Retrospective Analysis of Real-World Clinical Outcomes and Healthcare Resource Consumption in Patients With Chronic Kidney Disease With and Without Secondary Hyperparathyroidism in Italy

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POSB249

Introduction

Elevations in parathyroid hormone (PTH) concentration are observed in the early phase of chronic kidney disease (CKD) development. As CKD progresses, PTH increases and patients typically develop secondary hyperparathyroidism (sHPT)[1]. The alterations in PTH and mineral metabolism in SHPT have been associated with increased morbidity and mortality in CKD patients [1].

Objective

The aim of the study was to evaluate the clinical and economic burden of sHPT in CKD Italian patients, in a real-world setting.

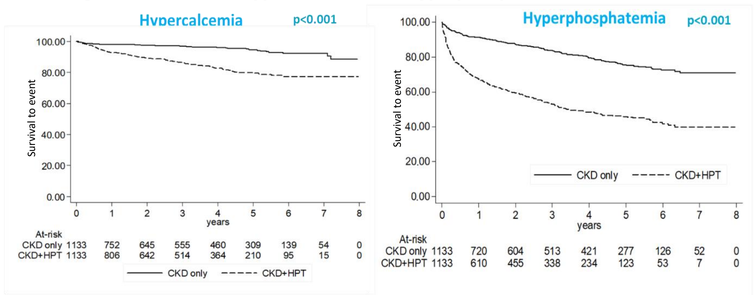
Methods

- A retrospective analysis of real-world data from administrative databases of 6 Italian Local Health Units was conducted.
- Adult non-dialysis CKD patients (stage 3-5) with at least one CKD hospitalization diagnosis (ICD-9-CM codes: 585.3 - 585.4 - 585.5) during 01/2012-03/2015 were included. The date of first diagnosis during this period was defined as “CKD-index date”.
- Among included patients, presence of sHPT diagnosis was identified during the first year after CKD-index date by:
  - at least one prescription of paricalcitol (ATC code: H05BX02) or calcitriol (ATC code: A11CC04), OR
  - a value of PTH ≥ 85 pg/ml OR
  - at least one hospitalization with primary or secondary discharge diagnosis of sHPT (ICD-9-CM: 252.0), OR
  - an active payment waiver code (code that allow to avoid the co-payment for services/treatments in presence of certain diseases) for sHPT (026.252.0)
- Included patients were assigned to one of the two mutually exclusive cohorts:
  - CKD without sHPT cohort (***CKD-cohort***) that included patients without sHPT diagnosis; the index date corresponded to CKD-index date;
  - ***CKD/sHPT-cohort*** including CKD patients with sHPT diagnosis; the index date was the first match with sHPT criteria.
- Patients were characterized during all data availability periods (starting from January 2009) before the index date (the characterization period) and followed-up from index date until 31/12/2019.
- Exclusion criteria included:
  - age <18 years at index date,
  - presence of dialysis at index date or during characterization period;
  - presence of cancer or HIV or HCV diagnosis or cirrhosis at index date or during characterization period;
  - active pharmacological treatment indicated for sHPT (paricalcitol, ATC code H05BX02) during characterization period.
- The Propensity-Score-Matching (PSM) analysis was applied to adjust covariate variability among the two cohorts.
- After PSM, the following outcomes were evaluated during follow up period: dialysis, fractures, hypercalcemia, and hyperphosphatemia. Incidence rate of outcomes was calculated per 1000-person years of follow-up.
- During the follow-up, the annual direct healthcare costs/patients covered by the Italian National Health System (INHS) were assessed.
- *The present study has been approved by the Ethics Committee of each Entities involved in the analysis.*
- *The integration of administrative datasets makes it possible to represent the patient's entire clinical history and not just individual prescriptions. The analyses were conducted on exclusively anonymous data in full compliance with privacy regulations. Clicon s.r.l. has obtained the approval as per legislation by all the Ethics Committees to analyse these data. The results are exclusively in aggregated form and never attributable to a single institution, department, doctor, individual, or individual prescribing behaviours. The study was conducted in full compliance with current legislation for retrospective studies.*

Results

A total of 2,444,064 patient-records were screened, and 7,510 (0.3%) had a CKD 3-5 diagnosis. After application of exclusion criteria, the number decreased to 5,710 included patients: **3,998 (70%) were assigned to the CKD only cohort**, **1,712 (30%) to the CKD/sHPT cohort**.
In the selected population, an update analysis was carried out. After the PSM, 1,133 CKD patients (mean age 78.5, 56.3% male) and 1,133 CKD/sHPT patients (mean age 77, 56.1% male) were included. As extensively reported, the alteration of mineral metabolism in SHPT has significant consequences for patients with CKD, as the increase of calcium and phosphorus concentrations represent the major risk factors for vascular calcification, coronary artery disease, and overall-mortality in these patients[2]. The survival to hypercalcemia and hyperphosphatemia events were significantly lower in CKD/HPT patients vs. CKD only cohort (Figure 1).

Figure 1. Survival to hypercalcemia and hyperphosphatemia events curves



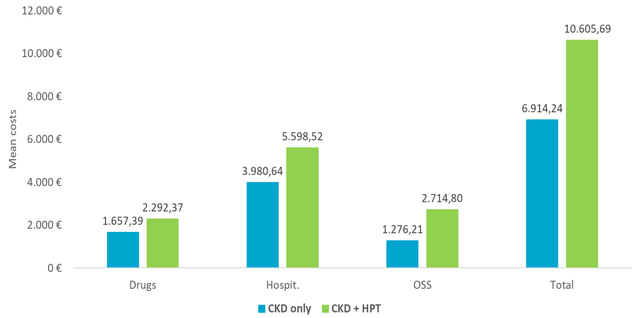
The occurrence of dialysis in overall patients and in those stratified by CKD stages and by age classes (update analysis) was reported in Table 1. **In CKD/sHPT cohort versus the CKD cohort**, the incidence rate of dialysis was significantly higher in overall patients, in patients at stage 3, 4 and 5, and also in patients under and over 65 years old (Table 1). In patients stratified by age classes, the occurrence of fractures was evaluated and reported in table 1. In patients under 65 years, the incidence of fractures were significantly higher (P<0.05) in CKD/sHPT cohort versus the CDK only cohort.

Table 1. Incidence rate of dialysis and fractures, post PSM.

	Dialysis (p<0.001)		Dialysis CKD stage 3 (p<0.001)		Dialysis CKD stage 4 (p<0.001)		Dialysis CKD stage 5 (p<0.001)		Dialysis <65 years (p<0.001)		Dialysis >65 years (p<0.001)		Fractures <65 years (p<0.05)		Fractures >65 years	
	CKD only	CKD/ sHPT	CKD only	CKD/ sHPT	CKD only	CKD/ sHPT	CKD only	CKD/ sHPT	CKD only	CKD/ sHPT	CKD only	CKD/ sHPT	CKD only	CKD/ sHPT	CKD only	CKD/ sHPT
Patients with events (n)	80	310	38	111	25	117	17	82	24	89	56	221	0	7	45	36
Person years of follow-up	3,357	2,791	2,071	1,695	1,033	885	253	210	618	472	2,738	2,319	655	760	2,758	2,727
Incidence rate/1000-person years	**23.83**	**111.08**	**18.35**	**65.47**	**24.2**	**132.18**	**67.22**	**390.12**	**38.81**	**188.72**	**20.45**	**95.29**	**0.00**	**9.22**	**16.32**	**13.2**
Follow-up (mean years ± SD)	3.0 (2.4)	2.5 (2.0)	3.2 (2.4)	2.8 (2.0)	2.7 (2.3)	2.3 (2.0)	2.4 (2.8)	1.5 (1.9)	4.4 (2.1)	3.0 (2.2)	2.8 (2.4)	2.4 (2.0)	4.6 (2.1)	4.8 (1.6)	2.8 (2.4)	2.8 (2.1)

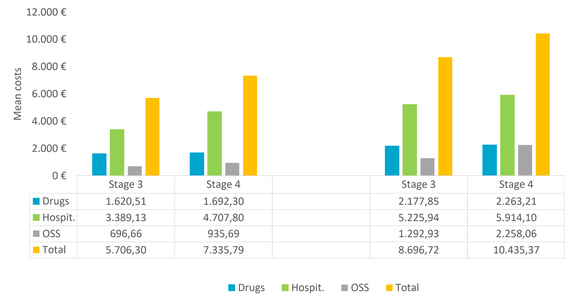
The overall direct cost evaluated during one-year of follow-up (index date excluded), tended to be higher in CKD/sHPT-cohort (10,605,69€) versus the CKD-cohort (6,914.24€) (Figure 2). The same trend was observed for OSS, hospitalization and drugs-related costs.

Figure 2. Direct healthcare costs during the first year of follow up, index date excluded, post PSM



The update analysis of stratification of patients by CKD stage has shown that the overall direct cost in CKD patients stage 3 and 4 averaged 5,706.30€ and 7,335.79€, respectively, and tended to be lower to the overall cost of CKD/sHPT patients stage 3 (8,696.72€) and stage 4 (10,435.37€)(Figure 3).

Figure 3. Direct healthcare costs during the first year of follow up in CKD stage 3 and 4 patients, index date excluded, post PSM



	Stage 3	Stage 4		Stage 3	Stage 4
Drugs	1.620,51	1.692,30		2.177,85	2.263,21
Hospit.	3.389,13	4.707,80		5.225,94	5.914,10
OSS	696,66	935,69		1.292,93	2.258,06
Total	5.706,30	7.335,79		8.696,72	10.435,37

Conclusion

The analysis of real-world data of patients with CKD disease with and without sHPT allowed us to evaluate patients' clinical management and economic impact. We showed that secondary HPT might worsen CKD disease progression rate in mineral imbalance, dialysis and fractures occurrence, especially in later-stage patients and younger patients. In addition, an increase direct costs was observed in the CKD/sHPT cohort. Further analyses focused on other clinical outcomes among stage-stratified CKD patients will be performed to get more insights on the impact of sHPT on CKD disease burden.

References

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2. Block GA et al. Am J Kidney Dis. 1998, 31: 607-617. 10.1053/ajkd.1998.v31.pm9531176.

Presented at Virtual ISPOR EU; 1st-3rd December, 2021
This study was supported by Vifor Pharma, Glattbrugg, Switzerland