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Diabetes Mellitus and Cardiomyopathy

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Introduction:
It seems there are changes in the structure and function of the myocardium in diabetic cardiomyopathy associated with diabetes mellitus. They are not directly attributable to other related factors such as coronary heart disease or hypertension.

Purpose: The purpose of this study is to search and find the impact of diabetes mellitus on the incidence of heart disease, such as cardiomyopathy and its treatment.

Review Method: A bibliographic search was conducted through "Medline" database and "Google Scholar" search engine using the keywords: diabetes, heart disease, cardiomyopathy, for the time period 2010-2020. The language except for English and Greek was the exclusion criterion for the study.
It is a known fact that diabetics are at high risk of developing cardiovascular disease. In fact, cardiovascular disease is the leading cause of morbidity and mortality in diabetics. Diabetes is responsible for the increased and diffuse atherosclerosis in the large arteries (carotid, aortic, femoral arteries) and the increased incidence of atherosclerosis in the peripheral vessels of the heart. [1]
The concept of Diabetic Cardiopathy was first introduced by Rubler and his colleagues and was then widely used by epidemiologists and clinicians. [2]
Diabetic cardiopathy is a common cardiovascular complication of diabetes, which is associated with an increased risk of morbidity and mortality. Diabetic cardiopathy describes changes in the structure and function of the myocardium associated with diabetes that are not directly attributable to other confounding factors such as coronary heart disease or hypertension. [1] The pathophysiological mechanisms considered to be responsible for the development of Diabetic Cardiomyopathy are metabolic substrate management disorder by the diabetic heart, co-existing insulin resistance, small heart disease, and autonomic cardiac neuropathy. These lead to myocardial cell damage, reactive hypertrophy, interstitial fibrosis, and the progressive development of heart failure. [3]
It is important to note that in many patients, especially those with type 2 diabetes, the changes associated with diabetes are exacerbated by the presence of these comorbid conditions, which are likely to increase the development of left ventricular hypertrophy, heart sensitivity for ischemic injury and the overall likelihood of developing heart failure. [4]
The purpose of this review is to present all the data and information related to diabetic cardiomyopathy, to investigate the impact of diabetes on the manifestation of myocardial infarction and its treatment.
The work was based on the literature review of Greek and international literature with keywords such as diabetes, heart disease, cardiomyopathy. Electronic databases such as Medline Pubmed, Scopus, and Google Scholar search engine were used. Exclusion criteria for articles were the language, except English and Greek.
Talking about diabetic cardiomyopathy
Diabetic cardiomyopathy is a heart disease that appears to be due solely to diabetes. It is a modification of the structure and function of the myocardium despite the absence of hypertension and coronary heart disease. [3]
Diabetic cardiopathy is characterized by diastolic dysfunction and myocardial ischemia, which is due to hyperglycemia and insulin resistance that cause left ventricular hypertrophy. Risk factors also include long-term alcoholism and smoking, long-term high blood pressure, heart disease such as sarcoidosis, and family history. [5]
The condition involves left ventricular dysfunction, and is also accompanied by diastolic dysfunction that becomes more severe if the diabetic also suffers from hypertension or myocardial ischemia. Diabetes is therefore a well-recognized risk factor for heart failure. [6]
The pathophysiological mechanisms that lead patients with diabetes to the gradual development of heart failure are direct myocardial damage, tumor overload, and pressure overload. [7]
Diabetes mellitus not only accelerates the development of atherosclerotic coronary heart disease, but also promotes the development of microangiopathy. In addition, Diabetic Myocardial Infarction, by exacerbating hypertension, leads to an increase in left ventricular transfusion, while through diabetes-induced renal impairment (diabetic nephropathy), it leads to fluid retention and tumor overload. [8]
In the early stages of Diabetic Cardiomyopathy, patients are usually asymptomatic. At an advanced stage of the disease, there is obvious heart failure. Patients develop symptoms compatible with frontal (weakness, discharge, angina, syncope) and backward (shortness of breath, increased central venous pressure, hepatomegaly, and edema of the lower extremities) heart failure. [9]
Initially, Diabetic Cardiomyopathy in the first stage does not cause changes in the structural architecture of the myocardium and therefore the mass of the left ventricle, the thickness of the walls and the internal dimensions of the heart cavities are controlled normally by echocardiography.
However, lesions occur at the myocyte level, which are functionally expressed and can be detected with the latest sensitive echocardiography techniques (tissue Doppler imaging, Strain, Strain rate). [10]
In a second stage, the myocardial damage becomes apparent, expressed as loss of myocardial cells, hypertrophy and interstitial fibrosis. At this stage they begin to become visible, with the classic ultrasound cardiogram, the changes in the structure of the myocardium (mass, wall thickness and cavity

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dimensions), but mainly diastolic dysfunction (abnormal type of dimethroid flow) and possible systolic dysfunction of the left ventricle (reduction of its systolic markers). [11]

In the final stage of the disease, the structural and functional lesions of the heart are now clinically evident in the form of diastolic or systolic heart failure and are easily detected by all imaging methods of the heart. [12]

The degree of myocardial fibrosis in the myocardium of diabetic patients can be determined with the help of ultrasound and cardiac magnetic resonance imaging (CMR). [13]

The changes caused by Diabetes Mellitus II in the geometry of the left heart (central hypertrophy) are, as demonstrated by cardiac magnetic resonance, independent of gender and age. [14]

The most common echocardiographic finding in asymptomatic diabetic patients is left ventricular diastolic dysfunction with or without hypertrophy. [15]

There is also evidence that diabetic patients have an increased risk of arrhythmias, including sudden cardiac death. [16]

Of crucial importance in its approach is its detection in primary stages. This is achieved through the use of echocardiography and in particular the application of new echocardiographic techniques. There are no established specific treatment strategies that can be recommended for Diabetic Cardiomyopathy. [17] The aforementioned pathophysiological mechanisms, which are thought to be responsible for the development of diabetic myocardial infarction, suggest that different treatment directions may be effective in preventing, delaying progression, and ultimately treating heart failure. Crucial in the approach of Diabetic Cardiomyopathy is its detection in primary stages. This is achieved through the use of echocardiography and in particular the application of new echocardiographic techniques. [17, 18]

Strict glycemic control is a key element of treatment, as hyperglycemia increases free fatty acid levels, stimulates oxidative stress, activates growth factors, disrupts calcium homeostasis and lipid metabolism, ultimately leading to lipid overload. [19]

Modern therapeutic quiver has many effective drugs for the treatment of diabetes such as metformin, sulphonylureas, glycazones, insulin, but also newer agents such as GLP1 agonists and DPP4 antagonists. [20]

The European Society of Cardiology's 2013 guidelines for diabetes, prediabetes and cardiovascular disease consider strict glycemic control (HbA1c <7%) as an indication of class I to reduce microvascular complications and indication of class IIa for the prevention of cardiovascular disease. [21, 22]

The treatment of diabetic cardiomyopathy is also based on the general rules for the treatment of heart failure, since so far there is no specific treatment. According to the 2013 guidelines of the European Society of Cardiology for diabetes, prediabetes and cardiovascular disease, three neurohormonal antagonists - angiotensin converting enzyme inhibitors or angiotensin receptor blockers and antagonists - are the mainstay of treatment for patients with heart failure, including patients with diabetes. These three competitors can be combined with a diuretic to relieve congestion and supplement with ivabradine. [23]

The general goals of treatment are the satisfactory regulation of diabetes, the treatment of its symptoms, the control of the risk factors of the disease and the prevention of its possible worsening. In addition to lifestyle changes, exercise and weight management can significantly improve the coexistence of insulin resistance and hyperinsulinemia. [24]

Exercise, in addition to the beneficial effect on the metabolic profile (glucose, lipids, hypertension), seems to have additional beneficial effects on Diabetic Cardiomyopathy. Improves endothelial dysfunction, suppresses the overactivity of the neurohormonal axis, promotes thrombosis-fibrinolysis balance and improves the function of the heart and peripheral skeletal muscles. [25]

Smoking cessation, a healthy diet low in fat, sugar and salt, weight control within the desired range, and weight loss, as well as aerobic exercise [26] are among the cornerstones of a healthier lifestyle. It has been accepted that in diabetic patients a decrease in body weight and an increase in aerobic activity have led to a drastic reduction in the incidence of Diabetic Cardiomyopathy. [27, 28]

Psychopathology

The symptoms of low blood sugar get worse the lower the blood sugar goes. It can affect one's mood and make it difficult for them to think. They might get a headache, feel dizzy, have poor coordination, or have trouble walking or talking. Severely low blood sugar can cause seizures or convulsions, make someone pass out, or put them in a coma. This condition, called hypoglycemia unawareness, happens when the brain has trouble noticing low blood sugar levels. When that happens, they do not get the usual early symptoms of low blood sugar, such as nausea, hunger, shakiness, cold or clammy skin, or a pounding heart.

The specific mechanisms that mediate cognitive decline in diabetes are not clear. Macrovascular pathways may link hyperglycaemia, hyperlipidaemia, hypertension and low-grade systemic inflammation to structural changes, brain volume loss and cognitive decline, as has been proposed elsewhere [31, 32, 33]

Additional microvascular pathways are also supported. Increasing severity of diabetic retinopathy has been cross-sectionally associated with lower verbal fluency, mental flexibility and processing speed in men but not women [Ding et al. 2010]. Retinopathy has also been associated with the 10-year decline in verbal fluency and processing speed, though this relationship was not restricted to diabetic retinopathy, but was also found with hypertensive retinopathy [34]. The findings suggest that cerebral microangiopathy, as reflected in

retinopathy, contributes to structural brain changes and ensuing cognitive decline.

The association of hypoglycaemia with cognitive decline and dementia risk has been examined, with inconsistent results. Severe hypoglycaemia was not associated with cognitive decline, but individuals with dementia appeared to be at risk of future severe hypoglycaemia in one study [35]. In contrast, another study suggested hypoglycaemia frequency and severity appeared to increase risk of dementia [36]. These discordant results from two large type 2 diabetes cohorts indicate the care required in evaluating cohorts prospectively, since it might be expected that older individuals with baseline cognitive dysfunction may already be on a dementia trajectory and are more likely to make decisions that increase hypoglycaemia risk, such as missing a meal or making an inappropriate medication adjustment.

Diabetes leads to Diabetic Cardiomyopathy, both through the enhancement of classical risk factors and through the direct damage it causes to the myocardium. Diabetic cardiomyopathy is a pathological entity that can independently lead to progressive development of heart failure, regardless of the coexistence of coronary heart disease, hypertension or other cardiovascular risk factors. [29]
Lifestyle changes and eating habits play an important role in the treatment and treatment of both diabetes and diabetic heart disease. The treatment of diabetic cardiomyopathy is based on the general rules for the treatment of heart failure, since so far there is no specific treatment. Thus further research is needed to improve our knowledge of this complex syndrome. [30]

Results: Diabetic cardiomyopathy is characterized by diastolic dysfunction and myocardial ischemia, which is due to hyperglycaemia and insulin resistance causing left ventricular hypertrophy. Risk factors also include long-term alcohol abuse, smoking, hypertension, heart diseases such as sarcoidosis, and family history. The treatment aims for properly regulating diabetes, treating its symptoms, controlling risk factors for the disease and preventing it from getting worse. Regular exercise could reduce several risk factors for heart disease and improve glycemic control along with medication. Smoking must also be stopped. Finally, a healthy diet, low in fatty acids sugar and salt, and weight control within the desired range, is vital.

Conclusion: Lifestyle changes and eating habits play an important role in as regards the treatment of both diabetes and diabetic cardiomyopathy.

References

1. E. L. Kolomtsas. Diabetic cardiomyopathy: heart failure due to diabetes http://cardiometabolism.gr/2017/03/28/diavitiki-myokardiopathia-i-kardiaki-aneparkia-pou-ofilete-sto-diaviti/
2. Rubler S, Dlugash J, Yuceoglu YZ, Kumral T, Branwood AW, Grishman A. New type of cardiomyopathy associated with diabetic glomerulosclerosis. Am J Cardiol 1972, 30: 595−602
3. D.Z. Mytas, I.A. Kyriazis. Diabetic cardiomyopathy. Archives of Hellenic Medicine 2008, 25 (4): 432–441
4. Giannoglou G, Giannakoulas G. Diabetic cardiomyopathy, New aspects. Hellenic Diabetol Chron 2002; 2: 94 - 101
5. Konstantinos Trachanas, Skevos Sideris, Konstantina Aggeli, Emmanouil Poulidakis, Konstantinos Gatzoulis, Dimitrios Tousoulis, Ioannis Kallikazaros. Diabetic Cardiomyopathy: From Pathophysiology to Treatment. ELLINIKI KARDIOLOGIKI, 398- 406 https://hellenicjcardiol.gr/UsersFiles/documents/previouspubs/PAGE_398-406.pdf
6. Boudina S, Abel ED. Diabetic cardiomyopathy revisited. Circulation. 2007 Jun 26; 115 (25): 3213-23.
7. Goyal BR, Mehta AA. Diabetic cardiomyopathy: pathophysiological mechanisms and cardiac dysfunction. Hum Exp Toxicol. 2013; 32: 571-59
8. Voulgari C, Papadogiannis D, Tentolouris N. Diabetic cardiomyopathy: from the pathophysiology of the cardiac myocytes to current diagnosis and management strategies. Vasc Health Risk Manag.2010; 6: 883-903
9. Fang ZY, Prins JB, Marwick TH. Diabetic cardiomyopathy: evidence, mechanisms, and therapeutic implications. Endocr Rev. 2004; 25: 543-567
10. Aneja A, Tang WH, Bansilal S, Garcia MJ, Farkouh ME. Diabetic cardiomyopathy: insights into pathogenesis, diagnostic challenges, and therapeutic options. Am J Med. 2008; 121: 748-757
11. Schannwell CM, Schneppenheim M, Perings S, Plehn G, Strauer BE. Left ventricular diastolic dysfunction as an early manifestation of diabetic cardiomyopathy. Cardiology. 2002; 98: 33–39.
12. Fang ZY, Prins JB, Marwick TH. Diabetic cardiomyopathy: Evidence, mechanisms and therapeutic implications. Endocr Rev 2004, 25: 543−567
13. Ng AC, Delgado V, Bertini M, et al. Findings fromleft ventricular strain and strain rate imaging in asymptomatic patients with type 2 diabetes mellitus. Am J Cardiol. 2009; 104: 1398-1401
14. Velagaleti RS, Gona P, Chuang ML, et al. Relations of insulin resistance and glycemic abnormalities to cardiovascular magnetic resonance measures of cardiac structure and function: the Framingham Heart Study. Circ Cardiovasc Imaging. 2010; 3: 257- 263
15. Ha JW, Lee HC, Kang ES, et al. Abnormal left ventricular longitudinal functional reserve in patients with diabetes mellitus: implication for detecting subclinical

myocardial dysfunction using exercise tissue Doppler echocardiography. Heart. 2007; 93: 1571-1576
16. Nakou ES, Mavrakis H, Vardas PE. Are diabetic patients at increased risk of arrhythmias? Hellenic J Cardiol. 2012; 53: 335-339
17. Aguilar D, Chan W, Bozkurt B, Ramasubbu K, Deswal A. Metformin use and mortality in ambulatory patients with diabetes and heart failure. Circ Heart Fail. 2011; 4: 53-58
18. Kourkouta L, Papathanasiou V I, Koukourikos K, Kleisiaris Ch, Fradelos C. E, Tsaloglidou A. (2015) Circulatory System's Diseases in the Elderly. Journal of Pharmacy and Pharmacology 3 (12): 591-595.
19. Xie Z, Lau K, Eby B, et al. Improvement of cardiac functions by chronic metformin treatment is associated with enhanced cardiac autophagy in diabetic OVE26 mice. Diabetes. 2011; 60: 1770- 1778
20. Sharma AK, Srinivasan BP. Triple verses glimepiride plus metformin therapy on cardiovascular risk biomarkers and diabetic cardiomyopathy in insulin resistance type 2 diabetes mellitus rats. Eur J Pharm Sci. 2009; 38: 433-444
21. Brown A, Reynolds LR, Bruemmer D. Intensive glycemic control and cardiovascular disease: an update. Nat Rev Cardiol. 2010; 7: 369-375
22. Akritidou S., Tsaklis P., Tsaloglidou A., Kazakos K. (2015). The use of therapeutic communication tools in patients with type 2 diabetes in order to improve glycemic control and self-care. 1st annual conference "Care in Diabetes", Thessaloniki 12-14 June 201
23. Rydén L, Grant PJ, Anker SD, et al. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: The Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). Eur Heart J. 2013; 34: 3035- 3087
24. Tahrani AA, Varughese GI, Scarpello JH, Hanna FW. Metformin, heart failure, and lactic acidosis: is metformin absolutely contraindicated? BMJ. 2007; 335: 508-512
25. Kodama S, Tanaka S, Heianza Y, et al. Association between physical activity and risk of all-cause mortality and cardiovascular disease in patients with diabetes: a meta-analysis. Diabetes Care. 2013; 36: 471-479
26. Kourkouta, L. Ouzounakis, P., Tsaloglidou, A. (2010). Exercise and diabetes. 3rd Panhellenic and 2nd Pan-European Scientific and Professional Conference ENE, Ioannina.
27. Eurich DT, McAlister FA, Blackburn DF, et al. Benefits and harms of antidiabetic agents in patients with diabetes and heart failure: systematic review. BMJ. 2007; 335: 497
28. Tsaloglidou, A., Rouska, E., Harokopos, N. (2007). The effect of exercise on the vascular endothelium. Cardiology, 2: 117-123.
29. Tsaloglidou, A. (2009). Does audit improve the quality of care? International Journal of Caring Sciences, 2 (2): 65-72.
30. Tsaousoglou, A., Koukourikos, K. (2007). Quality and health services. MOMENT, 15 (2): 18-24Kloppenborg R., Van Den Berg E., Kappelle L., Biessels G. (2008) Diabetes and other vascular risk factors for dementia: which factor matters most? A systematic review. Eur J Pharmacol 585: 97–108
31. Reijmer Y., Van Den Berg E., Ruis C., Kappelle L., Biessels G. (2010) Cognitive dysfunction in patients with type 2 diabetes. Diabetes Metab Res Rev 26: 507–519
32. Strachan M. (2011) R D Lawrence Lecture 2010. The brain as a target organ in type 2 diabetes: exploring the links with cognitive impairment and dementia. Diabet Med 28: 141–147
33. Lesage S., Mosley T., Wong T., Szklo M., Knopman D., Catellier D., et al. (2009) Retinal microvascular abnormalities and cognitive decline: the ARIC 14-year follow-up study. Neurology 73: 862–868
34. Bruce D., Davis W., Casey G., Clarnette R., Brown S., Jacobs I., et al. (2009) Severe hypoglycaemia and cognitive impairment in older patients with diabetes: the Fremantle Diabetes Study. Diabetologia 52: 1808–1815
35. Whitmer R., Karter A., Yaffe K., Quesenberry C., Jr, Selby J. (2009) Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. JAMA 301: 1565–1572