

4. SPECIAL CONDITIONS

BIOPSY SPECIFIC CHARACTERISTICS ARE IMPORTANT IN DETECTING AMYLOID IN PATIENTS WITH AMYLOIDOSIS

F.G. Weverling¹, A. Vinkenborg¹, R.J. Leguit², M.C. Minnema¹✉

¹Department of Hematology, University Medical Center Utrecht, The Netherlands; ²Department of Pathology, University Medical Center Utrecht, The Netherlands

<https://doi.org/10.3324/haematol.2026.s2.14088>

Background. In amyloidosis, amyloid deposits are identified using Congo red (CR) staining, followed by identification of the precursor protein using immunohistochemistry, immuno-electron microscopy (immuno-EM), ELISA, or mass spectrometry. Certain patient characteristics such as male sex are associated with a CR negative stain in fat aspirations. In this single-center study we investigated whether biopsy-specific characteristics also affect sensitivity of CR-staining and influence the results of amyloid typing by immuno-EM.

Methods. The pathology database was searched between January 2020 and January 2025 and all reports describing the presence or absence of amyloid were selected by screening for “amyloid”. Only patients with proven amyloidosis, defined as having at least one amyloid positive biopsy or cytology result (identified by Systematized Nomenclature of Medicine [SNOMED] terms), were included in the study. As multiple biopsies and/or cytology results were available for most patients, CR staining sensitivity was calculated by comparing positive and negative results within patients with amyloidosis. For immuno-EM, we calculated sensitivity only on CR-positive samples. We evaluated biopsy- and patient-specific characteristics relevant to CR staining and immuno-EM typing and expressed them as relative risks (RRs). For CR staining, sensitivity differences between cytological and histological subcutaneous fat pad samples were evaluated using within-patient matched samples obtained at the same time, expressed as RR.

Results. A total of 730 reports were identified from 335 amyloidosis patients. The median age was 67 yrs (IQR

59-74), 36% were female. Almost two-thirds of the patients had light chain (AL) amyloidosis. Of the 730 reports, 655 (90%) were histologic biopsies of which bone marrow (30%) and subcutaneous tissue (22%) biopsies were most prevalent. The remaining 75 cytology reports consisted predominantly of subcutaneous tissue aspirations (90%). A positive CR-stain was observed in 529 (72%) reports. Factors associated with a CR-positive stain were the presence of vascular structures (RR 1.29, 95% CI 1.18-1.41), periosteum in bone marrow biopsy (RR 1.68, 95% CI 1.44-1.96) and cytologically obtained subcutaneous tissue (RR 1.58, 95% CI 1.18-2.13). Immuno-EM was performed in 253 (52%) of 485 CR-positive histologic biopsy reports. In 84% of cases, an amyloid precursor protein was identified. Factors associated with amyloid precursor protein identification with immuno-EM were female sex (RR 1.16, 95% CI 1.04-1.28) and a younger age (<67 yrs; RR 1.16, 95% CI 1.05-1.28). Biopsy-specific characteristics were not significant.

Conclusions. In conclusion, this explorative study suggests that positive amyloid detection by CR-staining is more likely in the presence of vascular structures and, in bone marrow samples, by the presence of periosteum (biopsy-specific characteristics), whereas amyloid typing by immuno-EM is more dependent on sex and age (patient-specific factors). Cytological subcutaneous fat aspirations demonstrated higher sensitivity than histological fat biopsies. Given the challenges of sampling and interpretation of CR-stainings, improving diagnostic yield is essential to reduce diagnostic delay. Cytological fat pad aspiration represents a simple and minimally invasive approach that may facilitate earlier amyloid detection.