Original Article

Comparison of Left Ventricular Hypertrophy Regression on Echocardiography in Hypertensive Patients with and without Diabetes Mellitus Treated with a Candesartan-Based Regimen

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Abstract

Background: Hypertension is 2-3 times more common in type 2 diabetes (T2DM) patients than in non-diabetics. For hypertensive diabetics, maintaining blood pressure below 130/80 mm Hg is crucial to reduce LVH risk. Angiotensin receptor blockers are particularly effective, as antihypertensive drugs differ in their ability to reverse LVH.

Objective: To compare the regression of Left Ventricular Hypertrophy (LVH) on echocardiography in hypertensive patients with and without diabetes mellitus using Candesartan based regimen.

Methods: The study was conducted at Mayo Hospital, Lahore. Non-probability convenience sampling technique was used to collect data of 45 hypertensive patients with diabetes and 45 hypertensive patients without diabetes. Blood pressure was measured at baseline and during all follow ups by the researcher himself. The patients received candesartan-based treatment for six months. Patients were treated with an initial dose of 8 mg Candesartan once a day. Left ventricular mass index was calculated by echocardiography and follow ups were done on the 1st, 3rd and 6th months.

Results: The average age of patients was 52.81 years (range: 35–65). There were 40 men (44.44%) and 50 women (55.56%). Based on BMI, 33.33% had normal weight, 42.22% were overweight, and 24.44% were obese. After six months, LVH regression was observed in 57.8% of diabetic patients and 35.6% of non-diabetic patients, showing significantly better outcomes in the diabetic group ($p < 0.05$).

Conclusion: This study concludes that a candesartan-based regimen effectively regresses left ventricular hypertrophy in diabetic hypertensive patients, highlighting the importance of tailored treatment strategies to optimize cardiovascular outcomes.

Keywords: Hypertension, Diabetes Mellitus, Echocardiography, Left Ventricular Hypertrophy.

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Introduction

Left ventricular hypertrophy (LVH), a critical target organ damage in hypertension, increases the risk of atrial fibrillation, heart failure, coronary artery disease, and mortality.[1] Hypertension is 2–3 times more common in patients with type 2 diabetes mellitus (T2DM), and

the coexistence of these conditions significantly heightens the risk of both microvascular and macrovascular complications.[2,3] LVH is a preclinical marker of cardiovascular diseases and an independent risk factor for adverse outcomes, especially in hypertensive diabetic patients.[4,5] The pathogenesis of LVH in diabetes involves complex interactions between hyperglycemia, insulin resistance, obesity, dyslipidemia, and hypertension. These factors contribute to cardiomyocyte growth and extracellular matrix remodeling, leading to increased left ventricular mass.[6] Systemic hypertension, the most significant risk factor for LVH, exacerbates myocardial hypertrophy and fibrosis, altering left ventricular geometry and function. Hypertension leads to Extracellular Matrix (ECM) remodeling of cardiomyocytes through mechano-transduction, fibroblast activation, and dysregulated ECM turnover, contributing to myocardial fibrosis and stiffness. Candesartan inhibits LVH directly by blocking AT1 receptor-mediated hypertrophic signaling in cardiomyocytes and indirectly by reducing fibroblast-mediated fibrosis, oxidative stress, and inflammation. These combined effects help restore normal cardiac structure and function. Effective blood pressure control below 130/80 mm Hg and optimal glucose regulation are critical in managing hypertensive diabetic patients.[6]

Regression of LVH is a critical objective in managing hypertension due to its association with adverse cardiovascular outcomes. Among antihypertensive medications, angiotensin receptor blockers (ARBs), such as Candesartan, have shown significant efficacy in promoting LVH regression.[7-9] Factors such as the duration of diabetes and patient age influence the effectiveness of Candesartan-based regimens in reducing echocardiographic LVH (ECH-LVH) in hypertensive patients.[10] While other antihypertensive drugs, such as Amlodipine, have demonstrated some benefits—such as reducing left ventricular mass index and posterior wall thickness — they show limited effects on other parameters like the LV end-diastolic diameter.[11] This underscores the need for effective medications that can comprehensively regress LVH in diabetic hypertensive patients, thereby preventing complications. Although research has been done in this field results from previous studies vary with some reporting improvement in both groups while others report no significant difference.[12,13] Echocardiography, being more sensitive and reliable than electrocardiography, is the preferred method for detecting and monitoring LVH regression.[9] This study aims to compare the regression of echocardiographic LVH in hypertensive patients with and without diabetes mellitus using a Candesartan-based regimen.

Methods

This Quasi experimental interventional study was done at Medical Outdoor and Indoor departments of Mayo Hospital, Lahore (Jan 2015-Jan2016). The study was approved by King Edward Medical University's institutional review board(No. 51/PEC/RC/KEMU). The sample size was calculated using the prevalence of LVH as 72% in hypertensive patients with diabetes and 32% in hypertensive non-diabetic patients. The expected difference in LVH regre-ssion between diabetic and non-diabetic hypertensive patients was also considered. The calculation was per-formed with 99% study power, a 95% level of significance, and a 5% margin for Type I error using the WHO sample size calculator.[14] After taking informed consent, all patients were enrolled who were fulfilling the inclusion and exclusion criteria in this study from outpatient department and indoor medical department, Mayo hospital Lahore by non-probability convenience sampling. The study included patients aged 25 to 65 years of either gender with a known history of hypertension for a minimum of three years or those diagnosed with left ventricular hypertrophy on echocardiography and hypertensive patients diagnosed with Diabetes Mellites for at least three years. Patients with triggered atrial fibrillation, heart blocks, or a prior diagnosis of heart failure were excluded. Other exclusion criteria included a known malignancy, concurrent renal disease, or any other significant comorbid condition. Furthermore, patients with contraindications to angiotensin receptor blockers, renal artery stenosis, a history of stroke, or those already on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers were not included. Individuals with valvular or congenital heart disease and pregnant female patients were also excluded from the study. Basic demographical information (age, gender, occupation, etc.) was obtained. The presence of cardiovascular risk factors, target organ dysfunction and associated clinical ailments including diabetes mellitus, was noted from the clinical history and investigation. Hypertensive patients with diabetes were enrolled in group A and hypertensive patients without diabetes was enrolled in group B. Blood pressure was measured at baseline and during all follow ups. At a single occasion 3 different readings were taken 10 minutes apart and their average was taken. The patients received treatment

for six months using a regimen based on candesartan. Left ventricular mass index was calculated. Tablet Candesartan 8 mg once day (OD) was the initial dose given to the patients.

They were followed at 1st, 3rd and 6th months. Candesartan was titrated up to a maximum of 16 mg OD at the end of the first month if the desired blood pressure objective was not reached. Diabetic patients were given appropriate anti-diabetic therapy and their HbA1c was monitored. Metformin and Glimipride or Metformin and injection Humulin 70/30 can be used. Dose can be modified to keep HbA1c below 6.5. Frequent monitoring of renal function tests was conducted, and individuals were excluded from the research if their renal profiles worsened.

All data was entered and analyzed using computerized software i.e. SPSS version 20. Qualitative data like gender and Occupation was presented in form of frequency (%). Shapiro Wilk test was applied to check the distribution of data. Quantitative data like age, onset of disease, blood pressure and ECH-LVH were presented in form of Mean ± S.D. Independent sample t test was applied to compare mean (BP, ECH-LVH) in both study groups (diabetic and non-diabetic groups), at each follow up. Paired T test was used to check the difference in each parameter at 1st, 3rd and 6-month values. The Chi-square test was applied to compare the qualitative attributes (like status of hypertension) in both groups. P-value < 0.05 was considered as significant.

Results

The mean age of patients was 52.81 ± 7.85 years with minimum and maximum age of 35 and 65 years. The mean age in diabetic and non-diabetic group was 54.44 ±8.04 and 51.18 ± 7.38 years. The mean age of diabetic

TableI: *Comparison of blood pressure in both study groups at different follow-ups*

		Mean ± SD				**p-value
	Study groups	Baseline	1st	3rd	6th	Baseline vs. 6th months
Systolic	Diabetic	147.44±6.79	136.67±7.07	130.22±12.52	133.56±10.48	<0.001
	Non-Diabetic	150.11±5.06	141.33±5.48	135.78±8.39	137.78±5.99	< 0.001
*p-value		0.037	0.001	0.0105	0.021	
Diastolic	Diabetic	95.67±6.09	86.00±6.18	85.84±9.32	86.00±5.39	< 0.001
	Non-Diabetic	97.00±6.61	89.78±6.57	87.56±7.73	88.89±10.71	< 0.001
*p-value		0.332	0.006	0.346	0.110	

*p value 0.05 considered significant, **p value calculated by paired t test, *p value calculated by independent sample t test*

Table II: *Comparison of different measurements in both study groups*

		Mean ± SD				**p-value
	Study groups	Baseline	1st	3rd	6th	Baseline vs. 6th months
Ejection fraction	Diabetic	61.51±7.76	61.51±7.76	58.93±9.11	61.44±6.22	0.963
	Non-Diabetic	61.44±7.59	61.47±7.28	62.51±7.29	61.47±5.83	0.987
*p-value		0.967	0.978	0.043	0.986	
LVEDD	Diabetic	44.60±6.22	44.38±6.52	46.93±10.09	45.02±5.24	0.712
	Non-Diabetic	45.02±7.01	45.16±6.94	45.24±6.80	46.47±8.09	0.347
*p-value		0.763	0.585	0.354	0.317	
IVSd	Diabetic	13.44±1.60	13.44±1.60	12.71±1.74	12.49±1.25	0.002
	Non-Diabetic	12.38±1.17	12.36±1.15	11.91±0.97	11.91±0.92	0.026
*p-value		0.001	<0.001	0.009	0.015	
PWd	Diabetic	11.82±3.15	11.82±3.15	12.00±3.09	11.53±1.47	0.598
	Non-Diabetic	11.24±1.93	11.27±1.95	11.33±1.41	11.84±2.26	0.182
*p-value		0.297	0.317	0.192	0.440	

*LVEDD=Left ventricular end diastolic volume, IVSd=interventricular septum thickness in diastole, PWd=Pulse Wave Doppler, LVMI=Left ventricular Mass Index, p value ≤ 0.05 considered significant, **p value calculated by paired t test, *p value calculated by independent sample t test*

Table III: *Comparison of LVMI in both study groups at different follow ups*

		Mean ± SD				*p-value
	Study groups	Baseline	1st	3rd	6th	Baseline vs. 6th months
LVMI	***Diabetic***	116.56±48.89	115.29±48.91	115.09±48.23	113.04±24.63	0.8
	Non-Diabetic	121.96±32.65	120.42±44.48	120.36±44.54	120.06±44.14	0.549
***p-value**		0.592	0.604	0.701	0.05	

*LVMI=Left ventricular Mass Index, p value ≤ 0.05 considered significant, **p value calculated by paired t test, *p value calculated by independent sample t test*

patients was higher than non-diabetic, p-value = 0.048. There were 40(44.44%) male and 50(55.56%) female patients with male to female ratio of 1:1.25. In diabetic group there were 19(42.2%) male and 26(56.8%) female patients while in non-diabetic group there were 21(46.7%) male and 24(53.3%) female patients. The gender distribution in both groups was similar, with no significant difference (p > 0.05). The mean BMI in the diabetic and non-diabetic groups was 28.08 ± 2.95 and 27.30 ± 3.60, respectively, with no statistically significant difference (p > 0.05). Based on BMI, 33.33% of patients were normal weight, 42.22% were overweight, and 24.44% were obese. In the diabetic group, 22.22% were normal weight, 51.1% were overweight, and 26.7% were obese, while in the non-diabetic group, 44.4% were normal weight, 33.3% were overweight, and 22.2% were obese. In the diabetic group, blood pressure decreased significantly (p value < 0.001) from 147.44 ± 6.79 / 95.67 ± 6.09 to 133.56 ± 10.48 / 86.00 ± 5.39. There was a significant reduction in the non-diabetic group as well as shown in Table I. A comparison of different echocardiography parameters measurements in both groups is shown in Table II.

Table IV: *Comparison of Echocardiographic LVH regression (at 6th month) in both study groups*

		Study groups		Total
		Diabetic	Non-Diabetic	
Echocardiographic LVH regression (at 6th month)	**Yes**	26	16	42
		57.8%	35.6%	46.7%
	No	19	29	48
		42.2%	64.4%	53.3%
Total		45	45	90
		100.0%	100.0%	100.0%

LVH = Left ventricular Hypertrophy, Chi-square =4.46, p-value = 0.035, p value ≤ 0.05 considered significant, p value calculated by Chi-square

The difference in mean LVMI (Left ventricular Mass Index) was statistically same in both study groups till 3rd month but it was significantly lower in diabetic group at 6th month (p-value = 0.05) as shown in Table III. The difference from baseline to 6th months was insignificant within the group in both study groups (Table III). In diabetic and non-diabetic groups, echocardiographic LVH regression at 6th month was observed in 26(57.8%) and 16(35.6%) of the patients, the regression in diabetic group was higher as compared to non-diabetic group at a significant level (p-value < 0.05) as shown in Table IV.

Discussion

A common harmful effect of hypertension is left ventricular hypertrophy (LVH), which significantly increases the risk of cardiovascular morbidity and mortality. Hypertension is diagnosed when systolic blood pressure exceeds 140 mm Hg or diastolic blood pressure exceeds 90 mm Hg, or if a person is already on antihypertensive medication.[15] Hypertension is classified into primary and secondary types, with primary (essential) hypertension accounting for 90-95% of adult cases, while secondary hypertension, caused by factors like vascular, renal, and endocrine issues, represents 2-10% of cases.[16] One independent predictor of poor cardiovascular outcomes is the onset of left ventricular hypertrophy (LVH) as a result of hypertension. On the other hand, LVH regression is linked to a better outcome.[17] In order to enhance patient outcomes, recent research has highlighted the significance of both reversing LVH and regulating blood pressure.

Research demonstrates that patients treated with candesartan have a significant reduction in left ventricular mass index (LVMI) compared to those on other antihypertensive agents, with diabetic patients showing particularly strong benefits. This is due to the exacerbated impact of hypertension in diabetic individuals, who often have additional complications like insulin resistance and altered neurohormonal activation.[18] LVH regression should be the prime objective in management of hypertension. Available antihypertensive drugs vary in their efficacy to cause LVH regression and the drugs which blocks Angiotensin receptor have been considered to

be very useful in this regard. Echocardiography is the more sensitive than electrocardiographic in early detection of LVH. Candesartan is widely used to manage hypertension, with doses ranging from 8–32 mg daily. It has been shown to reduce the risks associated with hypertension, including stroke, cardiovascular mortality, and renal failure.[19] Clinical evidence suggests that candesartan is as effective as other ARBs like valsartan and telmisartan and offers superior antihypertensive benefits over losartan.[20,21] The renin-angiotensin system is a target site for a number of antihypertensive medications and is essential for maintaining volume homeostasis and controlling blood pressure. It is a compound known for its prolonged duration and highly selective in mode of action.[22] According to Barrios V et al., the impact of a candesartan-based regimen on ECH-LVH in hypertensive patients is also influenced by the patient's age and the duration of diabetes mellitus.[23] The research has clearly demonstrated the advantages of blood pressure management, which lowers the risk of heart failure and stroke.

The current study also shows significant reductions in blood pressure in both diabetic and non-diabetic hypertensive patients after treatment with candesartan. However, while LVMI decreased in both groups, the change was not statistically significant, indicating a need for further investigation. Moreover, a significant decrease in blood pressure was observed in present study in the diabetic group, with values improving from baseline to the 6th month. This result indicates the effectiveness of the treatment regimen in managing hypertension in diabetic patients. Regarding LVMI, it decreased in both diabetic and non-diabetic patients from baseline to the 6th month. In diabetic patients, LVMI reduced from 115.09±48.23 to 113.04±24.63, while in non-diabetic patients, it decreased from 120.36±44.54 to 124.96 ± 32.65. However, the change in LVMI from baseline to 6 months was not statistically significant in either group. A study conducted in 2003 reported significant reductions in systolic and diastolic blood pressure following treatment with candesartan cilexetil, as well as a decrease in LVMI, measured both by MRI and echocardiography but the results were not compared in hypertensive patients with and without diabetes.[24]

A 2009 study by Barrios et al. on diabetic and non-diabetic hypertensive patients found that both groups experienced a significant reduction in blood pressure with candesartan treatment. The incidence of ECG-LVH also decreased in both groups, with a more pronounced reduction in diabetics. The relative risk reduction of ECG-LVH was higher in diabetic patients, especially when assessed using the Cor P (Cornell product) and Sok P (Sokolow-Lyon product) criteria, compared to non-diabetic patients.[23] The current study reported that echocardiography-based regression of LVH in patients using Candesartan regime is more useful for diabetic hypertensive patients. In support are the findings of the study by Cuspidi C et al., 2019 who reported similar findings. They showed that systolic/diastolic blood pressure was reduced by 19.3 ± 8/9.4±5 mmHg ($p<0.001$ for both) and left ventricular mass index (LVMI) declined to 17.01 g/m^2 (95%CI: -13.2 to -20.99; $p<0.001$) whereas LVMI-related echocardiographic parameters significantly decreased after therapeutic treatment with the candesartan-based drugs moreover, they demonstrated that diabetes ($p < 0.05$) was predictive of LVH regression.[25] LVH regression at 6th month was observed in the present study in 42(46.67%) patients. Moreover, the LVH regression at 6 months was significantly higher in diabetic patients (57.8%) compared to non-diabetic patients (35.6%). suggesting that candesartan may be particularly effective in diabetic hypertensive patients. The use of candesartan in a comprehensive management plan not only addresses blood pressure but also targets the structural changes in the heart. This is particularly relevant considering that LVH is often under-recognized in clinical practice. The goal of future studies should be to better understand the processes underlying the differential regression of LVH in people with and without diabetes who have hypertension. Longitudinal studies are required to evaluate the long-term outcomes of LVH regression on cardiovascular events in these populations. Additionally, exploring combination therapies that integrate ARBs with other classes of antihypertensive medications may enhance regression outcomes.

Conclusion

In conclusion, this study affirms that a candesartan-based regimen effectively promotes left ventricular hypertrophy (LVH) regression, particularly in diabetic hypertensive patients. The significant difference in LVH regression between diabetic and non-diabetic patients highlights the importance of personalized treatment plans for managing hypertension and its cardiovascular risks. This approach not only improves patient outcomes but also contributes to reducing long-term cardiovascular morbidity, underscoring the role of individualized therapeutic strategies in enhancing overall health.

Conflict of Interest: None

Funding Disclosure: None

Ethical consideration: The study was approved by the ethical review board. Informed written consent was obtained from the participants, and the confidentiality of their data was clearly explained.

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Authors Contribution: All the authors contributed equally, in accordance with ICMJE guidelines and are accountable for the integrity of the study.

1. **NRR:** Conception, design, data analysis, and initial and final draft-making
2. **RR:** analysis and interpretation, initial and final draft making
3. **NF:** initial and final draft-making, analysis and design work
4. **HL:** Revising the initial and final draft, data collection and data analysis
5. **MA:** Data analysis, initial and final draft revision
6. **MA:** Initial and final draft-making, data analysis

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