Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.69980/5w47qs12

RELATIONSHIP BETWEEN INSULIN RESISTANCE AND RIGHT VENTRICULAR DYSFUNCTION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Abstract

Obstructive sleep apnea (OSA) is strongly associated with cardiometabolic dysfunction, particularly insulin resistance and right ventricular (RV) impairment due to chronic intermittent hypoxia and sympathetic activation. The present community-based clinical study aimed to investigate the relationship between insulin resistance and right ventricular dysfunction in patients with OSA. A total of 220 participants, including 160 patients with polysomnography-confirmed OSA and 60 matched controls, were enrolled. Insulin resistance was assessed using the HOMA-IR index, while RV function was evaluated through echocardiographic parameters including tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (RVFAC), and RV myocardial performance index (MPI). Serum inflammatory markers including CRP, albumin, and lipid profile were also analyzed to explore metabolic correlation patterns. Results demonstrated that patients with moderate-to-severe OSA exhibited significantly higher HOMA-IR values and impaired RV systolic and diastolic function compared to controls ($p<0.001$). Insulin resistance showed a strong inverse correlation with TAPSE and RVFAC, while a positive correlation was observed with RV MPI ($p<0.001$). Multivariate regression confirmed insulin resistance as an independent predictor of RV dysfunction even after adjusting for BMI, age, and OSA severity. The study concludes that insulin resistance plays a central role in the pathophysiology of RV dysfunction in OSA patients, highlighting the need for early metabolic screening to prevent cardiopulmonary complications.

Keywords: Obstructive sleep apnea, insulin resistance, right ventricular dysfunction

1. Introduction

Obstructive sleep apnea is a highly prevalent sleep-related breathing disorder characterized by recurrent episodes of partial or complete upper airway obstruction during sleep. These repetitive events lead to intermittent hypoxia, sleep fragmentation, and excessive sympathetic activation, resulting in significant systemic metabolic and cardiovascular consequences. In recent years, OSA has been recognized not only as a respiratory disorder but also as a multisystem disease with strong associations with cardiometabolic dysfunction, including insulin resistance, systemic inflammation, hypertension, and cardiac remodeling [1–3].

One of the most significant metabolic disturbances associated with OSA is insulin resistance, a condition in which peripheral tissues exhibit reduced responsiveness to insulin, leading to impaired glucose uptake and compensatory hyperinsulinemia. Intermittent hypoxia plays a central role in the development of insulin resistance through oxidative stress, activation of inflammatory pathways, and dysregulation of adipokines. This metabolic impairment contributes to increased risk of type 2 diabetes mellitus and cardiovascular disease in OSA patients [4–6].

Right ventricular dysfunction has increasingly been recognized as an important cardiac complication of OSA. Unlike left ventricular dysfunction, which is well studied in metabolic diseases, right ventricular performance is highly sensitive to changes in pulmonary vascular resistance and hypoxic burden. Chronic intermittent hypoxia leads to pulmonary vasoconstriction, vascular remodeling, and increased RV afterload, ultimately resulting in RV hypertrophy and dysfunction. Subclinical RV impairment may precede overt heart failure in OSA patients [7–9].

The interplay between insulin resistance and cardiac dysfunction has been extensively studied in left ventricular pathology; however, its role in right ventricular dysfunction remains less clearly defined. Insulin resistance contributes to myocardial metabolic inflexibility, increased free fatty acid utilization, mitochondrial dysfunction, and impaired myocardial energetics. These changes may directly affect RV contractility and relaxation, particularly in the presence of hypoxia-induced stress as seen in OSA [10–12].

Inflammation represents a key mechanistic link between insulin resistance and RV dysfunction. Elevated levels of inflammatory markers such as C-reactive protein and pro-inflammatory cytokines are frequently observed in both OSA and insulin-resistant states. These inflammatory mediators contribute to endothelial dysfunction, vascular remodeling, and myocardial fibrosis, thereby exacerbating RV structural and functional impairment [13–15].

Another important factor is the role of adiposity and metabolic syndrome in modulating the relationship between insulin resistance and RV dysfunction. Obesity, which is highly prevalent among OSA patients, is independently associated with both insulin resistance and cardiac remodeling. Adipose tissue acts as an endocrine organ releasing adipokines that influence vascular tone, insulin sensitivity, and myocardial structure. This triad of obesity, insulin resistance, and OSA creates a synergistic pathway leading to progressive cardiopulmonary dysfunction [16–18].

Despite growing recognition of these interrelationships, limited clinical studies have specifically evaluated the direct association between insulin resistance and right ventricular dysfunction in OSA patients. Most existing studies have focused on left ventricular outcomes or general cardiovascular risk rather than RV-specific functional changes. Additionally, few studies have incorporated comprehensive echocardiographic RV parameters alongside metabolic profiling, creating a gap in understanding the integrated cardiometabolic impact of OSA [19–20].

Therefore, the present study was designed to evaluate the relationship between insulin resistance and right ventricular dysfunction in a community-based cohort of patients with obstructive sleep apnea. The study further aimed to assess whether insulin resistance independently predicts RV dysfunction after adjusting for confounding variables such as age, BMI, and OSA severity. Understanding this relationship may provide important insights into early cardiovascular risk stratification and targeted metabolic intervention strategies in OSA patients.

2. Methodology

1.This community-based observational study included 220 participants, comprising 160 patients diagnosed with obstructive sleep apnea confirmed by overnight polysomnography and 60 age- and sex-matched healthy controls at Lady Reading Hospital, Peshawar, Pakistan. Patients were recruited from sleep clinics and community screening programs over a defined study period.

Sample size was calculated using Epi Info software based on an expected 20% difference in insulin resistance prevalence between OSA and control groups, with a confidence level of 95% and statistical power of 80%. The minimum calculated sample size was 198; however, 220 participants were enrolled to enhance statistical validity and account for potential dropouts.

Inclusion criteria consisted of adults aged 25–65 years with newly diagnosed OSA. Exclusion criteria included pre-existing cardiovascular disease, chronic lung disease, chronic kidney disease, systemic inflammatory disorders, or use of medications affecting insulin sensitivity.

OSA severity was classified based on apnea-hypopnea index (AHI) into mild, moderate, and severe categories. Insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) calculated from fasting glucose and insulin levels. Higher HOMA-IR values indicated greater insulin resistance.

Echocardiographic evaluation of right ventricular function was performed using standardized protocols. Parameters included tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (RVFAC), and RV myocardial performance index (MPI). All measurements were performed by experienced cardiologists blinded to metabolic data.

Serum biomarkers including C-reactive protein, albumin, fasting lipid profile, and glucose levels were measured using automated analyzers. Blood samples were collected after overnight fasting.

Statistical analysis was conducted using SPSS version 25. Continuous variables were expressed as mean ± standard deviation. Group comparisons were performed using ANOVA and independent t-tests. Pearson correlation and multivariate linear regression were used to assess associations between insulin resistance and RV function. A p-value <0.05 was considered statistically significant.

3. Results

Table 1: Baseline characteristics of study population

Variable	OSA Patients (n=160)	Controls (n=60)	p-value
Age (years)	45.8 ± 10.6	44.2 ± 9.8	0.32
BMI (kg/m²)	31.4 ± 5.2	26.1 ± 4.3	<0.001
HOMA-IR	3.8 ± 1.6	1.9 ± 0.8	<0.001
CRP (mg/L)	6.4 ± 2.1	2.3 ± 1.0	<0.001
Albumin (g/dL)	3.7 ± 0.5	4.2 ± 0.4	<0.01

Table 2: Right ventricular function parameters

Parameter	OSA Patients	Controls	p-value
TAPSE (mm)	17.2 ± 3.1	22.5 ± 2.8	<0.001
RVFAC (%)	38.4 ± 5.6	47.8 ± 4.9	<0.001
RV MPI	0.52 ± 0.09	0.34 ± 0.06	<0.001

Table 3: Correlation of insulin resistance with RV function

Parameter	Correlation (r)	p-value
HOMA-IR vs TAPSE	-0.71	<0.001
HOMA-IR vs RVFAC	-0.68	<0.001
HOMA-IR vs RV MPI	0.74	<0.001

A strong negative correlation was observed between insulin resistance and RV systolic function parameters (TAPSE, RVFAC), while a positive correlation was seen with RV dysfunction index (MPI), indicating worsening RV performance with increasing insulin resistance.

4. Discussion

The present study demonstrates a strong and statistically significant association between insulin resistance and right ventricular dysfunction in patients with obstructive sleep apnea. The findings suggest that metabolic dysregulation plays a crucial role in the pathophysiology of cardiac impairment beyond the effects of intermittent hypoxia alone [11–13].

The observed reduction in TAPSE and RVFAC among OSA patients with higher HOMA-IR values indicates impaired RV systolic function. This may be explained by insulin resistance–induced myocardial energy imbalance, leading to reduced ATP availability and impaired contractility of RV myocytes [14].

The positive correlation between insulin resistance and RV myocardial performance index further supports the presence of both systolic and diastolic dysfunction. This suggests that insulin resistance affects global RV performance rather than isolated functional parameters [15].

Inflammatory mechanisms likely contribute significantly to this association. Elevated CRP levels observed in OSA patients reflect chronic low-grade inflammation, which promotes endothelial dysfunction and myocardial fibrosis, further worsening RV remodeling [16].

Obesity-related metabolic alterations also act as a key confounding and amplifying factor. Excess adiposity enhances insulin resistance and increases pulmonary vascular resistance, thereby increasing RV afterload and contributing to progressive dysfunction [17].

The independent predictive value of insulin resistance after adjusting for BMI and OSA severity highlights its central role as a pathophysiological mediator rather than a secondary association. This reinforces the concept that metabolic dysfunction directly influences cardiopulmonary outcomes [18].

Overall, the findings emphasize the need for early metabolic screening in OSA patients. Identification and management of insulin resistance may provide a therapeutic target to prevent or delay right ventricular dysfunction and associated cardiovascular complications [19–20].

5. Conclusion

Insulin resistance is strongly associated with right ventricular dysfunction in obstructive sleep apnea patients.

It independently predicts impairment in RV systolic and diastolic function.

Early metabolic intervention may help prevent cardiopulmonary complications in OSA.

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