

# GLUCAGON LIKE PEPTIDE AGONIST AND CARDIOVASCULAR DISEASE IN TYPE 2 DIABETES

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In the first decade of the 21st century, some important studies (ACCORD, ADVANCE, VADT) using conventional glucose lowering drugs, showed a significant reduction in the levels of HbA1c in patients with type 2 diabetes treated with an intensified in comparison to a "standard" strategy. However, they didn't obtain a similar reduction in the major adverse cardiovascular events. This suggested an end of the "glucocentric paradigm" in cardiovascular disease in diabetes. In the last decade, a new generation of researches using two new types of medications (GLP1 analogs and SGLT2 drugs) were carried out. In some of the researches using GLP1 analogs, a significant reduction in the rate of cardiovascular mortality and major cardiovascular events was demonstrated despite just a moderate decrease in HbA1c levels.

The main objective of this revision was to analyze the known and potential effects of the GLP1 analogs over the cardiovascular system.

Expresion of the GLP1 receptor in the left atrium

Direct action over cardiomyocytes

Antiinflammatory effects of the GLP1

Action of the GLP1 agonist on the endothelium cells

Action of the GLP1 agonist on the renin, angiotensin, aldosterone system

Natriuretic effect of the GLP1 agonist

Action on the atrial natriuretic peptide

Stabilization of the atherosclerotic plaque

Reduction in systolic and diastolic blood pressure.

Effects on lipids

Reduction of the hypoglycemic risk

The GLP1 analogs differ in some pharmacokinetics and pharmacodynamics characteristics but they share a common beneficial effect over the cardiovascular system as was demonstrated by recent researches (LEADER, SUSTAIN, HARMONY, REWIND)

## INTRODUCTION:

The cardiovascular disease and the kidney disease constitute the main cause of mortality in type 2 diabetes patients so it matters to know the relative value of the creatinine level and the presence of albuminuria in the prediction of cardiovascular events (CVE) in these patients.

**OBJECTIVES:** to know the strength of association between creatinine levels and the presence of albuminuria with the presence of cardiovascular events (CVE) in type 2 diabetes patients, comparing the relative value of both determination in their prediction.

## MATERIALS METHODS

In 270 type 2 diabetic patients, age  $66 \pm 10$  years, male 138/female 132, we analyzed the average of the last three determinations of creatinine

(modified Jaffe method) and the quotient albuminuria/creatininuria by nephelometry in the first urine sample. In those patients were registered main cardiovascular events (CVE): Atherosclerotic cardiovascular disease (ASCVD): myocardial infarction, angina pectoris, angioplasty, myocardial revascularization surgery or of the lower limbs. Non atherosclerotic cardiovascular events (NASCVD): heart failure and arrhythmias

**STATISTICAL ANALYSIS:** Chi 2 (Yates), ANOVA one way, parametric and non parametric correlation, ROC curve, logistic regression univariate and multiple

## RESULTS:

31,5% of the patients had some CVE. In the univariate analysis was registered a significant association between the creatinine values and CVE in the ROC curve, with a cutoff value of 1,42 mg/dl (AUC: 0,595) ( $p < 0,001$ ). A cutoff value of albuminuria/creatininuria more than 88 mg/g was associated with more numbers of CVE although the ROC curve was not significant (AUC: 0,507,  $p > 0,07$ ). In the multivariate analysis by logistic regression, adjusting other variables (BMI, smoke habit, systolic and diastolic blood pressure, total cholesterol, HDL and triglycerides), the creatinine level, age and cholesterol HDL levels were significantly associated with CVE (178% increased risk for creatinine levels equal or over 1,42 mg/dl) while the albuminuric levels were non significantly associated with CVE (OR: 1,49;  $p > 0,298$ )

## CONCLUSION:

In the univariate analysis both variables (creatinine and albuminuria) were associated with more number of CVE events. However, in the multivariate analysis, only the creatinine level remained significantly associated with CVE

## Biography

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## Recent Publications:

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3. Keane WF, Brenner BM, de Zeeuw D, Grunfeld JP, McGill J, Mitch WE, Ribeiro AB, Shahinfar S, Simpson RL, Snapinn SM, Toto R: The risk of developing end-stage renal disease in patients with type 2 diabetes and nephropathy: the RENAAL study. Kidney Int 63:1499-1507, 2003

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