Prevalence and outcomes of cardiac amyloidosis in all-comer referrals for bone scintigraphy

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Objectives:

Cardiac amyloidosis (CA) is increasingly identified as a cause of heart failure due to diagnostic advances and enhanced disease awareness. Screening ascertainments have unveiled a significant proportion of (coexisting) CA for various cardiac conditions, but the true prevalence of CA in the general population as well as prognostic implications remain unknown

Methods:

Consecutive all-comer referrals for 99mtechnetium-3,3-diphosphono-1,2-propanodicarboxylic acid (DPD) bone scintigraphy between January 2010 and August 2020 were included retrospectively. CA was defined as positive cardiac tracer uptake (grade 1: subclinical CA; grade 2/3: clinical CA). Owing to the study design, CA subtype (transthyretin vs. light chain) was not consistently assessed. Indications for DPD, laboratory, and clinical data were retrieved from medical records. All-cause mortality, cardiovascular (CV) death and heart failure hospitalization (HHF) served as endpoints and were captured from the Austrian death registry and medical records, respectively. Outcome analysis was performed using Kaplan Meier estimates and multivariate Cox regression.

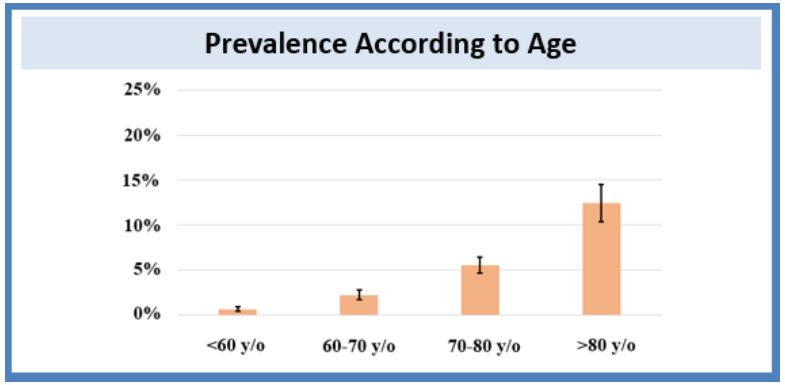


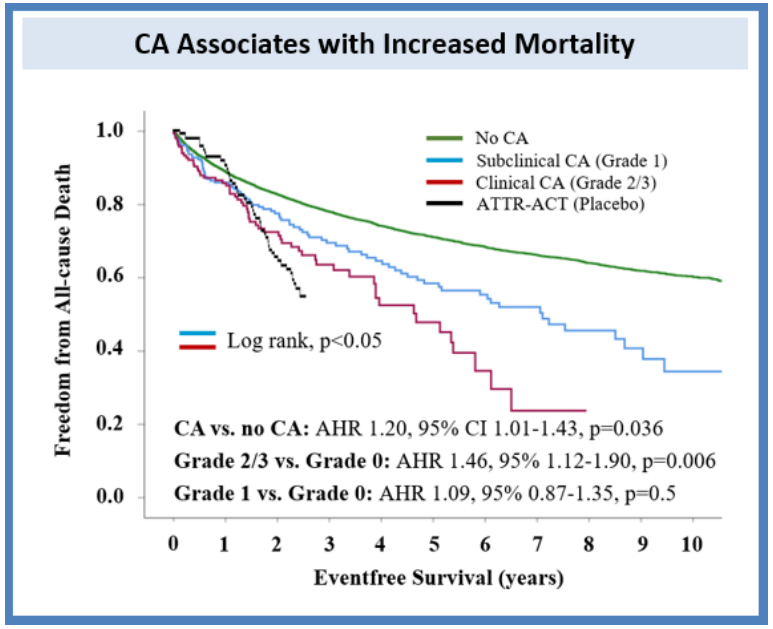
Figure 1: Increasing prevalence of cardiac amyloidosis in higher age levels.

Results:

17387 scans from 11527 subjects (61±16 y/o, 63.0% female, 73.6% cancer) were analyzed. Follow-up scans documented patients with progression from subclinical to clinical CA. Overall prevalence of CA was 3.3% (n=376/11527; grade 1: 1.8%, grade 2/3: 1.5%), increased with age (<60 y/o: 0.6% vs. 60-70 y/o: 2.2% vs. 70-80 y/o: 5.5% vs. >80 y/o: 12.4%; p for trend <0.001, **Figure 1**) and was higher in cardiac vs. non-cardiac referrals (18.2% vs. 1.7%). Across all age groups of non-cardiac referrals, CA patients more often had atrial fibrillation and cardiomyopathy, and displayed worse renal function (p for all<0.05). Independent predictors of CA were carpal tunnel syndrome, atrial fibrillation, chronic heart failure, male sex, and increased age.

After a median of 6 years, clinical event rates were: 29.4% mortality, 2.6% CV death, and 1.5% HHF, all independently predicted by CA. Adverse outcomes were driven by clinical CA (clinical CA vs. no CA, mortality: adjusted hazard ratio [AHR] 1.46 [95% confidence interval 1.12-1.90]; **Figure 2**; CV death: AHR 2.34 [1.49-3.68]; HHF: AHR 2.25 [1.51-3.37]), whereas subclinical CA performed equally to no CA (all p>0.3).

Figure 2: Clinical but not subclinical CA was associated with increased mortality compared to no CA.



Conclusions:

Cardiac amyloidosis is prevalent in elderly patients undergoing bone scintigraphy. The presence of clinical CA (grade 2/3) independently associates with adverse clinical outcomes. Conversely, patients with subclinical CA (grade 1) – which may progress to clinical CA over time – perform equally to those without CA. This opens a window of opportunity. If diagnosed and treated at a subclinical stage, adverse outcome implications conferred by CA may potentially be avoided.

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