Risk Factor Correlation with Diastolic Dysfunction and Pulmonary Hypertension in Patients with Chronic Cardiovascular Conditions

Emad Ali S. Al Khoufi [1,2]

1:Internal Medicine Department, College Of Medicine, King Faisal University Al Ahsa, Saudi Arabia,
2: King Faisal Graduate, Saudi Associate Professor, A Cardiolgy Consultant
Email : Ealkhoufi@kfu.edu.sa
ORCID:0000-0002-4427-8579 Scopus ID: 55923737700

KEYWORDS

Diastolic dysfunction, Pulmonary hypertension, Cardiovascular risk factors, Echocardiography, Saudi Arabia

ABSTRACT

Background: Diastolic dysfunction and pulmonary hypertension are significant contributors to cardiovascular morbidity and mortality. This study aimed to investigate the prevalence of these conditions and their associations with cardiovascular risk factors in a Saudi Arabian population.

Methods: A cross-sectional observational study was conducted on 246 patients with chronic cardiovascular conditions at a secondary care hospital in Hofuf, Saudi Arabia. Echocardiographic assessments were performed to evaluate left ventricular function, diastolic dysfunction, and pulmonary hypertension. Demographic data and cardiovascular risk factors were collected from medical records.

Results: Diastolic dysfunction was present in 68.3% of patients, with 43.1% showing Grade 1 dysfunction. Pulmonary hypertension was observed in 19.5% of patients. Strong associations were found between diastolic dysfunction and diabetes mellitus (84.1%, $p<0.001$), hypertension (76.0%, $p<0.001$), and dyslipidemia (72.4%, $p=0.02$). Pulmonary hypertension was significantly associated with atrial fibrillation (55.2% of AF patients had PH, $p<0.001$). Left atrial dilation was observed in 47.1% of patients.

Conclusions: This study reveals a high prevalence of diastolic dysfunction and pulmonary hypertension in patients with chronic cardiovascular conditions, strongly associated with traditional risk factors. The significant relationship between atrial fibrillation and pulmonary hypertension highlights the complex interplay between cardiac rhythm disturbances and pulmonary vascular disease. These findings emphasize the need for comprehensive cardiac evaluation and aggressive risk factor management in high-risk populations

Introduction:

Diastolic dysfunction and pulmonary hypertension (PH) significantly contribute to the global burden of cardiovascular disease (CVD), a primary cause of morbidity and mortality globally [1]. The aging demographic and the rising incidence of chronic cardiovascular ailments, including heart failure, coronary artery disease, hypertension, and valvular heart disease, have highlighted the intricate relationship between these conditions and their effects on patients' quality of life and clinical outcomes. Diastolic dysfunction, defined by the compromised

capacity of the left ventricle to relax and fill properly during diastole, frequently results in heart failure with preserved ejection fraction (HFpEF), a disease with few therapeutic alternatives and a bleak prognosis [3,4]. Pulmonary hypertension, characterized by high pressure in the pulmonary arteries, often coexists with diastolic dysfunction, worsening its clinical progression and resulting in considerable hemodynamic compromise and heightened mortality risk [5]. The two illnesses possess shared risk factors; however, their association remains inadequately comprehended, underscoring the want for additional research [3,6,7].The incidence of diastolic dysfunction and pulmonary hypertension is escalating concurrently with global trends of aging populations and a rise in risk factors, including obesity, diabetes, hypertension, and sedentary lifestyles. Diastolic dysfunction is widely acknowledged as a major contributor to heart failure hospitalizations, especially in older adults, as a rising percentage of heart failure patients are now diagnosed with HFpEF [9]. The pathophysiology of diastolic dysfunction encompasses various mechanisms, such as myocardial stiffness, impaired relaxation, and elevated ventricular filling pressures. However, its diagnosis is complicated by the subtlety of symptoms and the dependence on echocardiographic criteria, which may not fully represent the disease's spectrum. Individuals with diastolic dysfunction frequently exhibit exercise intolerance, tiredness, and dyspnea, which are nonspecific symptoms that coincide with other illnesses, hence impeding prompt diagnosis and management [11]. The interaction between diastolic dysfunction and pulmonary hypertension complicates the clinical scenario, since pulmonary hypertension intensifies the hemodynamic strain on the heart, resulting in progressive right heart failure, a significant factor contributing to adverse outcomes in these patients [12].Pulmonary hypertension is a diverse condition categorized into five groups according to its etiology, with group 2 pulmonary hypertension, or PH secondary to left heart disease, being the most prevalent. This kind of pulmonary hypertension frequently arises from chronic hypertension, heart failure, or valvular heart disease, and is intricately associated with the pathophysiology of diastolic dysfunction [1]. In patients with left heart disease, pulmonary hypertension is a significant predictor of negative outcomes, since it indicates the persistent increase in left atrial pressure and pulmonary venous congestion associated with decreased left ventricular relaxation. Chronic increasing pulmonary pressures induce remodeling of the pulmonary vasculature and augment right ventricular afterload, ultimately culminating in right ventricular dysfunction and failure [15]. The coupling between the right ventricle and pulmonary artery is essential for assessing the prognosis of patients with pulmonary hypertension, as right ventricular failure is a significant cause of mortality in this group. Furthermore, the existence of pulmonary hypertension frequently results in reduced exercise tolerance, increased hospitalizations, and a compromised quality of life in affected patients [17].

Identifying risk variables linked to diastolic dysfunction and pulmonary hypertension is essential for enhancing patient outcomes and informing therapeutic decision-making [18,19]. Conventional cardiovascular risk factors, including age, obesity, hypertension, and diabetes, have been associated with the onset of both disorders; however, their specific roles and the mechanisms via which they facilitate disease progression continue to be subjects of ongoing research [20,21]. Age is a significant predictor of diastolic dysfunction, characterized by myocardial stiffness and poor relaxation, which are indicative of the aging heart [22,23]. Hypertension, frequent among older adults, elevates left ventricular afterload and hypertrophy, hence exacerbating diastolic dysfunction [24,25]. Obesity, frequently associated with metabolic syndrome and insulin resistance, imposes further hemodynamic and inflammatory strain on the cardiovascular system, worsening diastolic dysfunction and facilitating pulmonary vascular remodeling that results in pulmonary hypertension.

Despite increasing acknowledgment of the significance of risk factors in the onset of diastolic dysfunction and pulmonary hypertension, a gap persists in comprehending the specific mechanisms via which these factors interact to intensify disease progression [28]. Moreover, the influence of genetic predisposition on the susceptibility to these conditions requires additional investigation, as research indicates that individuals with a familial history of heart failure or pulmonary hypertension face a heightened risk of developing these ailments [29]. Comprehending the genetic and molecular foundations of diastolic dysfunction and pulmonary hypertension may unveil novel therapeutic opportunities, especially in the context of precision medicine, where tailored treatment approaches based on a patient's distinct risk profile and genetic makeup are becoming more attainable.

Methods

Study Design

This research is a cross-sectional observational study aimed at examining the relationship between many risk variables and the onset of diastolic dysfunction and pulmonary hypertension (PH) in individuals with chronic cardiovascular diseases. The research was conducted at a secondary care hospital in Hofuf, Al-Ahsa, Saudi Arabia, enrolling patients with chronic cardiovascular conditions including heart failure, coronary artery disease, and hypertension. Data collection transpired during six months, from January 2024 to June 2024, involving patient assessments via clinical evaluations, echocardiographic investigations, and medical history reviews.

Setting

The research was performed in the cardiology department of a secondary care hospital situated in Hofuf, Al-Ahsa, Saudi Arabia. This hospital predominantly caters to patients from Al-Ahsa and adjacent areas, providing specialist cardiovascular services such as diagnostic echocardiography, interventional cardiology, and management of chronic cardiovascular conditions. The hospital's secondary care designation afforded access to a varied patient demographic, primarily from urban and suburban areas, hence enabling the examination of prevalent risk factors within this community.

Study Population

The study population included adult patients diagnosed with chronic cardiovascular conditions who visited the cardiology clinic or were admitted to the cardiology ward during the study period. Inclusion criteria for participation in the study were as follows:

1. Age ≥ 18 years.
2. Diagnosis of a chronic cardiovascular condition, including heart failure (with preserved or reduced ejection fraction), coronary artery disease, or hypertension.
3. Availability of echocardiographic data.
4. Informed consent provided by the patient or their legal representative.

Exclusion criteria included:

1. Patients with acute cardiovascular events, such as myocardial infarction or unstable angina, within the last three months.
2. Patients with severe mitral or aortic valve disease that could interfere with echocardiographic assessment.
3. Patients with significant non-cardiovascular comorbidities that would limit their participation in the study.

Data Collection

Data were collected from medical records and echocardiographic assessments of the enrolled patients. The following variables were recorded for each patient:

- **Demographic Information**:
  - Patient file number (MRN)
  - Gender (male/female)
  - Age
- **Cardiovascular Risk Factors**:
  - Presence of diabetes mellitus (Yes/No)
  - Presence of hypertension (Yes/No)
  - Dyslipidemia (Yes/No)
  - History of post-percutaneous coronary intervention (PCI) (Yes/No)
- **Echocardiographic Parameters**:
  - **Left Ventricular Ejection Fraction (EF%)**: EF was classified as normal (55-60%), mildly reduced (45-50%), moderately reduced (40-45%), or severely reduced (below 40%).
  - **Diastolic Dysfunction**: Graded based on echocardiographic assessment:
    1. Normal
    2. Grade 1 (Mild)
    3. Grade 2 (Moderate)
    4. Grade 3 (Severe)
    5. Cannot assess due to mitral annular calcification, moderate or severe mitral regurgitation, or tachycardia.
  - **Pulmonary Hypertension**: Classified based on pulmonary artery systolic pressure (PASP):
    1. Absent (< 25 mmHg)
    2. Mild (25-40 mmHg)
    3. Moderate (41-55 mmHg)
    4. Severe (> 55 mmHg)
  - **Atrial Fibrillation**: Presence or absence of atrial fibrillation (AF) was recorded.
  - **Left Atrium Size**: Measured and classified as normal (16-34 ml/m²), mildly dilated (35-41 ml/m²), moderately dilated (42-48 ml/m²), or severely dilated (above 48 ml/m²).

These data points were chosen based on their known associations with diastolic dysfunction and pulmonary hypertension, as well as their prognostic significance in chronic cardiovascular disease management

Procedure

All echocardiographic evaluations were conducted by certified cardiologists utilizing conventional 2D echocardiography equipment. The left ventricular ejection fraction was quantified utilizing Simpson's method, while diastolic dysfunction was evaluated through a combination of Doppler echocardiographic techniques, including the measurement of mitral inflow velocities (E/A ratio), tissue Doppler imaging of the mitral annulus (E'/A' ratio), and pulmonary vein flow profiles.Pulmonary artery systolic pressure was assessed by utilizing the tricuspid regurgitant jet velocity, supplemented by the right atrial pressure obtained via echocardiography. Patients with pulmonary hypertension were categorized into mild, moderate, and severe classifications based on the estimated pulmonary artery systolic pressure (PASP).Demographic information and cardiovascular risk factors of patients were obtained from their medical records. The medical history of each patient including diabetes, hypertension, dyslipidemia, and prior cardiac treatments was documented during their clinic visit or hospitalization. A thorough clinical assessment was performed to verify that the documented data were current and indicative of the patient's present health condition.

Statistical Analysis

IBM SPSS Statistics (Version 27.0) was implemented to analyze the data. Descriptive statistics were computed for all variables, including means and standard deviations for continuous variables and frequencies and percentages for categorical variables. The distribution of risk factors, as well as the prevalence of diastolic dysfunction and pulmonary hypertension in the study population, was ascertained.Bivariate analyses were implemented to evaluate the correlation between echocardiographic findings (pulmonary hypertension and diastolic dysfunction) and cardiovascular risk factors (diastolic dysfunction, dyslipidemia, diabetes, hypertension, and history of percutaneous coronary intervention). Depending on the normality of the data, independent t-tests or Mann-Whitney U tests were implemented for continuous variables. The categorical variables were compared using Fisher's exact tests or chi-square tests.A multivariate logistic regression analysis was performed to identify independent predictors of pulmonary hypertension and diastolic dysfunction. Variables that were clinically pertinent and significant in the bivariate analyses were incorporated into the models. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were computed for each variable. A p-value of less than 0.05 was established as the threshold for statistical significance.

Ethical Considerations

The ethical principles delineated in the Declaration of Helsinki were adhered to during the execution of this investigation. The Institutional Review Board (IRB) of the hospital granted ethical approval for the study. Prior to enrollment in the study, all patients or their legal representatives submitted written informed consent. Throughout the investigation, patient confidentiality was preserved, and data were anonymized to safeguard the participants' identities.

.

Results

Table 1 provides an overview of the gender and age distribution, as well as the prevalence of key comorbidities such as diabetes mellitus (DM), hypertension (HTN), dyslipidemia, and post-percutaneous coronary intervention (PCI). A majority of the patients were male (52.8%) and aged between 40 and 79 years (81.7%). Additionally, the prevalence of HTN and DM was high, at 78% and 59%, respectively, indicating a substantial burden of cardiovascular risk factors within the study population.

Table 1: Demographic and Clinical Characteristics of the Study Population (n=246)

Variable	Frequency	Percentage (%)
Gender		
Male	130	52.8%
Female	116	47.2%
Age Group		
20-39	30	12.2%
40-59	103	41.9%
60-79	98	39.8%
80+	15	6.1%
Comorbidities		
Diabetes Mellitus	145	59.0%
Hypertension	192	78.0%
Dyslipidemia	152	61.8%
Post-PCI	74	30.1%
Atrial Fibrillation (AF)		
Present	58	23.6%
Absent	188	76.4%

Table 2 and figure 1 outlines the echocardiographic parameters, including left ventricular ejection fraction (LVEF), diastolic dysfunction, and left atrial size. Most patients had preserved LVEF (66.7%), with 13.4% showing mild reductions and only 4.9% having severely reduced LVEF (<30%). Diastolic dysfunction was prevalent, with 43.1% having Grade 1 dysfunction, indicating early signs of cardiac impairment. Furthermore, 25.2% of patients had mild left atrial dilation, reflecting early cardiac remodeling.

Table 2: Echocardiographic Findings in the Study Population (n=246)

Echocardiographic Finding	Frequency	Percentage (%)
Left Ventricular Ejection Fraction (LVEF%)		
<30%	12	4.9%
30-40%	33	13.4%
40-50%	37	15.0%
50-60%	164	66.7%
Diastolic Dysfunction		
Normal	78	31.7%
Grade 1	106	43.1%
Grade 2	37	15.0%
Grade 3	25	10.2%
Left Atrium Size		
Normal	130	52.8%
Mild Dilated	62	25.2%
Moderate Dilated	36	14.6%
Severe Dilated	18	7.3%

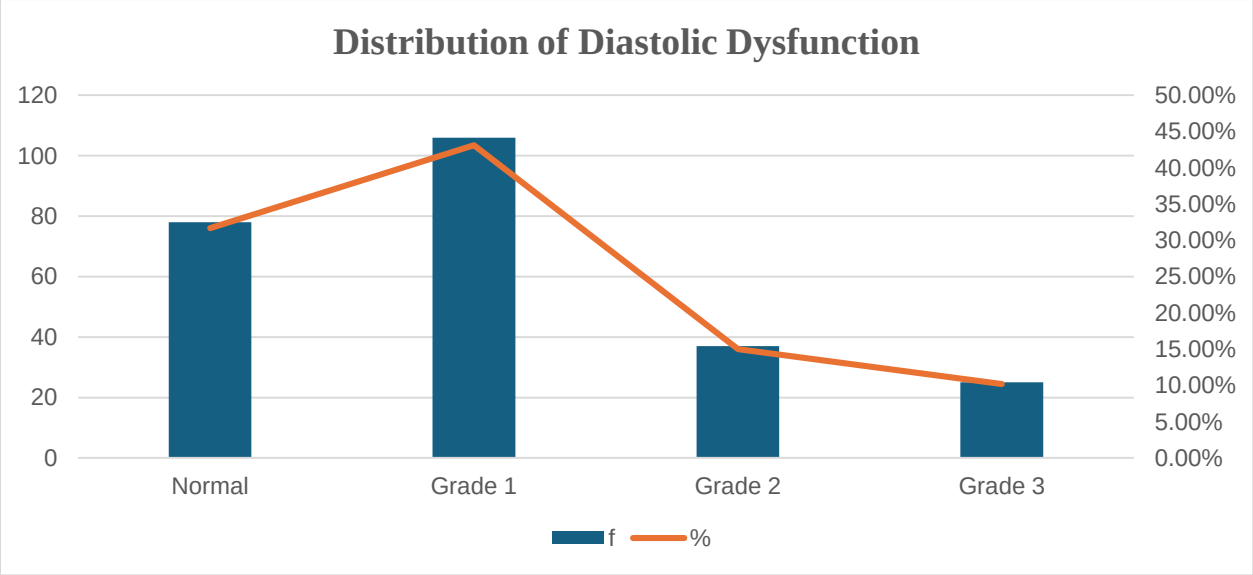

Figure 1: Diastolic Dysfunction

Pulmonary hypertension was present (Table 3) in 19.5% of the patients, with the majority having mild or moderate PH. This table highlights the significant association between PH and comorbidities such as hypertension, dyslipidemia, and atrial fibrillation ($p < 0.001$ for HTN and AF). PH was particularly prevalent in patients with atrial fibrillation (55.2%), indicating a higher cardiovascular burden in these individuals. The strong correlation between PH and cardiovascular risk factors suggests that these patients require early detection and management to prevent further cardiac deterioration.

Table 3: Pulmonary Hypertension (PH) Prevalence and its Relationship with Comorbidities (n=246)

Variable	Pulmonary Hypertension	No Pulmonary Hypertension	Total	p-value
Overall Prevalence of PH	48 (19.5%)	198 (80.5%)	246	
Relationship with Comorbidities				
Dyslipidemia	35 (23.0%)	117 (77.0%)	152	0.03
Diabetes Mellitus	32 (22.1%)	113 (77.9%)	145	0.02
Hypertension	45 (23.4%)	147 (76.6%)	192	<0.001
Atrial Fibrillation	32 (55.2%)	26 (44.8%)	58	<0.001

Table 4 examines the associations between diastolic dysfunction and key cardiovascular risk factors. Diabetic patients had a significantly higher prevalence of diastolic dysfunction (84.1%, $p < 0.001$), with a similar trend seen in hypertensive (76.0%, $p < 0.001$) and dyslipidemic patients (72.4%, $p = 0.02$). The presence of diastolic dysfunction in post-PCI patients (71.6%, $p = 0.04$) also suggests that procedural intervention may not fully mitigate the risks of cardiac dysfunction.

Table 4: Relationship Between Risk Factors and Diastolic Dysfunction (n=246)

Risk Factor	Diastolic Dysfunction	No Diastolic Dysfunction	Total	p-value
Diabetes Mellitus	122 (84.1%)	23 (15.9%)	145	<0.001
Hypertension	146 (76.0%)	46 (24.0%)	192	<0.001
Dyslipidemia	110 (72.4%)	42 (27.6%)	152	0.02
Post-PCI	53 (71.6%)	21 (28.4%)	74	0.04
Atrial Fibrillation	37 (63.8%)	21 (36.2%)	58	0.01

Table 5 shows a strong relationship between atrial fibrillation (AF) and pulmonary hypertension ($p < 0.001$), with over half (55.2%) of the patients with AF also exhibiting PH. This underscores the high cardiovascular burden in patients with AF and the need for comprehensive cardiac evaluation in these patients. The correlation suggests that PH may be an important contributing factor to the morbidity associated with AF and highlights the need for targeted management strategies to address both conditions simultaneously.

Table 5: Relationship Between Atrial Fibrillation and Pulmonary Hypertension (n=246)

Atrial Fibrillation (AF)	Pulmonary Hypertension	No Pulmonary Hypertension	Total	p-value
Present	32 (55.2%)	26 (44.8%)	58	<0.001
Absent	16 (8.5%)	172 (91.5%)	188	
Total	**48**	**198**	**246**	

Discussion

In a Saudi Arabian population with chronic cardiovascular diseases, this research sheds light on the frequency and connections between diastolic dysfunction and pulmonary hypertension (PH). Important implications for clinical treatment and future research avenues are offered by the results, which emphasize the substantial burden of these illnesses and their strong relationships with established cardiovascular risk factors.With 68.3% of patients showing some kind of malfunction, the prevalence of diastolic dysfunction in our research cohort was quite high. Consistent with other research, this data confirms that diastolic dysfunction is common among individuals with cardiovascular risk factors [31]. With 43.1% of patients experiencing

Grade 1 diastolic dysfunction, it's clear that many are experiencing mild cardiac impairment; hence, there's a chance to intervene early and stop the condition from becoming worse. Despite the lack of obvious signs of heart failure, this high frequency highlights the need of screening for diastolic dysfunction on a regular basis in individuals with cardiovascular risk factors [10].Diastolic dysfunction is strongly associated with many known cardiovascular risk factors, including diabetes mellitus (84.1%), hypertension (76.0%), and dyslipidemia (72.4%), according to our data. These results corroborate earlier studies that found these factors to be major risk factors for diastolic dysfunction [32]. Diastolic dysfunction is quite common in diabetic individuals (84.1%), which highlights the need for frequent cardiac screenings in this group. The complicated pathophysiology alterations in diabetic hearts, such as metabolic abnormalities, increased myocardial fibrosis, and poor calcium handling, may account for this connection [33]. It is necessary to aggressively treat high-risk people with antihypertensive medication due to the substantial correlation between hypertension and diastolic dysfunction (76.0%), which emphasizes the importance of controlling blood pressure in maintaining heart function [34,35].Our research cohort had a substantial prevalence of pulmonary hypertension (19.5%), which is similar to rates reported in earlier studies of individuals with chronic cardiovascular problems [36]. The need of raising clinician knowledge and doing more screenings for PH is highlighted by this study, which highlights the heavy burden of the disease in this patient group. It is probable that reactive pulmonary vascular remodeling and passive transmission of high left ventricular pressures are both contributors to the pathogenesis of PH in these individuals [37]. Our research found a particularly remarkable and warrants additional investigation high connection between PH and atrial fibrillation (AF), with 55.2% of AF patients having PH ($p < 0.001$). There may be a two-way street here; increased left atrial pressure and pulmonary venous congestion cause AF to exacerbate PH, whereas right atrial dilatation and stretch cause PH to exacerbate AF [38]. Comprehensive cardiac evaluations, including examination of pulmonary pressures, are necessary in patients with atrial fibrillation (AF) due to the high incidence of pulmonary hypertension (PH) [39].Our findings support the idea of heart failure with preserved ejection fraction (HFpEF) as a multi-organ systemic illness, which is supported by the correlation between diastolic dysfunction and pulmonary hypertension [40]. Although several of our patients showed signs of diastolic dysfunction and PH, 66.7% of them had intact left ventricular ejection fraction. This adds to the mounting evidence that HFpEF is a complex condition involving a wide variety of pathophysiological variables, some of which are located outside the heart [41]. Diastolic dysfunction and PH often occur together, which raises questions about the relationship between the left and right sides of the heart and emphasizes the need of taking a holistic approach to these patients' cardiac evaluation and treatment [42].The rising prevalence of cardiovascular risk factors in Saudi Arabia and other Middle Eastern nations is reflected in our research population's high prevalence of hypertension (78%), dyslipidemia (61.8%), and diabetes mellitus (59%). Improving primary preventive efforts and aggressively managing these risk factors are urgently needed to lower the occurrence of diastolic dysfunction and PH, as shown by our results. To address the underlying causes of these cardiovascular risk factors, public health campaigns should focus lifestyle adjustments such changing one's diet, increasing physical exercise, and quitting smoking [44].A history of percutaneous coronary intervention (PCI) was also significantly associated with diastolic dysfunction in our sample (71.6 percent, $p = 0.04$). Although percutaneous coronary intervention (PCI) successfully treats coronary artery stenosis, this research implies that treatment could not completely reduce the danger of diastolic dysfunction. Diastolic function evaluation, along with continuous cardiac monitoring and control of risk factors, should be prioritized in patients after percutaneous coronary intervention (PCI) [45]. Coronary revascularization may not resolve the underlying causes of diastolic dysfunction in these individuals, which might be due to microvascular dysfunction,

myocardial fibrosis, or other reasons [[46]]. This finding emphasizes the need of treating epicardial coronary stenosis as part of a holistic strategy for managing coronary artery disease.Notable left atrial dilatation is seen in a large percentage of patients (47.1% with moderate to severe dilation), which probably indicates that many of these patients have persistent diastolic dysfunction. Atrial fibrillation and thromboembolic events are more likely to occur in patients with left atrial remodeling, which is a hallmark of chronic diastolic dysfunction [47]. The importance of identifying and treating diastolic dysfunction early on to avoid negative cardiac remodeling is highlighted by the significant incidence of left atrial dilation in our group. Moreover, it implies that the size of the left atrium might be a significant indicator of prognosis in individuals suffering from chronic cardiovascular diseases [48].Cardiac dysfunction in individuals with several cardiovascular risk factors is complicated, since our research found that diastolic dysfunction, pulmonary hypertension, and atrial fibrillation all interact with each other [49]. Due to the multifaceted nature of cardiac and pulmonary vascular disease, it is essential that patients be managed by a team of experts from several fields, including cardiologists, pulmonologists, and others [50]. Furthermore, our results provide credence to the idea that new treatments targeting common pathways in pulmonary hypertension and diastolic dysfunction might be useful, for example, treatments that seek to decrease inflammation, oxidative stress, or fibrosis [51].

Implications of the Study

In individuals with chronic cardiovascular problems, this research sheds light on the relationship between diastolic dysfunction, pulmonary hypertension, and important risk factors for cardiovascular disease. The results show that diastolic dysfunction is common, especially in those who have diabetes, high blood pressure, and dyslipidemia. Important implications for clinical practice arise from these data. Heart failure with preserved ejection fraction (HFpEF) is difficult to treat and has poor results; hence, it is important to identify and manage diastolic dysfunction early on to avoid it from progressing to more severe types of heart failure.Thorough cardiac examinations are necessary for individuals with atrial fibrillation due to the significant correlation between the two conditions and the development of pulmonary hypertension. In order to avoid right heart failure and determine the best course of treatment, clinicians should check these patients for pulmonary hypertension on a regular basis. Additionally, the research emphasizes the need of controlling risk factors aggressively, such as blood pressure, glucose, and lipids, in order to lessen the impact of diastolic dysfunction and pulmonary hypertension. Public health initiatives aimed at reducing cardiovascular risk factors should also emphasize the need of making positive adjustments to people's lifestyles, such as managing weight, quitting smoking, and being more physically active.Furthermore, the results of the research imply that percutaneous coronary interventions (PCI) would not completely reduce the danger of diastolic dysfunction, even if they might treat coronary artery disease. It is crucial to continue monitoring the heart and managing risk factors in individuals who have had percutaneous coronary intervention (PCI). In sum, the findings of this study provide the groundwork for future studies and give therapeutic recommendations that may enhance the health of those who are at high risk for cardiovascular disease.

Limitations of the Study

Several caveats should be thought about in interpreting the data, despite the fact that the research did provide some useful insights. To start, we can't draw any firm conclusions about a cause-and-effect relationship between the variables that increase the risk of cardiovascular disease and the onset of diastolic dysfunction and pulmonary hypertension since this research is cross-sectional. Although there is evidence of links between these characteristics, it is not yet obvious what the direction or timing of these interactions are. To learn more about the ways these circumstances change over time in reaction to cardiovascular risk factors, a longitudinal research is the way to go.The second limitation is that the research only included one secondary

care hospital, therefore the results may not apply to other populations or healthcare systems. Cardiovascular disease prevalence and development may be affected by some population-specific variables unique to Saudi Arabia, such as food habits and environmental influences. These variables may not be relevant in other contexts.Also, there is a chance that the results might be skewed due to measuring method and interpretive uncertainty when using echocardiographic data to diagnose diastolic dysfunction and pulmonary hypertension. Heart magnetic resonance (CMR) and other cutting-edge imaging techniques may one day allow for more accurate evaluations of the heart's anatomy and function. Last but not least, the research failed to account for potential confounding variables, such as a hereditary propensity to diastolic dysfunction and pulmonary hypertension. To improve the results' generalizability and robustness, future research should fix these shortcomings and incorporate more risk variables.

Conclusion of the Study

Especially when combined with more conventional risk factors like diabetes, high blood pressure, and dyslipidemia, this research highlights the substantial impact of diastolic dysfunction and pulmonary hypertension on patients suffering from chronic cardiovascular diseases. The results highlight the need of screening for diastolic dysfunction on a regular basis in individuals with cardiovascular risk factors, even if they do not have obvious signs of heart failure. Improving patient outcomes and preventing the worsening of cardiovascular illnesses may be possible with the early diagnosis and treatment of diastolic dysfunction and pulmonary hypertension.Patients with atrial fibrillation should frequently undergo thorough cardiac examinations, as the research emphasizes the complicated relationship between diastolic dysfunction, pulmonary hypertension, and the condition. With this method, underlying heart dysfunction may be more easily identified, and the right therapy techniques can be followed.Research like this highlights the importance of aggressively controlling risk factors, such as dietary changes and medication, since cardiovascular risk factors are so common in the community under investigation. Expanding upon these results, future research should examine the effectiveness of innovative treatments that target both diastolic dysfunction and pulmonary hypertension concurrently, as well as the long-term consequences of individuals with both diseases. In conclusion, the findings of this research provide light on the pathogenesis of cardiovascular illnesses and point to ways in which early diagnosis and intervention might improve patient care.

References :

1. de Jesus Perez, V.A.; Haddad, F.; Zamanian, R.T. Diagnosis and Management of Pulmonary Hypertension Associated with Left Ventricular Diastolic Dysfunction. *Pulm. Circ.* **2012**, *2*, 163–169, doi:10.4103/2045-8932.97598.
2. Roth, G.A.; Mensah, G.A.; Johnson, C.O.; Addolorato, G.; Ammirati, E.; Baddour, L.M.; Barengo, N.C.; Beaton, A.Z.; Benjamin, E.J.; Benziger, C.P.; et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. *J. Am. Coll. Cardiol.* **2020**, *76*, 2982–3021, doi:10.1016/j.jacc.2020.11.010.
3. Obokata, M.; Reddy, Y.N.V.; Borlaug, B.A. Diastolic Dysfunction and Heart Failure With Preserved Ejection Fraction. *JACC Cardiovasc. Imaging* **2020**, *13*, 245–257, doi:10.1016/j.jcmg.2018.12.034.
4. Maharaj, R. Diastolic Dysfunction and Heart Failure with a Preserved Ejection Fraction: Relevance in Critical Illness and Anaesthesia. *J. Saudi Hear. Assoc.* **2012**, *24*, 99–121, doi:10.1016/j.jsha.2012.01.004.
5. Lai, Y.-C.; Potoka, K.C.; Champion, H.C.; Mora, A.L.; Gladwin, M.T. Pulmonary Arterial Hypertension. *Circ. Res.* **2014**, *115*, 115–130, doi:10.1161/CIRCRESAHA.115.301146.

6. Sharma, K.; Kass, D.A. Heart Failure With Preserved Ejection Fraction. *Circ. Res.* **2014**, *115*, 79–96, doi:10.1161/CIRCRESAHA.115.302922.
7. Stoicescu, L.; Crişan, D.; Morgovan, C.; Avram, L.; Ghibu, S. Heart Failure with Preserved Ejection Fraction: The Pathophysiological Mechanisms behind the Clinical Phenotypes and the Therapeutic Approach. *Int. J. Mol. Sci.* **2024**, *25*, 794, doi:10.3390/ijms25020794.
8. Mills, K.T.; Stefanescu, A.; He, J. The Global Epidemiology of Hypertension. *Nat. Rev. Nephrol.* **2020**, *16*, 223–237, doi:10.1038/s41581-019-0244-2.
9. Harper, A.R.; Patel, H.C.; Lyon, A.R. Heart Failure with Preserved Ejection Fraction. *Clin. Med.* **2018**, *18*, s24–s29, doi:10.7861/clinmedicine.18-2-s24.
10. Suárez, J.C.; López, P.; Mancebo, J.; Zapata, L. Diastolic Dysfunction in the Critically Ill Patient. *Med. Intensiva (English Ed.* **2016**, *40*, 499–510, doi:10.1016/j.medin.2016.06.006.
11. Xanthopoulos, A.; Starling, R.C.; Kitai, T.; Triposkiadis, F. Heart Failure and Liver Disease. *JACC Hear. Fail.* **2019**, *7*, 87–97, doi:10.1016/j.jchf.2018.10.007.
12. Miller, W.L.; Grill, D.E.; Borlaug, B.A. Clinical Features, Hemodynamics, and Outcomes of Pulmonary Hypertension Due to Chronic Heart Failure With Reduced Ejection Fraction. *JACC Hear. Fail.* **2013**, *1*, 290–299, doi:10.1016/j.jchf.2013.05.001.
13. Goldberg, A.B.; Mazur, W.; Kalra, D.K. Pulmonary Hypertension: Diagnosis, Imaging Techniques, and Novel Therapies. *Cardiovasc. Diagn. Ther.* **2017**, *7*, 405–417, doi:10.21037/cdt.2017.04.11.
14. Ltaief, Z.; Yerly, P.; Liaudet, L. Pulmonary Hypertension in Left Heart Diseases: Pathophysiology, Hemodynamic Assessment and Therapeutic Management. *Int. J. Mol. Sci.* **2023**, *24*, 9971, doi:10.3390/ijms24129971.
15. Dayer, N.; Ltaief, Z.; Liaudet, L.; Lechartier, B.; Aubert, J.-D.; Yerly, P. Pressure Overload and Right Ventricular Failure: From Pathophysiology to Treatment. *J. Clin. Med.* **2023**, *12*, 4722, doi:10.3390/jcm12144722.
16. Bernardo, R.J.; Haddad, F.; Couture, E.J.; Hansmann, G.; Perez, V.A. de J.; Denault, A.Y.; Man, F.S. de; Amsallem, M. Mechanics of Right Ventricular Dysfunction in Pulmonary Arterial Hypertension and Heart Failure with Preserved Ejection Fraction. *Cardiovasc. Diagn. Ther.* **2020**, *10*, 1580–1603, doi:10.21037/cdt-20-479.
17. Burkhoff, D.; Borlaug, B.A.; Shah, S.J.; Zolty, R.; Tedford, R.J.; Thenappan, T.; Zamanian, R.T.; Mazurek, J.A.; Rich, J.D.; Simon, M.A.; et al. Levosimendan Improves Hemodynamics and Exercise Tolerance in PH-HFpEF. *JACC Hear. Fail.* **2021**, *9*, 360–370, doi:10.1016/j.jchf.2021.01.015.
18. Ottosen, C.I.; Nadruz, W.; Inciardi, R.M.; Johansen, N.D.; Fudim, M.; Biering-Sørensen, T. Diastolic Dysfunction in Hypertension: A Comprehensive Review of Pathophysiology, Diagnosis, and Treatment. *Eur. Hear. J. - Cardiovasc. Imaging* **2024**, doi:10.1093/ehjci/jeae178.
19. Azaredo Raposo, M.; Inácio Cazeiro, D.; Guimarães, T.; Lousada, N.; Freitas, C.; Brito, J.; Martins, S.; Resende, C.; Dorfmüller, P.; Luís, R.; et al. Pulmonary Arterial Hypertension: Navigating the Pathways of Progress in Diagnosis, Treatment, and Patient Care. *Rev. Port. Cardiol.*, doi:10.1016/j.repc.2024.03.004.
20. Powell-Wiley, T.M.; Poirier, P.; Burke, L.E.; Després, J.-P.; Gordon-Larsen, P.; Lavie, C.J.; Lear, S.A.; Ndumele, C.E.; Neeland, I.J.; Sanders, P.; et al. Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation* **2021**, *143*, doi:10.1161/CIR.0000000000000973.
21. Volpe, M.; Gallo, G. Obesity and Cardiovascular Disease: An Executive Document on Pathophysiological and Clinical Links Promoted by the Italian Society of Cardiovascular Prevention (SIPREC). *Front. Cardiovasc. Med.* **2023**, *10*,

doi:10.3389/fcvm.2023.1136340.
22. Sanders, D.; Dudley, M.; Groban, L. Diastolic Dysfunction, Cardiovascular Aging, and the Anesthesiologist. *Anesthesiol. Clin.* **2009**, *27*, 497–517, doi:10.1016/j.anclin.2009.07.008.
23. Parikh, J.D.; Hollingsworth, K.G.; Wallace, D.; Blamire, A.M.; MacGowan, G.A. Normal Age-Related Changes in Left Ventricular Function: Role of Afterload and Subendocardial Dysfunction. *Int. J. Cardiol.* **2016**, *223*, 306–312, doi:10.1016/j.ijcard.2016.07.252.
24. Lalande, S.; Johnson, D.B. Diastolic Dysfunction: A Link between Hypertension and Heart Failure. *Drugs of Today* **2008**, *44*, 503, doi:10.1358/dot.2008.44.7.1221662.
25. Oh, G.C.; Cho, H.-J. Blood Pressure and Heart Failure. *Clin. Hypertens.* **2020**, *26*, 1, doi:10.1186/s40885-019-0132-x.
26. Vilariño-García, T.; Polonio-González, M.; Pérez-Pérez, A.; Ribalta, J.; Arrieta, F.; Aguilar, M.; Obaya, J.; Gimeno-Orna, J.; Iglesias, P.; Navarro, J.; et al. Role of Leptin in Obesity, Cardiovascular Disease, and Type 2 Diabetes. *Int. J. Mol. Sci.* **2024**, *25*, 2338, doi:10.3390/ijms25042338.
27. Willson, C.; Watanabe, M.; Tsuji-Hosokawa, A.; Makino, A. Pulmonary Vascular Dysfunction in Metabolic Syndrome. *J. Physiol.* **2019**, *597*, 1121–1141, doi:10.1113/JP275856.
28. Rosenkranz, S.; Howard, L.S.; Gomberg-Maitland, M.; Hoeper, M.M. Systemic Consequences of Pulmonary Hypertension and Right-Sided Heart Failure. *Circulation* **2020**, *141*, 678–693, doi:10.1161/CIRCULATIONAHA.116.022362.
29. Austin, E.D.; Loyd, J.E. The Genetics of Pulmonary Arterial Hypertension. *Circ. Res.* **2014**, *115*, 189–202, doi:10.1161/CIRCRESAHA.115.303404.
30. Bustin, S.A.; Jellinger, K.A. Advances in Molecular Medicine: Unravelling Disease Complexity and Pioneering Precision Healthcare. *Int. J. Mol. Sci.* **2023**, *24*, 14168, doi:10.3390/ijms241814168.
31. Fischer, M. Prevalence of Left Ventricular Diastolic Dysfunction in the Community Results from a Doppler Echocardiographic-Based Survey of a Population Sample. *Eur. Heart J.* **2003**, *24*, 320–328, doi:10.1016/S0195-668X(02)00428-1.
32. Russo, C.; Jin, Z.; Homma, S.; Rundek, T.; Elkind, M.S.V.; Sacco, R.L.; Di Tullio, M.R. Effect of Diabetes and Hypertension on Left Ventricular Diastolic Function in a High-risk Population without Evidence of Heart Disease. *Eur. J. Heart Fail.* **2010**, *12*, 454–461, doi:10.1093/eurjhf/hfq022.
33. von Bibra, H.; St John Sutton, M. Diastolic Dysfunction in Diabetes and the Metabolic Syndrome: Promising Potential for Diagnosis and Prognosis. *Diabetologia* **2010**, *53*, 1033–1045, doi:10.1007/s00125-010-1682-3.
34. Park, S.-J. The Role of Systolic Blood Pressure Reduction in Diastolic Dysfunction: RAAS Inhibition versus Non-RAAS Blood Pressure Lowering. *J. Cardiovasc. Imaging* **2020**, *28*, 183, doi:10.4250/jcvi.2020.0083.
35. Chun, K.-H.; Kang, S.-M. Blood Pressure and Heart Failure: Focused on Treatment. *Clin. Hypertens.* **2024**, *30*, 15, doi:10.1186/s40885-024-00271-y.
36. Wijeratne, D.T.; Lajkosz, K.; Brogly, S.B.; Lougheed, M.D.; Jiang, L.; Housin, A.; Barber, D.; Johnson, A.; Doliszny, K.M.; Archer, S.L. Increasing Incidence and Prevalence of World Health Organization Groups 1 to 4 Pulmonary Hypertension. *Circ. Cardiovasc. Qual. Outcomes* **2018**, *11*, doi:10.1161/CIRCOUTCOMES.117.003973.
37. Maron, B.A. Revised Definition of Pulmonary Hypertension and Approach to Management: A Clinical Primer. *J. Am. Heart Assoc.* **2023**, *12*, doi:10.1161/JAHA.122.029024.

38. Rottlaender, D.; Motloch, L.J.; Schmidt, D.; Reda, S.; Larbig, R.; Wolny, M.; Dumitrescu, D.; Rosenkranz, S.; Erdmann, E.; Hoppe, U.C. Clinical Impact of Atrial Fibrillation in Patients with Pulmonary Hypertension. *PLoS One* **2012**, *7*, e33902, doi:10.1371/journal.pone.0033902.
39. Ilonze, O.J.; Ebong, I.A.; Guglin, M.; Nair, A.; Rich, J.; McLaughlin, V.; Tedford, R.J.; Mazimba, S. Considerations in the Diagnosis and Management of Pulmonary Hypertension Associated With Left Heart Disease. *JACC Hear. Fail.* **2024**, *12*, 1328–1342, doi:10.1016/j.jchf.2024.04.031.
40. Kim, H.-L.; Jo, S.-H. Arterial Stiffness and Heart Failure With Preserved Ejection Fraction. *J. Korean Med. Sci.* **2024**, *39*, doi:10.3346/jkms.2024.39.e195.
41. LeWinter, M.M.; Meyer, M. Mechanisms of Diastolic Dysfunction in Heart Failure With a Preserved Ejection Fraction. *Circ. Hear. Fail.* **2013**, *6*, 1112–1115, doi:10.1161/CIRCHEARTFAILURE.113.000825.
42. Agrawal, V.; Byrd, B.F.; Brittain, E.L. Echocardiographic Evaluation of Diastolic Function in the Setting of Pulmonary Hypertension. *Pulm. Circ.* **2019**, *9*, 1–11, doi:10.1177/2045894019826043.
43. Munawir Alhejely, M.M.; Shibli, K.Y.; Hamed Almalki, W.A.; Felemban, G.M.B.; Alluhaybi, H.S.; Majrashi, B.M.; Bakhsh, B.Y. Influence of Lifestyle Changes on Cardiovascular Diseases in Saudi Arabia: A Systematic Literature Review. *Cureus* **2023**, doi:10.7759/cureus.40075.
44. Rippe, J.M. Lifestyle Strategies for Risk Factor Reduction, Prevention, and Treatment of Cardiovascular Disease. *Am. J. Lifestyle Med.* **2019**, *13*, 204–212, doi:10.1177/1559827618812395.
45. Aggarwal, P.; Sinha, S.K.; Marwah, R.; Nath, R.K.; Pandit, B.N.; Singh, A.P. Effect of Percutaneous Coronary Intervention on Diastolic Function in Coronary Artery Disease. *J. Cardiovasc. Echogr.* **2021**, *31*, 73–76, doi:10.4103/jcecho.jcecho_128_20.
46. Hong, D.; Lee, S.H.; Shin, D.; Choi, K.H.; Kim, H.K.; Ha, S.J.; Joh, H.S.; Park, T.K.; Yang, J.H.; Song, Y. Bin; et al. Prognostic Impact of Cardiac Diastolic Function and Coronary Microvascular Function on Cardiovascular Death. *J. Am. Heart Assoc.* **2023**, *12*, doi:10.1161/JAHA.122.027690.
47. El Aouar, L.M.M.; Meyerfreud, D.; Magalhães, P.; Rodrigues, S.L.; Baldo, M.P.; El Aouar, S.M.; El Aouar, N.A.; Mill, J.G.; Campos Filho, O. Relationship Between Left Atrial Volume and Diastolic Dysfunction in 500 Brazilian Patients. *Arq. Bras. Cardiol.* **2013**, doi:10.5935/abc.20130109.
48. Thomas, L.; Marwick, T.H.; Popescu, B.A.; Donal, E.; Badano, L.P. Left Atrial Structure and Function, and Left Ventricular Diastolic Dysfunction. *J. Am. Coll. Cardiol.* **2019**, *73*, 1961–1977, doi:10.1016/j.jacc.2019.01.059.
49. Rosenkranz, S.; Gibbs, J.S.R.; Wachter, R.; De Marco, T.; Vonk-Noordegraaf, A.; Vachiéry, J.-L. Left Ventricular Heart Failure and Pulmonary Hypertension. *Eur. Heart J.* **2016**, *37*, 942–954, doi:10.1093/eurheartj/ehv512.
50. Rosenberg, M.A.; Manning, W.J. Diastolic Dysfunction and Risk of Atrial Fibrillation. *Circulation* **2012**, *126*, 2353–2362, doi:10.1161/CIRCULATIONAHA.112.113233.
51. Bousseau, S.; Sobrano Fais, R.; Gu, S.; Frump, A.; Lahm, T. Pathophysiology and New Advances in Pulmonary Hypertension. *BMJ Med.* **2023**, *2*, e000137, doi:10.1136/bmjmed-2022-000137.