**RELEATION OF**

 **GLOMRULAR FILTRATION RATE**

**WITH LEFT VNTRICULAR MASS MEASURMENTS IN PATIANTS HAD RENAL IMPAIRMENT AND CHRONIC KIDNEY DISEASE**

*A thesis*

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 **بسم الله الرحمن الرحيم**

 **)**وَمَا أُوتِيتُم مِّن الْعِلْمِ إِلاَّ قَلِيلاً**)**

صَدَقَ اللَّه العَظيم

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**Dedication**

**To …**

***My family and my wife***

**Aknowledgment**

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**ABSTRACT**

Background

Left Ventricular Hypertrophy (LVH) is associated with end-stage renal disease and chronic kidney disease, but the association of LVH with mild impairment in kidney function is not known.Left ventricular hypertrophy (LVH) is an early, subclinical marker of cardiovascular disease and heart failure risk.In patients with end-stage renal disease, LVH is common, and is an independent predictor of cardiovascular disease and mortality.

**Method**

This was a cross sectional study of patients who havechronic kidney disease or they had renal impairment in albasra general hospital and alsader teaching hospital who had echocardiographic study

In this study, we included every patient with renal impairment and chronic kidney disease as evident by abdominal ultrasound examinations that show small size kidney and sent them for echocardiography to estimate left ventricular mass by M-mode measurements of left ventricular dimensions

The patient was (n=100) ,55% men and 45% female , their age between 16 and 75 for duration of five months from July 2010 to December 2010

In the estimation of glomerular filtration rate or creatinine clearance I had use Cockcroft-Gault equation

**Results:**

There is strong relation between reduction in glomerular filtration rate and increased left ventricular mass especially at or more than stage 3 of chronic kidney disease as evident in this study

**Conclusions:**

Left ventricular mass is an independent predictor of cardiovascular disease mortality and heart failure in patients with ≥ stage three chronic kidney disease, defined as a creatinine-based estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m2. Among patients with chronic kidney disease, increased LV mass is correlated with severity of GFR impairment.

**Introduction**

Definition of chronic kidney disease

The Renal NSF adopted the US National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) classification of CKD1. This classification divides CKD into five stages defined by evidence of kidney damage and level of renal function as measured by glomerular filtration rate (GFR). Stages 3–5 may be defined by GFR alone, whilst stages 1 and 2 also require the presence of persistent proteinuria, albuminuria, haematuria or structural abnormalities1,2. Stage 5 CKD may be described as established renal failure (also called end stage renal disease (ESRD)), and is CKD which has progressed so far that renal replacement therapy (regular dialysis treatment or kidney transplantation) may be required to maintain life. Established renal failure is an irreversible, long-term condition. A small number of people with established renal failure may choose conservative management only. The classification of CKD into 5 stages has been widely adopted but as understanding of the epidemiology of CKD has developed, it has been criticized as not being sufficiently sophisticated for clinical needs.

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| --- | --- | --- |
| **Stage** | **Description** | **GFR (ml/min/1.73m2)** |
| 1 | Kidney damage with normal or increased GFR | ≥90 |
| 2 | Kidney damage with mild reduction in GFR | 60–89 |
| 3 | Moderate reduction in GFR | 30–59 |
| 4 | Severe reduction in GFR | 15–29 |
| 5 | Kidney failure | <15 (or dialysis) |

Chronic kidney disease (CKD) and ESRD, treated with conventional hemo- or peritoneal dialysis are both associated with a high prevalence of an increase in left ventricular mass (left ventricular hypertrophy [LVH]), intermyocardial cell fibrosis, and capillary loss2. Cardiac magnetic resonance imaging is the best way to detect and quantify these abnormalities, But M-Mode and 2-D echocardiography can also be used if one recognizes their pitfalls. The mechanisms underlying these abnormalities in CKD and ESRD are diverse but involve afterload (arterial pressure and compliance), preload (intravascular volume and anemia), and a wide variety of afterload/preload independent factors3. The hemodynamic, metabolic, cellular, and molecular mediators of myocardial hypertrophy, fibrosis, apoptosis, and capillary degeneration are increasingly well understood3,4. These abnormalities predispose to sudden cardiac death, most likely by promotion of electrical instability and re-entry arrhythmias and congestive heart failure. Current treatment modalities for CKD and ESRD, including thrice weekly conventional hemodialysis and peritoneal dialysis and metabolic and anemia management regimens, do not adequately prevent or correct these abnormalities. A new paradigm of therapy for CKD and ESRD that places prevention and reversal of LVH and cardiac fibrosis as a high priority is needed. This will require novel approaches to management and controlled interventional trials to provide evidence to fuel the transition from old to new treatment strategies. In the meantime, key management principles designed to ameliorate LVH and its complications should become a routine part of the care of the patients with CKD and ESRD4,5,6,7.

**Left Ventricular Measurements**

Left ventricular mass is generally calculated as the difference between the epicardium and the left ventricular chamber volume multiplied by an estimate of myocardial density8. Following this principle, several methodologies have been used to calculate left ventricular mass and to define hypertrophy with its own flaws and strengths on each step, resulting in a wide range of values. Probably, the most significant echocardiographic limitation is related to inadequate quality imaging15,16. Population-based studies are not able to obtain complete imaging in almost a quarter of screened patients. mainly due to inappropriate acoustic windows. M-mode echocardiography is used most widely to measure left ventricular mass because of its wide availability, moderate expense, anatomic and prognostic validation and lack of radiation or claustrophobia; however, this technique is expertise-dependent and may give erroneous results in distorted ventricles. Two-dimensional and especially three-dimensional echocardiography increase the precision with which left ventricular mass is measured but they are more time-consuming and difficult to perform on a large scale. Magnetic resonance imaging provides highly accurate left ventricular mass measurements and permits tissue imaging but its use is limited by expensive, fixed facilities and claustrophobia. Cine computed X-ray tomography also measures left ventricular mass accurately and permits perfusion assessment with contrast injection but it involves radiation and the use of fixed facilities of limited availability. Understanding the strengths and limitations of available techniques can facilitate selection of the most appropriate method to measure left ventricular mass in a particular setting16.

**Calculating Left Ventricular Mass Formulas**

The most commonly used formulas to estimate LV mass are all variations of the same mathematical principle, based in the volume formulas. Original calculations from Troy and coworkers were the first to be recommended as standard to estimate LV mass from M mode measurements (Formula 1) .

***Formula 1: LV mass(Troy) = 1.05 ([LVIDD + PWTD +IVSTD]3- [LVIDD]3) g.***

*Where: LVIDD = Left Ventricular Internal Diameter in Diastole*

*PWTD = Posterior Wall Thickness in Diastole*

*IVSTD = Interventricular Septum Thickness in Diastole*

Subsequently, Devereux and colleagues suggested a slightly modified regression equation, using the Penn convention as the border definition criteria (Formula 2).Their prediction equation in this pivotal study was derived from necropsy findings of 34 patients .

***Formula 2: LV mass(Penn) = 1.04 ([LVIDD + PWTD + IVSTD]3- [LVIDD]3) -13,6 g.***

As depicted above, each regression equation was derived based on a specific border limits convention, an issue that is source of great confusion when interpreting different studies .As expected, LV mass calculations derived from both formulas are linearly correlated, but final crude estimations may differ by more than 20%. Devereux and colleagues proposed a new adjusted equation, validated on necropsy findings of 52 individuals , using the ASE (American Society of Echocardiography )convention and accounting for this discrepancy (Formula 3).

***Formula3: LV mass (ASE): 0.8 (1.04 ([LVIDD + PWTD + IVSTD]3- [LVIDD]3))+ 0,6 g.***

This latter convention (ASE) is the most accepted border definition criteria, becoming the standard recommendation for M-mode estimations, and uses the leading edge of each layer20 . Some critical aspects must be acknowledged regarding LV mass formulas. First, all necropsy validation studies have limited sample sizes and evaluate heterogeneous ventricular configurations. Second, these formulas may not perform adequately in distorted ventricles, where a two dimensional approach is preferred. Different formulas may yield distinct cut point values, as demonstrated by Levy and coworkers in the Framingham cohort . Finally, other post-mortem study showed only moderate correlation between echocardiographic and autopsy LV mass estimations (correlation coefficients ranging from 0.58 to 0.67)

|  |
| --- |
| **Left ventricular hypertrophy cut points (Healthy reference group from The Framingham cohort).** |
|  **Men** |  **Women** |
|  | **Mean** | **Mean + 2sd** |  **Mean** |  **Mean + 2sd** |
| **LVM(ASE) (g)** | **208** | **294** | **145** | **198** |
| **LVM(Penn) (g)** | **177** | **259** | **118** | **166** |
| **LVM/BSA(ASE) (g/m2)** | **109** | **150** | **89** | **120** |
| **LVM/BSA(Penn) (g/m2)** | **92** | **131** | **72** | **100** |
| **LVM/Ht(ASE) (g/m)** | **17** | **163** | **89** | **121** |
| **LVM/Ht(Penn) (g/m)** | **99** | **143** | **73** | **102** |

**Role of additional factors in left ventricular mass and hypertrophy determination**

Gender and body size are clearly identified as predictors of LV mass and LVH Definitions are usually corrected and/or stratified for these factors10,11,12 . Many others constitutional factors and exposures may lead to changes in LV mass. Some of these factors are pathophysiologically involved in LVH and, moreover, interact among themselves, limiting the interpretation of the independent role of each one. Although the best strategy to adjust LVM for obesity is a matter of debate, obesity is increasingly recognized as an independent predictor of cardiovascular morbidity and mortality . The increase in LV mass related to obesity is probably more than a mere physiologic adaptation13. Obesity has been shown to be independently associated to LVH, particularly in populations with a high prevalence of hypertension and other metabolic risk factors . Despite this association, the impact of obesity on LVH may be less than expected LV mass progressively increases during aging , particularly parietal thickness , which was seen in both normotensive and hypertensive patients . Heart size increases during infancy and adolescence due to body size enlargement and, at this stage, the gender differences become prominent. The rate of LV mass increase due to age changes in magnitude, weakening its independent role at older individuals, when other risk factors play a greater role. LVH is particularly prevalent in African-Americans. In these analyses, two particular aspects deserve consideration14. An increased crude prevalence of LVH in African-Americans and Hispanics is more evident using height-indexed LV mass than with body surface area-indexed LV mass , suggesting that obesity may partially explain the reported ethnic differences. Furthermore, adaptive response to hypertension may differ across ethnic groups. Hypertensive African-Americans, in comparison with hypertensive whites, have increased relative wall thickness, resulting in an increased frequency of concentric remodeling, given equivalent LV mass estimates16. However, Afro-American ancestry has been identified as an independent risk factor for LVH.Numerous population based studies have unequivocally shown an association between hypertension and LVH . Other reports usually stratify their analysis by or restrict to those with hypertension to allow better evaluation of additional risk factors17  . It is interesting that even within the normal range, increases in blood pressure is related to an increased LV mass  . This increment may be attributed to the classical pathophysiological concept of hypertrophic response to increased overload, although neuro-humoral and genetic factors have been also implicated. LVH association with hypertension is so evident that it is recognized as target organ damage in hypertensive disease by several clinical practice guidelines, representing an intermediate unfavorable prognostic marker.Together with obesity and hypertension, diabetes has been implicated as an important determinant of left ventricular mass in most population-based studies18,19 . Myocardial and systemic mechanisms, as an increased extra-cellular matrix, vascular hypertrophy and vasoconstriction, have been attributed to this hypertrophic response. An adaptive response has been shown to diverse degrees of altered carbohydrate metabolism, as in Cardiovascular Health Study and in The Strong Heart Study cohort, where diabetes  , impaired glucose tolerance and insulin levels where associated with increased LV mass. Although associated with an increase in left ventricular mass, hyperinsulinemia and insulin resistance show a stronger association with concentric remodeling22,23. Concentric hypertrophy is more pronounced in diabetes presenting with microalbuminuria, which could imply a progressive adaptive process.A gender difference in the left ventricular response to diabetes, with an increase in parietal thickening, rather than hypertrophy, being prominent in women has been suggested. LV mass increase is also seen in individuals with other known risk factors, as in those linked to the metabolic syndrome, where pathophysiological aspects related to this syndrome may directly affect ventricular adaptive mechanisms25.26.

**Aim of study**

1. To see the effects of glomerular filtration reduction on left ventricular mass
2. To see the relation of increase left ventricular mass and the presence of hypertention and heart failure

**Patients and Methods**

A cross-sectional study enrolled 100 Iraqi patients with renal impairment and chronic kidney disease ,55% men and 45% women their ages between 16 and 75 from inpatient addmitions in Albasra general hospital and Alsader teaching hospital. In this study we exclude patients with acute renal failure

Each patient sent for echocardiographic heart study to estimate the left ventricular mass by M –mod measurements of left ventricle dimensions in diastolic state, then we use the Americans society of Echocardiography (ASE) formula to produce left ventricular mass in grams

For each patient we calculate the glomerular filtration rate estimated by Cockcroft-Gault equation

**Statistical Analysis:**

Data were coded and fed on computer. Analysis was done on SPSS (Statistical Package for Social Science Analysis). For the determination of statistical significance among different variables, a descriptive statistics like mean together with analytic statistics like chi squared test, have been done when appropriate. A p-value less than 0.05 was considered significant. A p-value more than 0.05 was considered not significant (NS).

**Results and discussion**

The study enrolled 100 patients, the frequency of sex showed in table(1). Those patients classified in frequency of body mass index values into three groups as showed in table(2) and the patient frequency according the associated diseases (hypertension ,diabetes mellitus , ischemic heart disease and low ejection fraction ) showed in table (3) . the frequency of patients according to stage of CKD showed in table (4) ,and the frequency of patients in relation to reference range of left ventricular mass,showed in table (5)

By doing correlations between the available variables as showed in tables (6,7,8,9,10) we notes the following

1. The patients in stage 4 are 66.7% of all, p.value 0.04
2. Patients on dialysis 66.7% of them had left ventricular mass value above reference range , p.value 0.001
3. Patients who are obese or over weight had left ventricular mass value above reference range , p.value 0.08
4. Patients who are hypertension had left ventricular mass value above reference range , p.value 0.042
5. Patients who are in chronic kidney disease ,in stage 3 or more , had left ventricular mass value above reference range , p.value ـــ 0.215

So from those findings we conclude that,,(left ventricular mass increase in patient with chronic kidney disease at stage 3 and above ) also those patients who are obese or over weight or hypertensive , had larger left ventricular mass

**Tables**

**Table 1 frequency of patients according to sex**

|  |  |  |  |
| --- | --- | --- | --- |
| **Sex** | **Frequency** | **Percent** | **Total** |
| **Male** | **55** | **55%** | **100%** |
| **Female** | **45** | **45%** |

**Table 2 frequency of patients according to body mass index**

|  |  |  |
| --- | --- | --- |
| **Body mass index** | **Frequency** | **Percent** |
| **Less than 25** | **81** | **81%** |
| **26-30** | **15** | **15%** |
| **More than 30** | **4** | **4%** |
| **Total**  | **100** | **100%** |

**Table 3 frequency of patients according to associated disease and dialysis**

|  |  |
| --- | --- |
|  | **Frequency** |
| **Hypertension**  | **65** |
| **Diabetes mellitus**  | **45** |
| **Ischemic heart disease** | **34** |
| **Ejection fraction less than 50%** | **22** |
| **On dialysis**  | **30** |

**Table 4 frequency of patients according to stages of chronic kidney disease**

|  |  |  |
| --- | --- | --- |
| **Stages of CKD** | **Frequency** | **Percent** |
| **Stage 1** | **0** | **0%** |
| **Stage 2** | **2** | **2%** |
| **Stage 3** | **46** | **46%** |
| **Stage 4** | **51** | **51%** |
| **Stage 5** | **1** | **1%** |

 **Table 5 frequency of patients according to value of LVM reference ranges**

|  |  |  |
| --- | --- | --- |
| **Left ventricular mass** | **Frequency** | **Percent** |
| **Above reference ranges** | **42** | **42%** |
| **Within normal ranges** | **24** | **24%** |
| **Below reference ranges**  | **34** | **34%** |
| **Total**  | **100** | **100%** |

**Table 6 correlation of chronic kidney disease stages with patients on dialysis**

|  |  |  |  |
| --- | --- | --- | --- |
| **Stages of CKD** | **Patients on Dialysis** | **Percent** | **P .value** |
| **Stage 1** | **0** | **0%** |
| **Stage 2** | **1** | **3.3%** | **0.041** |
| **Stage 3** | **8** | **26.7%** |
| **Stage 4** | **20** | **66.7%** |
| **Stage 5** | **1** | **3.3%** |

**Table 7 correlation of left ventricular mass with patients on dialysis**

|  |  |  |  |
| --- | --- | --- | --- |
| **Left ventricular mass** | **Patients on Dialysis** | **Patients without Dialysis** | **P .value** |
| **Above reference ranges** | **66.7%** | **31.4%** | **0.001** |
| **Within normal ranges** | **3.3%** | **32.9%** |
| **Below reference ranges**  | **30.0%** | **35.7%** |
| **Total**  | **100%** | **100%** |

**Table 8 correlation of left ventricular mass with patients body mass index**

|  |  |  |
| --- | --- | --- |
| **Body mass index** | **Left ventricular mass** | **P .value** |
| **Above ref.range(no)** | **Within normal range** | **Below ref. range** |
| **Less than 25** | **(34) 42%** | **(23) 28.4%** | **(24) 29.6%** | **0.08** |
| **26-30** | **(5) 33.3%** | **(1) 6.7%** | **(9) 60%** |
| **More than 30** | **(3) 75%** | **0.0%** | **(1) 25%** |

**Table 9 correlation of left ventricular mass with patients associated diseaes**

|  |  |  |
| --- | --- | --- |
|  | **Left ventricular mass** | **P .value** |
| **Above ref.range(no)** | **Within normal range** | **Below ref. range** |
| **Hypertension**  | **49.2%** | **16.9%** | **33.8%** | **0.042** |
| **Diabetes mellitus**  | **42.2%** | **31.1%** | **26.7%** | **0.22** |
| **Ischemic heart dis.** | **38.2%** | **17.6%** | **44.1%** | **0.22** |

 **Table 10 correlation of left ventricular mass with patients at different stages of chronic kidney disease**

|  |  |  |
| --- | --- | --- |
|  | **Left ventricular mass** | **P .value** |
| **Stages of CKD** | **Above ref.range(no)** | **Within normal range** | **Below ref. range** |
| **Stage 1** | **0.0%** | **0.0%** | **0.0%** | **ـــ 0.215** |
| **Stage 2** | **50%** | **0.0%** | **50%** |
| **Stage 3** | **32.6%** | **23.9%** | **43.5%** |
| **Stage 4** | **49%** | **25.5%** | **25.5%** |
| **Stage 5** | **100%** | **0.0%** | **0.0%** |

**Recommendations**

1. Larger study with large sample size and multiple centers to confirm this study and to find how much is significant.

2. To increase awareness of physician about this relation between reduction of glomrular filtration rate and increase left ventricular mass and so increase mortality in patients with chronic kidney diseaes

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