocardial Disease – Diagnostic Methods

Background:
Tissue accumulation of misfolded transthyretin (TTR) may occur because of TTR gene mutations (variant amyloid TTR amyloidosis, ATTRv), or as an age-related phenomenon (wild-type ATTR, ATTRwt). Cardiac sympathetic denervation has been reported in ATTRv, but has never been investigated in ATTRwt.

Methods:
Fifteen consecutive patients with ATTRwt cardiomyopathy (81% men, median age 82 years, no one with prior myocardial infarction) underwent Cadmium Zinc Telluride tomographic imaging for amyloid burden (99mTc-hydroxymethylene diphosphonate - 99mTc-HMDP), innervation (123I-metaiodobenzylguanidine - 123I-MIBG), and perfusion (99mTc-tetrofosmin).

Results:
Median summed 99mTc-HMDP score was 60 (58-62), denoting a severe and diffuse amyloid burden. Planar 123I-MIBG examination showed decreased early and late H/M ratios (late H/M ratio: 1.5 [1.3-1.6], range 1.2-1.9, reference value ≥2.0). Summed 123I-MIBG score was 12 (6-22), with the most prominent denervation in the infero-septal, inferior, and infero-lateral regions; summed rest score was 7 (5-11), with lowest degrees of myocardial perfusion in the inferior and infero-septal regions. The correlation between amyloid burden (as relative 99mTc-HMDP uptake) and innervation (as relative 123I-MIBG uptake) did not achieve statistical significance at both segmental (p=0.252) and regional level (p=0.251). Nevertheless, denervation tended to worsen in parallel with the amyloid burden, and 123I-MIBG scores increased with 99mTc-HMDP scores. Segments and regions with more prominent hypoperfusion were those showing the more intense denervation (r=0.500 and 0.591, respectively; both p<0.001).

Conclusions:
Patients with ATTRwt cardiomyopathy display cardiac sympathetic denervation, particularly in the inferior and septal myocardial wall. Myocardial hypoperfusion has a similar regional pattern, while the amyloid burden is more extensive.