Cent. Eur. J. Med. • 9(1) • 2014 • 15-20
DOI: 10.2478/s11536-013-0233-y

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Central European Journal of **Medicine**

Ischemic and non-ischemic dilated cardiomyopathy

Research Article

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Received 3 January 2013; Accepted 26 June 2013

Abstract: Dilated Cardiomyopathy is a high-incident disease, which diagnosis of and treatments are clinical priority. The aim of our study was to evaluate the diagnostic potential of cardiac magnetic resonance (CMR) imaging; echocardiography and the biochemical parameters that can help us differentiate between the post-ischemic and non-ischemic dilated cardiomyopathy. Materials and methods. The study enrolled 134 patients with dilated cardiomyopathy: 74 with the post- ischemic form and 60 with the non-ischemic one. All patients underwent a coronary imaging test, with echocardiogram, cardiac magnetic resonance and a blood test. Pro-inflammatory cytokines were evaluated using Luminex kit. Data was compared between the two groups. Results. Echocardiography allowed recognition of Left Ventricular Non Compaction in 2 patients. Longitudinal and circumferential strains were significantly different in the two groups ($p<0.05$). Using CMR imaging a post-myocarditis scar was diagnosed in 2 patients and a post-ischemic scar in 95% of patients with the chronic ischemic disease. The interleukin IL-1, IL-6 and TNF-α levels were higher in the post-ischemic group compared with the non-ischemic one. Conclusions. The use of second level techniques with a high sensitivity and specificity would help distinguish among different sub-forms of dilated cardiomyopathy.

Keywords: *Dilated cardiomyopathy • Cardiac magnetic resonance*

1. Introduction

Dilated Cardiomyopathy (DCM) is a disease with a high incidence and has a great social impact on patients [1]. The main cause for development of DCM is an ischemic heart disease, which is thought to be responsible for ventricular dilatation in more than 60% of cases of DCM. The diagnostic and therapeutic approaches to ischemic heart disease are well coded, thus allowing effective treatment of patients [2]. On the other hand, the diagnostic and therapeutic strategies for non-ischemic DCM are usually insufficient; in fact, the definition of "non-ischemic DCM" incorporates many different sub forms with different etiology, clinical diagnosis, treatments and outcomes, such as left ventricular non-compaction (LVNC), familial dilated cardiomyopathy, Takotsubo cardiomyopathy, post-myocarditis dilated cardiomyopathy and peripartum cardiomyopathy [1,3-6]. Also, it is not uncommon that the protocols for diagnosis of patients with the post-ischemic DCM are incorrectly used to diagnose patients with the non-ischemic DCM.

The aim of our study was to evaluate the diagnostic potential of cardiac magnetic resonance (CMR) imaging, echocardiography (ECG) and some biochemical parameters to differentiate between the ischemic DCM and the non-ischemic DCM,

2. Materials and methods

A total of 134 patients with dilated cardiomyopathy were enrolled in the study. All patients underwent invasive

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and non-invasive coronary evaluation to diagnose post-ischemic DCM, using coronary imaging test, echocardiography and the CMR. We studied the presence of cardiovascular risk factors such as hypertension, dyslipidemia, diabetes, smoking history, DCM familiarity and obesity, that were assessed according to the stipulated guidelines (see Table 1) [7-10].

All patients underwent a venous blood sample to investigate the following biochemical parameters: serum creatinine levels, peak of leukocytes, fibrinogen, C-reactive protein (CRP), peak of CK-MB, troponin, total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides (TG) levels. The following normal range of these parameters was considered, for the serum creatinine levels (0.7-1.3 mg/dl in men; 0.6-1.1 mg/dl in women), leukocytes peak (3.8-11.0 10^3/ml), fibrinogen (200-400 mg/dl), CRP (<1.0 mg/L), CK MB (38-120 ng/ml), troponin peak (<0.01 ng/ml), LDL-cholesterol (<130 mg/dl), HDL-cholesterol (30-75 mg/dl) and for TG (50-200 mg/dl).

In all patients, we analyzed 5 different cytokines (IL-1β, IL-1ra, IL-6, IL-10, TNF-α), pointing out pro-inflammatory cytokines and proliferating cell inducers; these cytokines were evaluated using Luminex kit (R&D Systems). The assays were performed within the following limits of sensitivity for the measured cytokines: TNF-α>10pg/mL, IL-1ra>5pg/ml, IL-1β>15pg/mL, IL-6>3 pg/mL and IL-10>5 pg/mL. The normal ranges of values for these cytokines were: IL-1β (0.0-2.4 pg/ml), IL-1ra (0.0-2.8 pg/ml), IL-6 (0.0-5.6 pg/ml), IL-10 (0.0-6.3 pg/ml), and TNF-α (0.0-13.3 pg/ml).

All patients underwent coronary imaging test, echocardiography and CMR imaging.

The left ventricle ejection fraction (EF) was evaluated along with the global and focal function of the left ventricle, left ventricular end-systolic and end-diastolic diameters, shortening fraction, left ventricle wall thickness, valve structure and function, diastolic mitral flow and aortic outflow through 2D-echocardiography. Moreover, we studied the texture of pericardium and the left ventricle wall and considered the ratio of a non-compacted to compacted myocardium greater than >2, as a tool for diagnosis of LVNC.

In addition to the 2D-echocardiography we proceeded with tissue Doppler imaging, strain (ε) and strain rate, speckle tracking and X strain; these methods allowed the assessment of longitudinal, circumferential and radial myocardial deformation. The normal range of values for ECG were: left ventricle ejection fraction, 55-70%; longitudinal strain from -15.9% to -22.1%; circumferential strain from -20.9% to -27.8% and the radial Strain between 35.1-59.0%.

The CMR was performed using both CINE sequences and T1 and T2-weighted inversion recovery sequences after injection of gadolinium.

All enrolled patients were asked to sign the consent form for further use of their personal data in agreement with the law 675/96, and every patient was given to read informative report regarding personal data protection, according to the same law.

All data was collected in an Excel database (Microsoft); statistical analysis was carried out using Student T-test for univariate analysis and $\chi 2$ test for multivariate analysis, considering statistical significant for *P* value <0.05.

Table 1. The characteristics of the patients enrolled in the study. Dilated Cardomyopathy: DCM.

Risk factors	Ischemic DCM	Non-Ischemic DCM	P value (p<0.05)
Hypertension	67%	55%	0.136
Diabetes	23%	28%	0.478
Dyslipidemia	39%	30%	0.267
Smoking hystory	41%	40%	0.949
Familiarity	63%	55%	0.317
Obesity	33%	27%	0.468

3. Results

In total, 134 patients were enrolled in the study; 74 man (59%) with post-ischemic DCM and 60 (41%) woman with a non-ischemic DCM. Among the patients with non-ischemic DCM, 2 had left ventricular non-compaction, 2 were affected by myocarditis, 27 had a primary dilated cardiomyopathy (patients with high familiarity for DCM and without any other possible cause of DCM), and 1 patient had a Takotsubo cardiomyopathy. All remaining patients were diagnosed with the idiopathic dilated cardiomyopathy. The average patient age was 54±22 years.

The biochemical parameters of the studied population are given in Table 2.

The pro-inflammatory pattern was assessed by cytokine evaluation and showed higher blood concentrations of some pro-inflammatory interleukins in patients with ischemic DCM than in patients with non ischemic DCM (Table 3); in fact, patients with post-ischemic DCM had higher concentration of IL-1β, IL-6 and TNF-a compared with the patients with non-ischemic DCM (*P<0.05).

With regard to the imaging techniques, echocardiogram has helped identify the LVNC in 2 patients.

Moreover, the assessment of diastolic dysfunction allowed us to observe that there is a reduction of longitudinal, radial and circumferential function in all

patients (see Table 4); however, the longitudinal and circumferential strains were found to be significantly reduced (*P<0,05) in patients with ischemic etiology compared with those with the primitive non-ischemic dilated cardiomyopathy.

Finally, the use of Delay enhacement (DE) in CMR imaging, has made it possible to identify:
- post myocarditis scar in 2 patients and
- post infarction scar in 95% of patients with chronic ischemic heart disease.

We also documented the presence of fibrosis in some patients who did not have a compaction of the left ventricle.

Using CMR imaging it was possible to evaluate the different frames of imaging in patients with the LVNC and in patients with idiopathic dilated cardiomyopathy. In patients with LVNC we considered the hypertrabecular pattern, the possible involvement of the right sections and the absence of perfusion defects. In patients with the idiopathic dilated cardiomyopathy we evaluated the evedence for a dilated heart, a globally altered regional kinesia, the absence of perfusion defects and the absence of DE.

The results of use of DE in CMR imaging and results of measurements of EF using echocardiography in our population are given in Table 5.

Table 2. Biochemical parameters evaluated in the studied population. CRP: C-Reactive Protein, CK MB: Creatine Kinase-MB; LDL:Low Density Lipoprotein; HDL: High Density Lipoprotein; TG:triglicerids; Dilated Cardomyopathy: DCM.

	Mean detected values in ischemic DCM	Mean detected values in non-ischemic DCM	Normal range	P value (p<0.05)
Serum creatinine (mg/dl)	1.15 ± 1.2	1.29 ± 1.1	0.7 - 1.3 men 0.6 - 1.1 women	0.487
Leukocytes peak (10^3/ml)	10.0 ± 9.48	9.69 ± 11.4	3.8 - 11.0	0.863
Fibrinogen (mg/dl)	388.33 ± 119.7	402.33 ± 114.7	200 - 400	0.494
CRP (mg/L)	2.91 ± 6.7	2.80 ± 7.7	< 1.0	0.929
CK MB (ng/ml)	88.99 ± 110.6	87.22 ± 109.0	38 - 120	0.926
Troponin peak (ng/ml)	14.67 ± 21.0	12.52 ± 19.3	<0.01	0.542
LDL-cholesterol (mg/dl)	110.0 ± 4.0	106.33 ± 5.8	< 130	<0.05
HDL-cholesterol (mg/dl)	45.85 ± 19.0	48.9 ± 15.0	30 - 75	0.310
TG (mg/dl)	140 ± 69.0	132.45 ± 91.0	50 - 200	0.860

Table 3. Cytokine pattern in the enrolled population distinguishing between ischemic and non-ischemic dilated cardiomyopathy. IL: interleukin; TNF: Tumor Necrosis Factor. DCM: Dilated Cardiomyopathy.

	Ischemic DCM	Non-Ischemic DCM	Normal range	P value (P<0.05)
IL-1β (pg/ml)	326.9 ± 41.09	249.09 ± 34.0	0.0 - 2.4	<0.0001
IL-1ra (pg/ml)	1420.67 ± 5608.5	225.69 ± 310.32	0.0 - 2.8	0.1019
IL-6 (pg/ml)	37.08 ± 62.91	15.21 ± 29.09	0.0 - 5.6	0.0142
IL-10 (pg/ml)	20.99 ± 35.74	18.09 ± 55.60	0.0 - 6.3	0.7155
TNF-α (pg/ml)	27.93 ± 19.95	15.19 ± 13.47	0.0 - 13.3	0.0001

Table 4. Radial, Circumferential and Longitudinal strain evaluation through tissue Doppler imaging and 2-D speckle tracking in patients with ischemic and non-ischemic dilated cardiomyopathy: Circumferential and Longitudinal Strains are significantly reduced in patients with ischemic dilated cardiomyopathy; there was not a difference with respect to the radial strain. DCM: Dilated Cardomyopathy.

	Ischemic DCM	Non-Ischemic DCM	P value (p<0.05)
Radial strain (%)	5.6 ± 2.2	5.5 ± 3.2	0.8310
Circumferential Strain(%)	8.0 ± 2.43	11.5 ± 3.3	<0.0001
Longitudinal Strain (%)	7.8 ± 2.43	9.0 ± 3.1	0.0156

Table 5. Evaluation of the use of Delay Enhancement with cardiac magnetic resonance (CMR) imaging to measure the ejection fraction versus use of 2-D echocardiography in enrolled patients. Delay Enhancement (DE), Ejection fraction (EF), DCM: Dilated Cardomyopathy.

	All patients	Ischemic DCM	Non-Ischemic DCM	P value ($p<0.05$)
DE^+	60	70	0	<0.0001
DE^-	74	4	60	<0.0001
EF (%)	36.75 ± 8.8	37.6 ± 6.5	35.3 ± 12.5	0.1726

Table 6. Cineventriculography in the enrolled patients.

Coronary status	Number of patients
No occlusion	62
Bivasal occlusion	27
Trivasal occlusion	13
Monovasal occlusion	32

The results obtained using the CMR imaging were compared with the results of cardiac ventriculography (CVG) (see Table 6). It appears that there is a good correspondence between the presence of subendocardial or transmural DE at CMR and the presence of ischemic heart disease diagnosed by the CVG (92% specificity and 83% sensitivity).

4. Discussion

The European and American epidemiological data show a rapidly increasing trend for patients with the DCM; this entails an increase number of hospitalizations, clinical controls, prescription of drugs and the need for social support network for these patients, who often lose their self-sufficiency.

In order to reduce the inconveniences caused to patients and the costs of healtcare, it is extremely important to find strategies that would allow an early diagnosis of this disease as well as the identification of tailored and effective therapeutic pathways.

In our work we evaluated the diagnostic potential of the cardiac diagnostic imaging tests and biochemical parameters in defining the clinical pattern of patients with dilated cardiomyopathy, aimed at a tailored therapy.

The main cause of DCM today is ischemic heart disease, which is thought to be responsible for the ventricular dilatation in more than 60% of cases of DCM. The diagnostic and therapeutic strategies for ischemic heart diseases are well coded and they have allow an effective treatment of patients for many years [2,11-13].

In fact, all patients with DCM (that is not related to the ischemic heart diseases) are usually incorporated in the cauldron of non-ischemic dilated cardiomyopathy, which includes many diseases with very different etiology, such as myocarditis, familial dilated cardiomyopathy, LVNC, Takotsubo cardiomyopathy, forms associated with systemic diseases etc.[1]

The diagnostic and therapeutic approaches for these patients are usually improperly unified, and protocols designed for patients with post-ischemic DCM are often incorrectly used for patients with the non-ischemic DCM.

Using the imaging techniques we performed, most of the times it was possible to distinguish between the patients with post-ischemic and non-ischemic disease. Among the 134 patients, 60 were diagnosed with a non-ischemic DCM. In more than half of the patients, it was also possible to distinguish a specific etiology. MRI allowed the identification of 27 patients with dilated primitive cardiomyopath, 2 with myocarditis and 2 with LVNC, while echocardiogram also allowed the diagnosis of the LVNC.

Many recent studies in the literature are demonstrating the potential role of CMR in diagnosing DCM [14-19]. Athanasiadis et al., in their recent review paper have focused on the evidence available to date, supporting the late gadolinium enhancement imaging as a tool for prediction of future cardiovascular events in patients with ischemic and non-ischemic cardiomyopathies [18]. Grothoff et al., stated that CMR can distinguish LVNC from other cardiomyopathies as well as the normal hearts with high sensitivity and specificity; and that the follow-up examinations would be helpful to assess a potential change of non-compacted or compacted mass in a chronological sequence [19].

Therefore, CMR can be a useful tool in the evaluation of patients with dilated cardiomyopathy as it allows tissue characterization, the perfusion study at rest and after pharmacological stress and the evaluation of fibrosis.

Echocardiographic techniques allowed us to identify regional deformations due to myocarditis in two patients, and to distinguish between post-ischemic and non-ischemic dilated forms through the assessment of myocardial longitudinal and circumferential deformation.

The humoral evaluation allowed us to demonstrate that the pro inflammatory status of the patients with

ischemic heart disease is higher in patients with non-ischemic heart disease. As demonstrated in the literature, inflammation plays a major role in coronary heart disease: multiple pro-inflamatory cytokines and chemokines such as interleukin IL-1β and IL-6 are higher in patients with coronary heart disease [21-24]. Hence, in line with literature and our observations we can infer that the activation of pro-inflammatory cytokines may now be considered as a marker of coronary artery diseases. Considering these results, we believe that the routine use of more sophisticated diagnostic tools as those used in our study, which use is spreading and which are more and more easily available, allows not only a greater accuracy in the identification of subtypes of DCM but also a tailored therapy for these patients. Combined use of several diagnostic procedures, performed simultaneously to distinguish between different subforms of non-ischemic dilated cardiomyopathies (such as the detection of Takotsubo cardiomyopathy through echocardiography, myocarditis by CMR, LVNC by both echocardiography and CMR imaging) should result in a greater prescriptive effectiveness and less waste of economic resources.

5. Conclusions

Dilated cardiomyopathy is a high incident disease, which causes a growing social spending. Although the diagnostic approaches to ischemic heart disease are well coded, on the other hand the diagnostic strategies for non-ischemic DCM are usually inappropriate. Our study highlights the clinical utility of echocardiography, CMR imaging and pro-inflamatory cytokines in dilated cardiomyopathy as an important tool to discern between ischemic and non-ischemic subforms. In particular, CMR imaging can reliably diagnose many of the non-ischemic dilated cardiomyopathies and, along with the perfusion study, it allows the detection of post-infarction scar. Due to the study with second level imaging techniques it is now possible to distinguish between the different sub-forms of dilated cardiomyopathy with an overall accuracy of 83% and a specificity of 92%.

List of abbreviations

Dilated Cardiomyopathy (DCM),
Cardiac Magnetic Resonance (CMR),
left ventricular non-compaction (LVNC),
ejection fraction (EF),
Delay enhacement (DE),
cardiac ventriculography (CVG).

Conflicts of interest

None declared.

References

[1] Maron BJ, Towbin JA, Thiene G, et al. Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. Circulation 2006; 113: 1807-16

[2] Thygesen K, Alpert JS, Jaff AS et al. Third universal definition of myocardial infarction. Circulation. 2012; 126: 2020-2035

[3] Fatkin D; members of the CSANZ Cardiac Genetic Diseases Council Writing Group.Guidelines for the diagnosis and management of familial dilated cardiomyopathy. Heart Lung Circ. 2011; 20:691-3

[4] Novo S, Akashi Y, Arbustini, Assennato P, Azzarelli S, Barbaro G, Fazio G, Fedele F, Giordan M, Mazzarotto P, Modena MG, Novo G, Parodi G, Rapezzi C, Sconci F, Sganzerla P, Tona F, Salerno-Uriarte JA. Takotsubo Cardiomyopathy: a Consensus document. G Ital Cardiol (Rome), 2008; 9: 785-797

[5] Sliwa K, Hilfiker-Kleiner D, Petrie MC, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Eur J Heart Fail 2010; 12:767

[6] Manolio TA, Baughman KL, Rodeheffer R et al. Prevalence and etiology of idiopathic dilated cardiomyopathy (summary of a National Heart, Lung and Blood Institute Workshop). Am J Cardiol 1992; 69: 1459-1466

[7] Mancia G, De Backer G, Dominiczak A et al 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society

of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2007; 28:1462-1536

[8] Jellinger PS, Smith DA, Mehta AE, et al American Association of Clinical Endocrinologists' Guidelines for Management of Dyslipidemia and Prevention of Atherosclerosis. Endocr Pract. 2012 Mar-Apr; 18 Suppl 1:1-78

[9] Rydén L, Standl E, Bartnik M et al Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Eur Heart J. 2007; 28:88-136

[10] WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004 10; 363:157-163

[11] Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F, Gershlick AH, Giannuzzi P, Halvorsen S, Huber K, Juni P, Kastrati A, Knuuti J, Lenzen MJ, Mahaffey KW, Valgimigli M, van 't Hof A, Widimsky P, Zahger D. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012 Oct; 33(20):2569-619

[12] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Third universal definition of myocardial infarction. Eur Heart J. 2012 Oct; 33(20):2551-2567

[13] La Grutta L, Runza G, Gentile G, Russo E, Lo Re G, Galia M, Bartolotta TV, Alaimo V, Malagò R, Cademartiri F, Cardinale AE, Midiri M. Prognostic outcome of routine clinical noninvasive multidetector-row computed tomography coronary angiography in patients with suspected coronary artery disease: a 2-year follow-up study. Radiol Med. 2011 Jun; 116(4):521-531

[14] Stirrat J, White JA. The prognostic role of late gadolinium enhancement magnetic resonance imaging in patients with cardiomyopathy. Can J Cardiol. 2013; 29:329-336

[15] Giesbrandt KJ, Bolan CW, Shapiro BP, Edwards WD, Mergo PJ. Diffuse diseases of the myocardium: MRI-pathologic review of cardiomyopathies with dilatation. AJR Am J Roentgenol. 2013; 200:W274-82

[16] Fazio G, Visconti C, D'angelo L, Grassedonio E, Lo Re G, D'Amico T, Sutera L, Novo G, Ferrara F, Midiri M, Novo S. Diagnosis and definition of biventricular non-compaction associated to Ebstein's anomaly. Int J Cardiol. 2011; 150:e20-4

[17] Gulati A, Ismail TF, Jabbour A, Ismail NA, Morarji K, Ali A, Raza S, Khwaja J, Brown TD, Liodakis E, Baksi AJ, Shakur R, Guha K, Roughton M, Wage R, Cook SA, Alpendurada F, Assomull RG, Mohiaddin RH, Cowie MR, Pennell DJ, Prasad SK. Clinical utility and prognostic value of left atrial volume assessment by cardiovascular magnetic resonance in non-ischaemic dilated cardiomyopathy. Eur J Heart Fail. 2013 Jun; 15(6):660-670

[18] Athanasiadis A, Schneider B, Sechtem U. Role of cardiovascular magnetic resonance in takotsubo cardiomyopathy. Heart Fail Clin. 2013; 9:167-176

[19] Grothoff M, Pachowsky M, Hoffmann J, Posch M, Klaassen S, Lehmkuhl L, Gutberlet M. Value of cardiovascular MR in diagnosing left ventricular noncompaction cardiomyopathy and in discriminating between other cardiomyopathies. Eur Radiol. 2012;22:2699-709

[20] Koenig W, Khuseyinova N Biomarkers of atherosclerotic plaque instability and rupture. Arterioscler Thromb Vasc Biol 2007; 27:15-26

[21] Khan DA, Ansari WM, Khan FA Pro/anti-inflammatory cytokines in the pathogenesis of premature coronary artery disease. J Interferon Cytokine Res. 2011 Jul;31(7):561-567

[22] Rothenbacher D, Kleiner A, Koenig W, Primatesta P, Breitling LP, Brenner H. Relationship between inflammatory cytokines and uric acid levels with adverse cardiovascular outcomes in patients with stable coronary heart disease. PLoS One. 2012;7(9):e45907

[23] Shibasaki I, Nishikimi T, Mochizuki Y, Yamada Y, Yoshitatsu M, Inoue Y, Kuwata T, Ogawa H, Tsuchiya G, Ishimitsu T, Fukuda H. Greater expression of inflammatory cytokines, adrenomedullin, and natriuretic peptide receptor-C in epicardial adipose tissue in coronary artery disease. Regul Pept. 2010 Dec 10;165(2-3):210-217

[24] Ikonomidis I, Michalakeas CA, Parissis J, Paraskevaidis I, Ntai K, Papadakis I, Anastasiou-Nana M, Lekakis J. Inflammatory markers in coronary artery disease. Biofactors. 2012 Sep-Oct; 38(5):320-328