Impacto de los inhibidores de SGLT2 sobre la función renal en ancianos con diabetes tipo 2 durante el primer año de tratamiento

Impact of SGLT2 inhibitors on renal function in elderly with type 2 diabetes in the first-year of treatment

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ABSTRACT

Objectives: This study aims to evaluate the effect of iSGLT2 on estimated glomerular filtration rate (eGFR) and albuminuria in elderly patients during the first year of treatment.
Methods and Methodologies: Retrospective cohort study including elderly patients (>65 years) with type 2 diabetes (T2D) treated with iSGLT2. Data were collected at the beginning of treatment, 3, 6, 9 and 12 months after.
Results: A total of 115 elderly patients were included, 48.7% male, mean age 72.4±5.2 years, median HbA1c 8.4±1.7% and median T2D duration of 17±12 years. Dapagliflozin was initiated in 60.9% and empagliflozin in 39.1%. An eGFR of 30-60mL/min/1.73m2 was observed in 21.7%, with moderately increased albuminuria in 12.2% and severely increased albuminuria in 4.3%.
Throughout the first year, there was a significant reduction in HbA1c (-0.32%±1,6%; p<0.038). Regarding eGFR, no significant differences at the beginning of treatment or after 1-year were observed, nonetheless, a non-significant reduction was observed in the first semester, followed by a significant increase in eGFR (71.4-84.9mL/min/1.73m2; p<0.006) in the second semester. As to the variation of eGFR yearlong, there were no significant differences between dapagliflozin and empagliflozin, although in the first semester, empagliflozin presented a greater variation in eGFR(p=0.021). There was no significant reduction in albuminuria(p=0,074).
Conclusions: In our sample, iSGLT2 seems to preserve the glycemic effects, without worsening renal function in an elderly population during the first-year treatment. It seems that the nephroprotective effect is also preserved in the elderly in real life.

Keywords: SGLT2 inhibitors; Type 2 diabetes; elderly; renal function; glomerular filtration rate.

RESUMEN

Objetivos: Evaluar el efecto de iSGLT2 sobre la tasa de filtración glomerular estimada (TFGe) y la albuminuria en ancianos durante el primer año de tratamiento.
Métodos: Estudio coorte retrospectivo que incluyó a pacientes ancianos (>65 años) con diabetes tipo 2(DM2) tratados con iSGLT2. Los datos se recogieron al inicio del tratamiento, 3, 6, 9 y 12 meses después.
Resultados: Se incluyeron 115 ancianos, 48,7% varones, edad media 72,4±5,2 años, mediana de HbA1c 8,4±1,7% y de duración de la DM2 de 17±12 años. Se inició dapagliflozina en 60,9% y empagliflozina en 39,1%.
Se observó una TFGe de 30-60 ml/min/1,73m2 en 21,7%, con un aumento moderado de la albuminuria en 12,2% y un aumento grave de la albuminuria en 4,3%.
Durante el primer año, hubo una reducción significativa de la HbA1c (-0,32%±1,6%; p<0,038). En la TFGe no se observaron diferencias significativas al inicio del tratamiento ni al año, sin embargo, se observó una reducción no significativa en el primer semestre, seguida de un aumento significativo (71,4-84,9ml/min/1,73m2; p<0,006) en el segundo semestre. La variación de la TFGe a lo largo del año no presentó diferencias significativas entre dapagliflozina y empagliflozina, aunque en el primer semestre la empagliflozina presentó una mayor variación (p=0,021). No se ha demostrado una reducción significativa de la albuminuria (p=0,074).
Conclusiones: En nuestra muestra, iSGLT2 parece preservar los efectos glucémicos, sin empeorar la función renal en una población anciana durante el primer año de tratamiento. Por tanto, parece mantenerse el efecto nefroprotector en mayores de 65 años en vida real.

Palabras clave: Inhibidores de SGLT2; diabetes tipo 2; ancianos; función renal; tasa de filtración glomerular.

INTRODUCTION

Type 2 diabetes mellitus (T2D) is highly prevalent among adults, with more than 500 million people diagnosed in 2018 worldwide[1]. Since T2D is a chronic disease, the increase in average life expectancy results in a rising prevalence of T2D in the elderly population[1,2]. Poor metabolic control is associated with T2D complications and premature death, being an important cause of renal disease[2]. Diabetic kidney disease is more commonly diagnosed in patients with more than 60 years of age, furthermore, aging itself and T2D duration are associated with renal function worsening[3].

Diabetic patients experience geriatric syndromes more often and polypharmacy is frequent[1,3]. As this population have multiple comorbidities associated with polypharmacy, they are more prone to drugs adverse effects[1], making it difficult to combine multiple antidiabetic medications.

Since December 2013, a new therapeutic class for the treatment of T2D is available - selective sodium-glucose cotransporter inhibitors 2 (iSGLT2)[2]. iSGLT2 treatment results in a decrease in albuminuria and has reno-protective effect in diabetic kidney disease[4]. Prior to the introduction of iSGLT2, the only treatment used for renoprotection in patients with T2D was renin-angiotensin-aldosterone system inhibitors (RAASi)[5].

The role of iSGLT2 in glycemic control, its reno-protective effect and low risk of hypoglycaemia[6] makes it an interesting drug for the treat-

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ment of T2D in the elderly, although there is a lack of studies regarding the use of this therapeutic class in patients older than 65 years.

Therefore, this study aims to evaluate the effect of iSGLT2 on estimated glomerular filtration rate (eGFR) and albuminuria in elderly patients during the first year of treatment.

MATERIALS AND METHODOLOGIES

This was a single-centre retrospective cohort study, carried out from January 2017 to December 2019 in a tertiary hospital. All T2D patients with follow-up in Internal Medicine – Diabetes consultation and prescribed with iSGLT2 were included. Those taking iSGLT2 for less than 12 months and patients without creatinine evaluation at the beginning of treatment with iSGLT2 were excluded. Patients were separated in two groups considering their age: the elderly group included patients aged 65 years or more, and the other group patients with less than 65 years.

Data were collected from patient's medical file at the date of iSGLT2 introduction and 3, 6, 9 and 12 months of treatment.

For all patients, demographic data (including age and gender), T2D duration and vascular risk factors (including arterial hypertension, obesity, dyslipidaemia and current smoking habits) were collected. Regarding medication, it was evaluated which iSGLT2 patients were taking (dapagliflozin or empagliflozin), the use of other classes of antidiabetic drugs (metformin, insulin, glucagon-like peptide-1 receptor agonist (GLP1ra), dipeptidyl-peptidase 4 inhibitors (iDPP4), sulfonylurea, pioglitazone or nateglinide) and RAASi. All side effects related to the use of iSGLT2 were also considered. Glycosylated haemoglobin (HbA1c), uric acid and albuminuria were evaluated at 0 and 12 months treatment with iSGLT2. Creatinine was registered each trimester and glomerular filtration rate was calculated using CKD-EPI formula considering gender and age. Patients were also grouped according to their eGFR: stage 1 (eGFR > 90 mL/min/1.73m^2), stage 2 (89 > eGFR > 60 mL/min/1.73m^2), stage 3 (59 > eGFR > 30 mL/min/1.73m^2), stage 4 (30 > eGFR > 15 mL/min/1.73m^2) and stage 5 (eGFR < 15 mL/min/1.73m^2).

The study was approved by the Hospital Ethics Committee, which exempted the need to seek written informed consent due to the observational nature of the study. All the data collected were anonymized.

Statistical Analysis

Statistical analysis was performed with IBM-SPSS® 26.0 (SPSS Inc., Chicago, Illinois, USA). Categorical variables are presented as frequency and percentage. Continuous variables are presented as mean and standard deviation or median and interquartile range depending on normal distribution. A comparative bivariate analysis was also carried out between elderly and patients < 65 years, using a Qui-saquare or Fisher test for categorical variables, a Student's t test for continuous variables with normal distribution and a ManWhitney test for continuos variables with non normal distributions. To evaluate the variation between two temporal moments of eGFR, HbA1c, uric acid and albuminuria were perform a paired sample test using the Wilcoxon signed rank test for non-parametric variables and a paired samples t-test for normal distribution variables. Statistical significance was considered when p<0.05. Due to the multiple comparations performed to evaluate the eGFR during the first year, was performed a Bonferroni correction.

RESULTS

A total of 208 patients with T2D were under treatment with iSGLT2, including 115 elderly and 93 patients under 65 years old. The elderly group (EG) presented a higher prevalence of woman (51.3%), in opposite to the younger group (YG), which had a higher prevalence of man (60.2%). In the elderly group, the mean age was 72.4 ± 5.2 years with a mean T2D duration of 17.4 ± 9.4 years.

Regarding vascular risk factors, the most prevalent in the elderly group was dyslipidemia (85.2%) followed by arterial hypertension (80.9%), obesity (46.1%) and active smoking (15.7%). When comparing with the younger group, arterial hypertension was most prevalent in the elderly group (YG 60,2% vs EG 80,9%; p=0.001) and current smoking were less frequent (YG 36,6% vs EG 15,7%; p=0.001).

The number of antidiabetic drugs were similar between the two groups (p=0.344), with a mean of 1.8 ± 0.8 antidiabetic drugs in the elderly (vs 1.7 ± 0.9). Only dapagliflozin an empagliflozin were used, presenting a more frequent use of dapagliflozin in both groups (elderly group – 60.9%; younger group – 66.7%). The most used antidiabetic drugs, in descending order, following the iSGLT2, were metformin, iDPP4, insulin, GLP1ar, sulfunylurea, pioglitazone and nateglinide. The use of these drugs was similar in both groups and are presented in Table 1.

Approximately 62.6% of the elderly and 48.4% of the youngers were taking renin-angiotensin-aldosterone system inhibitors (RAASi) (p=0.048).

Baseline characteristics of patients in both groups are described in Table 1.

There was no statistically significant difference in HbA1c at the date of iSGLT2 initiation between both groups (Table 1). After 1 year of treatment, we observed a statistically significant decrease in HbA1c in the elderly group (0m: 8.4 (6.7-10.1)% vs 12m: 8.3 (6.8-9.8) %; p=0.038) with a median decrease of -0.31 (-1.9-1.3)%. Also, the younger group presented a statistically significant decrese in HbA1c (0m: 8.9 (7.1-10.7) vs 12m: 8.0 (6-10); p<0,001) with a median decrease of -0,8% (-2.4% – 0.8%). During the first year, there were no significant differences between HbA1c decrease in elderly when comparing with HbA1c decrease in young group (YG: - 0,8% (-1.5% – 0.15%) vs EG: -0,31 ± 1,6%; p=0.091). Glycemic control during the first year of treatment with iSGLT2 is represented in Table 2.

At the time of iSGLT2 initiation, elderly patients had a median eGFR of 74.6 ± 17 mL/min/1.73m^2, lower than patients under 65 years old. In the elderly group, 20.2% patients were in stage 1 of CKD, 57.8% in stage 2 and 6.6% in stage 3. No patients in stage 4 or 5 of CKD were started on a iSGLT2.

eGFR was significantly lower in the elderly group at the beginning of the treatment, 3, 6 and 12 months after initiating iSGLT2 treatment (Figure 1).

Table 1. Characteristics of patients at baseline

	Elderly group (n=115)	Under 65 years old group (n=93)	P
Age (years, mean ± SD)	72.4 ± 5.2	57,0 ± 6,4	<0.001
Man (frequency (%))	56 (48.7)	56 (60.2)	0.098
T2D duration (years, mean (SD))	17.4 ± 9.4	13,7 ± 7.1	0.006
Vascular Risk Factors			
Dyslipidemia (frequency (%))	98 (85.2)	75 (80.6)	0.381
Arterial Hypertension (frequency (%))	93 (80.9)	56 (60.2)	0.001
Obesity (frequency (%))	53 (46.1)	47 (50.5)	0.523
Current smoking (frequency (%))	18 (15.7)	34 (36.6)	0.001
Antidiabetic drugs (mean ± SD)	1.8 ± 0.8	1.7 ± 0.9	
iSGLT2 Dapagliflozin (frequency (%)) Empagliflozin (frequency (%))	 70 (60.9) 45 (39.1)	 62 (66.7) 31 (33.3)	 0.388 0.388
Metformin (frequency (%))	90 (78.3)	80 (86)	0.15
iDPP4 (frequency (%))	72 (62.6)	51 (54.8)	0.257
ARGLP1 (frequency (%))	23 (20)	17 (18.3)	0.754
Sulfonylurea (frequency (%))	15 (13)	11 (11.8)	0.792
Pioglitazone (frequency (%))	9 (7.8)	2 (2.2)	0.111
Nateglinide (frequency (%))	0 (0)	1 (1.1)	0.447
Insulin (frequency (%))	58 (50.4)	49 (52.7)	0.746
RAASi (frequency (%))	72 (62.6)	45 (48.4)	0.048
eGFR at iSGLT2 initiation (mL/min/1.73m2, median (IQR) | mean ± SD)	77.5 (62.1-87.0)	90.9 ± 19.0	<0.001
CKD stage at iSGLT2 initiation			
Stage 1 (frequency (%))	22 (20.2)	60 (65.9)	<0.001
Stage 2 (frequency (%))	63 (57.8)	25 (27.5)	<0.001
Stage 3 (frequency (%))	6 (6.6)	24 (22)	0.005
Uric acid at iSGLT2 initiation * (mg/dL, mean (SD); median (IQR))	5.0 ± 2.1	5 (4.5-5.9)	0.804
Albuminuria at iSGLT2 initiation ** (mg/g, median (IQR))	21.2 (5.3 – 136.9)	18.4 (3.2-18.8)	0.087

SD- standard deviation; T2D – type 2 diabetes mellitus; IQR - interquartile range; iSGLT2- selective sodium-glucose cotransporter inhibitors 2; iDPP4 - dipeptidyl-peptidase 4 inhibitors; GLP1ra- glucagon-like peptide-1 receptor agonist; RAASi - renin-angiotensin-aldosterone system inhibitors; eGFR – estimated glomerular filtration rate.

* missing: 82; **missing: 76

Table 2. Glycemic control during first year treatment with iSGLT2

	Elderly group (n=115)	Under 65 years old group (n=93)	P
HbA1c at beginning of treatment (%, median (IQR*))	8.4 (6.7-10.1)	8.9 (7.1-10.7)	0.594
HbA1c after 12 months treatment (%, median (IQR))	8.3 (6.8-9.8)	8.0 (6-10)	0.844
HbA1c variation during the first year treatment (%, median (IQR))	-0.31 (-1.9-1.3)	-0.8 (-2.4-0.8)	0.091

*IQR - interquartile range

We observed a decrease, although not statistically significative, in eGFR in the first semester after the initiation of iSGLT2 in the elderly group, followed by a significant increase in the second semester (first semester: 77.5 (62.1-87.0) mL/min/1.73m2 vs 71.4 ± 19.0 mL/min/1.73m2; p=0.18, with Bonferroni adjustment; second semester: 71.4 ± 19.0 mL/min/1.73m2 vs 12m: 74.9 ± 18.8 mL/min/1.73m2; p=0.018, with Bonferroni adjustment). The younger group presented a significative decrease in eGFR during the first semester but without significant differences in the second semester (first semester: 90.9 ± 19.0 mL/min/1.73m2 vs 87.6 ± 20.0 mL/min/1.73m2; p=0.006, with Bonferroni adjustment; second semester: 87.6 ± 20.0 mL/min/1.73m2 vs 97.2 (85-106.2) mL/min/1.73m2; p=0.14, with Bonferroni adjustment). There were no statistically significant differences between eGFR variation in first (EG -1.2 ± 8.5 mL/min/1.73m^2 vs YG -2.3 (-8.3 – 1.2) mL/min/1.73m^2; p=0.23) or second semester (EG 1.4 (-4.5 – 3.0) mL/min/1.73m^2 vs YG 1.2 (-1.6 – 7.2) mL/min/1.73m^2; p=0.76) when comparing both groups. Also, neither of the two groups presented a statistically significant difference in eGFR during the first year of treatment (EG - 0m: 90.9 ± 19.0 mL/min/1.73m^2 vs 12m: 74.9 ± 18.8 mL/min/1.73m^2; p=0,354, with Bonferroni adjustment; YG – 0m: 90.9 ± 19.0 mL/min/1.73m^2 vs 12m: 97.2 (85-106.2) mL/min/1.73m^2; p=0,95, with Bonferroni adjustment). The eGFR evolution in the first year of treatment is represented in Fig 1.

In the elderly group, treatment with dapagliflozin and empagliflozin was compared, as represented in Fig 2. Both drugs were not associated to significant differences in eGFR during first year treatment (dapaliflozin: 0m: 75.7 ± 15.7 mL/min/1.73m^2 vs 12m: 76.7 ± 18 mL/min/1.73m^2, p=0.174, with Bonferroni adjustment; empagliflozin - 0m: 69.6 ± 17 mL/min/1.73m^2 vs 12m: 65.7 (50.7 – 83.9) mL/min/1.73m^2; p=0.264, with Bonferroni adjustment). Empagliflozin presented a higher negative variation in eGFR during the first semester (empagliflozin: -4.4 ± 8.2 mL/min/1.73m^2 vs dapagliflozin: -0.6 ± 8.5 mL/min/1.73m^2; p=0.021). Nevertheless, there were no differences in the eGFR variation in the second semester (empagliflozin: 0.3 (-2.3 – 6.2) mL/min/1.73m^2 vs dapagliflozin: 1,6 (-1.1 – 4.9) mL/min/1.73m^2; p=0.852) or during the first-year treatment (empagliflozin: - 1.5 (-5.4 – 2.7) mL/min/1.73m^2 vs dapagliflozin -2.5 ± 9.4 mL/min/1.73m^2; p=0.124) between the two drugs in the elderly group.

At iSGLT2 initiation, elderly patients had a mean uric acid of 5.0 ± 2.1 mg/dL and a median albuminuria of 21.2 (5.3 – 136.9) mg/g, both without significant differences comparing to the younger group (Table 1). Neither uric acid (0 months (n=28): 5.0 ± 2.1 mg/dL; 12 months (n=17): 5.6 (3.9-7.3) mg/dL; p=0.362) nor albuminuria values (albumin-creatinine ratio: 0 months (n=41): 21.2 (5.3 – 136.9) mg/g; 12 months (n=42): 18.9 (3.5 - 180) mg/g; p=0.074) were significantly different in the first-year treatment with iSGLT2 in the elderly group.

In total, only 9 patients had adverse effects associated with iSGLT2 therapy, including 4 urinary tract infections, 4 genital infections and 1 euglycemic ketoacidosis. There were no statistically significant differences between the frequency of adverse effects in elderly or in younger subjects.

DISCUSSION

According to *Instituto Nacional de Estatistica* (Statistics Portugal) data for 2019, elderly represent approximately 22% of the total Portuguese population[7]. In 2015, approximately 24% of individuals between 65 and 74 years were diagnosed with T2D[8].

Our sample presented a higher percentage of elderly in T2D patients, with more than half of our sample represented by patients with 65 or more years. Although, longer T2D duration in elderly (table 1) often associated with more complex therapeutic regimens for glycemic control may result in a greater referral of elderly diabetic patients to hospital appointments.

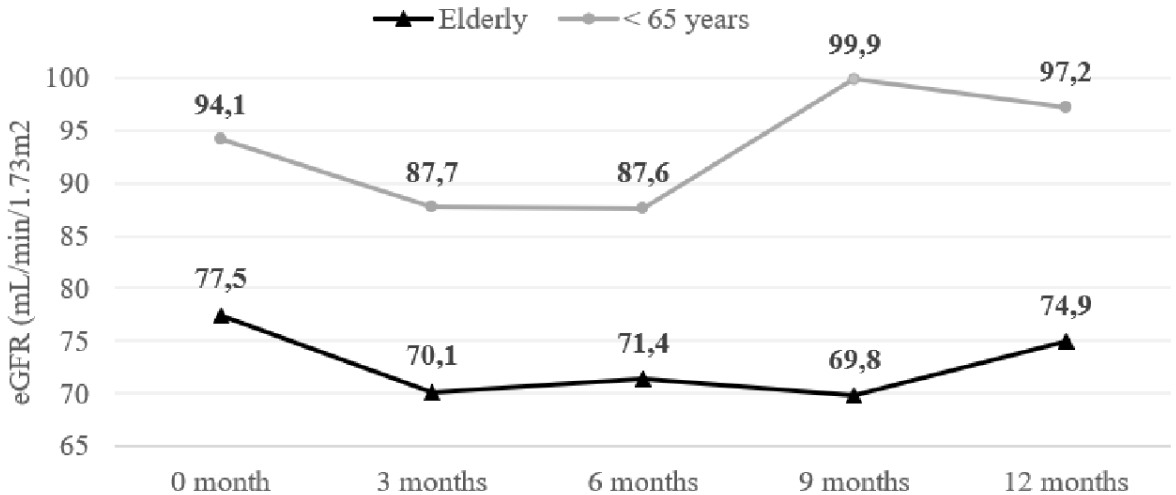
The higher prevalence of female patients in the elderly group is probably associated with higher life expectancy described in woman.

Similar diabetic drugs were used in elderly and in young adults and so, age does not seem to be a limiting factor in the choice of antidiabetics.

The use of RAASi was higher in elderly probably related with higher prevalence of arterial hypertension and higher prevalence of CKD in this group.

HbA1c at treatment beginning was similar in both groups and had a significant decrease after 12 months of therapy, nonetheless slightly

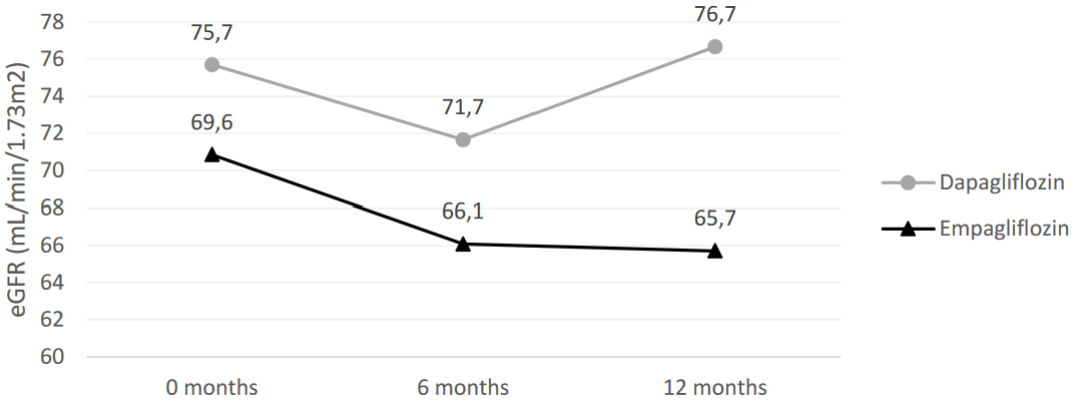
Fig 1. eGFR evolution during the first year of iSGLT2 treatment comparing elderly with patients under 65 years old.



	0 month	3 months	6 months	9 months	12 months
<65 years (mL/min/1.73m²)	90.9 ± 19.0	87.7 ± 19.1	87.6 ± 20.0	99.9 (84.9-107.0)	97.2 (85-106.2)
Elderly (mL/min/1.73m²)	77.5 (62.1-87.0)	70.1 ± 20.0	71.4 ± 19.0	69.8 ± 19.3	74.9 ± 18.8
p value	< 0.001	<0.001	< 0.001	< 0.001	< 0.001

Elderly group presented a no significant decrease in eGFR in the first semester after the initiation of iSGLT2 (p=0.18, with Bonferroni adjustment), followed by an increase in eGFR in the second semester (p=0.018, with Bonferroni adjustment), without statistically significant differences in eGFR during the first year of treatment (p=0,354, with Bonferroni adjustment).
Under 65 years old patients presented a significant decrease in eGFR in the first semester after the introduction of iSGLT2 (p=0.006, with Bonferroni adjustment), followed by a no significant increase in eGFR in the second semester (p=0.14, with Bonferroni adjustment), without statistically significant differences in eGFR during the first year of treatment (p=0,95, with Bonferroni adjustment).
0 month: elderly group - n = 115; under 65 years old group - n= 93
3 months: elderly group - n = 53; under 65 years old group - n= 39
6 months: elderly group - n = 79; under 65 years old group - n= 62
9 months: elderly group - n = 30; under 65 years old group - n= 27
12 months: elderly group - n = 76; under 65 years old group - n=73

Fig 2. eGFR evolution during the first year of treatment with dapagliflozin or empagliflozin in elderly.



No statistically significant differences were observed in eGFR between dapagliflozin initiation date and after 12 months treatment (p=0.174, with Bonferroni adjustment). No statistically significant differences were observed in eGFR between empagliflozin initiation date and after 12 months treatment (p=0.264, with Bonferroni adjustment).
0 month: dapagliflozin - n = 70; empagliflozin - n= 45
6 months: dapagliflozin - n = 47; empagliflozin - n= 32
12 months: dapagliflozin - n = 52; empagliflozin – n= 24

higher in patients under 65 years. The median HbA1c reduction in elderly was -0.31% (-1.9% – 1.29%) which is inferior to the usual HbA1c reduction of -0,5% to -0,7% previously described in general population[9,10].

There was no significant variation in eGFR after 12 months of treatment with iSGLT2 in elderly, although it reduced in the first semester, without statistically significant, it was followed by a significant improvement in the next semester. The initial worsening in eGFR with subsequent recovery is also described in general population studies[4,11]. Elderly patients had a lower eGFR during all the first-year treatment, although there were no statistically significant differences in eGFR variation in the first or second semester, when compared with patients under 65 years. This may indicate that iSGLT2 nephroprotective effect remains even in elderly populations, despite presenting a more advanced CKD. The secondary analyses of EMPA-REG Outcome trial, focusing renal outcomes, favors the use of empagliflozin in incident or worsening nephropathy, even in the elderly (included 1818 elderly in empagliflozin group)[4]. Also, CREEDENCE included 1009 elderly in the group exposed to canagliflozin and favors it use to reduce the combined outcome of end-stage kidney disease, doubling of the serum creatinine level from baseline or death from renal or cardiovascular disease[5]. The secondary analyses of DECLARE-TIMI 58 enrolled 3951 elderly in dapagliflozin group and favors it use in opposite to placebo to prevent the composed outcome of sustained decrease in eGFR by at least 40% to less than 60 mL/min per 1.73 m², end-stage renal disease or renal death[11]. At last, DAPA-CKD incorporated in dapagliflozin group 905 patients above 65 years old, with or without T2D, and dapaglifozin sems to be better than placebo in composed outcome of sustained decline in the estimated GFR of ≥50%, end-stage kidney disease, or death from renal or cardiovascular causes[12].

In the elderly group, empagliflozin was associated with a greater worsening in the eGFR in the first 6 months than dapagliflozin, however, empagliflozin was initiated in patients with lower eGFR, even though, in 12 months treatment, both drugs did not show eGFR worsening. This is in accordance with EMPA-REG and DECLARE-TIMI 58 trial results that proven empagliflozin and dapagliflozin role in delaying the progression of CKD and improving renal outcomes[4,11]. Also, DIAMOND verified an acute reversible decline in eGFR in patients with CKD medicated during 6 weeks with dapagliflozin[13].

Although this paper does not show significant differences in uric acid levels during the first-year treatment with iSGLT2, this data must be carefully analysed, as fewer patients had data regarding acid uric values at the treatment initiation and after 12 months. The same must be applied to albuminuria results. Although, DIAMOND did not prove an effect of dapagliflozin in proteinuria[13].

iSGLT2 seems to be a safe therapeutic class even in elderly patients, as there were few adverse effects reported, without significant differences between the elderly and the younger group. Even in patients with stage 3 CKD, iSGLT2 seems to be safe.

This paper has some limitations, especially inherent to its retrospective design. Not all patients had results for the studied variables (such as eGFR, uric acid and albuminuria), mainly at the third and ninth months. As the data were collected from the patients file, the adverse effects may be underestimated. Also, there is a selection bias, as it only included patients followed in a hospital appointment, so our sample may include patients with more advanced T2D with poor metabolic control and patients with more comorbidities.

CONCLUSION

In conclusion, iSGLT2 seems to preserve the glycemic effects, without worsening renal function in an elderly population during the first-year treatment. There is a non significative decreasing in eGFR during the first 6 months with a recovery in the second semester. This makes us suspect that the nephroprotective effect is also preserved in the elderly in the real life. However, longer-term prospective studies in elderly patients are lacking to assess the impact of iSGLT2 on this population.

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Not applicable.

CONFLICTS OF INTEREST
There are no conflicts of interest.

ETHICS APPROVAL
The study was approved by Ethics Committee of the Centro Hospitalar Vila Nova de Gaia/Espinho.

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