Short Communication

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2024.54.008616

# Dipeptidyl Peptidase-4, Heart Failure and Obesity: Current Status and Perspective

**Carmine Finelli[1]* and Simone Dal Sasso[2]**

[1]*Department of Internal Medicine, Italy*

[2]*Independent Researcher, Italy*

***Corresponding author:** Carmine Finelli, Department of Internal Medicine, ASL Napoli 3 Sud, Via di Marconi, 66, 80035 Torre del Greco (Napoli), Italy

**ARTICLE INFO**

**Received:** January 22, 2024

**Published:** February 07, 2024

**Citation:** Carmine Finelli and Simone Dal Sasso. Dipeptidyl Peptidase-4, Heart Failure and Obesity: Current Status and Perspective. Biomed J Sci & Tech Res 54(5)-2024. BJSTR. MS.ID.008616.

**ABSTRACT**

**Abbreviations:** LV: left Ventricular; WD: Western Diet; IR: Insulin Resistance; TGF: Transforming Growth Factor; GIP: Gastric Inhibitory Polypeptide; NAFLD: Nonalcoholic Fatty Liver Disease; DD: Diastolic Dysfunction

## Short Communication

Given that obesity increases the amount of blood that must be supplied to peripheral tissue, it is linked to a higher chronic cardiac workload. The increased demands of increased lean body mass are primarily responsible for the high cardiac output, which is sustained by an increase in ventricular mass, a high normal heart rate, and an increased stroke volume [1]. An increase in non-muscular tissue, which contributes to the development of electrical abnormalities, heart failure, and sudden death, is also implied by an increase in left ventricular (LV) mass [1]. One of the main risk factors for heart failure is obesity itself. The variable degrees of systolic and diastolic dysfunction linked to obesity-related left ventricular hypertrophy are difficult to identify with conventional techniques, but they may be curable with appropriate, stable, moderate weight loss [1]. A high-fat/high-fructose Western diet (WD) has been associated with an increase in heart disease and obesity, especially diastolic dysfunction, which is a feature of early obesity and metabolic cardiomyopathy [2]. Growing research indicates that oxidative stress, fibrosis, and inflammation play a part in the pathophysiology of metabolic cardiomyopathy [2]. Patients with obesity, heart failure, and insulin resistance (IR) have been found to have elevated levels of the circulating exopeptidase dipeptidyl peptidase-4 (DPP-4), in their plasma [2]. Myocardial fibrosis brought on by obesity may result in diastolic dysfunction and eventually heart failure [3]. The pathophysiology of obesity-induced myocardial fibrosis may involve the activation of the transforming growth factor (TGF)-βl and its downstream Smad2/3 pathways [3]. The antidiabetic dipeptidyl peptidase 4 inhibitors (DPP4i) may have an impact on these pathways [3].

DPP-4 is a serine protease that quickly inactivates glucose-dependent insulinotropic polypeptide, glucagon-like peptide-1, and incretin peptides to control glycemia and postprandial islet hormone secretion [4]. By modifying the activity of hormones such as glucagon-like peptide (GLP)-1 and gastric inhibitory polypeptide (GIP), DPP4 controls blood glucose levels. In order to maintain balanced glucose levels, these hormones increase the production of insulin and reduce the synthesis of glucagon. Moreover, several stress-induced responses have led to the identification of DPP4 as a possible contributor to cardiovascular disease. In the context of nonalcoholic fatty liver disease

(NAFLD), obesity, and type 2 diabetes (T2D), DPP-4 also has nonglycemic effects by regulating the progression of inflammation [4]. Direct interactions between proteins may have a greater influence over this regulation of inflammation thandoes catalytic activity. The development of metabolic dysregulation may be influenced by the immune system's chronic subclinical activation brought on by an inability to resolve inflammation [4]. DPP4 thus demonstrates a wide range of effects that can impact the development of metabolic disease through both its cleavage and regulation of the bioactivity of peptide hormones as well as its impact on inflammation [4]. Moreover, DPP-4 inhibitors' long-term effects on blood pressure, cardiovascular, and renal health are still up for debate. It was suggested that long-term DPP4 inhibitor treatment may be harmful in certain genetic backgrounds and provide an animal model to investigate the mechanisms underlying DPP4 inhibitor-induced pathological conditions and test preventative measures [5].

Future cardiovascular events are predicted by diastolic dysfunction (DD), a primary defect in heart failure with preserved ejection fraction and a hallmark of obesity [6]. It reported that linagliptin, a dipeptidyl peptidase-4 inhibitor, in Zucker Obese rats, a genetic model of obesity and hypertension, improved DD [6]. Therefore, linagliptin's suppression of DPP-4 activity reverses WD-induced DD, potentially through interfering with TRAF3IP2 expression and the inflammatory signaling it triggers [6]. Because DPP4 plays a crucial role in the regulation of glucose, DPP-4 inhibitors have become attractive therapeutic options for the management of type-2 diabetes [7,8]. In clinical trials, these inhibitors have demonstrated improvements in glycated hemoglobin levels and effectively lower blood sugar levels by targeting the DPP-4 enzyme, all without worsening hypoglycemia or causing weight gain. Nonetheless, there has been discussion and investigation regarding the impact of DPP-4 inhibitors on cardiovascular health [9]. One common comorbidity in patients with diabetes mellitus is heart failure. DPP-4 inhibitor-treated diabetes mellitus patients may or may not have the same heart failure risk factors as the general population [10]. According to preliminary research, there may be cardiovascular benefits because of improved metabolic parameters, such as decreased inflammation and weight gain.

## Disclosure Statement

The authors declare that there are no conflicts of interest.

## References

1. Contaldo F, Pasanisi F, Finelli C, de Simone G (2002) Obesity, heart failure and sudden death. Nutr Metab Cardiovasc Dis 12(4): 190-197.
2. Bostick B, Habibi J, Ma L, Aroor M, Nathan R, et al. (2014) Dipeptidyl peptidase inhibition prevents diastolic dysfunction and reduces myocardial fibrosis in a mouse model of Western diet induced obesity. Metabolism 63(8): 1000-1011.
3. Hong SK, Choo EH, Ihm SH, Chang K, Seung KB, et al. (2017) Dipeptidyl peptidase 4 inhibitor attenuates obesity-induced myocardial fibrosis by inhibiting transforming growth factor-βl and Smad2/3 pathways in high-fat diet-induced obesity rat model. Metabolism 76: 42-55.
4. Trzaskalski NA, Fadzeyeva E, Mulvihill EE (2020) Dipeptidyl Peptidase-4 at the Interface Between Inflammation and Metabolism. Clin Med Insights Endocrinol Diabetes13: 1179551420912972.
5. Jackson EK, Mi Z, Gillespie DG, Cheng D, Tofovic SP, et al. (2021) Long-Term Dipeptidyl Peptidase 4 Inhibition Worsens Hypertension and Renal and Cardiac Abnormalities in Obese Spontaneously Hypertensive Heart Failure Rats. J Am Heart Assoc 10(6): e020088.
6. Aroor AR, Habibi J, Kandikattu HK, Mona GK, Brady B, et al. Dipeptidyl peptidase-4 (DPP-4) inhibition with linagliptin reduces western diet-induced myocardial TRAF3IP2 expression, inflammation, and fibrosis in female mice. Cardiovasc Diabetol 16(1): 61.
7. Evans M, Kuodi P, Akunna CJ, Nicole M, Morten D, et al. (2023) Cardiovascular and renal outcomes of GLP-1 receptor agonists vs. DPP-4 inhibitors and basal insulin in type 2 diabetes mellitus: A systematic review and meta-analysis. Diab Vasc Dis Res 20(6): 14791641231221740.
8. Sivaraman SA, Sabareesh V (2024) An Update on Dipeptidyl Peptidase-IV Inhibiting Peptides. Curr Protein Pept Sci.
9. Tan X, Liang Y, Rajpura JR, Larisa Y, Josh N, et al. (2023) Once-weekly glucagon-like peptide-1 receptor agonists vs dipeptidyl peptidase-4 inhibitors: cardiovascular effects in people with diabetes and cardiovascular disease. Cardiovasc Diabetol 22(1): 319.
10. Matsuzaki A, Momo K, Watanabe A, Hiromi K, Yuka K, et al. (2023) Risk Assessment for Heart Failure in Patients with Type 2 Diabetes Mellitus Treated with Dipeptidyl Peptidase 4 Inhibitor Using a Large Claims Dataset. Biol Pharm Bull 46(9): 1217-1222.

**ISSN: 2574-1241**

DOI: 10.26717/BJSTR.2024.54.008616

**Carmine Finelli.** Biomed J Sci & Tech Res



**Submission Link**: https://biomedres.us/submit-manuscript.php