

Diagnosis of Light Chain (AL) Amyloidosis

Enhancing clinical suspicion, confirming diagnosis, biopsy strategy by suspected organ involvement, and cardiac assessment.

GRADE

Strong Rec

Conditional Rec

Good Practice Statement

1 Enhancing Clinical Suspicion

STATEMENT	GRADE
Suspected cardiac amyloidosis: SIFE + UIFE + serum free light chain (sFLC) to increase suspicion of cardiac AL amyloidosis	1 · Strong (Mod)
Unexplained proteinuria: paraprotein testing (SIFE/UIFE/sFLC) to increase suspicion of AL amyloidosis	2 · Conditional (Low)
Positive SIFE/UIFE/sFLC + abnormal cardiac biomarkers + non-diagnostic echo : perform cardiac MRI (CMR)	2 · Conditional (Mod)
Positive SIFE/UIFE/sFLC + abnormal cardiac biomarkers + echo consistent with amyloidosis : skip CMR, go to tissue biopsy	2 · Conditional (V.Low)

GPS

Serum/urine **protein electrophoresis alone is not sufficient** as a screening or confirmatory test – electrophoresis + immunofixation on serum and urine, plus serum free light chains, are all required.

2 Confirming Diagnosis — Bone Scintigraphy

STATEMENT	GRADE
Suspicion of AL amyloidosis: against bone scintigraphy (PYP/DPD/HMDP) for diagnosis of AL cardiac amyloidosis	1 · Strong (Mod)
No plasma cell disorder (normal sFLC, no monoclonal protein) + suspected cardiac amyloidosis: bone scintigraphy for cardiac ATTR amyloidosis	1 · Strong (Mod)

GPS

Bone scintigraphy should be performed with **SPECT** (not planar-only imaging) to confirm myocardial (not blood-pool) tracer uptake. Offer genetic counseling for suspected/confirmed ATTR amyloidosis regardless of family history.

3 Biopsy Strategy by Suspected Organ Involvement

CLINICAL SCENARIO	PREFERRED APPROACH	GRADE
Suspected cardiac AL amyloidosis (abnormal biomarkers + echo + positive serology)	Start with fat pad + bone marrow biopsy , or endomyocardial biopsy	2 · Conditional (Low)
Suspected renal amyloidosis + positive serology	Fat pad + bone marrow biopsy over renal biopsy	2 · Conditional (Mod)
Monoclonal gammopathy + peripheral/autonomic neuropathy	Fat pad + bone marrow biopsy over nerve biopsy	2 · Conditional (V.Low)
Suspected multiorgan AL amyloidosis	Surrogate biopsies (fat pad + BM) if expeditious; else biopsy the most feasible symptomatic target organ	2 · Conditional (Low)
Plasma cell dyscrasia (MM/SMM) with existing bone marrow biopsy	Congo red staining on already-performed BM biopsy	2 · Conditional (V.Low)

GPS

Fat pad sampling technique must be optimized to allow validated subtyping. Once amyloid deposits are proven on histology, **subtype promptly** using a validated method. If highly suspected but fat pad/BM biopsy negative, **biopsy the affected organ**. Historical pathology (within 3 yr) may be tested retrospectively for amyloidosis.

4 Cardiac Involvement Assessment at Diagnosis

STATEMENT	GRADE
Proven AL amyloidosis, no cardiac symptoms : cardiac biomarkers (hs-troponin, BNP/NT-proBNP) + cardiac imaging to define presence/extent of cardiac involvement	1 · Strong (Low)

GPS

Echocardiography should include **global longitudinal strain** (sensitivity 72%; apical-sparing pattern may be absent in ~28%). **NT-proBNP** is preferred where available; BNP is an acceptable alternative. CMR offers higher diagnostic accuracy than echo but is often limited by cost/availability.