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Association Between Albuminuria and Left Ventricular Diastolic Dysfunction

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Abstract:

Introduction: Left ventricular diastolic dysfunction (LVDD) causes heart failure symptoms and accounts for many hospitalizations worldwide. The diagnosis of LVDD is challenging. In this regard, simple modalities and diagnostic algorithms are becoming more important to aid the diagnosis. Albuminuria is a prevalent finding within patients having heart failure with an established prognostic value and a potential diagnostic benefit. However, its role in LVDD diagnosis is still under investigation.

Aim: We aim to study the association between albuminuria (microalbuminuria and macroalbuminuria) and LVDD in patients presented to Fayoum University Hospital.

Subjects and Methods: Hospital-based cross-sectional research involved 200 Patients presenting with exertional dyspnea (NYHA II/III) and an ejection fraction of 50% or more. First-morning mid-stream urine samples were collected and analyzed for UACR. Micro-albuminuria has been identified as a UACR of 30 mg/gCr, although macro-albuminuria is described as a UACR of 300 mg/gCr or more. Average E/e', Septal e' velocity and Lateral e' velocity. TR peak velocity and LA volume index were used to identify patients with LVDD.

Results: We found albuminuria levels (detected by urinary albumin creatinine ratio) show a statistically significant positive correlation with the four recommended echo variables of LVDD: annular e' velocity septal (r =0.31, p <0.01), lateral (r =0.23, p <0.01), average E/e' ratio (r =0.38, p <0.01), LA maximum volume index(r =0.29 with a p-value of <0.01), and peak TR velocity (r =0.25, p <0.01). This correlation was obvious in the comparison of albuminuria levels at different diastolic function states, which revealed a statistically significant higher level of Albuminuria (UACR) among cases with diastolic dysfunction (p <0.01).

Conclusions: There is an association between albuminuria and LVDD. As a simple and cheap investigation, it has the potential to be used as a test in patients with suspected diastolic dysfunction.

Keywords: HFpEF; Albuminuria; UACR; Diastolic dysfunction.

1. Introduction

Worldwide, heart failure (HF) is a prominent contributor to both death and disability. Around 50% of patients who present with the clinical syndrome of heart failure also possess a preserved ejection fraction (HFpEF) [1]. Cases diagnosed with heart failure now have a significantly better prognosis than when the initial treatment trials were published several decades ago. Nevertheless, this enhancement was limited to individuals who exhibited a substantial decline in HFrEF (left ventricular systolic function) [2]. HFpEF has the same prognosis regarding hospital stay, HF relapses, and NYHA functional class progression [1].

Despite the concerning rise in the prevalence of HFpEF, recognizing it remains difficult, particularly in euvolemic patients who present with exertional dyspnea. Better understanding and diagnosis of LVDD may aid HFpEF diagnosis.

Diastolic dysfunction (DD) occurs when there is myocardial rigidity, excluding endocardial and pericardial pathologies. Both the extracellular matrix and cardiomyocytes have an impact on myocardial rigidity. By way of matrix proteins, alterations in the rigidity of cardiomyocytes are conveyed to the extracellular matrix [2].

Within cases having heart failure, albuminuria remains a robust indicator of deleterious events, including mortality and hospitalization, despite controlling for concomitant renal disease, diabetes, and hypertension [3]. However, data about the prevalence of urinary albumin excretion in patients with HFpEF is limited [4]. That is in part because the HFpEF cohorts are usually limited in most studies in comparison to the HFrEF patients. Therefore, the results are mostly driven by the HFrEF cohorts.

Regarding the correlation between urinary albumin creatinine ratio and left ventricular diastolic dysfunction, insufficient evidence exists. Hence, the objective of this research endeavor was to ascertain the association between albuminuria (microalbuminuria and macroalbuminuria) and LVDD within cases presented having unexplained exertional dyspnea.

2. Subjects & Methods

2.1. Subjects

200 subjects have been involved in the research.

Inclusion criteria

Patients presenting with exertional dyspnea (NYHA II/III) and an ejection fraction of 50% or more.

Exclusion criteria

- Any other cardiovascular disease (ejection fraction <50% (current or previous), important valvular cardiac disease (more than moderate regurgitation or more than mild stenosis), primary cardiomyopathies, constrictive pericarditis, pulmonary arterial hypertension).
- non-cardiovascular entities that might mimic heart failures, such as renal failure or nephrotic syndrome, cirrhosis or liver failure, anemia, 1ry pulmonary hypertension, a lung disease with or without cor-pulmonale, and chronic respiratory failure hypoventilation syndrome.

2.2. Study design

A cross-sectional study in which First-morning mid-stream urine samples were collected and analyzed for UACR. Micro-albuminuria has been described as a UACR of thirty mg/gCr, although macro-albuminuria has been described as a UACR of 300 mg/gCr or more [5]. Four echo variables were evaluated to diagnose patients with abnormal diastolic function. The following variables and their irregular cutoff values are suggested: annular e' velocity (septal e' < seven cm/sec, lateral e' < ten cm/sec), average E/e' ratio > fourteen, LA maximum volume index > thirty-four mL/m2, and peak TR velocity > 2.8 m/sec [6]. LV diastolic function is considered typical if the cutoff values to detect improper function are not met by over half of the available variables. These cutoff values indicate the presence of LV diastolic dysfunction when over half of the available parameters meet them. If the cutoff values are not met by half of the parameters, the research is inconclusive [6].

2.3. Statistical Methods

Standard deviations are used for assessing the dispersion of quantitative parametric data, while arithmetic means are used to measure central tendency. Qualitative data is represented by numbers and percentages in a simple descriptive

analysis. The One-Sample Kolmogorov-Smirnov test has been utilized to verify the normality of the quantitative data in each examined group. Subsequently, inferential statistical tests have been performed. The Kruskal-Wallis test was utilized for comparing over 2 independent groups for quantitative parametric data. The correlation among quantitative non-parametric variables was evaluated using the bivariate Spearman's correlation test. Statistical significance has been observed when the *P*-value < 0.05.

3. Results

The average age among the examined groups was (48.6±15.2) years old, with a mean BMI of (29.8±5.9). 37% were males, versus 63% were females (**Table 1**).

Table 1: Description of general characteristics within the examined group.

Variables		**Number (n=200)**	
		Mean ±SD	Median (Range)
	Age (years)	48.6 ±15.2	49.5 (18-77)
	BMI (kg/m^2)	29.8 ±5.9	29 (19-44)
Sex	Male	74 (37%)	
	Female	126 (63%)	

As illustrated in **Table 2**, the E/e' average among the study group was (8.6 ±3.03), septal annular e' velocity was (5.3 ±2.4), lateral annular e' velocity was (8.1 ±3.6), peak TRV was (2.7 ±0.4) m/s, and LA maximum volume index was (30.1 ±4.7).

Table 2: Description of echo findings within the examined group.

Variables	Number (n=200)
E/e' average	8.6 ±3.03
Peak TRV	2.7 ±0.4
Septal annular e' velocity	5.3 ±2.4
Lateral annular e' velocity	8.1 ±3.6
LA	30.1 ±4.7

Table 3 illustrates that the mean ACR within the examined group was (87.6±139.1) and the mean creatinine was (0.88±0.21). 22% of them show Micro-albuminuria and 10.5% of them show Macro-albuminuria with 67.5% of them showing normal levels. LVDD among the study population with 57% showing normal diastolic function, versus 43% having LVDD (Table 3). Comparison of albuminuria levels according to diastolic function revealed a statistically significant higher level of albuminuria (ACR) among cases with LVDD (p <0.01) (**Table 4**).

Table 3: Description of albuminuria, creatinine level, and diastolic function within the examined group.

Variables		Number (n=200)
ACR		87.6±139.1
Albuminuria	Normal	135 (67.5%)
	Micro-albuminuria	44 (22%)
	Macro-albuminuria	21 (10.5%)
Diastolic function	Normal	114 (57%)
	LVDD	86 (43%)

Table 4: Comparison of albuminuria levels according to diastolic function.

Diastolic function	ACR	*P*- value
Normal function	28.5 ±53.2	<0.01
LVDD	171.1 ±88.2	

As illustrated in **Table 5**, there was a statistically significant positive association (p <0.05) among echo parameters of LVDD and the ACR.

Table 5: Correlation between ACR and different variables among cases.

Variables	ACR	
	R	*P*-value
E/e' average	0.38	<0.01
Peak TRV	0.25	<0.01
Septal annular e' velocity	0.31	<0.01
Lateral annular e' velocity	0.23	<0.01
LA	0.29	<0.01

4. Discussion

We hypothesized that Albuminuria is a potentially useful biomarker for LVDD screening within cases having unexplained dyspnea based on various studies that investigated the correlation between albuminuria and LVDD within many groups with established risk factors such as obesity and hypertension [3, 7].

The present study revealed that albuminuria levels (detected by urinary albumin creatinine ratio) show a statistically significant positive correlation with the four recommended echo variables of LVDD: annular e' velocity septal (r = 0.31, p <0.01), lateral (r =0.23, p <0.01), average E/e' ratio (r =0.38, p <0.01), LA maximum volume index(r

=0.29, p <0.01), and peak TR velocity (r =0.25, p <0.01). This correlation was obvious in the comparison of albuminuria levels at different diastolic function states, which revealed a statistically significant higher level of Albuminuria (UACR) among cases with diastolic dysfunction (p <0.01).

Although clinically these values may not be discriminatory on their own, further diagnostic multivariate scores may include albuminuria as a complementary tool, especially in indeterminate groups, being easy to perform and a cheap biomarker that can aid the diagnosis.

Similarly, in another research by Wang T et al. that included 870 hypertensive patients, to evaluate the severity of albuminuria, the urinary albumin to creatinine ratio (UACR) has been computed. Of the 870 cases, 765 (87.9%) had typical albuminuria, 28 (3.2%) had macroalbuminuria, and 77 (8.9%) had microalbuminuria [7]. As the UACR raised the percentage of LVH and LVDD increased. In cases having typical albuminuria, UACR was independently related to LVH and LVDD. This suggests that even low-grade albuminuria, which is described as the greatest tertile within typical albuminuria for each sex (8.1-29.6 mg/g within men and 11.8-28.9 mg/g within women) [7], may be utilized as a marker of diastolic dysfunction.

A similar result has been found in cross-sectional research by Minoo et al., (2014) which revealed an adversely significant linear correlation between the UACR measurement and diastolic function (r =-0.184, p =0.012) [8]; but, this association was insignificant for systolic function (r =0.007, p =0.926) [8]. Moreover, multivariable linear regression analysis demonstrated that the UACR index had a significant reverse association with diastolic function [8].

Limitations include a small sample size. It needs to be carried out in a larger size and different communities to yield a more generalized result. Moreover, our results depend on correlations, so a causality evaluation is needed. Another significant limitation is the fact that we did not correlate our findings with the gold-standard invasive tests, so further validation with the gold-standard investigation may be needed to know the actual diagnostic accuracy of albuminuria. The discriminatory power of our results may be increased if included in further modelling strategies as a complementary tool in multivariable scores.

5. Conclusion

Our results recommend that albuminuria may be an efficient modality in screening for LVDD. However, further research is needed to confirm these findings in larger and more diverse populations.

Ethical committee approval: The study protocol was approved by the research ethical committee of the faculty of medicine, at Fayoum University following the guidelines of ethical considerations of the Helsinki Declaration.

Competing interests: All authors declare no conflict of interest.

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