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DILATED CARDIOMIOPATHY - ANATOMIC-CLINICAL STUDY

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Abstract:

Introduction. Dilated cardiomyopathy (DCM) is characterized by global cardiac dilation associated with left ventricular (LV) systolic dysfunction without valvar substrate or ischemic heart disease. Diagnosis of idiopathic DCM can only be sustained after excluding other non-genetic causes.

Methods. This study was performed on a cohort of 256 patients who died in Emergency County Hospital of Oradea and had diagnosis of DCM; the study was performed on a period of 2 years, from January 2014 until the end of December 2015. These patients were differentiated according to social criteria, background, department of admission, number of autopsies and co-morbidities.

Results and Discussion. Diagnosis of DCM was more common in male patients up to the age of 70; after this age the tendency is towards equalization. In patients aged 61-80 years, DCM played a major role in tanatogenesis. Existing clinical trials have shown that patients with idiopathic DCM have a lower mortality than patients with cardiac ischemic disease.

Conclusions. Despite the possibility of diagnosis with increased sensitivity and the large number of therapeutic options, multicentre studies and registries are needed to improve the life expectancy of these patients.

Keywords: *dilative cardiomyopathy, tanatogenesis, mortality.*

Rezumat

Introducere. Cardiomiopatia dilatativă (CMD) se caracterizează prin dilatarea globală cardiacă asociată cu disfuncția sistolică a ventriculului stâng (VS) fără avea ca și substrat boli valvulare sau ischemice. Diagnosticul de CMD idiopatică poate fi susținut doar după excluderea altor cauze non-genetice.

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Material și metodă. Studiul de față a fost efectuat pe un lot de 256 pacienți decedați în Spitalul Județean de Urgență Oradea care prezentau la externare diagnosticul de CMD în perioada Ianuarie 2014 până la finalul lunii Decembrie 2015. S-au diferențiat pacienții decedați în funcție de criterii sociale, mediul de proveniență, secția clinică, număr de cadavre necropsiate și comorbidități.

Rezultate și discuții. Diagnosticul de CMD a fost mai des întâlnit la pacienții de sex masculin până la vârsta de 70 ani; după această vârstă tendința este spre egalizare. La pacienții cu vârste cuprinse între 61 – 80 ani, CMD a avut un rol major in tanatogeneză. Studiile clinice existente au demonstrat că pacienții cu CMD idiopatică au o mortalitate mai scăzută decât pacienții cu boală ischemică cardiacă.

Concluzii. În ciuda posibilităților de diagnostic cu o sensibilitate crescută și a multitudinilor de opțiuni terapeutice, sunt necesare studii și registre multicentrice aprofundate pentru a putea îmbunătății speranța de viață a acestor pacienți.

***Cuvinte cheie**: cardiomiopatie dilatativă, tanatogeneză, mortalitate.*

Introduction

Dilated cardiomyopathy (DCM) is characterized by global cardiac dilation associated with left ventricular (LV) systolic dysfunction without substrate in valvar or ischemic disease.[1]

Although a universal definition of cardiomyopathies is not universally accepted, they were divided into two categories: primary and secondary. Primary cardiomyopathies include DCM, hypertrophic-obstructive cardiomyopathy (HOCM), restrictive cardiomyopathy (RCM), right ventricular arrhythmia dysplasia (RVAD), and non-compaction of LV.[2]

Secondary cardiomyopathies occur in accordance with other pathological conditions affecting the myocardial function.

Primary DCM, which has long been characterized as idiopathic, has a genetic etiopathogen in most cases, describing familial forms, especially when at least 2 family members are targeted.[2,3]

Diagnosis of idiopathic DCM can be sustained only after excluding other non-genetic causes.[4]

Secondary DCM occurs during infectious diseases (myocarditis, parasitic infections or rickets), endocrine (hyperthyroidism,

Statistical characteristics in deceased patients with DCM			
Analysed criterion	Patients deceased with DCM diagnosis in 2014 (n=121)	Patients deceased with DCM diagnosis in 2015 (n=135)	Patients deceased with DCM diagnosis in 2014–2015 (n=256)
Number of patients without necropsy	51	62	113
Number of patients exempt from necropsy	70	73	143
Deaths occurred in the emergency units	12	18	30
Deaths occurred in clinical departments	109	117	226
Number of patients with DCM as main death diagnosis	64	67	131
Number of patients with DCM as secondary diagnosis	57	68	125
Male patients	82	84	166
Female patients	39	51	90
Average age of patients	72.04± 8,72 years	71,93 ± 7,91 years	71.985±8,35 years
Urban areas patients	59	67	126
Rural areas patients	62	68	130

Table 1: *Characteristics studied in deceased patients with DCM*

pheochromocytoma, Cushing's syndrome), autoimmune (systemic lupus erythematosus, scleroderma, giant cell arteritis, Kawasaki disease), thesaurisomes (Fabry disease, amyloidosis , Hurler's disease), tachyarrhythmia, thermal shock, sleep apnea. Secondary DCM may also develop after consumption of toxic substances (alcohol, cocaine, ampheta-mines, lithium, metisergide) or even therapeutic after oncologic, irradiation therapies, or after the use of antiretroviral therapies. [3]

The onset of the disease occurs most frequently in adults (20-60 years) with an average age at presentation of 50 years[5], but juvenile cases are known and defined (family forms).

Pathophysiologically, DCM translates into systolic dysfunction which will produce a reduced volume with increased telesist and telediadial volumes at LV level, resulting in a very low LV ejection fraction, dilated ventricular cavities, parietal tension, and thinning the wall of the LV. All these phenomena occur in the absence of an abnormal ventricular load (high blood pressure, valvar disease) or a coronary pathology.[6]

Inflammatory DCM includes a group of diseases that have the substrate as a

myocardial infiltrate and must be distinguished from cases where an immune response is associated with another injury (ischemia or genetic substrate is present).

At present, cardiac magnetic resonance imaging (MRI) is considered to be the highest degree of sensitivity and specificity in assessing fibrosis (through the gadolinium capture technique).[7] In DCM, the degree of fibrosis is a predictor of overall mortality but also of the rate of respiration. Some studies have shown that DCM patients with a delay in gadolinium uptake are at an increased risk of developing ventricular arrhythmias. This technique is also useful in assessing the size and function of LV, but has proven its superiority to echocardiography by providing additional information. Also, this delay in substance capture was correlated with the presence of myocardial interstitial oedema and the presence of an inflammatory infiltrate at this level (cases were correlated with histological examinations from biopsy fragments or post-transplantation examination of the hearts).

Patients with DCM may experience symptoms and signs of congestive heart failure (HF) (paroxysmal nocturnal dyspnoea, orthopnoea, swelling of the legs, asteno-fatigue, pulmonary rheum, pressure increase in the jugular vein) or thromboembolic complications, malignant arrhythmias or even sudden cardiac death. In the advanced stages of dilation, signs of valvar damage (mitral or tricuspid insufficiency) appear.

The hygienic-dietary regime of DCM patients includes hydrosaline restriction, physical tolerability limits and risk factor control. Current clinical guidelines discuss extensively the management and the multitude of existing therapeutic options but draw attention to the use of anticoagulants only in cases where atrial fibrillation (FA), valvar prostheses or intracavitary thrombi are associated.

The WATCH study that evaluated the effectiveness of antithrombotics in patients with FEVS <35% did not show significant differences in patient mortality. *The WARCEF study* based on the same considerations, with similar inclusion criteria, compares the effect of warfarin with that of aspirin without significant differences in the overall mortality prevention. Cardiovascular recovery in these patients improves symptoms and may reduce overall mortality by up to 20% in 5 years. The overall prognosis of patients with DCM without cardiac transplantation is without hope.[8]

Purpose

We wanted to evaluate the incidence and prevalence characteristics of DCM-deceased patients in our clinic. We also performed an assessment of clinical-pathological inconsistencies.

Differentiation of DCM patients by age and background in 2014					
Age	Male patients from urban areas	Male patients from rural areas	Female patients from urban areas	Female patients from rural areas	Total patients
< 40 years	0	0	0	1	1
41-50 years	3	0	0	0	3
51-60 years	6	5	2	1	14
61-70 years	11	11	2	3	27
71-80 years	13	14	10	11	48
>81 years	7	10	5	6	28
Total patients	40	40	19	22	121

Table 2: *Differentiation of DCM patients by age and background in 2014*

Differentiation of DCM patients by age and background in 2015					
Age	Male patients from urban areas	Male patients from rural areas	Female patients from urban areas	Female patients from rural areas	Total patients
< 40 years	0	0	0	1	1
41-50 years	2	0	0	1	3
51-60 years	8	7	1	0	16
61-70 years	14	12	5	6	37
71-81 years	12	14	10	11	47
>81 years	7	8	8	8	31
Total patients	43	41	24	27	135

Table 3: *Differentiation of DCM patients by age and background in 2015*

Material and method

This study was performed on a lot of 256 patients deceased in the Emergency County Hospital of Oradea who presented the diagnosis of DCM at discharge from January 2014 until the end of December 2015. Excluded from the study were patients with violent death diagnoses and those who did not have the description of the diagnosis of DCM in the finding certificate or in the necropsy report. Observatory sheets, medical certificates of death, necropsy reports and histopathological results of fragments taken during necropsy were studied.

Deceased patients were differentiated according to social criteria, origin, clinical department, the number of corpses necropsied and comorbidities.

The study was conducted with the approval of the ethics committee of the health unit where the study was conducted in accordance with the ethical recommendations of the Declaration of Helsinki 1975. The necrophagic examination was carried out according to the legislation in force and was in line with the wish of the legal guardians.[9]

The data was processed using the SPSS 18 and Microsoft Excel Software. The results were expressed by the mean ± standard and median deviation (IQR).

Results and discussions

Of the 256 patients enrolled in the study, most were hospitalized in the Departments of Cardiology and Internal Medicine. A significant percentage of them were exempt from necropsy because DCM was the primary diagnosis of death, and there was no doubt about clinical diagnosis. On the other hand, those admitted to the surgical wards were diagnosed with DCM only after necropsy, which requires incomplete clinical and laboratory examination. These cases have been proposed for verification in the monthly death analysis commission that takes place in the pathological service department of the sanitary unit.

Table 1 can identify patients in the study diagnosed with DCM, with differences of gender, background, place of death and reporting as primary or secondary diagnosis.

Diagnosis of DCM was more common in male patients up to the age of 70 years; after this age the tendency is towards equalization, a result similar to the current statistics. In patients aged 61-80 years, DCM played a major role in tanatogenesis, which supports the theory that advanced age would be an independent risk factor for mortality.[10,11]

There were no significant differences between urban and rural area patients, which is encouraging because access to medical services is proving to be easier for those in

the rural environment. Table 2 and Table 3 show differences in the different age groups of the study group and their correlation with patient gender and background for 2014 and respectively 2015.

In the last period, the incidence and prevalence of DCM increased significantly as a result of early diagnosis by both family screening programs and improved diagnostic techniques. Even if we diagnose younger patients, mortality is higher in elderly patients, this may be due to the effectiveness of new cardiac remodelling therapies. These new therapies can provide a more favourable long-term prognosis.[12]

In the United States, pump failure has been shown to be the leading cause of death in patients with DCM. However, existing clinical trials have shown that patients with idiopathic DCM have a lower mortality than patients with cardiac ischemic disease.[13]

According to the decompensated IC registry *(ADHERE)*, 47% of patients admitted with IC were diagnosed with non-ischemic DCM.[14]

The 5-year mortality of patients with non-ischemic DCM is very high, 20% of whom may have sudden cardiac death. Implantation of cardiac defibrillators, a therapeutic option based on the LV ejection fraction (below 35%), is included in the current guidelines for the prevention of sudden cardiac death.[15,16]

Pulmonary and systemic embolism, feared complications of DCM, may be the consequence of blood stasis in dilated cavities with hypokinesia and secondary activation of coagulation cascade.[17]

Conclusions

Globally, DCM is known to be the most common cause of congestive heart failure (CHF) in the adult population, representing a socio-economic burden on health systems.

Mortality reduction is the major objective of studies conducted so far and of on-going studies.

Despite the possibility of diagnosis with increased sensitivity and the multitude of therapeutic options, in-depth multicentre studies and registries are needed to improve the life expectancy of these patients.

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