Left ventricular hypertrophy among hypertensive patients with diminished glomerular filtration rate

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Abstract: Background and Purpose: To study the left ventricular mass by ECHO in a groups of hypertensive patients with reduction of kidney function, free of CV diseases. **Aim of Work:** To assess the prevalence of LVH among hypertensive patients with diminished renal function. We evaluated the relationship between reduced estimated glomerular filtration rate (eGFR) and LVH diagnosed with echocardiography (ECHO)**. Methods:** The study was performed at Shiekh Zayed hospital in cooperation with Al Azhar University hospital, during the study period from 1/10/2015 to 1/11/2016 on group of patients who are known to be hypertensive(defined according to the European Society of Hypertension (ESH)/European Society of Cardiology (ESC) Guidelines were included in this study, according to glomerular filtration rate patients will divided into group with normal GFR (control group), and group with mild to moderate reduction of GFR, data were collected and analyzed by SPSS program and ANOVA. **Results:** The current study showed that there was a significant statistical difference between the 3 groups Regarding LVMI. We found that LVMI showed a progressive rise with increase in severity of renal failure. **Conclusion:** High prevalence of LVH in patients with mild or moderate renal dysfunction. The progressive increase of LVH prevalence and left ventricular mass are likely to contribute to the high prevalence of cardiovascular events of this population.

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Keywords: Left ventricular; hypertrophy; patient; glomerular filtration rate

1. Introduction

Left ventricular hypertrophy is the most powerful risk factor for coronary heart disease, ventricular arrhythmias, congestive heart failure and sudden cardiac death ***(Tocci et al, 2008)***.

The progressive increase of LVH prevalence and left ventricular mass along with decreasing renal function ***(Levy et al., 1990)***.

Recent epidemiological studies confirmed that a moderate reduction of glomerular filtration rate (GFR) is associated with the increase of CV risk, and that renal function is an independent predictor of CV mortality and all cause death ***(Manjunath et al., 2003)***.

Cardiovascular diseases are the leading cause of death for patients with chronic kidney disease. Cardiovascular risk of chronic kidney disease patients is significantly higher than in the general population, and the risk of a fatal cardiovascular event is higher than the risk than their renaldisease, the increase of risk is alarming for patients with end- stage renal disease ***(Nardi et al, 2012)***.

Hypertension in itself represents a powerful risk factor for cardiovascular disease in chronic kidney disease and is almost invariably present in patients with renal failure **(*Cerasola et al., 2011)***.

Hypertension also plays a major role in cardiac damage in chronic kidney disease via changes in left ventricular remolding and left ventricular hypertrophy induction ***(Norris et al, 2009)***.

Left ventricular hypertrophy (LVH), a common expression of hypertension-related target-organ damage, is an independent predictor of CV morbidity and mortality; ***(Sundstrom et al., 2001)*** this is true is, in some studies, higher than 70% **(*Stack et al., 2002).***

Aim of Work

The aim of this work is to study the relationship between left ventricular mass and mild to moderate reduction of kidney function in a group of hypertensive patients.

2. Patients and Methods

The present study was performed at Shiekh Zayed hospital in cooperation with Al Azhar University hospital, during the study period from 1/10/2015 to 30/10/2016on group of patients who are known to be hypertensive(defined according to the European Society of Hypertension (ESH)/European Society of Cardiology (ESC) Guidelines ***(Mancia et al., 2007)*** were included in this study, according to glomerular filtration rate patients will divided into group with normal GFR (control group), and group with mild to moderate reduction of GFR.

The patients will be selected according to the following criteria:

Inclusion criteria:

- Hypertension.
- Age ≤ 65 years.

- Males and females.

Exclusion criteria:

1- Patients with diagnosed heart failure.

2- History or clinical signs of coronary artery disease.

3- History of valvular or congenital heart diseases.

4- History of endocrine or malignant hypertension.

5- History or clinical signs of cerebrovascular disease.

6- Patients with a GFR of less than 30 mL/min per 1.73 m2.

The participants will be classified into three groups according to the levels of renal function*:*

Using the cut-off values of GFR proposed by the National Kidney Foundation Kidney Disease Outcome Quality Initiative (K/DOQI 2002).

- **Group (I):** (normal kidney function).

Control group includes 20 hypertensive patients with blood pressure >140/90 & normal kidney function (GFR of 90 mL/min per 1.73 m2 or more).

- **Group (II):** (mild reduction of kidney function).

Includes 30 hypertensive patients with blood pressure >140/90 & mild reduction of GFR (GFR of 60–89 mL/min per 1.73 m2).

- **Group (III):**(moderate reduction of kidney function).

Includes 30 hypertensive patients with blood pressure >140/90 & moderate reduction of GFR (GFR 30–59 mL/min per 1.73 m2).

GFR estimated from plasma creatinine by Cockcroft & Gault Formula (***Cockcroft DW et al.*, 1976**).

Laboratory assessment:-

- Serum creatinine concentrations.
- Serum electrolytes.
- Blood glucose level.

Echocardiographic assessment:

By Conventional Transthoracic Echocardiography (TTE):

► Echocardiographic measurements and calculation will be done according to recommendations of American Society of Echocardiography **(*Sahn D et al.*, *1978*)**.

Two-dimensional (2D) echocardiography. All the patients will be examined in the left lateral decubitus position. Echocardiographic images will be acquired from the standard views (parasternal long-axis, parasternal short axis at papillary muscle level, apical four –chamber, apical five –chamber and apical two- chamber).

The Echocardiographic assessment will focus on:

Left ventricular dimensions.

Left atrium dimensions and volume.

Left ventricular diastolic function.

Left ventricular mass index:

By measuring the following parameters on the M-mode echocardiogram:

– left ventricular diastolic dimension (LVDd, cm).

– interventricular septum diastolic thickness (IVS, cm).

– left ventricular posterior wall diastolic thickness (LVPW, cm).

The measurements will be obtained at the peak of the R wave on the ECG.

Statistics:

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, The Wilcoxon tests, linear correlation coefficient, Analysis of variance [ANOVA] tests Paired t-test and chi-square by SPSS. Significant results is considered if p-value < 0.05 and highly significant results is considered if p-value < 0.01. All statistical analyses were performed using SPSS 11.0 J for Windows.

3. Results

A total of 80 subjects comprised the study population. The participants were classified into three groups according to the levels of renal function:

Group (1): (normal kidney function) included 20 hypertensive patients & normal kidney function (GFR of 90 mL/min per 1.73 m2 or more).

Group (2): (mild reduction of kidney function) included 30 hypertensive patients & mild reduction of GFR (GFR of 60–89 mL/min per 1.73 m2).

Group (3): (moderate reduction of kidney function) included 30 hypertensive patients & moderate reduction of GFR (GFR 30–59 mL/min per 1.73 m2).

Table (1): Gender distribution among study groups.

Sex	Group I (n=20)	Group II (n=30)	Group III (n=30)	Total (n=80)
Male	50% (n= 10)	53.3% (n= 16)	60% (n= 18)	55% (n= 44)
female	50% (n= 10)	46.7% (n= 14)	40% (n= 12)	45% (n= 10)

The following Results Were Obtained:

I- Demographic criteria of study population:

Age

The study population age ranged from 39 to 63 yrs (54 ± 5.8) yrs.

Group I age mean was (50.7 ± 6) yrs.

Group II age mean was (51.9 ± 4.7) yrs.
Group III age mean was (59.2 ± 2.9) yrs.

Sex

The study population included 45 (56%) males and 35 (44%) females.

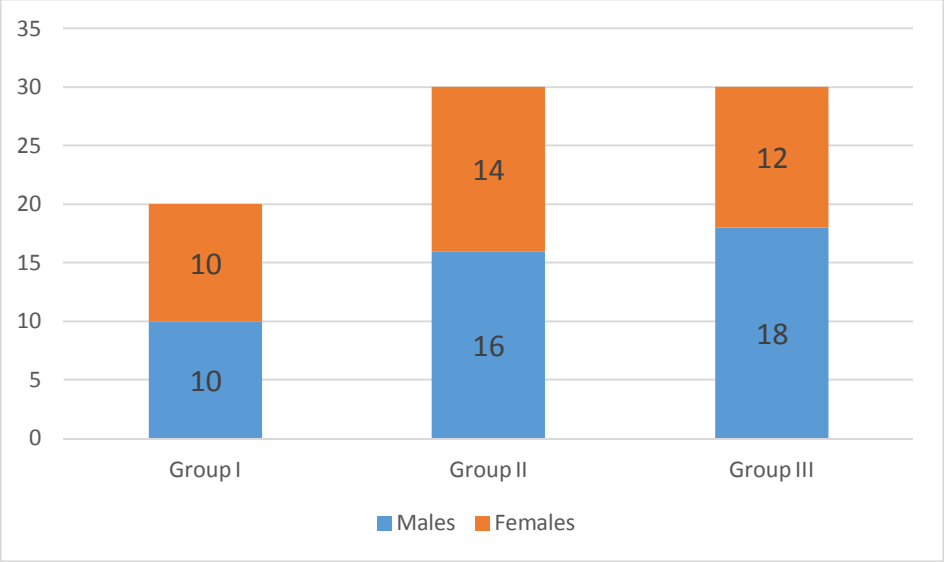

Figure (1): comparison between groups regarding gender.

Systolic blood pressure

The study population systolic blood pressure ranged from 130 to 155 Hmmg (146.25±6.58) Hmmg.

Group I systolic blood pressure mean was (138 ± 4.7) Hmmg.

Group II systolic blood pressure mean was (146 ± 4) Hmmg.

Group III systolic blood pressure mean was (151.7±2.4) Hmmg.

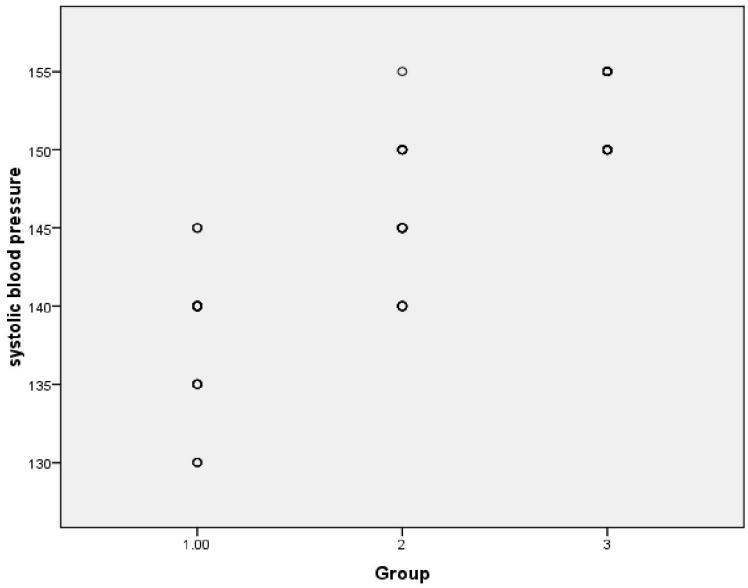

Figure (2): comparison between groups regarding systolic blood pressure.

Diastolic blood pressure

The study population systolic blood pressure ranged from 80 to 100 Hmmg (91.1 ± 5.4) Hmmg.

Group I systolic blood pressure mean was (86 ± 4.8) Hmmg.

Group II systolic blood pressure mean was (91.3 ± 2.9) Hmmg.

Group III systolic blood pressure mean was (93.7 ± 5.5) Hmmg.

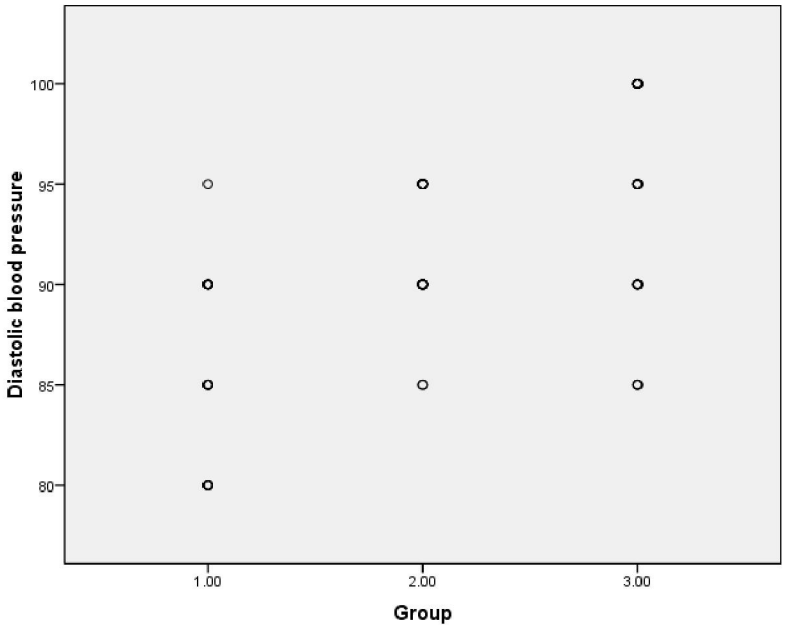

Figure (3): comparison between groups regarding diastolic blood pressure.

Heart Rate

The study population heart rate ranged from 60 to 103 b/m (85.5 ± 10.4) b/m.

Group I heart rate mean was (79 ± 13) b/m.

Group II heart rate mean was (86.7 ± 10.8) b/m.

Group III heart rate mean was (88.7 ± 5.8) b/m.

Left ventricular mass

The study population left ventricular mass ranged from 166 to 450 g (297.59 ± 51.9) g.

Group I left ventricular mass mean was (235 ± 31) g.

Group II left ventricular mass mean was (301.6 ± 20.5) g.

Group III left ventricular mass mean was (245.1 ± 50.8) g.

Left ventricular mass index

The study population left ventricular mass ranged from 83 to 185 g/m² (151.1 ± 23.1) g/m².

Group I left ventricular mass index mean was (118 ± 16.8) g/m².

Group II left ventricular mass index mean was (152.4 ± 6.2) g/m².

Group III left ventricular mass index mean was (172.55 ± 5.7) g/m².

Left atrium

The study population left atrium ranged from 3.70 to 4.20 cm (3.96 ± 0.137) cm.

Group I left atrium mean was (3.9 ± 0.16) cm.

Group II left atrium mean was (3.97 ± 0.13) cm.

Group III left atrium mean was (3.99 ± 0.11) cm.

Ejection fraction

The study population ejection fraction ranged from 50 to 78 % (61.33 ± 7.4) %.

Group I left atrium mean was (65.4 ± 8) %.

Group II left atrium mean was (61 ± 6.6) %.

Group III left atrium mean was (59.3 ± 7.4) %.

Diastolic dysfunction

The study population included 58(72.5%) with grade I diastolic dysfunction, 19(23.8%) grade II diastolic dysfunction and 3(3.8%) grade III diastolic dysfunction

Table (2): Diastolic dysfunction among study groups.

Diastolic dysfunction	Group I, n=20	Group II, n=30	Group III, n=30	Total, n=80
Grade I	85% (n= 17)	83% (n= 25)	53% (n= 16)	72.5% (n= 58)
Grade II	15% (n= 3)	17% (n= 5)	37% (n= 11)	23.8% (n= 19)
Grade III	(n=0)	(n=0)	10% (n= 3)	3.8% (n= 3)

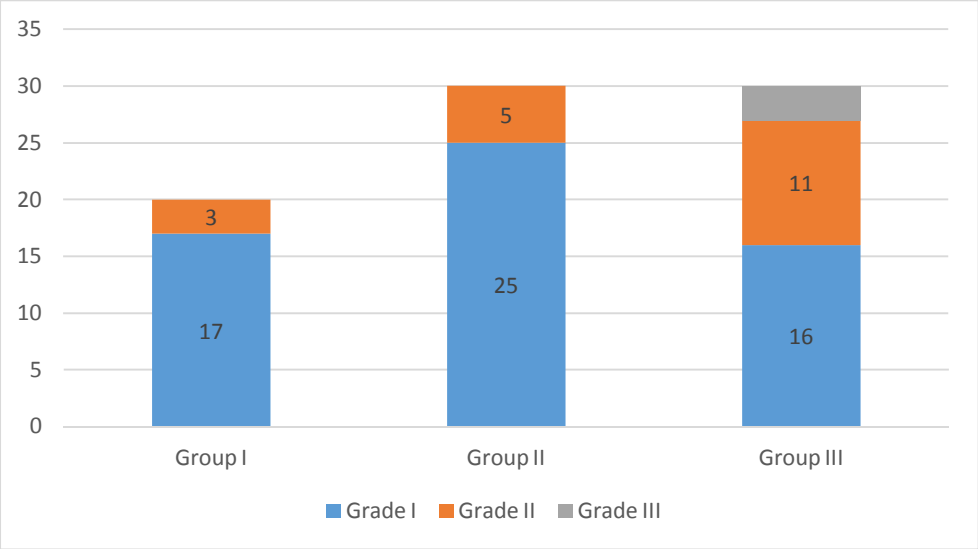

Figure (4): comparison between groups regarding diastolic dysfunction.

Creatinine clearance

The study population creatinine clearance ranged from 40 to 125 ml/min (68.85 ± 22.31) ml/min.

Group I creatinine clearance mean was (101 ± 9.7) ml/min.

Group II creatinine clearance mean was (69.9 ± 5.9) ml/min.

Group III creatinine clearance mean was (45.1 ± 4) ml/min.

Medication

The study population included 10(12.5%) no medication, 50(62.5%) on Beta blocker and 20(25%) on ACEI

Table (3): Study groups regarding antihypertensive medications.

Medication	Group I (n=20)	Group II (n=30)	Group III (n=30)	Total (n=80)
No medication	20%(n=4)	7.6%(n=2)	13.3%(n=4)	12.5% (n=10)
Beta blocker	50%(n=10)	46.7%(n=14)	86.7%(n=26)	62.5% (n=50)
ACEI	30%(n=6)	46.7%(n=14)	(n=0)	25% (n=20)

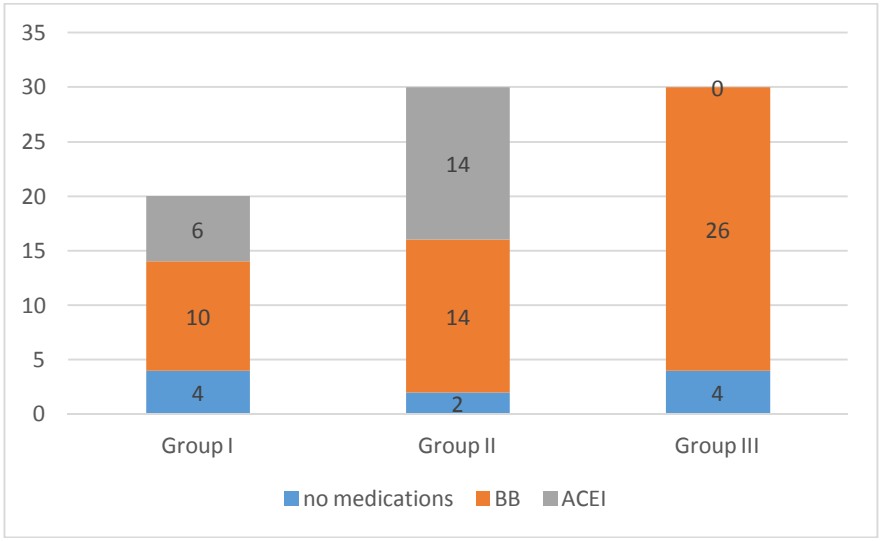

Figure (5): comparison between study groups regarding antihypertensive medications

II- Analytic statistics:

Table (4): Correlation between creatinine clearance and different study variables ANOVA

	Mean square	F	Sig (p value)
sex	0.395 (0.114)	3.473	< 0.001
age	61.648 (9.104)	6.772	< 0.001
systolic blood pressure	87.336 (2.591)	33.701	< 0.001
Diastolic blood pressure	59.202 (2.744)	21.576	< 0.001
Heart Rate	218.028 (10.018)	21.763	< 0.001
DiastolicDysfunction	0.610 (0.001)	164.34	< 0.001
Ejection fraction	103.906 (10.064)	10.325	< 0.001
Left atrium diameter	0.033 (0.006)	5.499	< 0.001
Left ventricular mass index	1099.250 (11.915)	92.260	< 0.001
Medication	0.691 (0.061)	11.329	< 0.001

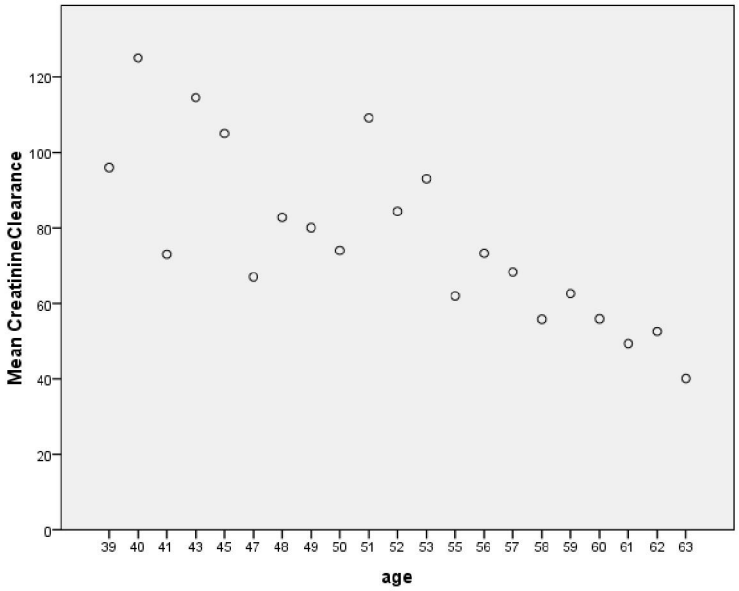

Figure (6): comparison between mean creatinine clearance and age.

Table (5): Correlation between left ventricular mass index LVMI and different study variables ANOVA

	Mean square	F	Sig (p value)
sex	0.309 0.216	1.432	0.131
age	87.552 5.185	16.887	< 0.001
Diabetic	0.353 0.195	1.813	0.032
systolic blood pressure	103.373 10.403	9.937	< 0.001
Diastolic blood pressure	70.505 7.609	9.266	< 0.001
Heart Rate	196.398 62.680	3.133	< 0.001
DiastolicDysfunction	0.713 0.063	11.286	< 0.001
Left atrium diameter	0.032 0.012	2.693	< 0.001
Ejection fraction	112.878 23.539	4.795	< 0.001

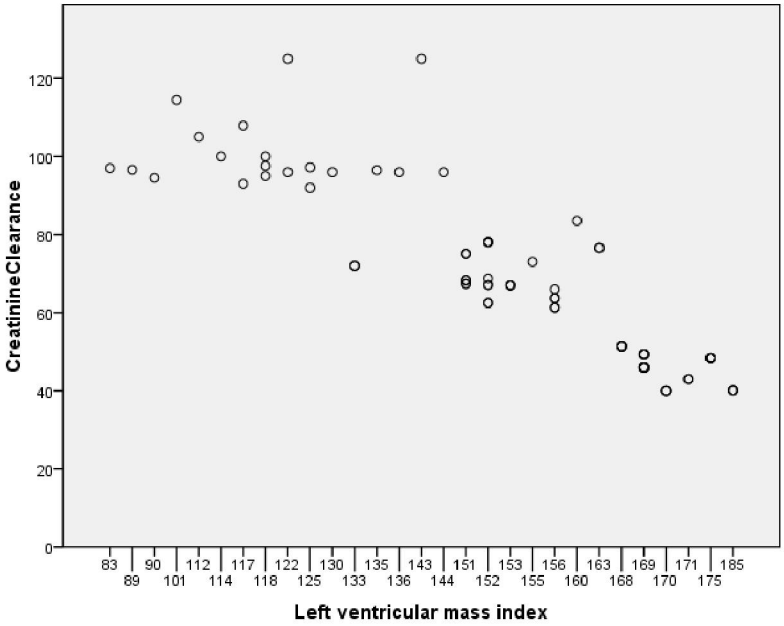

Figure (7): comparison between creatinine clearance and left ventricular mass index.

Table (7): Correlation between left ventricular mass index LVMI and different creatinine clearance among study groups ANOVA.

	Mean square	F	Sig (p value)
Group I	89.0 111.506	0.799	0.662
Group II	80.776 21.141	3.821	<0.005
Group III	78.882 1.281	61.565	<0.001

Table (8): Demographic characters means distributions among study groups

	Group I (n=20)	**Group II (n=30)**	**Group III (n=30)**
Age	50.7 ± 6	51.9 ± 4.7	59.2 ± 2.9
Systolic Blood Pressure	138 ± 4.7	146 ± 4	151.7 ± 2.4
Diastolic blood pressure	86 ± 4.8	91.3 ± 2.9	93.7 ± 5.5
Heart rate	79 ± 13	86.7 ± 10.8	88.7 ± 5.8
Left ventricular mass	235 ± 31	301.6 ± 20.5	345.1 ± 50.8
Left ventricular mass index	118 ± 16.8	152.4 ± 6.2	172.55 ± 5.7
Left atrium diameter	3.9 ± 0.16	3.97 ± 0.13	3.99 ± 0.11
Ejection fraction	65.4 ± 8	61 ± 6.6	59.3 ± 7.4
Creatinine	1.02 ± 0.1	1.38 ± 0.13	2.2 ± 0.49
Creatinine clearance	101 ± 9.7	69.9 ± 5.9	45.1 ± 4
Urea	26.2 ± 7.4	27.3 ± 5	32.5 ± 3.8
Sodium	136.2 ± 3	135.3 ± 2	139 ± 3.1
Potassium	4.3 ± 0.35	4.5 ± 0.36	4.6 ± 0.3

4. Discussion

Hypertension is the most important risk factor for death in industrialized countries. In the year 2000, it is estimated that nearly one billion people or "26% of the adult population have hypertension worldwide. ***(Kearney et al., 2005*)**.

It is important to remark that for many patients with CKD, the risk of a fatal CV events higher than

the risk that their renal disease may reach ESRD. ***(Shulman NB et al., 1989).***

Left ventricular hypertrophy (LVH), a common expression of hypertension-related target-organ damage, is an independent predictor of CV morbidity and mortality (***Sundstrom J et al., 2001).*** While for patients with ESRD data regarding the prevalence and the prognostic significance of LVH are well consolidated, less data are available about the relationship between LVH and less advanced CKD. However, published data seem to provide evidence that the prevalence of LVH among non-uremic CKD patients is 34–78%, with increasing prevalence along with decreasing renal function. **(*Levin et al., 1999*).**

In this study: we investigated the relationship between LV mass and mild-to-moderate reduction of kidney function in a group of hypertensive patients, free of CV diseases.

80 individuals were enrolled and divided into 3 groups:

- **Group (I)**: included 20 hypertensive patients with blood pressure >140/90 & normal kidney function (GFR of 90 mL/min per 1.73 m2 or more).
- **Group (II):** included 30 hypertensive patients with blood pressure >140/90 & mild reduction of GFR (GFR of 60–89 mL/min per 1.73 m2).
- **Group (III):** included 30 hypertensive patients with blood pressure >140/90 & moderate reduction of GFR (GFR 30–59 mL/min per 1.73 m2).

There was a significant statistical difference between the 3 groups Regarding Systolic Blood Pressure which was (151 ± 8), (156 ± 7) and (162 ± 6) in Group (I), Group (II) and Group (III) respectively (P value was < 0.05).

There was a significant statistical difference between the 3 groups Regarding Diastolic Blood Pressure which was (97.5 ± 6), (98.3 ± 7.3) and (101.8 ± 6.3) in Group (I), Group (II) and Group (III) respectively (P value was < 0.05).

A similar finding was reported by **(*Giovani Cerasola et al., 2011*)**, who studied 455 CKD patients divided into 3 Groups and Found a significant statistical difference between the 3 Groups regarding both systolic Blood Pressure which was (123±21) & (154±20) & (173±21) in Groups I, II, III respectively & the Diastolic Blood Pressure which was (91±15) & (92±15) & (102±16) in Groups I, II, III respectively.

Regarding LVMI:

The LVMI show a progressive rise with increase in severity of renal failure the pathomechanism of LVH in renal failure are explained by **(*Amman k et al., 1998*)** and concluded that both preload and after load are increased because of hypervolemia and increased peripheral vascular resistance respectively, the increasein preload induced by hypervolemia, causes serial additional of sarcomeres leading to lengthening of myofibers and eccentric hypertrophy. Also the increase in after load from increased peripheral resistance and increase impedance, causes parallel addition of sarcomeres, leading to thickening of myofibers and concentric hypertrophy.

A similar finding was reported by **(*Levin et al., 2007*)**, who studied 318 CKD patients And found that 34% had LVH, whose prevalence increased with the declining renal function, becoming near to 70% in the subgroup with ESRD.

Also, a similar finding was found In the Hoorn Study where the association between LVH and renal dysfunction has been evaluated in 742 subjects, nearly 70% of whom were hypertensive. While in women no relation between renal dysfunction and LVM was observed, it was found in men. The authors concluded that renal dysfunction, through an increase of arterial stiffness, leads to the increase of LVM (the authors found an increase of both LV diameter and wall thickness).

Another study by **(*Paoletti et al., 2005*)** evaluated the prevalence of LVH in 244 non-diabetic patients with CKD, reaching conclusions consistent with those by the Hoorn Study. An independent association between LVM and pulse pressure was demonstrated. The prevalence of hypertension was 66% and the prevalence of LVH was progressively higher along with the declining renal function, being 71% in stage 3 CKD.

This also agreed with study done by **(*Emilio Nardi et al., 2008*)**, who studied 293 patients with CKD and hypertension (men/women: 175/118, mean age 59.3±13.7 years) and found that LVH was observed in 47 % of patients with CKD and in 31% of essential hypertensive patients (P < 0.0001). They also found an increasingly higher left ventricular diameters, thicknesses, and mass from stage 2 to 5 CKD that reached more than 70% (73%) in patients with stage 5 CKD.

In the present study, we found that LVMI showed a progressive rise with increase in severity of renal failure. This is in concordance with the study done by **(*Greaves et al., 1995*)** who also found a similar trend of LVMI in patients of CRF.

A study done by **Harnett et al., 1993** revealed that, the course of hemodialysis significantly decreased LVMI in CRF patients.

2-Regarding the level of Blood Pressure & LVMI:

Pressure overload, caused, by hypertension, requires the generation of greater intracavitary pressure during ventricular contraction. This is achieved by arraying contractile protein units in parallel. Relatively, an increase in wall thickness.

In our study, There was a significant statistical positive correlation between the levels of Systolic

Blood Pressure & Diastolic Blood Pressure and LVMI (p value < o.o5).

A similar finding was found by **(*Foley et al., 1995*)** who found that Blood pressure is associated with LVH in the general & CRF individuals.

London et al., 2002 described systolic blood pressure (SBP) and pulse pressure as simplified markers of pressure load that result from interaction between cardiac factors, i.e., stroke volume, ejection velocity, and the opposition to left ventricular ejection.

And identified these factors as an important contributor to LVH, so it may be increased as a function of hypervolemia, anemia, or arteriovenous fistula.

Also, studies done by **London et al., 2003** have shown that peripheral resistance and mean arterial pressure as well as Diastolic Blood Pressure are frequently increased in early renal disease and CRF.

3- Regarding correlation between eGFR & Age:

In our study, there was a significant statistical correlation between age & eGFR among all study populations ($r = - 0.7068$, $p < 0.0001$).

This agrees with the study done by Mahboob **Rahman et al., 2004** *who* studied 40514 hypertensive patients 55 years or older who were enrolled in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) found that 75 % of patients had mild (60-89 mL/min per 1.73 m2), 17 % had moderate (30-59 mL/min per 1.73 m2), and 0.6% had severe (≤ 29 mL/min per 1.73 m2) reductions in GFR. The prevalence of LVH was higher in patients with moderate (6 %) and severe (11.2%) reductions in GFR than those with a normal GFR (3.9%) or a mild reduction (4.2%). (P ***≤ 0.05 for differences between groups)***.

Patients with moderate and severe reductions in eGFR were older and included a higher proportion of women compared with patients with a mild reduction in or a normal GFR with the mean age was 50.7 ± 6 in the Group of normal eGFR (no = 10 374 pt.) & 51.9 ± 4.7 in the group of mild reduction of eGFR (no = 22 965 pt.) & 59.2 ± 2.9 in the group of Moderate Reduction of eGFR (no = 6952 pt.) & 70.6 ± 9.0 in the group of Severe Reduction of eGFR (n = 223). (P ***≤ 0.05 for differences between groups)***. A decrease in GFR of 10 mL/min per 1.73m2 was independently associated with a 6% higher risk for CVD and 14% higher risk for ECG-LVH. The increase in risk was marked at a GFR of approximately 60 to 70 mL/min per 1.73 m2.

This also agreed with the study done by **(*Pierre Douville1 et al., 2009*)** who studied 773 outpatients from 18 to90 years old. Multiple linear regression was used to model the effect of age on glomerular filtration. Comparisons were made with the simplified MDRD and the MAYO equations. All equations show declining function with age, suggest that the GFR reduction is progressive after the age of 30 and continue to decline steadily after the age of 60.

Also, this agree with study done by ***(Crooks et al., 1976)*** and concluded that Diminution of glomerular filtration rate, renal plasma flow and associated tubular function with age have been well documented. Drug clearance comparisons between old and young have been carried out for only three renally excreted drugs — digoxin, propicillin and sulphamethizole. With digoxin and sulphamethizole, the evidence is that renal excretion is diminished in the elderly.

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