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Age and gender distribution of primary hyperparathyroidism and incidence of surgical treatment in a European country with a particularly high life expectancy

Laura Richert[a], *Andrea Trombetti*[a], *François R. Herrmann*[a], *Frédéric Triponez*[b], *Christian Meier*[c], *John H. Robert*[b], *René Rizzoli*[a]

[a] Service of Bone Diseases, Department of Rehabilitation and Geriatrics, University Hospitals of Geneva, Geneva, Switzerland
[b] Thoracic and Endocrine Surgery Unit, Department of Surgery, University Hospitals of Geneva, Geneva, Switzerland
[c] Division of Endocrinology, Diabetes and Clinical Nutrition, University Hospital of Basel, Basel, Switzerland

Summary

Objective: Primary hyperparathyroidism (PHPT) is a frequently encountered endocrine disease in the elderly, but little is known about its epidemiology in the aging European population. This study investigates the age- and sex-dependence of PHPT and the incidence of parathyroidectomy (PTX) in Switzerland, a country with a particularly high life expectancy.

Design: A population-based study was performed using data from the Swiss Federal Statistical Office covering years 2000 to 2004. Anonymised hospital discharge codes for PHPT and PTX were analysed, and the hospitalisation rate for PHPT and incidence of PTX were calculated.

Results: The mean annual hospitalisation rate of patients with PHPT was 8.3/100,000 inhabitants. The rate was approximately three times higher in women than in men, with the highest estimate found in women ≥80 years (63.7/100,000). The population-adjusted annual incidence of PTX was 3.8/100,000 inhabitants. PTX incidence was higher in individuals ≥50 years than in younger persons (8.7/100,000 vs 1.3/100,000), with a peak in patients aged 70–74 years.

Conclusions: In a European population with high life expectancy, the hospitalisation rate of PHPT is higher in women and increases continuously with age. Incidence of PTX is highest in patients aged 70–74 years. These findings underscore the need for further research on the impact of population aging on the treatment patterns of PHPT.

Key words: primary hyperparathyroidism; parathyroidectomy; age distribution; gender; Switzerland

Introduction

Primary hyperparathyroidism (PHPT) is a common endocrine disorder in the elderly. Over the last few decades, the epidemiology of PHPT has undergone marked changes. After the introduction of routine serum calcium measurements in the 1970s, facilitating the diagnosis of asymptomatic PHPT, epidemiological studies from the United States (US) reported a higher prevalence and incidence than previously presumed [1]. More recently, a constant decline in incidence has been observed [2], despite the demographic changes due to an aging US population.

In Europe, population aging is of a particularly important magnitude [3]. Yet, recent epidemiological estimates of PHPT in European countries are scarce. Prevalence reports from the 1990s in Scandinavian countries are either restricted to selected age groups or exclude the population over 75 years [4–7]. Moreover, different reporting methods limit their comparison and do not allow for any inference on the overall age distribution of PHPT. In a study analysing the changes in incidence of newly diagnosed PHPT in Danish hospitals, the mean patient age at the time of diagnosis increased significantly from 1980 to 1999 [8], thus suggesting a changing age pattern of the disease. Gender difference was documented by Adami et al. who reported a female predominance

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of 5:1 in older European PHPT patients [9]. However, the population-adjusted age- and gender distribution of PHPT was not assessed in these studies.

To our knowledge, no population-adjusted studies on the disease pattern of PHPT in Europe have been published recently. With Iceland, Switzerland shares the highest life expectancy at birth in Europe (81.8 and 81.7 years, respectively) [3]. In 2000, the proportion of subjects aged over 80 years was 3.9% in Switzerland, compared to 3.6% for the rest of Western Europe [3]. Thus, we hypothesize that the epidemiological characteristics of PHPT may be representative of an aging population. The aim of our study was to analyse the age and gender distribution of this disease in Switzerland and to assess the surgical treatment pattern.

Methods

Nationwide data from 2000 to 2004 were obtained from the Swiss Federal Statistical Office as follows and stratified by age and sex: population data, number of hospitalisations, and anonymous hospital diagnosis and surgical procedure codes for PHPT and parathyroidectomy (PTX), respectively. A diagnosis of PHPT in a hospitalised case was defined by the diagnostic code E21.0 according to the International Classification of Diseases, 10th revision (ICD-10) [10]. Both principal and secondary discharge diagnoses were taken into account. Of note, the diagnoses "secondary hyperparathyroidism" (E21.1) as well as "other" (E21.2) and "unspecified" hyperparathyroidism (E21.3), defined by distinct ICD-10 codes, were not included in the analysis. Surgical procedures in Switzerland are coded on the basis of the Swiss classification of surgical interventions (CHOP), a translation and adaptation of the US version of the International Classification of Diseases, 9th revision (ICD-9-CM), elaborated by the Swiss Federal Statistical Office [11]. In accordance with current encoding practice, the most appropriate surgical code for PTX in relation to PHPT was defined as CHOP 06.89 ("other parathyroidectomy"). The only other code for parathyroid surgery in Switzerland is "total parathyroidectomy", an uncommon procedure for PHPT.

Annual reporting of discharge codes to the Federal Statistical office has been compulsory for all hospitals since 1997, and hospital statistics have been published since 2000. Participation rates for public hospitals were 81.1% in 2000, 81.1% in 2001, 91.7% in 2002, 93% in 2003, and 93.5% in 2004 (rate of reported cases). Coding quality, evaluated in different subsets of Swiss hospitals between 2003 and 2005, has been reported to be good [12, 13]. If not specified otherwise, discharge statistics from private clinics were included in the present study.

All data obtained had to be reformatted for analysis. Due to the small absolute case numbers in the oldest age groups, data of cases aged 80 years and older were combined. With population data as a denominator, the mean annual hospitalisation rate (i.e. incidence of hospitalisation of patients with PHPT) and incidence of PTX were estimated by sex and age per 100,000 inhabitants. The analysis was then repeated with the number of hospitalisations as a denominator to obtain the in-hospital prevalence of PHPT per 100,000 hospitalisations. Private clinics were not taken into account for the estimation of the in-hospital prevalence since we had no information on the total number of hospitalisations in these institutions.

Additionally, the proportion of surgically-treated PHPT patients in the hospital setting was calculated by dividing the number of PTX by the number of hospitalised PHPT cases. However, due to the anonymisation of the data, no information was available as to whether diagnostic and surgical codes referred to identical cases. In Switzerland, PTX is only very rarely performed in an outpatient setting so that the numbers presented here correspond to >95% of all PTX performed in this country during the analysed time-period. Proportions were compared using a Chi-square test. P values <0.05 were considered significant.

Results

Population-based hospitalisation rate for PHPT and incidence of parathyoidectomy

Between 2000 to 2004, 3052 cases had a hospital discharge diagnosis of PHPT, including a principal diagnosis of PHPT in 1178 cases. Of the 3052 cases, 170 were treated in private clinics. During the same period, a total of 1381 parathyroidectomies were performed (84 in private clinics).

The principal and secondary diagnoses taken together, the mean annual population-based hospitalisation rate of patients with PHPT was estimated at 8.3 per 100,000 inhabitants. If only principal discharge diagnoses were taken into account, the hospitalisation rate resulted in 3.2/100,000 inhabitants. Since PHPT was rare in the younger population, estimates were computed separately for cases over 50 years. As expected, population-adjusted numbers of hospitalised PHPT cases increased with age (fig. 1), with a hospitalisation rate of 0.5/100,000 inhabitants in children and adolescents (0–19 years), 2.1/100,000 in the population aged 20 to 49 years, and 21.6/100,000 in those aged ≥50 years (principal and secondary diagnoses taken together for these and all following estimates). In both genders, the rate increased continuously up to the very old with the highest estimate of declared hospitalised PHPT cases being found in female patients aged ≥80 years (50.4/100,000). In men ≥80 years, the estimate was 23.8/100,000. Of note, gender difference was striking in the population ≥50 years, with a hospitalisation rate of 31.6/100,000 for women and 9.7/100,000 for men. This difference was less pronounced in those

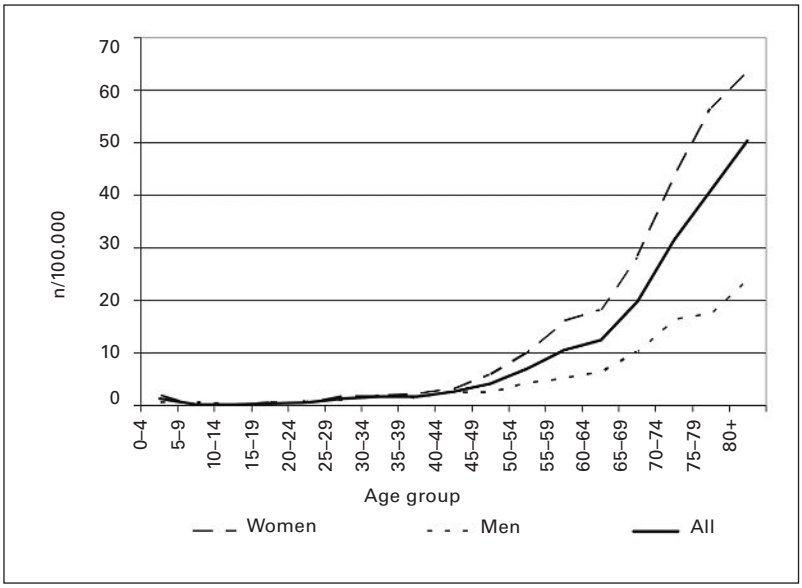

Figure 1

Annual mean hospitalisation rate of patients with primary hyperparathyroidism per 100,000 inhabitants in Switzerland, 2000–2004.

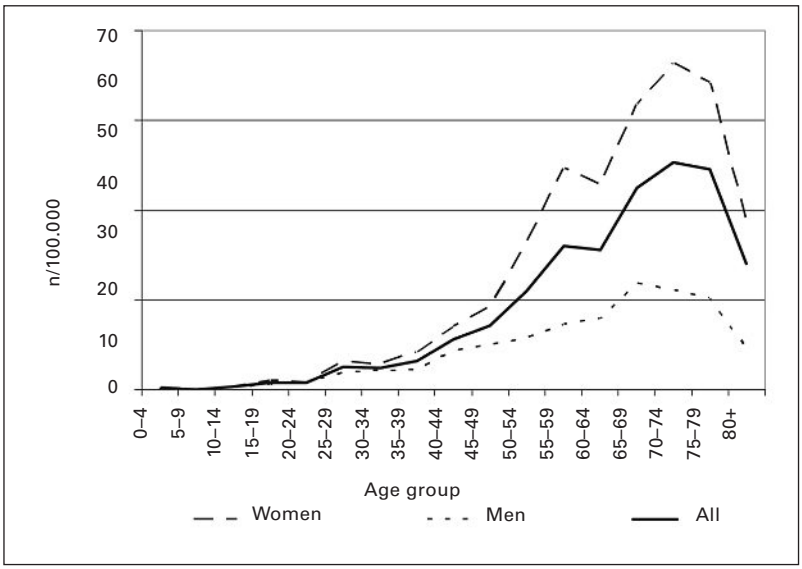

Figure 2

Annual mean incidence per 100,000 inhabitants of parathyroidectomy in Switzerland, 2000–2004.

<50 years (1.9/100,000 vs 1.2/100,000, respectively).

Mean annual incidence of PTX was estimated at 3.8/100,000 inhabitants. In accordance with an age-dependent increase in PHPT, the population-adjusted incidence of PTX was higher in persons aged ≥50 years (fig. 2). The peak of PTX incidence was observed in patients aged 70–74 years (12.7/100,000), with a decline thereafter. Overall estimates were higher in women than in men (5.6/100,000 vs 1.9/100,000, respectively). Moreover, PTX incidence was significantly higher in areas of south-west Switzerland than in the rest of the country (data not shown).

Table 1

In-hospital prevalence of primary hyperparathyroidism in Switzerland, 2000–2004.

Age group (years)	Prevalence /100,000 hospitalisations *		
	Women	Men	All
0–4	7.2	1.7	4.2
5–9	0.0	7.1	4.3
10–14	0.0	5.0	2.8
15–19	5.5	3.6	4.6
20–24	2.6	8.0	4.8
25–29	8.3	10.6	9.0
30–34	7.6	19.4	11.1
35–39	12.3	14.1	13.0
40–44	20.1	22.3	21.1
45–49	38.0	17.2	27.9
50–54	56.8	23.7	40.2
55–59	78.0	24.4	49.9
60–64	81.3	24.4	51.1
65–69	105.8	31.4	67.5
70–74	131.9	41.5	87.9
75–79	133.6	36.6	90.7
80+	130.4	41.3	97.4
Overall	61.2	22.7	43.8

*Nationwide annual mean prevalence of PHPT per 100,000 hospitalisations

In-hospital prevalence of primary hyperparathyroidism

Prevalence of PHPT among hospitalised patients was 61.2/100,000 in women and 22.7/100,000 in men, with an overall prevalence of 43.8/100,000. As illustrated in table 1, prevalence rose with increasing age to a maximum of 97.4/100,000 among hospitalised patients aged ≥80 years. In patients aged ≥50 years, female gender was predominant (108.6/100,000 vs. 32.3/100,000 in men). In younger patients, however, prevalence estimates were similar among the two genders (11.9/100,000 in women vs. 11.1/100,000 in men).

Proportion of surgically treated patients

The proportion of surgically treated patients among those hospitalised for PHPT was estimated at 45.2%, with a higher proportion found in those aged <50 years than in older patients (81.3% vs. 40.1%, p <0.001). Men were more likely to be treated surgically than women (48.7% vs. 44.2%, p <0.05).

Discussion

Based on hospital discharge statistics, we report estimates of epidemiological indicators of PHPT in Switzerland, a country with a high proportion of elderly people. From 2000 to 2004, we found a mean annual hospitalisation rate of patients with PHPT of 8.3/100,000 inhabitants, and an in-hospital prevalence of PHPT of 43.8/100,000 hospitalisations. These estimates are conservative since discharge codes of unspecified PHPT were not included in the analysis.

Although limited to in-patient statistics, our data provide an insight into the age and gender distribution of the disease in Switzerland. The hospitalisation rate and in-hospital prevalence increased with age in both genders, reaching a peak in patients ≥80 years of age. Interestingly, a recent update of population-based data from Rochester, Minnesota, indicated a peak in PHPT incidence in the population aged 65 to 74 years, with a decline thereafter [2]. This apparent discrepancy with our results may either be due to the use of different epidemiological indicators, or it may suggest a distinct disease pattern in Switzerland. As expected, all indices were markedly higher in women, thus reflecting the well-known preponderance of the disease in females. Of note, and as already reported by others, this gender imbalance seems to be less detectable in the younger population [2]. Indeed, in our population adjusted data the hospitalisation rate in women compared to men begins to diverge at the age of 45 years, which might indicate a possible relationship between PHPT occurrence and peri- or postmenopausal state. This contrasts with a recently published report by Miller et al. who hypothesized on the basis of absolute PTX numbers that gender distribution was not related to menopausal state [14]. In our view, this discrepancy underscores the importance of population adjusted estimates to assess gender and age distribution of a given disease. In addition, our data reflect that rare cases of PHPT may also occur in children and adolescents. Parathyroid adenoma, multiple endocrine neoplasia or familial hyperparathyroidism have been reported to be the main aetiologies of PHPT in patients <19 years [15].

There is a paucity of published literature on the community-based prevalence and incidence of PHPT and, to our knowledge, only three studies have been published in the last 10 years. Wermers et al. reported a population-based incidence rate of PHPT of 21.6 per 100,000 person-years between 1993 and 2001 in the USA [2]. In Norway, PHPT prevalence in the population <76 years was estimated at 0.17% in men and 0.45% in women in a study from the 1990s [5]. Finally, in Sweden, a PHPT prevalence of 2.1% was observed in women aged 55–75 years in the early 1990s [4]. No estimates of PHPT incidence were reported in these two Scandinavian studies. Unfortunately, there are no published data on the ratio of in-patients to out-patients with PHPT, which would allow for a rough appraisal of the overall epidemiological relevance of this disease in our study.

The overall incidence of PTX in our study was 3.8/100,000 inhabitants. Crude population-based incidence of PTX and its gender distribution seem to be fairly similar between Switzerland, USA, Australia and Hong Kong [16–18]. In the USA, the annual PTX procedure rate in 2004 was 4.8/100,000 in the general population [16]. In Australia, population based PTX rates of 7.6/100,000 in women and 2,7/100 000 in men have been reported in the late 1990s [17]. Lastly, in Hong Kong, the annual procedure rate of PTX has been estimated at 2.5/100,000 in the general population [18].

Although PTX is the only curative treatment for PHPT, some patients may be followed without surgery. Interestingly, in a survey evaluating referral patterns in Switzerland, endocrinologists reported referring 59 ± 24% of their PHPT patients for surgical treatment [19]. Based on this survey it could be hypothesized that the incidence of diagnosed PHPT cases in the overall Swiss population might be 27–65% higher than the incidence of PTX.

In our estimates, the crude incidence of PTX was highest in the population aged 70–74 years. Despite a continuing increase in PHPT hospitalisation rates with older age, a decline in PTX incidence was observed in the oldest (≥75 years). This finding may have several explanations: in the highest age groups, the number of comorbidities and the remaining life expectancy could affect the decision to intervene surgically. Moreover, the data may suggest an under-treatment of PHPT in the very old. Encouraging outcomes of surgical treatment in elderly patients with PHPT have been reported [20–22]. A comparative study suggests that unilateral neck exploration is cost-effective in patients up to 80 years of age [23]. However, more research is needed to evaluate the long-term outcome of different management strategies in this population.

The NIH consensus guidelines recommend surgery in patients <50 years [24]. Notably, a French consensus statement, even though advocating surgery more generally as a preferred treatment for PHPT, also specifies younger age as a formal indication for parathyroidectomy [25]. Hence, it is not surprising that in the analysed data the proportion of surgically-treated cases among those hospitalised with PHPT was higher in patients <50 years than in those ≥50 years.

The present study has some limitations, and our epidemiological estimates may be biased by errors inherent to hospital discharge statistics, such as miscoding and underreporting of secondary diagnoses. Moreover, since the analyses do not comprise out-patient data, little inference can be made

to the epidemiology of PHPT in the overall Swiss population. When interpreting the estimated hospitalisation rate, it is reasonable to assume that some patients might have been hospitalised more than once. PTX, however, confers a high cure rate and is most likely a procedure performed only once in a given patient [26]. It should also be noted that the surgical coding for PTX in our analysis might also comprise patients undergoing partial PTX for secondary or tertiary renal hyperparathyroidism, thus leading to an overestimation of cases. Nevertheless, we believe this effect to be minor since surgical treatment for secondary hyperparathyroidism is only undertaken in rare, severe cases. For instance, in one of the five Swiss university hospitals, approximately 10% of all PTX between 1990 and 2002 were performed for secondary hyperparathyroidism [27, 28 and personal unpublished results]. With the introduction of calcimimetics for the medical management of severe renal hyperparathyroidism, we consider this proportion to be smaller in the present data.

In summary, epidemiological indicators of PHPT based on hospital discharge data in Switzerland showed a female predominance and a continuous increase with rising age. Incidence of PTX was highest among patients aged 70–74 years. We suggest that demographic changes may have a major impact on the pattern of the disease and on the frequency of parathyroidectomies, but further research is necessary to assess community-based prevalence and incidence of PHPT and the need for surgical treatment in the European aging population.

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Correspondence:
Andrea Trombetti, MD
Service of Bone Diseases
Geneva University Hospital (HUG)
24, Rue Micheli-du-Crest
CH-1211 Geneva 14
Switzerland
E-Mail: andrea.trombetti@hcuge.ch

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