Left Ventricular Dysfunction in Prediabetic Patients: A review article

Mohammed Abdelrazek Elsenbsy[a,c], Ahlam M. Sabra[a], Abdulla Eliaw Mohamed Ali[b], Gehad Osama Fawzy Sayed[a], Hossam Eldin M. Mahmoud[a]

[a] Department of Internal Medicine, Faculty of Medicine, South Valley University, Qena, Egypt.

[b] Department of Clinical Pathology, Faculty of Medicine, South Valley University, Qena, Egypt.

[c] Department of Internal Medicine, Arabian University (AGU), Bahrain.

Abstract:

Background: Prediabetes is a common condition that indicates a state between normal glucose metabolism and diabetes. This is considered a dangerous condition because of the high risk of developing diabetes. A recent study in Europe shows that visually impaired fasting increases glucose and impaired glucose tolerance. Prevalence of impaired fasting glucose (IFG) levels range from approximately 3%to 5% in the 20 -44 age group and approximately 20% to 30% in the 65-74 age group. Evidence suggesting a link between the risk of neuropathy, nephropathy, early retinopathy, and macrovascular disease and prediabetes. Prediabetes is associated with a 20% increased risk of cardiovascular disease compared to normoglycemic individuals. Several studies have established systolic and diastolic left ventricular dysfunction in prediabetic patients. We aimed to highlight left ventricular dysfunction in prediabetic patients and to describe the possible underlying mechanisms of this association.

Conclusion: There is a significant association between left ventricular systolic and diastolic dysfunction and prediabetes. The defects underlying prediabetes which include insulin resistance, metabolic syndrome, dyslipidemia, and inflammation, have been implicated to predispose diabetic patients to increased risk of developing ventricular dysfunction.

Key Words: Prediabetes; left ventricular dysfunction, echocardiography.

Definition of Prediabetes

Preliminary diabetes is defined as a state of high blood sugar using two special parameters according to the World Health Organization. Oral Glucose tolerance test (OGTT) was defined as 2 h plasma glucose of 140–200 mg / dL after consuming a load of 75 grams of oral glucose or a combination of the two. **(WHO, 2006).** On the other hand, the American Diabetes Association (ADA) has a cut-off value similar to IGT (140-200 mg / dL), but a lower cut-off value for IFG (100-125 mg / dL), and a hemoglobin A1c (HbA1c) with added value. The standard for diagnosing prediabetes ranges from 5.7% to 6.4%. **(ADA, 2014).**

Pathophysiology of Prediabetes

The recognition of the well-known disease defects, which are the basis of T2DM, is becoming increasingly common in patients prone to diabetes. Famous disease defects, which are the basis of T2DM, are becoming increasingly recognized in prediabetes. **(Defronzo, 2009).**

Decreased digestive function includes insulin resistance, leading to significant pancreatic dysfunction **(Khaw et al., 2004).**

There are still major defects affecting the action of insulin as well as its secretion in people at risk of developing diabetes, as a result of impaired glucose tolerance. Many studies have done and many checks to carefully know the various causes of diabetes and T2DM. **(Halban et al., 2014)**.

Defects in prediabetes include an increase in fat breakdown, a decrease in glucagon-like peptide 1 (GLP-1) levels, and a violation of glucagon secretion by alpha cells in the pancreas. **(Mather et al., 2008).**

In addition, some studies have suggested that protein synthesis may contribute to the toxic environment of early-stage diabetes. For example, low levels of adiponectin have been found to be a predictor of early glucose tolerance to prediabetes, from prediabetes to diabetes II **(Jiang et al., 2016).**

The higher-level molecular markers e.g. intercellular adhesion molecule-1 are omitted, as well as exclusion of tumor necrosis factor-α (**Brannick and Dagogo-Jack, 2018**).

Also, the initial perception of microbes in the gut and associated cardiovascular diseases, such as diabetes, dyspepsia and obesity, has a strong relationship with diabetes. **(von Toerne et al., 2016).**

Cardiovascular complications

Large epidemiological studies have shown that people with impaired fasting glucose have a higher risk of developing

diabetes and cardiovascular disease (CVD) and a higher mortality rate. **(Kacker et al., 2018)**.

Macro-vascular diseases associated with prediabetes include cardiovascular disease (CVD), stroke, and peripheral vascular disease (PVD). **(Stacey et al., 2015).**

Several signaling pathways contribute to ventricular dysfunction in prediabetics **(Aroor et al., 2012).** Low blood sugar, increased blood lipids, and increased insulin resistance can damage heart cells, which is a precursor to oxidation. **(Maisch et al., 2011)**.

In addition, free fatty acids that cause fat poisoning in the heart cells increase in circulation. These events first and foremost cause diastolic obstruction before systemic disturbances. **(Zhang and Chen, 2012).** A meta-analysis of 35 recent studies showed that all Cardiovascular complications related to diabetic patients as myocardial infarction, congestive heart failure, coronary artery stenosis and atherosclerosis were all reported in prediabetic patients **(Huang et al., 2016).** In the EPIC-Norfolk study, a 1% increase in the normal range of HbA1c was associated with a 10-year cardiovascular mortality rate. **(Khaw et al., 2004).**

The results of the EPIC-Norfolk study are in line with the data of the Paris Prospects Research Group, which shows that the CVD mortality rate of IGT subjects is doubling compared to NGT subjects. **(Wang et al., 2014)**.

Finding an increase in mortality confirms that most patients with prediabetes have anti-insulin (metabolic syndrome), such as obesity, poor digestion, low HDL cholesterol, and high blood pressure. **(Wang et al., 2014).**

The components of the metabolic syndrome can be identified in prediabetes a few years before the diagnosis of type II diabetes. These functions lead to advanced atherosclerosis, which is most often caused by atherosclerotic-dependent vascular damage, impaired vascular smooth muscle function, and increased atherosclerosis. **(Papa et al., 2013).**

A recent study reported that a positive link between the prevalence of diabetes and atherosclerosis was reported, and that early intervention in the control of prediabetes prevents arterial involvement. **(Holman et al., 2017).** It is noteworthy that prediabetes is associated with a nearly 3-fold higher incidence of unrecognized myocardial infarction compared to normal glucose tolerance (NGT), which has been shown in a

multinational study of atherosclerosis (MESA). **(Stacey et al., 2015).**

Left Ventricular dysfunction

Diabetes mellitus is characterized by a weakening of both the heart and digestive system. Regular output and normal Doppler parameters are used for its evaluation **(Edvardsen et al., 2006).**

Echocardiography makes it possible to assess diastolic functions. LV shortens the ejection time and systolic function and increases the narrowing time of isovolometers**(Peterson et al., 2004)**. On the other hand, the diastolic dysfunction in the left ventricle increases the time of isovolemetric relaxation and changes the time of diastolic filling. (**Sliem and Nasr, 2011**).

Askin et al. Assessed 80 baseline diabetics (34 women and 46 men) and the same number of sex-matched healthy subjects (35 women and 45 men). All subjects underwent laboratory analyzes and echo heart tests, including myocardial performance index (MPI) measurements. The mean age of the initial diabetes and control groups was 64.0 ± 10.6 and 62.2 ± 11.6 years, respectively. Time (IVCT) was higher in the initial diabetic group (P = .016), and they found that the Functional Index (MPI) was associated with prediabetes in a multivariate retreat analysis (Odds Ratio (OR): 1.967, 95% confidence interval [CI]: 1.574–2.459, P <.001) **(Askin et al., 2018).**

Recent cross-sectional studies have shown that the incidence of diabetes increases in prediabetic patients, and that impaired diastolic function is associated with reduced glucose tolerance throughout the metabolic state. **(Stahrenberg et al., 2010).**

Ceyhan et al. used Tissue Doppler Echo Heart and Tension / Tension Rate Echocardiography on The left heart field to analyze systolic and diastolic function to diagnose left ventricular dysfunction in patients with diabetes and primary diabetes (LV). **(Ceyhan et al., 2012).**

Aslan and colleagues Evaluated 50 healthy controls and 47 healthy controls of the same age with prediabetes. PW Echo Heart Measurements show that in prediabetic patients, the value of IVRT and deceleration time (DT) was significantly longer and significantly decreased in E wave. Although the LA diameter was significantly larger in the patient group than in the control group (35.9 ± 3.9 cm and 33.7 ± 4.2 cm; p = 0.027, respectively). **(Aslan et al., 2014).**

Ardahanli et al. A prospective study enrolled fifty-three consecutive primary

diabetic patients (primary care group) and 48 normal individuals (control group). Not all sciences have a history of cardiovascular disease, and they were normal. Isovolumetric resting time (IVRT) was longer in the initial group than in the control group and was statistically significant (91 ± 15 and 83 ± 16 ؛ p = 0.019, respectively).

The ejection time (ET) was significantly longer in the control group than in the initial diabetes (264 ± 28 versus 241 ± 28 ؛ p <0.001). In the initial group, the MPI value was higher than in the control group (0.74 ± 0.12 vs 0.64 ± 0.09, respectively, p <0.001). **(Ardahanli et al., 2019).**

Akçay et al. They provide evidence of the prevalence of left ventricular and diastolic ventricular systolic abnormalities in prediabetes patients undergoing echocardiography (TDE). They estimated 94 patients with non-traumatic prediabetes and 70 healthy volunteers with similar demographic characteristics. The mean scores for myocardial infarction time (IVCTm), myocardial infarction time (IVRTm), and myocardial infarction index (MPI) were higher than in patients with preDM. (**Akçay et al. 2016**).

Conclusion:

Left ventricular systolic and diastolic dysfunction has a strong relationship between prediabetes .

Conflict of Interest:

The researcher does not contradict or contradict these publications.

References

- **Akcay M, Aslan AN, Kasapkara HA, Ayhan H, Durmaz T, Keles T, et al. (2016).**Assessment of the left ventricular function in normotensive prediabetics: a tissue Doppler echocardiography study. Arch Endocrinol Metab, 60(4): 341-7.
- **American Diabetes Association (2012).** Diagnosis and classification of diabetes mellitus. Diabetes Care, 35(Suppl 1):S64-71.
- **Askin L, Cetin M, Tasolar H and Akturk E (2018):** Left ventricular myocardial performance index in prediabetic patients without coronary artery disease. Echocardiography, 35:445–449
- **Aslan AN, Ayhan H, Çiçek ÖF, Akcay M, Durmaz T, Keles T, et al. (2014).** Relationship between aortic stiffness and the left ventricular function in patients with prediabetes. Intern Med, 53:1477–1484.
- **Bajraktari G, Koltai MS, Ademaj F, Rexhepaj N, Qirko S, Ndrepepa G, et al. (2006).** Relationship between insulin resistance and left ventricular diastolic dysfunction in patients with impaired glucose tolerance and type 2 diabetes. Int J Cardiol,10(2):206-11.

- **Barr EL, Boyko EJ, Zimmet PZ, Wolfe R, Tonkin AM, Shaw JE.(2009).** Continuous relationships between non-diabetic hyperglycaemia and both cardiovascular disease and all-cause mortality: the Australian Diabetes, Obesity, and Lifestyle (AusDiab) study. Diabetologia, 52(3):415-24.
- **Carluccio E, Biagioli P, Alunni G, Murrone A, Zuchi C, Biscottini E, et al. (2012).** Improvement of myocardial performance (Tei) index closely reflects intrinsic improvement of cardiac function: assessment in revascularized hibernating myocardium. Echocardiography, 29(3):298-306.
- **Ceyhan K, Kadi H, Koç F, Celik A, Oztürk A and Onalan O. (2012).** Longitudinal left ventricular function in normotensive prediabetics: a tissue Doppler and strain/strain rate echocardiography study. J Am Soc Echocardiogr, 25(3):349-56.
- **Cheng YJ, Gregg EW, Geiss LS, Imperatore G, Williams DE, Zhang X, et al. (2009):** Association of A1C and fasting plasma glucose levels with diabetic retinopathy prevalence in the U.S. population: Implications for diabetes diagnostic thresholds. Diabetes Care, 32(11):2027-32.
- **Møller JE, Søndergaard E, Poulsen SH and Egstrup K. (2001).** The Doppler echocardiographic myocardial performance index predicts left-ventricular dilation and cardiac death after myocardial infarction. Cardiology, 95:105–111.
- **Shimabukuro M, Higa N, Asahi T, Yamakawa K, Oshiro Y, Higa M, et al. (2011).** Impaired glucose tolerance, but not impaired fasting glucose, underlies left ventricular diastolic dysfunction. Diabetes Care, 34(3):686-90.
- **Stahrenberg R, Edelmann F, Mende M, Kockskmper A, Düngen HD, Scherer M, et al. (2010).** Association of glucose metabolism with diastolic function along the diabetic continuum. Diabetologia, 53(7):1331-40.
- **Kacker S, Saboo N, Jitender (2018).** Prediabetes: Pathogenesis and Adverse Outcome. Int J Med Res Prof,4(2):1-6.
- **Aroor AR, Mandavia CH, Sowers JR (2012):** Insulin resistance and heart failure: molecular mechanisms. Heart Fail Clin, 8:609–617.
- **Maisch B, Alter P, Pankuweit S (2011).** Diabetic cardiomyopathy—fact or fiction? Herz, 36:102–115.
- **Zhang X , Chen C (2012).** A new insight of mechanisms, diagnosis and treatment of diabetic cardiomyopathy. Endocrine, 41:398–409.
- **Edvardsen T, Helle-Valle T, Smiseth OA (2006).** Systolic dysfunction in heart failure with normal ejection. Prog Cardiovasc Dis, 49:207–214.
- **Peterson LR, Waggoner AD, Schechtman KB, Meyer T, Gropler RJ, Barzilai B, *et al*. (2004).** Alterations in left ventricular structure and function in young healthy obese women: Assessment by echocardiography and tissue Doppler imaging. J Am Coll Cardiol, 43:1399-404.
- **Sliem H , Nasr G (2011).** Left ventricular structure and function in prediabetic adults: relationship with

insulin resistance. J Cardiovasc Dis Res, 2011;2:23–28.

- **DeFronzo RA (2009).** From the triumvirate to the „ominous octet": a new paradigm for the treatment of type 2 diabetes mellitus. Clinical Diabetology, 10(3), 101-128.
- **Halban PA, Polonsky KS, Bowden DW, Hawkins MA, Ling C, Mather (2014).** β-cell failure in type 2 diabetes: postulated mechanisms and prospects for prevention and treatment. The Journal of Clinical Endocrinology & Metabolism, 99(6), 1983-1992.
- **Holman RR, Coleman RL, Chan JC, Chiasson JL, Feng H, Ge J, et al. (2017).** Effects of acarbose on cardiovascular and diabetes outcomes in patients with coronary heart disease and impaired glucose tolerance (ACE): a randomised, double-blind, placebo-controlled trial. The lancet Diabetes & endocrinology, 5(11), 877-886.
- **Huang Y, Cai X, Mai W, Li M, and Hu Y (2016).** Association between prediabetes and risk of cardiovascular disease and all cause mortality: systematic review and meta-analysis. Bmj, 355.
- **Jiang Y, Owei I, Wan J, Ebenibo S, and Dagogo-Jack S (2016).** Adiponectin levels predict prediabetes risk: the Pathobiology of Prediabetes in A Biracial Cohort (POP-ABC) study. BMJ Open Diabetes Research and Care, 4(1), e000194.
- **Mather KZ, Funahashi T, Matsuzawa Y, Edelstein S, Bray GA, Kahn SE, et al. (2008).** Adiponectin, change in adiponectin, and progression to diabetes in the Diabetes Prevention Program. Diabetes, 57(4), 980-986.
- **Nyenwe EA and Dagogo-Jack S (2011).** Metabolic syndrome, prediabetes and the science of primary prevention. Minerva endocrinologica, 36(2), 129-145.
- **Stacey RB, Leaverton PE, Schocken DD, Peregoy JA and Bertoni AG (2015).** Prediabetes and the association with unrecognized myocardial infarction in the multi-ethnic study of atherosclerosis. American heart journal, 170(5), 923-928.
- **von Toerne C, Huth C, de Las Heras Gala T, Kronenberg F, Herder C, Koenig W, et al. (2016).** MASP1, THBS1, GPLD1 and ApoA-IV are novel biomarkers associated with prediabetes: the KORA F4 study. Diabetologia, 59(9), 1882-1892.
- **Wang J, Liu L, Zhou Y, Wang C, Hu H, Hoff K, et al. (2014).** Increased fasting glucose and the prevalence of arterial stiffness: a cross-sectional study in Chinese adults. Neurological research, 36(5), 427-433.