Phenotyping Amyloidosis Subtypes in an Observational Database

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Abstract

Molecular subtypes of systemic amyloidosis can have overlapping clinical presentations and consequently, differentiating them with observational data can be challenging. We differentiated two subtypes of amyloidosis by whether the kidney or heart was the first organ with a positive biopsy result.

Background

Systemic amyloidosis, which results from tissue deposition of protein fibrils, is a cause of morbidity and mortality in the elderly. The amyloidosis subtypes are markedly different with respect to genetics, prevalence, pathophysiology, and treatment. For example, light chain amyloidosis (AL amyloidosis) results from the deposition of misfolded immunoglobulins and transthyretin amyloidosis (ATTR amyloidosis) results from deposition of misfolded transthyretin. However, the subtypes of amyloidosis can present with a similar set clinical symptoms. Therefore, phenotypes that can accurately differentiate among amyloidosis subtypes are valuable for observational research.

Methods

We designed phenotypes for AL and ATTR amyloidosis that favored specificity. We defined the AL amyloidosis phenotype as cases of amyloidosis that were diagnosed within 90 days following a renal biopsy. We excluded patients with a prior endomyocardial biopsy. Additionally, we restricted our cohort to patients who had a diagnosis of monoclonal paraproteinemia prior to the renal biopsy.

We used CPT code 50200 (“Renal biopsy; percutaneous, by trocar or needle”) to identify the renal biopsy. We identified amyloidosis with a separate set of codes, such as SNOMED code 17602002 (“amyloidosis”) or a related amyloidosis diagnosis. We identified monoclonal paraproteinemia with SNOMED code 267440005 (“monoclonal paraproteinemia”) and an endomyocardial biopsy with CPT code 93505 (“endomyocardial biopsy”).

We defined the ATTR phenotype as cases of amyloidosis that were diagnosed within 90 days following a heart transplant. We excluded patients with a prior history of chronic kidney disease or monoclonal paraproteinemia.

Results

A total of 16 patients with AL amyloidosis were identified in our database. The median age of the AL amyloidosis cohort was 60 [50-74] years. There were 8 (50%) male patients and 8 (50%) female patients in the cohort. The median prior observation time was 1.2 [0.1-11.9] years. A representative group of diagnoses antecedent to amyloidosis for the AL amyloidosis cohort are shown in Table 1.

A total of 15 patients with ATTR amyloidosis were identified in our database. The median age of the ATTR amyloidosis cohort was 62 [51-66] years. There were 14 (93.3%) male and 1 (6.7%) female patients. The median prior observation time was 0.6 [0.1-2.6] years. A representative group of diagnoses antecedent to amyloidosis for the ATTR amyloidosis cohort are shown in Table 2.

We used our algorithm for AL amyloidosis on an identified database to identify cases for validation. We reviewed 13 patients with AL amyloidosis. Of those, 9 (69.2%) had biopsy proven AL amyloidosis. We identified 15 patients with ATTR amyloidosis on the identified database with our ATTR amyloidosis algorithm. Of those, 10 (66.7%) had biopsy proven ATTR.

Results

Antecedent Condition	Count (Percent)
Proteinuria	13 (81.3%)
Essential Hypertension	9 (56.3%)
Chronic Kidney Disease	8 (50.0%)
Congestive Heart Failure	7 (43.8%)
Multiple Myeloma	6 (37.5%)
Type 2 Diabetes Mellitus	5 (31.3%)

Table 1: Medical Diagnoses Antecedent to Amyloidosis for the AL Amyloidosis Cohort

Antecedent Condition	Count (Percent)
Congestive Heart Failure	15 (100%)
Cardiomyopathy	14 (93.3%)
Peripheral Vascular Disease	7 (46.7%)
Essential Hypertension	5 (33.3%)

Table 2: Medical Diagnoses Antecedent to Amyloidosis for the ATTR Amyloidosis Cohort

Conclusions

AL and ATTR amyloidosis were distinguished in our database by whether the kidney or the heart was the first organ with a positive biopsy result.

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