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Newsletter

Cardiomyopathy and heart disease secondary to non-cardiological medical treatments

The assessment of cardiac function today

Authors

Dr John Evans,
Dr Dominique Lannes
Medical Directors at
SCOR Global Life

Left ventricular function is an essential parameter in assessing cardiomyopathy and heart disease in general. It is a predictor of short and long-term mortality.

Various examinations are used to assess cardiac function, but the first step is to take **the patient's medical history during the clinical examination**. For this first approach to the functional status of the heart, several classification systems are available, including the NYHA classification, which identifies four stages⁽¹⁾. In patients suffering from coronary heart disease, this classification provides a correlation between exercise capacity and twelve-year survival. For more prognostic information, cardiologists, in their day-to-day practice, rely on the **electrocardiogram (ECG)**. In insurance applications, any mention of changes in the ECG must be taken into consideration. The cardiac stress test is another useful aid to prognosis. More sensitive than the ECG, this test which assesses functional capacity, is a much more accurate predictor of survival.

However, Doppler echocardiography is the key procedure for assessing cardiac function.

This non-invasive, easily available and inexpensive examination provides a great deal of information and in particular it allows the calculation of the left ventricular ejection fraction⁽²⁾. This measurement of cardiac contractility is a good prognostic indicator for all heart diseases. Ejection fraction figures are available in underwriting files and must therefore be sought out. Doppler echocardiography is also the only examination that provides an evaluation of left ventricular diastolic function. Evaluating LV diastolic function is important because, in some diseases, filling abnormalities are observed before deterioration of the ejection fraction. The ejection fraction can also be measured by **ultrafast CT and MRI scanning**. However, these examinations have the disadvantage of being less widely available and more costly.

Editor

Bérangère Mainguy
Tél. : +33 (0)1 46 98 70 00
life@scor.com

SCOR Global Life SE

Societas Europaea with
a capital of €274,540,000
1, avenue du Général de Gaulle
92074 Paris La Défense Cedex
France
RCS Nanterre 433 935 558

www.scor.com

(1) New York Heart Association: Class 1: no difficulty in performing strenuous physical activities; Class 2: moderate difficulties in performing strenuous physical activities; Class 3: considerable difficulties in performing moderate physical activities; Class 4: difficulties in performing any physical activities.

(2) This is calculated by dividing the volume of blood ejected on each beat - difference between the end-diastolic volume (ventricle full) and the end-systolic volume (volume of the ventricle once it has been emptied by the muscle contraction) - also known as the stroke volume, by the end-diastolic volume.

Primary cardiomyopathy: from diagnosis to treatment

Cardiomyopathy is a group of heart muscle diseases characterised by a structural or functional abnormality of the myocardium not caused by coronary, valvular or congenital conditions or by hypertension.

The most common conditions are **dilated cardiomyopathy** and **hypertrophic cardiomyopathy**.

Epidemiology

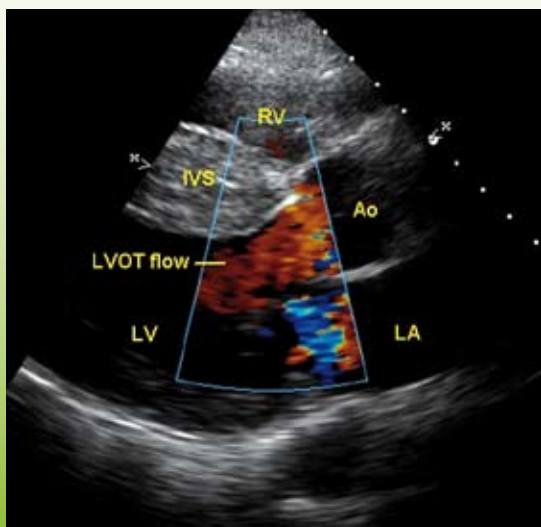
Dilated cardiomyopathy is characterised by dilation of the ventricular chambers, thin walls and reduced pump function. Prevalence in the general population is about 1 in 3,000. There is a family history of the disease in about 30% of cases. Many mutations have been found in various genes involving the cardiomyocyte proteins. Other aetiologies may be toxic (chemotherapy, alcohol, etc.), infectious (myocarditis, HIV, etc.), metabolic, endocrine, etc. In most cases, however, no cause is identified.

Hypertrophic cardiomyopathy differs from DCM in that it is characterised by significant thickening of the walls.

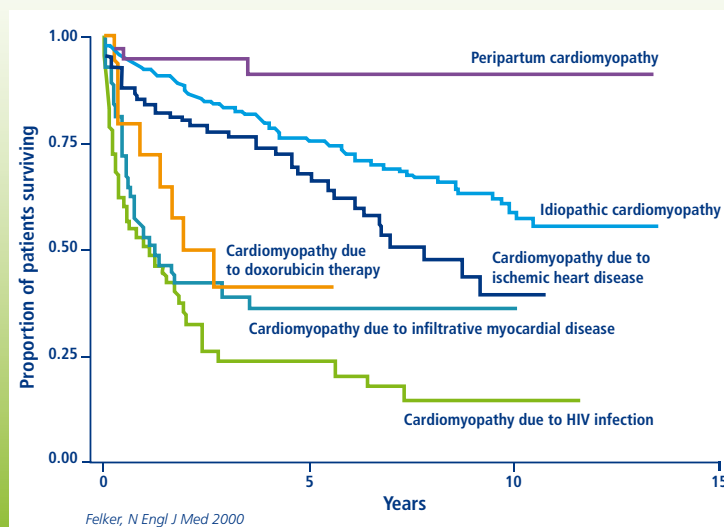
Often asymmetrical, the hypertrophy involves mainly the interventricular septum, which is the partition separating the two ventricles. It leads to abnormal ventricular filling. It also impairs ventricular ejection.

Relatively common in the general population, hypertrophic cardiomyopathy affects one adult in 500⁽³⁾. It is a familial disease in over 60% of cases. Due to the autosomal dominant mode of transmission, a child of a patient has a 50% chance of inheriting the mutation and, therefore, of the disease. Many genes are implicated, first and foremost the genes encoding sarcomere proteins. Worth noting: athlete's heart can sometimes mimic this type of cardiomyopathy.

Hypertrophic cardiomyopathy



Survival rate depending on cardiomyopathic causes



(3) Data taken from an echocardiographic study carried out on populations of healthy subjects.



Diagnosis and the place of genetic testing

Dilated cardiomyopathy may be discovered when a patient has a chest X-ray or ECG. **The diagnosis is confirmed by echocardiography, which will show reduced contraction (left ventricular ejection fraction < 45%) and left ventricular dilation (> 112% of the theoretical value).** Coronary angiography is usually performed to exclude coronary artery disease.

Hypertrophic cardiomyopathy may be revealed by a routine ECG or by family screening of a documented case. **It is confirmed by echocardiography showing abnormal hypertrophy of one of the ventricle walls** (Standard criterion: a wall thickness of more than 15 mm). Other examinations can be useful, such as MRI in the event of an unusual location of the hypertrophy.

Is there a place for genetic testing in screening and/or diagnosis? This test can be useful in hypertrophic cardiomyopathy to detect carriers of a known mutation within a family who have not yet developed the disease. If there is no family history and a mutation is not known to be present, it may be worthwhile to perform genetic testing for diagnosis in a doubtful case of hypertrophy in an athlete.

Severity criteria that are now well-known

Severity of dilated cardiomyopathy is determined using the same clinical or paraclinical criteria as those used for heart failure: severity of the symptoms (NYHA classification, syncope), severity of cardiac impairment in terms of dilation and reduced contraction (the lower the left ventricular ejection fraction, the poorer the prognosis), biological parameters (blood sodium, creatinine, natriuretic peptide or BNP), exercise capacity. A high heart rate and low blood pressure and intraventricular conduction disorders are also poor prognosis factors. Scoring systems⁽⁴⁾ exist to calculate patients' prognosis.

Severity of hypertrophic cardiomyopathy, on the other hand, is correlated above all to the severity of the symptoms (discomfort during effort, dyspnoea, syncope) and certain factors associated with an increased risk of sudden death: a family history of sudden death at a young age, a history of syncope, hypertrophy of one of the walls of more than 30 mm, ventricular rhythm disorders, abnormal blood pressure response during effort.

(4) Heart Failure Survival Score, Seattle Score.

(5) In a recently published study, BNP level was shown to correlate directly with the overall and cardiovascular mortality rate observed.

The benefits of biomarkers as markers of risk

BNP, or B-type natriuretic peptide, is a cardiac hormone released into the blood essentially in response to increased cardiac wall strain. The measurement of BNP and its metabolite, NT-proBNP, is used to diagnose heart failure, in particular in patients with effort dyspnoea. An increased level of this peptide is proportional to the severity of the heart failure⁽⁵⁾. **In dilated cardiomyopathy, BNP is an important risk marker.** Although BNP testing has not yet been introduced in the insurance field, it could well be considered for use in medical underwriting in the future.

Do treatments improve patients' life expectancy?

The clinical course of patients suffering from dilated cardiomyopathy is usually characterised by repeated hospital admissions for heart failure, and, in some cases, by sudden death. **However, with medical treatment many patients remain stable for many years.** What is treatment based on? First of all, on a healthy lifestyle and some dietary rules, which include reducing salt and alcohol intake. Drugs therapy based on diuretics, beta-blockers and ACE inhibitors are prescribed and a pacemaker, which may or may not be combined with a defibrillator, may be offered to some patients to resynchronise the ventricles. If the condition is severe and advanced, a heart transplant may be envisaged.

To improve patients' life expectancy, the treatment of hypertrophic cardiomyopathy must be adapted to the severity of the illness. Firstly, in totally asymptomatic patients with no signs of serious illness, no treatment is justified. In those with risk factors for sudden death, an automatic implantable cardioverter-defibrillator must be offered. In cases where there are significant symptoms and obstruction, the first-line treatment must be medical. If this fails, other strategies may be offered (surgery, septal alcoholic ablation, pacemaker). Finally, if there are symptoms but no obstruction, beta-blockers or diuretics are recommended.

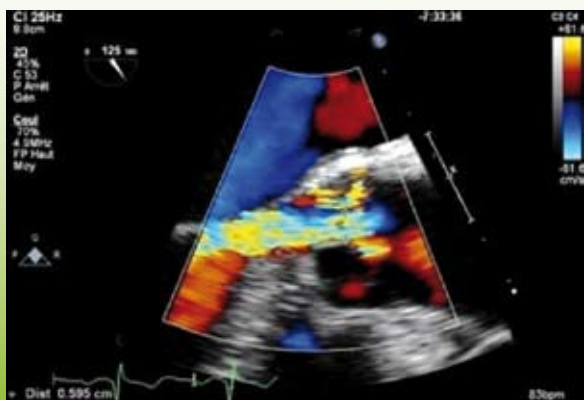
Heart diseases secondary to non-cardiological medical treatments

Non-cardiological medications can cause several types of cardiac complications: toxicity affecting the muscle or interstitial tissue (left ventricular dysfunction, heart failure), electrophysiological toxicity (reversible arrhythmia), vascular toxicity affecting the coronary arteries (angina pectoris and myocardial infarction). The extent to which such drugs are responsible for the cardiotoxicity can be determined by analysing prescription chronology and the course of the disease and by performing an echocardiogram.

Cardiac muscle toxicity: which are the types of drugs most often involved?

Toxicity affecting the muscle or interstitial tissue is classically associated with chemotherapy with anthracyclines prescribed to treat cancer. This type of treatment is known to cause abnormal left ventricular contraction, sometimes very severe and leading to symptoms of heart failure due to dilated cardiomyopathy. With some drugs such as doxorubicin, there is a cumulative, dose-dependent cardiotoxicity.

Toxicity of benfluorex



Should we be wary of the new anti-cancer drugs?

Although the complications affecting the heart muscle are now well-known and are becoming rare, we should be wary of the potential harmful effects of the new treatments acting on tyrosine kinase receptors used to treat breast and bowel cancer. Trastuzumab (Herceptin) and Bevacizumab (Avastin) are known to cause cardiac complications. Moreover, **Trastuzumab has been shown to increase the risk of left ventricular dysfunction when associated with anthracyclines, increasing their toxicity.**

Monitoring of patients treated with benfluorex

Launched as “an adjuvant to diet for patient with diabetes with overweight”, benfluorex (Mediator), an amphetamine derivative, has recently, but belatedly, been found to be linked to an excess risk of valvular heart disease. Indicated in the prevention of the complications of a disease and not for its treatment, this drug was prescribed for large numbers of patients (2 million subjects were treated from 1976, and 200,000 patients were still taking it when it was withdrawn from use in November 2009). **Regular monitoring and check-ups of patients who have taken benfluorex are essential to limit the severity of future complications.**

SCOR Global Life R&D Centre for Medical Underwriting and Claims Management has been following the latest research and publications in cardiology for several years.

Close collaboration with leading-edge medical research teams allow the Centre to respond rapidly to the latest clinical developments and understand and assess their implications for the insurance against exceptional risks. For further information on this subject please contact your normal contact at SCOR Global Life.