Patient screening for cardiac hemochromatosis, echocardiography or MRI?

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Hereditary hemochromatosis is autosomal recessive disorder associated with the HLA-A locus on the short arm of chromosome 6 [1]. Excessive iron deposition occurs mostly in the heart, pancreas and pituitary. In normal subjects, absorption of iron from the gut is inversely correlated with iron stores. In homozygous hereditary hemochromatosis there is increased absorption of iron, which is not regulated by iron stores [2]. This leads to progressive iron accumulation because there is no normal mechanism for excretion of excess iron once it has been absorbed into the body. The clinical manifestations of iron overload include liver disease in 75% of cases, weakness and lethargy in 74%, skin hyperpigmentation in 70%, diabetes mellitus in 48%, arthralgia in 44%, impotence in 45%, electrocardiographic abnormalities in 31% and heart failure and conduction disturbances in 15% [3, 4]. Repeated phlebotomy can prevent iron accumulation in the heart. At this moment T2* magnetic resonance imaging is the best way for early detection of iron overload in patients with hemochromatosis [5, 6]. However, magnetic resonance imaging is time

consuming and expensive. If echocardiography would be able to detect cardiac iron overload in the same way as T2* magnetic resonance imaging, this would be more cost effective and could be used to screen patients with hemochromatosis on the presence or absence of cardiac involvement. The study of Davidsen et al. in the current issue of the *International Journal of Cardiac Imaging* shows, that tissue Doppler imaging was able to detect hemochromatosis determination of S' [7]. A cut-off value of $S' = 10.88$ cm/s achieved a 56% sensitivity and 74% specificity for separating haemochromatosis from controls (Communication from the authors). This gives a positive predictive value of 68% and a negative predictive value of 57%. Although the discriminating value of S' is not extremely high, echocardiography with tissue Doppler imaging could be used as a screening tool to detect cardiac involvement in patients with haemochromatosis. One has to be aware that the negative predictive value is slightly higher than 50%. This means, that if no abnormalities can be found, additional imaging with T2* MRI is still needed. At this moment echocardiography and tissue Doppler imaging is not able to replace T2* magnetic resonance imaging. Even if echocardiographic abnormalities are found it will be prudent to perform additional imaging with T2* MRI.

However, because echocardiography and tissue Doppler imaging is a cheap, non-invasive and easy technique initial screening in patients with haemochromatosis can be done using this technique followed

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by magnetic resonance imaging. If the diagnosis of cardiac haemochromatosis is established, both echocardiography and T2* MRI could be used for follow-up guidance of left ventricular function after therapeutic phlebotomy and chelation therapy [8]. In this situation, estimation of iron stores in the heart would be very helpful in order to evaluate the efficacy of chelation therapy and determine the cardiac risk. Although the iron storage proteins like hemosiderin and ferritin are mostly intracellular, serum ferritin is highly correlated with the amount of iron deposition and can therefore be used as an index for intracardiac iron load [9]. However, ferritin levels can be affected by factors as fever or inflammation [10]. T2 relaxation time has a linear correlation with the total iron content in the heart [11]. Echocardiography with tissue velocity imaging is able to detect early ventricular function and ventricular dilation in thalassemia patients, but it does not detect cardiac iron load [12].

Therefore cardiac magnetic resonance imaging remains the preferred technique to image iron load in the myocardium in patients with haemochromatosis and guide chelation therapy.

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