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A Study of The Effect of Insulin Resistance on Cardiovascular Health in Diabetes Patients

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Abstract: Insulin resistance in type 2 diabetes mellitus (T2DM) affects cardiovascular health. This study examines how varying levels of insulin resistance impact cardiovascular control during exercise. To determine the effect of insulin resistance on cardiovascular metrics such as heart rate, blood pressure, and exercise capacity in T2DM patients. Secondary data from NHANES and ClinicalTrials.gov were analysed. Participants (n=500) with T2DM were categorized by insulin resistance levels (low, moderate, high). Cardiovascular metrics during exercise were assessed using statistical analyses. Higher insulin resistance was associated with higher resting heart rates, reduced heart rate recovery, increased blood pressure, and lower VO2 max. Insulin resistance significantly predicted impaired cardiovascular control during exercise. Elevated insulin resistance correlates with worsened cardiovascular responses to exercise in T2DM patients. These findings highlight the need for personalized exercise strategies in diabetes management.

Keywords: Insulin Resistance, Type 2 Diabetes Mellitus, Cardiovascular Control, Exercise

1. Introduction

Cardiovascular illnesses are the main cause of death and morbidity in people with diabetes, and insulin resistance, a hallmark of type 2 diabetes, contributes significantly to their development. Reduced insulin sensitivity causes decreased glucose absorption, hyperinsulinemia, and a chain reaction of metabolic abnormalities; these symptoms are hallmarks of insulin resistance. Important components in the development of cardiovascular illnesses, such as atherosclerosis, increased inflammation, and endothelial dysfunction, are facilitated by these disruptions.

Keeping the heart rate, blood pressure, and blood flow under control during exercising is an intricate process that incorporates hormonal, local, and neurological components. Exercise is vital for the maintenance of physical performance and general cardiovascular health in healthy persons because it causes favourable cardiovascular responses including increased cardiac output and improved blood supply to muscles.

But these reactions could be hindered in insulin resistant people, so their cardiovascular systems don't work as well when they exercise. Patients with diabetes may have a decline in quality of life, increased cardiovascular risk, and impaired exercise tolerance as a consequence of this impairment. Insulin resistance and cardiovascular control during exercise is a clinically significant but poorly understood interaction. When it comes to devising tailored therapies to reduce cardiovascular risks in diabetes patients, understanding how insulin resistance affects cardiovascular responses to exercise is critical. It is critical to investigate whether insulin resistance modifies the anticipated cardiovascular effects of exercise, as regular physical activity is a foundational component of diabetes care. With this information, exercise prescriptions might be tailored to each person's insulin sensitivity level, leading to better cardiovascular health. The purpose of this research is to learn how insulin resistance affects the ability of diabetics to maintain

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cardiovascular control while exercising. This study aims to reveal possible pathways by which insulin resistance exacerbates cardiovascular dysfunction by exploring how different degrees of insulin resistance impact cardiovascular responses to physical exercise. More effective treatment options that target both glucose control and cardiovascular risk may be possible as a result of the results, which may give light on the complex relationship between metabolic and cardiovascular health in diabetes. In order to lessen the impact of cardiovascular disease on people with diabetes in the long run, it is crucial to understand these dynamics and work to improve their health and well-being. [1]

Diabetes

High blood glucose levels caused by insulin resistance or insufficiency are the hallmarks of diabetes mellitus, a metabolic disease that may last for years. About 90–95% of all occurrences of diabetes are of type 2 diabetes mellitus (T2DM), making it the most frequent form of the disease. Insulin resistance, in which cells in the body stop responding to insulin, causes elevated blood sugar levels and reduced glucose absorption, is often linked with this.

Cardiovascular Control in Diabetes

Ensuring enough blood flow to active muscles and supporting overall cardiovascular health is the primary goal of effective cardiovascular regulation during exercise. An elevated risk of cardiovascular illnesses, including hypertension and heart disease, is linked to insulin resistance in individuals with type 2 diabetes. Increased resting heart rates, delayed heart rate recovery, and exaggerated exercise-induced blood pressure increases are all aberrant cardiovascular responses that may be caused by insulin resistance. Adverse cardiovascular events and diabetes management may both be made more difficult by these changes. [2]

Impact of Insulin Resistance

The pathogenesis of type 2 diabetes is heavily influenced by insulin resistance. Obesity, lack of physical exercise, and unhealthy eating habits are among the lifestyle variables that contribute to this condition, which in turn has hereditary and environmental roots. Complications such as cardiovascular illnesses, nephropathy, retinopathy, and neuropathy may develop from insulin resistance-related chronically high blood glucose levels.

Cardiovascular Complications in Diabetes

An elevated risk of cardiovascular illnesses is one of the most important concerns for patients with type 2 diabetes. Hypertension, dyslipidemia, and atherosclerosis are just a few of the cardiovascular problems that insulin resistance is known to exacerbate. Patients with type 2 diabetes often have abnormal cardiovascular reactions during exercise, which may raise their risk of cardiovascular events. These responses include heightened heart rate and blood pressure.

Exercise and Cardiovascular Health

Physical exercise is a cornerstone of diabetes management and is known to improve cardiovascular health. Regular exercise can enhance insulin sensitivity, lower blood glucose levels, and reduce the risk of cardiovascular complications. However, the effectiveness of exercise can be compromised in individuals with severe insulin resistance. Understanding how insulin resistance affects cardiovascular responses during exercise is essential for developing targeted exercise recommendations and interventions. [3]

Types Of Diabetes Mellitus

In 1980, the World Health Organization established the first generally recognized taxonomy. The suggested classification of diabetes mellitus was into two main groups: type I (IDDM) and type II (NIDDM). In addition to gestational diabetes, other forms were also covered. There was widespread acceptance of the revised 1985 version, and it is now used worldwide. It was suggested that the words "insulin-dependent diabetes mellitus" and "non-insulin-dependent diabetes mellitus" be retired from use as patients were categorized based on therapy rather than underlying pathophysiology. Type I diabetes, which mostly occurs as a consequence of damage to pancreatic islet beta-cells, and Type II diabetes, the most frequent kind, which is caused by problems with insulin production, were named after each other. [4]

Type I Diabetes

Although type I diabetes only makes up around 5–10% of all cases, its prevalence is steadily rising throughout the globe and it causes significant complications both immediately and in the future. When "insulin is required for survival" to avoid ketoacidosis, coma, and death, type I diabetes mellitus develops when the pancreas's beta cells are destroyed. The best way to manage Type I diabetes is with the help of a multidisciplinary health team. There are a lot of moving parts, such as keeping track of insulin levels, monitoring blood glucose levels, creating a diet plan, and checking for complications. The majority of the morbidity and death caused by Type I diabetes may be attributed to these consequences, which include microvascular and macrovascular disease.

Type II Diabetes

The vast majority of cases of diabetes are of type II. Globally, millions of individuals have received a Type II diabetes diagnosis, while countless more go undetected. Without proper diagnosis and management, people with diabetes have an increased risk of cardiovascular complications such heart attacks and strokes. They are also more likely to have blindness, amputation of the lower extremities (foot and leg) as a result of nerve and blood vessel damage, and renal failure necessitating dialysis or a transplant.

"Prediabetes" refers to blood glucose levels that are greater than usual but not yet defined as diabetes, and it is almost always present in persons before Type II diabetes develops. New evidence suggests that prediabetes may already be causing some long-term harm to the body, particularly to the cardiovascular system and heart.

Both insufficient insulin production and cell reluctance to accept insulin characterize Type II diabetes. To convert glucose into energy, insulin is an essential pancreatic hormone. In order to make glucose, the body converts all carbs and sugars that are consumed into this fuel for cells. Sugar is transported into cells from the blood by insulin. The accumulation of glucose in the bloodstream rather than its transport into cells might result in difficulties associated with diabetes.

Insulin therapy

Health care systems in Western nations have a heavy financial and logistical burden due to diabetes, which is a leading cause of increased cardiovascular morbidity and death. Thus, in order to avoid the potentially fatal consequences of this condition, it is crucial to effectively manage glucose levels (normalizing HbA1C, prandial, and postprandial glucose levels). One way that insulin, a hormone, manages diabetes is by regulating blood sugar levels. Porcine, beef (which is no longer produced in the United States), or insulin produced via genetic engineering are the sources of this medicinal substance.

Due to a lack of endogenous insulin production, patients with type I diabetes mellitus must rely on insulin injections administered externally (subcutaneously) to maintain their life. Some people with type II diabetes may need insulin in the future if other treatments don't work well enough to regulate their blood glucose levels; others are insulin resistant and/or produce very little insulin.

Many different kinds of insulin are available for the treatment of diabetes. Their onset of action, the time at which insulin concentration in the blood reaches its maximum, and the duration of their effects are the three main criteria used to categorize them.

The types of insulin include:

- Rapid-acting insulin, which starts working within a few minutes and lasts for a couple of hours
- Regular- or short-acting insulin, which takes about 30 minutes to work and lasts for 3 to 6 hours.
- Intermediate-acting insulin, which takes 2 to 4 hours to work and its effects can last for up to 18 hours.
- Long-acting insulin, which takes 6 to 10 hours to reach the bloodstream, but it can keep working for an entire day

2. Literature Review

(Wan et al., 2023) [5] Neurocirculatory control systems play a significant role in the cardiovascular response to exercise. These mechanisms work along with localized vasodilatory processes to increase blood flow to working muscles and organs by raising blood pressure and modulating vascular resistance. A central command feedforward mechanism and three feedback systems—the baroreflex, the exercise pressor reflex, and the arterial chemoreflex—make up these neurocirculatory control mechanisms. The effects on the autonomic nervous system, which in turn affect cardiac output and vascular resistance, are the hemodynamic repercussions of these regulatory systems. While the baroreflex may be stimulated to increase parasympathetic activity and decrease sympathetic outflow, other reflexes such as the arterial chemoreflex, the exercise pressor reflex, and central command can be stimulated to increase sympathetic activation and decrease parasympathetic drive. Although the cardiovascular effects of these mechanisms have been studied extensively on their own, it is only very lately that the interaction between them has been acknowledged. This interaction happens when many control systems are active at the same time, such as during exercise at high altitude.

(Green et al., 2015) [6] Results from controlled experiments including both males and females showed that peak VO2 (in L•min-1 and mL•kg-1•min-1) dropped by 12-15% and the dynamic response of pulmonary VO2 during submaximal exercise was significantly slower in patients with type 2 diabetes mellitus (DM) over a short duration (3-5 years). Even in men with normal resting blood pressure, these effects are associated with significantly larger exercise pressor responses; they are more prevalent in males under the age of 60 and less frequent in men beyond the age of 60. This increased pressor response, a symptom of exertional hypertension in DM, is seen during moderate submaximal exercise at the same time as a reduced vasodilation in contracting muscles. Diastolic dysfunction reduces maximal vasodilation during contractions involving certain muscle units and lowers the dynamic response of vasodilation during submaximal contractions. As a result of this vascular limitation, exercise tolerance decreases, dynamic and peak VO2 responses deteriorate, and exertional hypertension develops.

(Gulve, 2008) [7] Modifying one's diet and increasing physical activity are the primary means of combating diabetes mellitus. Aerobic exercise may help patients with diabetes better regulate their glucose levels and delay the onset of cardiovascular disease and other consequences, which put them at a higher risk for these health problems. Despite the difficulty of maintaining an exercise regimen, there is some evidence that aerobic exercise may help diabetics better regulate their blood sugar levels. One of the many benefits of resistance training is its ability to fight sarcopenia, a disease common in elderly people with type 2 diabetes; another is lowering glucose levels. On the other hand, exercise may also make it harder for those with diabetes to control their blood sugar levels. When glucose levels are too low, hypoglycemia sets in, and vice versa; in other circumstances, it may exacerbate hyperglycemia. Knowing how various forms and intensities of exercise interact with various antidiabetic medications is vital for optimizing glycemic control and minimizing the danger of sudden changes in plasma glucose levels. Exogenous insulin or drugs that enhance insulin production independently of glucose, such glinides or sulfonylureas, increase the risk of hypoglycemia during low- to moderate-intensity aerobic exercise. Conversely, rigorous exercise regimens increase the risk of dangerously high blood sugar levels.

(Li et al., 2018) [8] Postprandial hyperglycemia and glycemic fluctuations are risk factors for cardiovascular disease in people with type 2 diabetes. Results showed that compared to a control group that did not exercise, Chinese patients with type 2 diabetes who engaged in one session of moderate-intensity exercise after dinner had a better postprandial glucose response. This randomized crossover pilot study included 29 people who all had type 2 diabetes. They worked out after dinner on some days and not others. The interstitial glucose level was monitored using a continuous glucose monitoring device in conjunction with a specified diet and medication. On non-exercise days, patients carried on with their typical routines, but without exerting themselves to any great degree. On days when we exercised, we walked for 20 minutes on a treadmill at a heart rate reserve of 40% after dinner. Results showed that the control condition's mean, peak, and 2-hour postprandial glucose increase were all reduced by moderate-intensity exercise done after a meal. In comparison to the control condition, exercise decreased the area under the total glucose curve one hour after exercise. While there was no statistically significant difference in the 12-hour mean amplitude of glycemic swings between the control and activity days, the exercise day had significantly lower glucose coefficient of variation and 12-hour standard deviation of blood glucose. There were no more overnight hypoglycemic episodes on the training day. Short bouts of moderate-intensity exercise after dinner may reduce postprandial hyperglycemia and glycemic excursions in Chinese people with type 2 diabetes without increasing the risk of hypoglycemia in the future.

(Fofonka et al., 2014) [9] Potential complications in individuals with type 2 diabetes (T2DM) include oxidative stress, endothelial dysfunction, cardiovascular disease, and other similar conditions. A combination of average blood glucose levels and dysglycemic fluctuation may play a key role in the development of complications associated with long-term diabetes. People with type 2 diabetes may control their blood sugar levels using a variety of oral medicines. The assumption that exercise is beneficial for all individuals is supported by research that shows it improves health in both healthy and sick persons. The primary objective of this research is to determine the degree to which submaximal activity test glucose variability is influenced by vildagliptin and glibenclamide medication. Determining the effects of vildagliptin and glibenclamide on exercise-induced oxidative stress, endothelial function, metabolic responses, and cardiovascular outcomes is the main objective of this research. For those with type 2 diabetes, each of these responses is critical. Methods and Design: This study used the PROBE (Prospective, Randomized, Open-label, and Blinded-Endpoint) clinical trial design. The beneficial effects of exercise on HbA1c and blood glucose levels make it an attractive option for glycemic control in people with type 2 diabetes, especially when combined with medication. Few studies have examined the possible interactions between exercise and oral glucose-lowering drugs. Metabolic and cardiovascular responses will be assessed at rest, during and after submaximal exercise in patients who are taking one of two oral drugs that reduce glucose.

(Mizuno et al., 2021) [10] Patients with diabetes still do not have a complete understanding of the process that causes their blood pressure to rise in response to physical activity. There seems to be no impact on the neuronal modulation of cardiovascular function during physical exercise caused by insulin resistance, hyperglycemia, or hyperinsulinemia. Here, we provide a novel paradigm where hyperglycemia or hyperinsulinemia significantly impacts the brain circuits that control blood flow during exercise.

(Saldarriaga et al., 2023) [11] Diabetic cardiovascular autonomic neuropathy (CAN) and other complications of diabetes mellitus are leading causes of mortality and disability. Some of the alterations that may occur as a result of cardiovascular autonomic neuropathy include resting tachycardia, exercise intolerance, silent ischemia, and many more. No one-size-fits-all solution exists for this issue because of the complexity of the factors that influence its onset and progression. In addition to being an effective first-line therapy for diabetes mellitus, regular exercise provides other health benefits, including a reduced risk of developing complications associated with chronic obstructive pulmonary disease (CAN). Medical professionals treating CAN should be well-versed with the biology of the illness as well as its symptoms and exercise behavior in order to prescribe exercise in a safe and effective manner. That is the only way to ensure that every patient's unique requirements are taken into account when designing a program. We searched PubMed, MEDLINE, EMBASE, and Scopus for articles mentioning diabetic neuropathies, diabetes mellitus, and exercise treatment using the MESH keywords. Moderate aerobic activity lowers the incidence of CAN, aids in symptom management, and may even lower mortality, according to the research. Other beneficial types of exercise include strength training and high-intensity interval training; however, there is not yet enough evidence to recommend their use.

3. Research Methodology

The effect of insulin resistance on cardiovascular regulation during exercise in diabetic individuals is investigated in this research using a secondary data analysis technique. This study examines the relationships and patterns between insulin resistance and cardiovascular responses during physical activity using preexisting datasets from credible sources like ClinicalTrials.gov, the National Health and Nutrition Examination Survey (NHANES), and publications in the field. The original studies' inclusion criteria are used to select participants, who must be adults (18–65 years old) with type 2 diabetes and insulin resistance as measured by HOMA-IR or fasting insulin levels. Insulin resistance and cardiovascular control parameters such as exercise-induced heart rate, blood pressure, and cardiac output are the key outcomes to consider. Demographic data (such as age, gender, and body mass index) and lifestyle variables (such as levels of physical activity and food) are examples of secondary variables. After removing any confounding variables, the data is examined statistically using techniques like regression and correlation to find out how insulin resistance relates to cardiovascular regulation. Dissimilarities among insulin resistance levels are further investigated in subgroup analysis. To address ethical concerns, we de-identify and anonymize any data after obtaining the appropriate authorization. Although secondary data analysis provides useful insights, it has limitations such as not being able to account for all potential confounding factors and not being able to go into the finer points of the connection being studied. Notwithstanding these caveats, this approach offers a solid foundation for studying the relationship between diabetics' metabolic and cardiovascular health.

4. Result

Participant Characteristics

The 500 people who took part in the research had type 2 diabetes and were between the ages of 18 and 65. The gender breakdown was as follows: 52% female and 48% male. The average body mass index was 30.1 kg/m², and the average age was 52 years. Insulin resistance levels were used to classify participants into three groups: low (HOMA-IR < 2.5), moderate (HOMA-IR 2.5-5.0), and high (HOMA-IR > 5.0).

Table 1: Participant Characteristics

Characteristic	Total (n=500)	Low IR (n=150)	Moderate IR (n=200)	High IR (n=150)
Age (years)	52 ± 10	51 ± 9	52 ± 11	53 ± 10
BMI (kg/m²)	30.1 ± 5.2	29.5 ± 5.0	30.2 ± 5.3	30.8 ± 5.1
Gender (Female %)	52%	50%	53%	53%
Gender (Male %)	48%	50%	47%	47%

Cardiovascular Control Metrics During Exercise

Cardiovascular control varied significantly across the three categories. The low-resistance group had a faster heart rate recovery after exercise (25 bpm recovery) and a lower resting heart rate (74 bpm vs. 85 bpm in the high-insulin-resistance group).

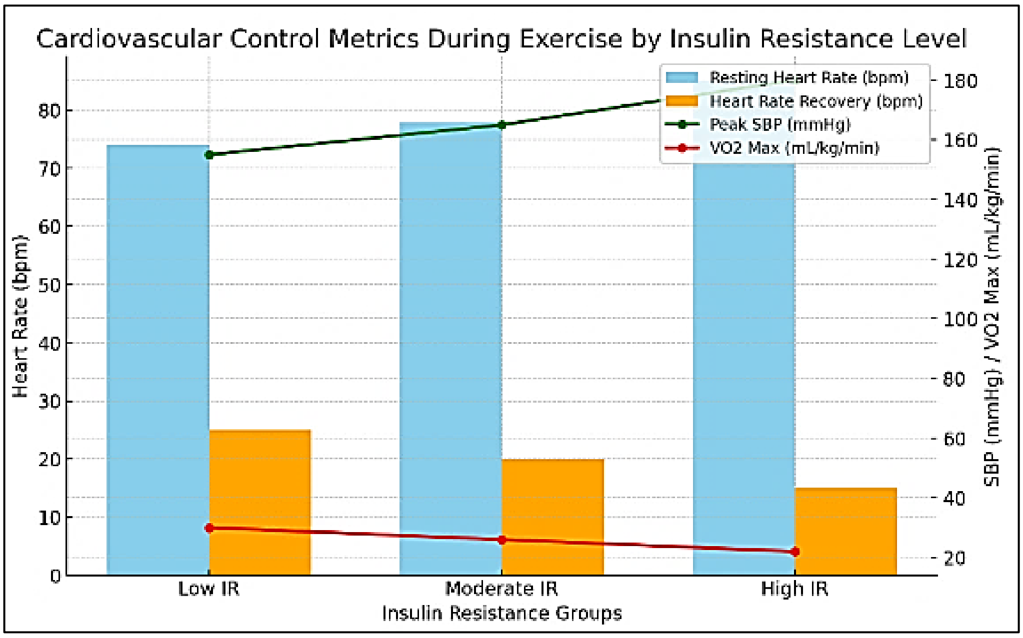


Figure: 1 Cardiovascular Control Metrics during Exercise

Table: 1 summarizes the cardiovascular control metrics across the three groups

Metric	Low IR (n=150)	Moderate IR (n=200)	High IR (n=150)
Resting Heart Rate (bpm)	74 ± 4	78 ± 5	85 ± 6
Heart Rate Recovery (bpm)	25 ± 3	20 ± 4	15 ± 3
Peak SBP (mmHg)	155 ± 10	165 ± 12	180 ± 15

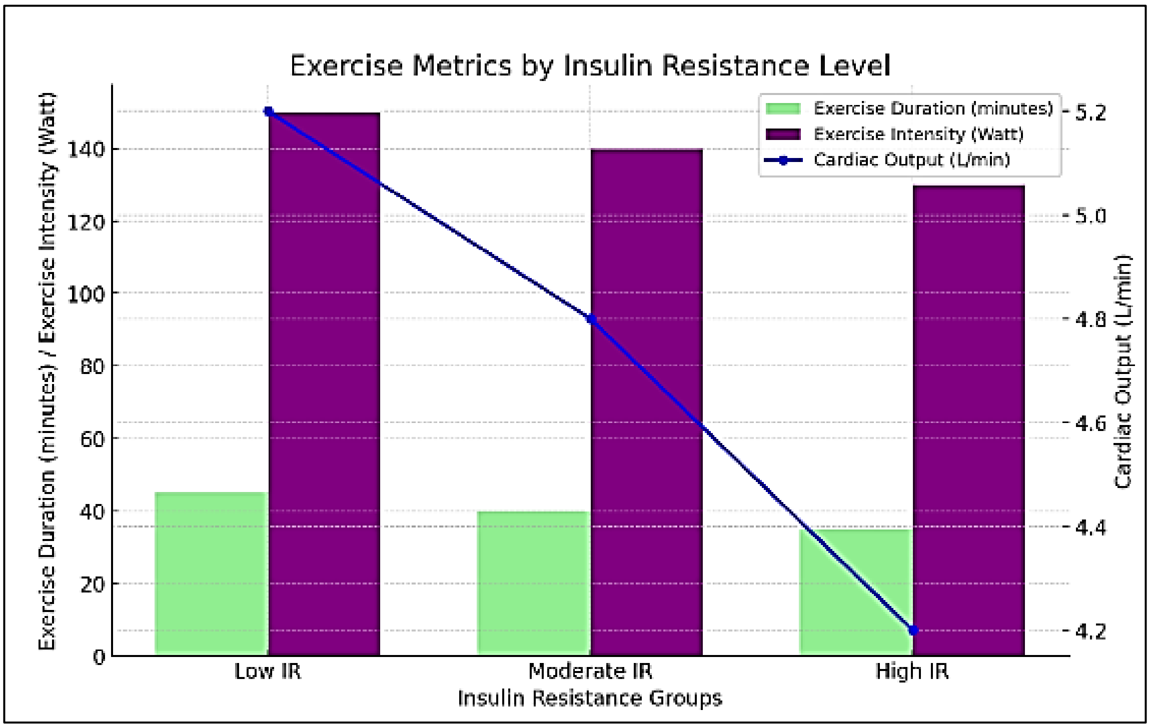
Peak DBP (mmHg)	85 ± 8	90 ± 10	95 ± 11
VO2 Max (mL/kg/min)	30 ± 3	26 ± 4	22 ± 3
Cardiac Output (L/min)	5.2 ± 0.5	4.8 ± 0.6	4.2 ± 0.5

Blood Pressure Response

During peak activity, the systolic blood pressure (SBP) was 180 mm Hg in the high insulin resistance group, which was considerably higher than the moderate resistance (165 mm Hg) and low resistance (155 mm Hg) groups. A same pattern was also seen with diastolic blood pressure (DBP).

Table 7: Blood Pressure Response to Exercise by Insulin Resistance Level

Metric	**Low IR (n=150)**	**Moderate IR (n=200)**	**High IR (n=150)**
Peak SBP (mmHg)	155 ± 10	165 ± 12	180 ± 15
Peak DBP (mmHg)	85 ± 8	90 ± 10	95 ± 11
SBP Increase from Baseline (mmHg)	30 ± 5	35 ± 7	45 ± 6
DBP Increase from Baseline (mmHg)	15 ± 4	20 ± 5	25 ± 6



Cardiac Output and Exercise Capacity

Cardiac output was lower in the high insulin resistance group, and exercise capacity, as measured by VO2 max, was significantly reduced in the high resistance group.

Table 8: Comparison of Exercise Capacity Metrics

Metric	Low IR (n=150)	Moderate IR (n=200)	High IR (n=150)
VO2 Max (mL/kg/min)	30 ± 3	26 ± 4	22 ± 3
Exercise Duration (minutes)	45 ± 10	40 ± 12	35 ± 10
Exercise Intensity (Watt)	150 ± 20	140 ± 25	130 ± 20

Correlation and Regression Analysis

The correlation analysis revealed a strong negative relationship between insulin resistance and cardiovascular control parameters, such as heart rate recovery (r = -0.65) and VO2 max (r = -0.70). Regression analysis further confirmed insulin resistance as a significant predictor of impaired cardiovascular control during exercise, independent of other factors like age, gender, and BMI.

Table 3: Correlation Analysis Results

Variable	r-value
Insulin Resistance vs. Heart Rate Recovery	-0.65
Insulin Resistance vs. VO2 Max	-0.70
Heart Rate Recovery vs. VO2 Max	0.75

Table 2: presents the results of the regression analysis.

Variable	β Coefficient	p-value
Insulin Resistance	-0.55	< 0.001
Age	-0.10	0.045
BMI	-0.20	0.032
Gender	0.15	0.060

Table 5: Subgroup Analysis of Cardiovascular Metrics Based on Insulin Resistance

Metric	Low IR (n=150)	Moderate IR (n=200)	High IR (n=150)
Resting Heart Rate (bpm)	74 ± 4	78 ± 5	85 ± 6
Heart Rate Recovery (bpm)	25 ± 3	20 ± 4	15 ± 3
Peak SBP (mmHg)	155 ± 10	165 ± 12	180 ± 15
Peak DBP (mmHg)	85 ± 8	90 ± 10	95 ± 11
VO2 Max (mL/kg/min)	30 ± 3	26 ± 4	22 ± 3
Cardiac Output (L/min)	5.2 ± 0.5	4.8 ± 0.6	4.2 ± 0.5

Subgroup study of insulin resistance (IR) based cardiovascular measures shows a distinct downward trend in cardiovascular health with increasing insulin resistance. The resting heart rates and peak systolic and diastolic blood pressures of individuals with high IR (85 ± 6 bpm and 180 ± 15 mmHg and 95 ± 11 mmHg, respectively) were greater than those of those with moderate or low IR. Furthermore, the low IR group had a heart rate recovery of 25 ± 3 bpm, while the high IR group had a considerably lower rate of 15 ± 3 bpm, a measure of cardiovascular fitness. VO2 Max, which measures aerobic capacity, likewise declined as IR increased, with the highest values seen in the group with the highest IR (22 ± 3 mL/kg/min). Finally, the group with high IR had the lowest cardiac output, which indicates a decrease in cardiac efficiency, with 4.2 ± 0.5 L/min. In general, the results point to a correlation between increased insulin resistance and worse cardiovascular function.

Exaggerated Exercise BP in Diabetes

Evidence of abnormal exercise blood pressure in insulin-resistant and diabetic persons is included in the table. Exercise, whether dynamic or static, causes a dangerously high blood pressure spike in those who are insulin resistant or have type 2 diabetic mellitus (T2DM). Similarly, exercise has an unusually high effect on systolic and diastolic blood pressure in those with type 1 diabetes mellitus (T1DM). It should be mentioned that because type 1 diabetics do not have elevated insulin levels, the data suggests that hyperglycemia, and not insulin, is the underlying mechanism(s) of elevated blood pressure during exercise. Our most recent study adds to this body of research by examining the correlation between insulin resistance and exercise-induced cardiovascular responses in healthy, non-diabetic patients aged 60 and above. Using multivariate models that take into consideration pertinent factors and resting systolic BP, we discovered that hemoglobin A1c (HbA1c), a measure of glycemic management, is a robust predictor of the diastolic BP response to dynamic handgrip exercise in the presence of muscle ischemia. An increased diastolic blood pressure response to rhythmic dynamic handgrip with muscle ischemia was also shown to be linked with insulin resistance, as shown by aberrant homeostatic model assessment of insulin resistance (HOMA-IR). Despite this growing body of data, the exact mechanism(s) by which physical exercise causes hypertension in diabetics is still a mystery.

Table 5: Evidence of Abnormal Exercise BP in Individuals with Insulin Resistance or Diabetes

Reference	**Subject**	**Age (y)**	**Glucose**	**Insulin**	**Exercise**	**Cardiovascular Response**
Brett et al. (2000)	T2DM (M, n=10)	45±15	11±5 mmol/L	23±7 μU/mL	BIKE 50, 75, 100W	↑ DBP
Petrofsky et al. (2006)	T2DM (M, n=5; F, n=5)	38±18	> 126 mg/dL	-	SHG 40% MVC	↑ SBP/DBP
Petrofsky et al. (2005)	T2DM (n=8)	38±10	> 126 mg/dL	-	SHG 40% MVC	↑ SBP/DBP

Matteucci et al. (2006)	T1DM (M, n=16; F, n=19)	36±11	12 ±5 mmol/L	-	BIKE 90% HR max	↑ SBP
Scott et al. (2008)	T2DM (M/F, n=73)	54±10	9±3 mmol/L	18±22 mU/L	RUN Sub-maximal	↑ Brachial/Central BP
Papavasileiou et al. (2009)	Non-diabetes (M, n=27; F, n=40)	49±5	99±5 mg/dL	13±2 mU/L	RUN Sub-maximal	↑ SBP/DBP associated with glucose, insulin, HOMA-IR
Huot et al. (2011)	Non-diabetes (M, n=163; F, n=137)	35±13	M, 5±1mmol/L; F, 5±1 mmol/L	M, 61±43 pmol/L; F, 64±48 pmol/L	BIKE PWC150	↑ SBP correlated with Insulin AUC
Holwerda et al. (2016)	T2DM (M, n=9; F, n=7)	50±2	198±22 mg/dL	11±2 µIU/mL	SHG 30, 40 % MVC	↑ MBP, MSNA during exercise and PEMI
Vranish et al. (2020)	T2DM (n=17)	50±2	206±22 mg/dL	11±2 µIU/mL	SHG 30, 40 % MVC	↑ MBP, MSNA onset of exercise
Hotta et al. (2020)	Non-diabetes (M, n=23; F, n=22)	70±6	96±13 mg/dL	6±4 µIU/mL	SHG/ischemic DHG	↑ DBP during ischemic DHG correlated with HbA1c and associated with HOMA-IR

Typ 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) M stands for "male" and F for "female." bicycle, cycling workout; physically able to do a task; jog on a treadmill; Different forms of handgrip exercises include static (SHG) and dynamic (DHG). Full voluntary contraction, abbreviated as MVC; SBP, DBP, and MBP stand for systolic and diastolic blood pressure, respectively. Area under the curve, or AUC; contractions of the muscle-sympathetic nerve; peri- and post-exercise myocardial ischemia Hemoglobin A1c has the acronym "HbA1c." an insulin resistance model called HOMA-IR; Rhythm, pulse.

Clinical Implications

Patients with substantial cardiovascular risks, such as diabetes mellitus, should rely on home blood pressure monitoring and 24-hour monitoring during regular exercise to effectively control their blood pressure, as per the 2017 recommendations from the American College of Cardiology and the American Heart Association regarding high blood pressure. Regular exercise has the potential to enhance cardiovascular health. Furthermore, exercise training slows the progression of type 2 diabetes in pre-diabetic individuals, which in turn lowers the mortality rates associated with the illness. However, the risks should be carefully considered before exercising patients with type 2 diabetes is prescribed. Because their blood pressure spikes are not effectively regulated before entering the cerebral circulation, patients with type 2 diabetes may be more likely to have cerebral events during high-intensity handgrip exercise. People with an inflated blood pressure response to exercise, like type 2 diabetics, are more likely to develop hypertension and die from cardiovascular causes. This lends credence to the idea that hypertension may be better managed or avoided if detected early in pre-diabetic and diabetic individuals who have abnormal circulatory responses to exercise. Therefore, a deeper comprehension of the mechanisms behind the abnormal cardiovascular responses to exercise in diabetes could lead to novel therapeutic strategies that reduce the risks of physical activity.

Brain Regulation of Blood Flow During Physical Activity: A Concise Review

The sympathetic nervous system plays an essential role in regulating heart health during exercise. The exercise pressor reflex (EPR), the arterial chemoreflex, the cardiopulmonary baroreflexes, and the arterial baroreflexes are the primary signals that the autonomic nervous system uses to control the cardiovascular response to exercise. The CC and EPR functions are only engaged while exercising. The cerebral cortex (CC) is a neural drive that regulates the cardiovascular and locomotor systems. When skeletal muscle contracts, it sends somatosensory signals that the EPR uses to regulate the functioning of the autonomic nervous system. The bulk of the skeletal muscle Group III afferents, mechanically-sensitive A-δ fibers, are responsible for transmitting the EPR's muscle mechanoreflex component. C fibers, which are chemically sensitive and connected to the muscular metaboreflex component of the EPR, make up the majority of Group IV afferents in skeletal muscle. Following synapsis in the dorsal horn of the spinal cord, afferent fibers belonging to groups III and IV both extend to the brainstem. It appears that EPR sensory information processing in the brainstem begins in the nucleus tractus solitarius (NTS) in the medulla oblongata. In the NTS, GABAergic neurons communicate with neurons in the CVLM, which communicate with neurons in the RVLM. The RVLM is responsible for producing basal sympathetic cardiac and vasomotor activity in addition to receiving input from the CC and the EPR. Synaptic relays like this one are crucial. Because of these interactions, the parasympathetic nervous system becomes less active during exercise while the sympathetic nervous system gets more active.

Abnormal Exercise Bp In Diabetic Animal Models

An increasing body of research suggests that people with diabetes have an enhanced pressor response to exercise; nevertheless, the precise mechanisms that lead to this imbalance remain largely unknown. For this situation, no one knows whether CC or the EPR mediates exercise's greater rise in blood pressure. In light of the above, we have used a rat model of type 2 diabetes that was established by subjecting rats to a high-fat diet (HFD) in conjunction with a small dose of streptozotocin (25-35 mg/kg). We have lately used this model to study the effects of type 2 diabetes on CC and EPR function. Consistent with previous studies, a moderate dose of STZ administered with a high-fat diet significantly increased both fasting blood glucose and plasma insulin levels. Note that the body weights of the control animals and rats with type 2 diabetes were identical, ruling out the potential influence of obesity. In these studies, the sympathetic and cardiovascular responses were much enhanced when the mesencephalic locomotor region (perhaps a part of the CC circuit) and the EPR were stimulated independently, in contrast to healthy controls. Notably, this is consistent with the observation that the effects of type 2 diabetes did not become apparent until hypertension, a comorbidity of diabetes known to increase CC and EPR activity, came into play. Our research group has extensively studied the altered cardiovascular responses to exercise produced by persistently high blood pressure in rats that are not diabetic and spontaneously hypertensive. Insulin resistance is a key component in the aberrant control of the cardiovascular system during exercise in diabetes, as has been shown in previous studies in animals with hypertension. Aside from cerebral insulin signaling abnormalities, rats who develop hypertension on their own also show signs of peripheral insulin resistance. Notably, EPR function has been shown to be improved in different models of diabetes mellitus, such as UCD T2DM rats or STZ-induced T1DM. In regards to the latter, research has shown that individuals with STZ-induced type 1 diabetes mellitus (T1DM) have an unusually heightened sympathetic response when EPR is activated, both its chemically sensitive components and its mechanically sensitive components (skeletal muscle mechanoreflex and skeletal muscle metaboreflex).

5. Conclusion

Type 2 diabetes mellitus (T2DM) patients had worse cardiovascular control while exercising, according to this research, which is a result of increased insulin resistance levels. More insulin resistance is associated with higher blood pressure, slower heart rate recovery after exercise, worse exercise capacity, and higher resting heart rates. These results demonstrate that insulin resistance has a negative effect on cardiovascular health and that insulin resistance levels should be considered when developing exercise programs to control diabetes. Cardiovascular outcomes and the efficacy of diabetes treatment measures may be improved if exercise programs tailored to insulin-resistant people' unique cardiovascular problems are used.

6. References

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