

Larix Publications

Singapore Journal of Cardiology





Vol. 1, Issue 2, 2020

ISSN: 2737-4025

## **Original Article**

Pulse Pressure Related to Type 4 Cardiorenal Syndrome and Peguero – Lo Presti Positive Index in Patients with Chronic Kidney Disease Stage G5.

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Received on: 06-08-2020; Revised and Accepted on: 13-08-2020

### **ABSTRACT**

The pulse pressure is the difference in between the systolic pressure and diastolic pressure. It has been considered as a total cardiovascular risk factor, the high blood pressure on the systolic side can favor the ventricular hypertrophy and the left ventricular failure, and, as well, the oxygen demand of the myocardic muscle, therefore, low pressure values on the diastolic pressure is a limiting factor of the coronary perfusion and thus, it elevates the risk of ischemia. Cardiorenal syndrome is an state of advanced non-regulation between myocardic muscle and kidney, which involves the organic damage of both organs, both acute or chronic which induces the disfunction of both of them, in which it's physiological functions will use a compensation mechanism that will develop long- term repercussions, leading to ventricular hypertrophy, dilation and heart failure.

**Objective:** correlate pulse pressure relating it to type IV cardiorenal syndrome and positive Peguero – Lo Presti Index on patients with chronic kidney disease stage G5.

**Methodology:** Observational, longitudinal – prospective study of 74 patients that meet the requirements of the inclusion criteria, Through the instrument the data has been collected and everyone had been examinated as well the pulse pressure functional capacity, 12 derivations electrocardiogram to determine the Peguero – Lo Presti index, transthoracic echocardiogram, creatinine and urea. **Results:** indicates that, Elevated Pulse Pressure on Type IV cardiorenal syndrome is a predictive factor of heart hypertrophy and dilation,

and, Peguero – Lo Presti index has a high sensibility and specificity to make electrocardiographic diagnosis on ventricular hypertrophy and dilation.

Keywords: Type IV cardiorenal syndrome, Peguero – Lo Presti, Pulse Pressure, heart failure.

### 1. INTRODUCTION:

Chronic kidney disease has been defined as the presence of alterations on the renal function and structure for at least three months and with implications on the health of the patients. Persons with CKD may have one or more of the following diagnosis criteria: pathologic abnormalities, markers of kidney damage (i.e.: imaging abnormalities and abnormalities in serum or urine, including proteinuria and abnormal urinary

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Marwan Michaell Chlaiwit Marín I.V.S.S. Dr. Rafael Calles Sierra and Universidad Nacional Experimental Francisco De Miranda (UNEFM) **Email:** mchlaitiwt@gmail.com **Phone:** +584121620502 DOI: doi.org/10.46978/sjc.20.1.2.9 sediment), or GFR less than 60 mL/min/1.73 m2 for at least three months [5].

Cardiorenal syndrome (CRS) is an state of advanced deregulation in both heart and kidney, which involves the affectation of both organs because of an acute or chronic disfunction of one of the organs which induce disfunction of the other organ, for which its physiological functions in both heartkidney relation, any of the two organs mentioned will use a compensation mechanism which will have important repercussions of the other organ. This definition has three fundamental characteristics: 1) relevance of the relation of both organs, 2) this affection can be acute or chronic and also functional or structural,

3) the interaction is bidirectional, characteristics which leads to a negative loop which leads to the decompensation of the circulatory system. It has been described five types of cardiorenal syndrome [5, 6]:

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Type 1 cardiorenal syndrome: or also known as acute cardiorenal syndrome, is defined as a quick compromise of the cardiac functions (i.e.: cardiogenic shock) that leads to an acute kidney injury. Biomarkers: ET-1, Troponin, CPK-MB [5, 6].

Type 2 cardiorenal syndrome: also known as chronic cardiorenal syndrome, is defined as the chronic abnormality of the cardiac function (i.e.: congestive heart failure) that can potentially lead progressively to a CKD. Biomarkers: ET-1, BNP [5, 6].

Type 3 cardiorenal syndrome: also known as acute renocardiac syndrome, is defined as a quick compromise of the renal function (i.e.: ischemic acute kidney injury, acute glomerulonephritis) which leads to an alteration of the cardiac functions (heart failures, ischemia). Biomarkers: TNF-alpha, IL-1, IL-6, IL-8 [5, 6].

Type 4 cardiorenal syndrome: also known as chronic renocardiac syndrome, is defined as the existence of a CKD that contributes to the deterioration of the cardiac function, leading to ventricular hypertrophy which elevates the risk of an adverse cardiovascular event. Biomarkers: Parathormone, copectine, cistatine c [5, 6].

Type 5 cardiorenal syndrome: also known as secondary cardiorenal syndrome, is defined as a systematic condition (diabetes mellitus, sepsis, and amyloidosis) that leads to a cardiac disfunction and kidney injury [5, 6].

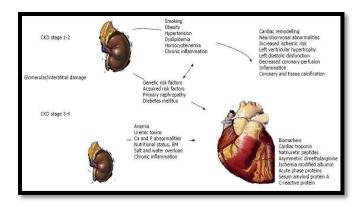


Fig.1: Physiopathology of 4 cardiorenal syndrome [5]

Pulse pressure is the difference between the systolic blood pressure and diastolic blood pressure, it is considered as a total cardiovascular risk factor [6].

The principal determinants of pulse pressure in every ventricular ejections are: cardiac output, heart rate, stiffness of high caliber arteries and early reflection wave of the heartbeat, thus, pulse pressure is a measurement that reflects vascular elasticity on blood pressure [7, 8].

The elevated pressure in systole favors the ventricular hypertrophy, leads to left ventricular failure and heightens the

oxygen requirements to the myocardic muscle; on the other hand, lower pulse pressure on diastole is a limiting factor of the coronary perfusion which leads to ischemia [9].

The etiology known factors of the high pulse pressure includes the reduction of the elastic fibers, which are replaced by collagen, the endothelial disfunction and a rising expression of vasoconstrictor substances (angiotensin II, endothelin, thromboxanes) and a lowering vasodilator substances (Nitric oxide, bradikynin) [9].

The normal range of pulse pressure is unknown; in a study with hypertensive patients, those who had a pulse pressure of 60 mmHg had the highest values of left ventricular mass compared to those who had lower values (50 mmHg), although they had similar pulse pressures. Vaccarino et al. informed that the rise of 10 mmHg heightens the risk of heart failure by 14%, coronary artery disease by 12% and every cause of mortality by 6% in population over 65 years. NHANES I study shown that a rise of pulse pressure of every 10 mmHg heightens the risk of death by cardiovascular disease by 26% in the patients within the ages of 25 – 45 years, and 10% on patients within 46 – 77 years old. Otherwise, lower pulse pressures below 45% with advanced heart failure is an independent mortality predictor [9].

Peguero et al. developed a new electrocardiographic criteria for the diagnosis of left ventricular hypertrophy (LVH) with a high sensibility; the adition of the deepest S wave in every electrocardiographic derivation plus the S wave in V4 exceeds 28 mm in male

patients or 23 mm in female patients, chances are of the probability of LVH. The criteria of the deepest S wave (SD) + SV4 has shown a better performance in comparison of the traditional LVH criteria when analyzed on the test and validation cohort separately. Although, when combined both cohorts, there was a significant difference which has been observed firstly on the sensitivity, favoring Peguero – Lo Presti Criteria [10, 11]

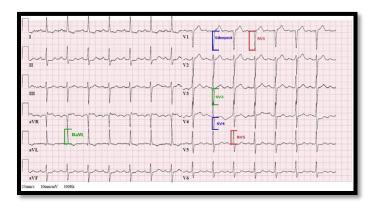


Fig. 2: Electrocardiographic criteria for diagnosis of LVH, JACC, Volume 69, Issue 13 (April 2017) [12]

Our aim is to correlate high pulse pressure and associate it in patients with Cardiorenal Syndrome type 4 and a positive Peguero – Lo Presti Index in patients with Chronic Kidney Disease stage G5.

# 1.1 METHODS

Observational, longitudinal, prospective study. A total of 87 patients were recruited for participation in the study, of both sexes, with ages of 18 years old onwards with diagnosis of Chronic Kidney Disease stage G5, in which 74 met the inclusion criteria. A clinical record of every patient was made in which we took comorbidities that lead them to hemodialysis and a physical examination of every patient; normal pulse pressure was defined as below 50 mmHg, while high pulse was define as above 50 mmHg; paraclinical essays were performed in which were included 12 derivation electrocardiography, transthoracic echocardiography, creatinine and urea levels in blood serum; graphical representation and tables were made in Microsoft Excel 2015 and IBM - SPSS ver. 21; Association of the studied variables were verified using Chi<sup>2</sup> and Pearson Correlation using the software SPSS 10.7.

# **1.2 INCLUSION CRITERIA:**

- 1. Adults above 18 years old of both sexes with diagnoses of Chronic Kidney Disease stage G5
- 2. Patients without arteriovenous fistula
- 3. Patients without the diagnoses of Anemia

- 4. Patients who aren't pregnant
- 5. Non-Critical ill patients
- 6. Patients without psychiatric disorders

# 1.3 RESULTS

A total of 74 patients were recruited and met the inclusion criteria, with a mean age of 49 years old, with ages between 18 and 71 years old, 51 of whom where male and 23 of them were female (68,9% and 31,1% respectively). Most of the patients had nephroangiosclerosis with 53 patients in total (71.6%), 8 of them had polycystic kidney disease (10.8%), 5 of them had unknown causes (6.8%), 3 of them had diabetic nephropathy (4.1%) and 4 of them had obstructive nephropathy in form of bilateral hydronephrosis. In relation of the pulse pressure, the mean pulse pressure was 78.22 mmHg with a Standard Deviation (SD) of ± 20,12 mm/Hg (Min. PP value: 40 mmHg vs Max. PP value; 142 mmHg). Most of the patients, 68 patients (91.9%) had elevated PP values, in comparison of 6 patients who had normal PP values (8.1%). In relation to mean arterial pressure (MAP), we had a mean MAP of 96.39 mmHg with a SD of ± 13.19 mmHg (Min. MAP value: 48 mmHg vs. Max MAP value: 135 mmHg).

Demographic properties		Frequency	Percentage
Age	< 35 Years old	4	5,4%
_	≥ 35 Years old	70	94,6%
	Female	23	31,1%
Sex	Male	51	68.9%

Table 1: Demographic properties of study population

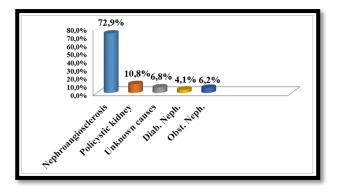
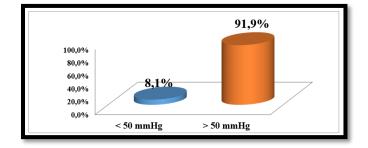
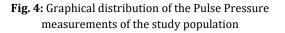


Fig. 3: Personal background and Causes of CKD of the study population.

Pulse Pressure		Frequency	Percentage
Pulse Pressure	Normal ( < 50 mmHg)	6	8,1%
(78,82 ± 20,12)	High Pulse Pressure ( > 50 mmHg)	68	91,9%





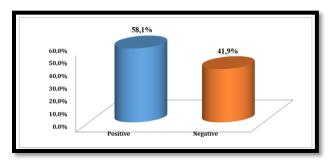
In relation of the categorization of the Cardiorenal Syndrome type 4, it has been determined that 54 patients (73%) met the diagnosis criteria while only 20 patients (27%) did not met the

diagnosis criteria for cardiorenal syndrome type 4. As mentioned before, Peguero – Lo Presti Index was used as the newly electrocardiographic criteria for the diagnosis of the Left Ventricular Hypertrophy (LVH), it should be noted that all the patients had echocardiographic studies were it has been noted with dilated cardiomyopathy in 55 (74.32 %) of the patients while 19 (25.67%) of them had left ventricular hypertrophy. 43 patients (58.1%) had a Peguero – Lo Presti positive index while 31 of them (41.9%) had a Peguero – Lo Presti negative index result. In relation of this results another test was ran but with only with the patients with dilated cardiomyopathy related to CKD diagnosed by transthoracic echocardiography, in which 33 patients (59.5%) had a Peguero – Lo Presti positive index and 22 patients (40.5%) had a Peguero – Lo Presti negative index

#### Table 3: Peguero – Lo Presti index results

Results		Frequency	Percentage
	Positive	43	58,1%
Peguero – Lo Presti Index	Negative	31	41,9%

Result	S	Frequency	Percentage
Peguero – Lo Presti Index in dilated cardiomyopathy related to Chronic	Positive	33	60%
Kidney Disease	Negative	22	40%



**Fig. 5:** Graphical distribution in relation of the results of the Peguero – Lo Presti Index

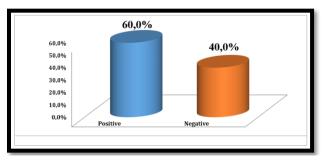


Fig. 6: Graphical distribution in relation of the results of the Peguero – Lo Presti Index in patients with dilated cardiomyopathy related to CKD

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and CKD it was used Chi Square test, an statistical, inferential, non-parametrical procedure, in which, the following

hypotheses are tested: Null Hypotheses vs. Alternative Hypothesis :

VARIABLES	Chi – Square value	d.f	SIGNIF.	P. value.
Pulse Pressure VS. Cardiorenal Syndrome type 4 criteria	3,855	1	.050	p < .05
Pulse Pressure vs. Peguero – Lo Presti Index	4,196	1	.048	p < .05

Chi-Square value of Pulse Pressure vs. Cardiorenal Syndrome Type 4 diagnosis criteria and Pulse Pressure vs. Peguero – Lo Presti Index were 3,855 and 4,196 respectively with 1 degree of freedom, and shown an asymptotic significance of .050 and 0.48 respectively, that brings a p = <.05, indicating that it is significant statistical differences and there's enough statistical evidences to accept the alternative hypotheses, concluding that pulse pressure is related to the diagnosis criteria for the Cardiorenal Syndrome Type 4 and Peguero – Lo Presti Index, with a confidence level of 95% and an error margin of 5%, meaning that a patient with CKD that has a high pulse pressure has a higher probability to develop Cardiorenal Syndrome type 4 and also has more probability to have Peguero With the porpoise of show the existent relation in patients with dilated cardiomyopathy and Peguero – Lo Presti positive index, it has been applied Chi Square test, showing that Chi Square value for the cardiomyopathy related to CKD vs. Peguero – Lo Presti positive index was 69.985 with 1 degree of freedom, showing an asymptotic significance of .000 which resulted less than .01 (p < 0.1), indicating that there's statistical differences to accept the alternative hypotheses concluding that a positive result on Peguero – Lo Presti index is related to dilated cardiomyopathy related to CKD verified via transthoracic echocardiography, with a confidence level of 99% and an error margin of 1%, meaning that a patient with a positive result on the Peguero – Lo Presti index has a high probability to have a cardiomyopathy related to CKD.

- Lo Presti positive index

	Value	d.f.	Asymptotic sig.	Exact Sig. (bilateral)	Exact Sig. (unilateral)
Chi Square	69,985	1	,000		
<b>Continuity correction</b>	66,028	1	,000		
Likelihood ratio	91,086	1	,000		
Fisher's exact statistic					
Linear by linear association	69,040	1	,000	,000	,000
N of valid cases	55				

Chi Square test.

With the intention of comparing the diagnosis of dilated cardiomyopathy and the positives results of the Peguero – Lo Presti index of the patients, it has been used the inferential statistic test of Cohen's Kappa Agreement Index. This test provides a measurement of the agreement existent between two diagnosis and judgments under the contrast of the following two hypothetical affirmations: Null Hypotheses vs. Alternative Hypotheses. For this test it was applied the statistical program IBM – SPSS with the results of both diagnosis:

## **Cohen's Kappa Coefficient**

		Value	Tip. Err asymptotic.	T approximated	Sig. approximated
Measure of agreement	Карра	0,972	,028	8,366	,000
N of valid cases		55			

The resultant Value of Cohen's Kappa Agreement Coefficient was 0.972; made an approximately significance of .000, which resulted in less than 1% (p > .01). This result let us to take the statistical decision of accepting the alternative hypotheses and concluding that there is a significative agreement between the two diagnoses, a significantly higher agreement than expected by chance. This reality can confirm with a higher statistical criteria that in both diagnosis there is more agreement than disagreement, in virtue of the fact that the percentage of coincidence between both findings reaches the percentage figure of 98.75%, which is why the Peguero – Lo Presti index is given a very high reliability for the diagnosis of dilated cardiomyopathy related to CKD verified by a transthoracic echocardiogram of the patients.

With the fair objective of determine the predictive value of Peguero – Lo Presti index in the diagnosis of the cardiomyopathy related to CKD of the patients, it was used the statistical program IBM – SPSS, for which it can realize the specificity, sensibility and predictive positive and negative values of the variables and the results obtained:

Predictive values of Peguero – Lo Presti Index.	Percentage
Sensibility	97,7%
Specificity	100%
Positive predictive value	100%
Negative predictive value	98,6%

It can be indicated that, Peguero – Lo Presti index has a capacity of 97.7% of determining an electrocardiography diagnosis of dilated cardiomyopathy related to CKD and a 100% of determining that the result can be positive in relation of its predictive value. This result can confirm with statistical criteria that Peguero – Lo Presti index has a lightly higher specificity than sensibility in this case.

# 1.4 DISCUSION:

The age range were the patients > 35 years old with a male predominance (Acle et al, Uruguay 2014), the predominant comorbidity on the development of the CKD was nephroangiosclerosis (Bodian, M et al, Dakar – Senegal 2014); high pulse pressure levels were found on most of the patients (91,9%) (Hashimoto et al, Japan 2014); most of the patients met the criteria for the Cardiorenal Syndrome type IV (73%) (Suresh et al, India 2017); in relation of the results of the electrocardiographic studies referred towards the Peguero – Lo Presti Index as a newly electrocardiographic criteria for the diagnosis of the left ventricular hypertrophy /LVH) was positive in the 58.1%, in relation of the results of the transthoracic echocardiography and Peguero – Lo Presti Index in dilated cardiomyopathy, 60% of the study population had a positive result on the Peguero – Lo Presti index. A patient with a higher pulse pressure in relation of CKD has a higher probability to match the diagnosis criteria for cardiorenal syndrome type 4 and also a high probability to have a positive result on the Peguero – Lo Presti index. A patient with a positive result on the Peguero – Lo Presti index has a higher probability of having a dilated cardiomyopathy related to CKD (97.7%) and a 100% to determined that the result can be negative, having a slightly more specificity than sensibility.

## 2. CONCLUSIONS

A patient with a high pulse pressure in relation of a CKD has a higher chance to meet the criteria for Cardiorenal Syndrome type 4 and also of having a positive result on the Peguero – Lo Presti index, which also has a high probability to have a dilated cardiomyopathy with a 97.7% on the population study and a 100% that the result can be negative, which can confirm with statistical criteria that the Peguero – Lo Presti Index has a slightly more specificity than sensibility in these cases.

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# Article Citation:

Authors Name. Marwan Michaell Chlaiwit Marín. Pulse Pressure Related to Type 4 Cardiorenal Syndrome and Peguero – Lo Presti Positive Index in Patients with Chronic Kidney Disease Stage G5. SJC 2020;1(2): 53 - 59 DOI: doi.org/10.46978/sjc.20.1.2.9

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