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## Bone scintigraphy reduces the need for biopsy in suspected cardiac amyloidosis

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FROM THE SPECIALTIES

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### **The gold standard to diagnose suspected cardiac amyloidosis is myocardial biopsy. In recent years, bone scintigraphy has partly replaced myocardial biopsy.**

Cardiac amyloidosis is an important cause of cardiac failure with preserved ejection fraction. Autopsy studies have shown presence of myocardial amyloid deposits in approximately 25 % of the population over the age of 80 years with a median survival of five years (1). Symptoms of cardiac amyloidosis include dyspnoea, oedema, fatigue, arrhythmia and syncope. Patients may also have extra-cardiac manifestations such as carpal tunnel syndrome and spinal stenosis. A myocardial biopsy with Congo red positive staining is the diagnostic gold standard when cardiac amyloidosis is suspected. Cardiac MRI as well as echocardiography may raise suspicion, but neither are diagnostic of amyloidosis. As bone scintigraphy has been included in the diagnostic workup in recent years, the need for myocardial biopsies can be reduced (2).

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### **Two types of amyloid affecting the heart**

Several types of amyloidosis can affect the heart. The two most common types are transthyretin amyloidosis and light chain amyloidosis, where amyloid fibrils are formed from transthyretin or from fragments of light chain immunoglobulins, respectively. Testing for clonal B-cell disease is necessary when cardiac amyloidosis is suspected. Detection of monoclonal components or a pathological kappa/lambda ratio must lead to haematological investigation for light chain amyloidosis with biopsy of bone marrow, fatty tissue, and possibly also myocardial biopsy. When light chain amyloidosis is ruled out, a positive bone scintigraphy is diagnostic for transthyretin amyloidosis.

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## Bone scintigraphy for cardiac diagnosis

A high affinity for cardiac transthyretin of common bone scintigraphy tracers such as bisphosphonates ( $^{99}\text{mTc}$ -DPD (3,3-Difosfono-1,2-propano-dicarboxic-acid) and  $^{99}\text{mTc}$ -HMDP (hydroxy-methylenediphosphonate)) has been known for decades. A role for bone scintigraphy in diagnostic algorithm of cardiac amyloidosis was established in the diagnostic workup after the publication by Gillmore et al. in 2016 demonstrating the high diagnostic yield for transthyretin cardiomyopathy (2).

Amyloid bone scintigraphy is performed after intravenous injection of approximately 700 MBq  $^{99}\text{mTc}$ -DPD/HMDP. Three hours after injection, a 20-minute whole body scan is performed. In case of cardiac uptake, proceeding with a SPECT/CT of the heart is recommended in order to characterise the localisation and distribution. Uptake of radiotracers is scored as described by Perugini (3). A positive amyloidosis bone scintigraphy (Perugini grade > 1) has > 98 % positive predictive value and specificity for transthyretin cardiac amyloidosis, provided that light chain amyloidosis is ruled out (1). If there is any evidence of monoclonal components and/or a pathologic kappa/lambda ratio, independent of Perugini score, light chain amyloidosis should be suspected (1).

In collaboration with colleagues from several medical specialities we have published updated Norwegian guidelines for diagnosis and treatment of amyloidosis (4).

Amyloid bone scintigraphy is available in all Norway's health regions for investigation of suspected cardiac amyloidosis. The method has high diagnostic accuracy for cardiac transthyretin and reduces the need for myocardial biopsy. Incidental cardiac uptake on a bone scan performed on other indications, such as malignancy, should result in a referral to a cardiologist.

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