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What are predictors of impaired quality of life in patients with hypoparathyroidism?

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Abstract

Context: Hypoparathyroidism (hypoPT) is a rare endocrine disorder. Little is known about what factors are associated with potential quality of life (QOL) impairments.

Design: HypoPT patients at a minimum of 6 months' post diagnosis were invited to participate in an online survey through their treating physician or through self-help organisations

Methods: Impairments of clinical importance in QOL were considered present if the score of the respective functioning scale of the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 exceeded a pre-defined threshold. Symptom burden was assessed using the HPQ-28. Multivariate logistic regression was used to identify factors associated with impairments in QOL.

Results: Data were available for 264 hypoPT patients. Impairments of clinical importance in QOL were reported for 40.4% in role functioning (RF), 40.6% in social functioning (SF), 60.8% in physical functioning (PF), 65.5% in cognitive functioning (CF) and 76.0% in emotional functioning (EF). Higher odds for reporting impaired QOL were seen for higher symptom burden (for almost all domains) and for being unable to work (for PF, RF and SF). Surgery for thyroid cancer being the cause of hypoPT was associated with lower odds in PF for patients and in PF and CF for patients with surgery for other thyroid-related diseases being the hypoPT cause.

Conclusions: HypoPT needs to be recognised as a disease which might be associated with impaired QOL and affect daily living. Symptom management is crucial for improving QOL in hypoPT patients but socioeconomic factors like work-ability need to be considered when treating hypoPT patients.

KEYWORDS

EORTC QLQ-C30, hypoparathyroidism, impairments, parathyroid, quality of life, survey, well-being

1 | INTRODUCTION

Chronic Hypoparathyroidism is an endocrine disorder defined hypocalcaemia with inappropriately normal or low parathyroid hormone[1,2] for more than 6 months but different definitions and times frames are also used in the literature.[3] The prevalence varies in countries with 9.4 per 100,000 in Norway,[4] 24 per 100,000 in Denmark[5,6] and 37 per 100,000 in the United States.[7] The current treatment options consist of calcium and vitamin D supplementation as the conventional treatment, and synthetic PTH analogue (PTH 1–34) and human recombinant parathormone (PTH 1–84) as new treatment options for patients whose hypocalcemia cannot be treated with the standard treatment.[1] Patients receiving standard treatment have been shown to report impairments in quality of life (QOL) compared to matched controls or norm populations.[8,9] Studies using PTH 1–34 or PTH 1–84 have been shown to improve QOL[10–12] and to maintain calcium levels in the normal target range.[9] Therapies and blood level parameters might play a role in influencing QOL in hypoPT patients, but the role of blood levels results in particular is conflicting in the literature.[4,9,11] The severity of symptoms and therefore their influence on QOL cannot be directly translated to serum calcium levels,[1] since calcium levels may vary throughout the day and therefore single measures might not explain effects on QOL.[13] Factors like symptoms, disease duration, aetiology of hypoPT, or sociodemographic factors may play an important role in the QOL of hypoPT patients.

Therefore, the aim of this study was to assess the share of hypoPT patients who report impairments in QOL of clinical importance and to identify factors which might be associated with impaired QOL.

2 | MATERIALS AND METHODS

2.1 | Design

Supported by the German Society of Endocrinology, Hormones, and Metabolism and the German Society of Nuclear Medicine, physicians were informed about the study and invited to provide information to their patients. Additionally, 294 physicians were contacted by mail and were asked for their support of the study with 22 (7.5%) actively consenting to support the study. The contact information of the physicians was obtained using the Kassenärztliche Budesvereinigung database. They then informed their patients about the study. Additionally, study information was distributed through the patient organisation Netzwerk Hypopara. Patients completed on online survey between 10/2020 and 10/2021. Next to the online questionnaire, a paper-based version of the questionnaire was available and was provided upon request.

Patients were eligible if they had been treated for hypoparathyroidism diagnosed by their physician. As per local regulations, no ethics committee approval was needed (confirmed by the Ethics-Committee of the Landesärztekammer Rhineland-Palatinate).

2.2 | Assessments

All data were provided by the patient through the online survey. QOL was assessed using the functioning scales [physical functioning (PF), role functioning (RF), emotional functioning (EF), cognitive functioning (CF), social functioning (SF)] and the global QOL scale of the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Core Questionnaire (QLQ-C30).[14] Response formats are on a four-point-Likert scale ('not at all', 'a little', 'quite a bit' and 'a lot'). The items are summarised and transformed into scores ranging from 0 to 100, with high values indicating lower impairments in the functioning and the QL scales.[15] Symptom Burden was assessed using the Hypoparathyroid Patient Questionnaire HPQ-28.[16] In the HPQ-28, 20 symptom items using a four point-Likert Scale (0 = 'not at all', 1 = 'slightly', 2 = 'moderately', 3 = 'severely/strongly') measure symptom burden and eight items for the assessment of depression and anxiety and vitality. The items cover symptoms related to *pain and cramps*, *gastrointestinal symptoms*, *neurovegetative symptoms*, *numbness or tingling*, *memory problems*, *heart palpitations*, *depression and anxiety* using a 4-week time frame. For categorising symptom burden, the mean value of all items (scores ranging from 0 to 3 per question) was calculated. Participants were categorised into *low symptom burden* (mean score 0 to <0.5), *medium symptom burden* (mean score ≥0.5 to <1.5), and *high symptom burden* (mean score ≥1.5). Education was defined by the highest educational certificate obtained resulting into the following categories: *below 10 years of education*, *10 years of education*, *and above 10 years of education*. Occupational status was assessed by the current employment situation. Four categories emerged from the question: *Employed/self-employed*, *retirement annuity (regular retirement)*, *unable to work*, and *others*. The *unable to work* category comprises patients who are early retired (before the age of 65), receive disability pension, reduced earning capacity pension, or are on long-term sick leave (more than 6 months). In the *other* category participants were included if the total numbers were too small to form a group (e.g., students, housewives). Time since diagnosis was assessed using the following categories: *0.5–1*, *1–2*, *2–5*, *5–10 years*, and *more than 10 years*.

2.3 | Statistical analysis

Scores for the functioning scales of the EORTC QLQ-C30 were calculated according to the scoring manual of the EORTC.[15] A value below the thresholds (PF: 83 points, RF: 58 points, SF: 58 points, EF: 71 points, and CF: 75 points) by Giesinger et al.[17] was considered to be an impairment of clinical importance in the respective scale. Univariate comparisons of QOL scores (non-surgical vs. surgical) were performed using Mann–Whitney-*U* tests.

Multivariate logistic regression with having impairments of clinical importance (no/yes) as the outcome and sociodemographic, clinical, and symptom burden as independent variables was performed for the five functioning scales of the EORTC QLQ-C30. All

TABLE 1 Patient characteristics ($n = 264$) using mean (SD) or n (%)

Characteristic	
Age (mean [SD])	54.5 (13.3)
Sex (n [%])	
Male	36 (13.6%)
Female	225 (85.2)
Missing	3 (1.1)
Education (n [%])	
Below 10 years	36 (13.6)
10 years	102 (38.6)
More than 10 years	125 (47.3)
Missing	1 (0.4)
Living situation (n [%])	
Alone	61 (23.1)
With someone	203 (76.9)
Occupation (n [%])	
Employed/self-employed	145 (54.9)
Regular retirement	57 (21.6)
Unable to work	45 (17.0)
Other	17 (6.4)
Member of self-help organization (n [%])	
No	167 (63.3)
Yes	97 (36.7)
Time since diagnosis (n [%])	
6 months–1 year	6 (2.3)
1–2 years	22 (8.3)
2–5 years	47 (17.8)
5–10 years	43 (16.3)
More than 10 years	145 (54.9)
Missing	1 (0.4)
Cause of HPT (n [%])	
Nonsurgical	21 (8.0)
Surgical	243 (92.0)
Surgery for thyroid cancer	100 (41.2)
Surgery for other thyroid related diseases	143 (58.8)
Symptom burden (n [%])	
None to low	59 (22.3)
Medium	75 (28.4)
High	130 (49.2)
Medication (n [%])	
Calcium	153 (58.0)
Calcitriol	152 (57.6)
Alphacalcidol	23 (8.7)
Colecalciferol	66 (25.0)
PTH	28 (10.6)
Magnesium	49 (18.6)
Dihydrotachysterol	31 (11.7)
Missing	13 (4.9)

statistical analyses were performed using R (R version 4.0.4, R Foundation for statistical computing).

3 | RESULTS

3.1 | Sample and patient characteristics

In total, 264 patients with hypoparathyroidism participated in the study. Four (2.3%) participants were excluded since their diagnosis was less than 6 months past and therefore it could not be ruled out that their hypoPT was only transient. The mean age of the study population was 54.5 (SD:13.3) years with 85.2% (225) being female and 92.0% (243) naming surgery the cause for their hypoPT. All patient characteristics can be found in Table 1.

3.2 | Quality of life

QOL scores for the total sample and for patients with non-surgical and surgical causes of hypoPT are presented in Table 2. No differences were seen when comparing the QOL scores of patients with a non-surgical and surgical cause using univariate analysis.

For role functioning and social functioning 40.4% and 40.6% of the patients reported impairments of clinical importance. For the three other functioning scales, the percentage of patients with impairments of clinical importance was 76.0% regarding emotional functioning, 60.8% in physical functioning, and 65.5% in cognitive functioning.

3.3 | Factors associated with impairments in QOL in patients with hypoparathyroidism

Symptom burden was associated with all functioning scales (Table 3). Compared to patients with a medium symptom burden, patients with low symptom burden had lower odds for impairments of clinical importance {PF (OR: 0.1; 95% CI [0; 0.3]), EF (OR: 0.2; 95% CI [0.1; 0.4]), SF (OR: 0.04; 95% CI [0.002; 0.2]), and CF (OR: 0.2; 95% CI [0.1; 0.6])} and patients with high burden reported higher odds

TABLE 2 Functioning in patients with hypoparathyroidism (HPT), stratified by cause of HPT (surgery vs. other causes)

		All (n = 264)	Non-surgical (n = 21)	Surgical (n = 243)	p-value non-surgical versus surgical)
Physical functioning (PF)	Mean (SD)	74.0 (21.5)	74.3 (17.2)	74.0 (21.9)	.75
	Median (Q1;Q3)	80 (60; 93.3)	73.3 (60; 80)	80 (60; 93.3)	
Role functioning (RF)	Mean (SD)	63.6 (32.5)	65.9 (35.9)	63.4 (32.3)	.62
	Median (Q1;Q3)	66.7 (33.3; 100)	66.7 (33.3; 100)	66.7 (33.3; 100)	
Social functioning (SF)	Mean (SD)	61.7 (33.4)	69.0 (33.5)	61.1 (33.4)	.28
	Median (Q1;Q3)	66.7 (33.3; 100)	83.3 (50; 100)	66.7 (33.3; 100)	
Emotional functioning (EF)	Mean (SD)	46.9 (30.1)	54.5 (30.5)	46.2 (30.0)	.22
	Median (Q1;Q3)	50 (25; 66.7)	58.3 (41.7; 75)	50 (22.2; 66.7)	
Cognitive functioning (CF)	Mean (SD)	56.9 (31.6)	63.5 (27.7)	56.3 (32.0)	.38
	Median (Q1;Q3)	66.7 (33.3; 83.3)	66.7 (50; 83.3)	66.7 (33.3; 83.3)	
Global Quality of Life (QL)	Mean (SD)	44.4 (21.3)	44.0 (21.8)	44.4 (21.3)	.84
	Median (Q1;Q3)	50 (33.3; 58,3)	50 (33.3; 58,3)	50 (33.3; 58,3)	

Note: Univariate comparison using Mann–Whitney-*U* tests.

{PF (OR: 4.3; 95% CI [2.1; 9.2]), RF (OR: 7.5; 95% CI [3.6; 16.4]), EF (OR: 7.9; 95% CI [3.0; 24.2]), SF (OR: 4.9; 95% CI [2.4; 8.8]), and CF (OR: 12.0; 95% CI [5.3; 29.8])} for impairments of clinical importance.

Patients who were unable to work (compared to patients being employed/self-employed) had higher chances of reporting impairments of clinical importance in PF (OR: 6.3; 95% CI [2.1; 21.7]), RF (OR: 5.6; 95% CI [2.2; 15.2], and SF (OR: 2.6; 95% CI [1.1; 6.6]). Surgery being the cause of hypoPT (compared to non-surgical patients) was associated with lower odds in PF (OR: 0.1; 95% CI [0; 0.5]) for patients with surgery for thyroid cancer and in PF (OR: 0.1; 95% CI [0; 0.4]) and CF (OR: 0.3; 95% CI [0.1; 0.9]) for patients with surgery for other thyroid-related diseases (e.g., goitre). Compared to the lowest education group (below 10 years of education), education of 10 years (OR: 0.2; 95% CI [0.1; 0.6]) and above 10 years (OR: 0.3; 95% CI [0.1; 0.9]) was associated with lower odds in PF. Age, living with someone, and time since diagnosis were not associated with impairments of clinical importance in the functioning scales. PTH replacement therapy did not alter the results of the regression analysis and did not show any significant associations (data not shown).

4 | DISCUSSION

Our study shows that a moderate to high share of patients report impairments of clinical importance across several QOL domains. Patients with a medium and high symptom burden had higher chances of reporting impairments in QOL. Being unable to work was also associated with higher odds of reporting impairments in PF, RF and SF of the EORTC QLQ-C30.

With 40.4% (for RF) and up to 76.0% (for EF), our study had a moderate to high share of hypoPT patients with impairments of clinical importance. These potential negative effects of hypoPT on QOL are in line with findings from other studies assessing the QOL in hypoPT patients.[8] Compared to various cancer populations, an equal or higher share of patients reported impairments of clinical importance in our study.[18,19] This is in line with findings from Astor et al.[4] who reported, using the SF-36, that Norwegian hypoPT patients had significantly lower scores compared to patients with Addison's disease or congenital adrenal hyperplasia. Oerlemans et al.[20] found that for thyroid cancer survivors large differences regarding self-reported cognitive functioning (using the EORTC QLQ-C30) compared to a norm population exist. Since it is estimated that up to 17%[21] of all patients with total thyroidectomy develop chronic hypoPT, the question arises if these impairments in cognitive functioning might not also be applicable to hypoPT among thyroid cancer survivors since cognitive functioning was the second highest domain with reported impairments in our study and the so-called brain fog being one of the typical hypoPT symptoms.[1] In general, the question arises if impairments in QOL of thyroid cancer patients and survivors might not be influenced be the occurrence of hypoPT in this population.[22] On the other hand, one can also discuss whether the cause of hypoPT (e.g., surgery for thyroid cancer) does have an effect on QOL itself. The aetiology hypoPT as an impact on QOL is controversially discussed in the literature. While some studies report worse QOL for surgical hypoPT patients compared to non-surgical,[4,9] this could not be confirmed in our study. In our study, having thyroid cancer as cause for surgery was even associated with lower odds in PF (OR: 0.1; 95% CI [0; 0.5]) of reporting impairments of clinical importance compared to non-surgical patients. One possible

TABLE 3 Variables associated with clinically impaired functioning in patients with hypoparathyroidism

	Physical functioning (PF)	Role functioning (RF)	Emotional functioning (EF)	Social functioning (SF)	Cognitive functioning (CF)
Age (continuous)	1.0 [1.0; 1.0]	1.0 [1.0; 1.1]	1.0 [0.9; 1.0]	1.0 [1.0; 1.0]	1.0 [0.9; 1.0]
Sex					
Male (ref.)	1	1	1	1	1
Female	1.5 [0.5; 4.3]	1.0 [0.4; 3.1]	1.0 [0.4; 2.6]	1.2 [0.4; 3.8]	0.8 [0.3; 2.2]
Education					
Below 10 years (ref.)	1	1	1	1	1
10 years	0.2 [0.1; 0.6]*	0.5 [0.2; 1.4]	0.8 [0.2; 2.6]	0.7 [0.3; 1.8]	1.3 [0.5; 3.6]
Mmore than 10 years	0.3 [0.1; 0.9]*	0.5 [0.2; 1.4]	0.9 [0.3; 2.7]	0.8 [0.3; 2.1]	1.6 [0.6; 4.5]
Living with someone					
No (ref.)	1	1	1	1	1
Yes	0.8 [0.4; 1.8]	0.5 [0.2; 1.1]	0.7 [0.3; 1.7]	0.7 [0.4; 1.5]	1.0 [0.4; 2.1]
Occupation					
Employed/self-employed (ref.)	1	1	1	1	1
Regular retirement	1.4 [0.4; 4.6]	0.6 [0.2; 1.8]	0.5 [0.1; 1.7]	0.7 [0.2; 2.1]	1.1 [0.3; 3.7]
Unable to work	6.3 [2.1; 21.7]*	5.6 [2.2; 15.2]*	0.9 [0.3; 2.9]	2.6 [1.1; 6.6]*	2.6 [0.9; 7.9]
Other	0.8 [0.2; 3.4]	1.1 [0.3; 3.9]	0.3 [0.1; 1.7]	1.9 [0.5; 7.8]	0.6 [0.1; 2.6]
Cause of HPT					
Non-surgical (ref.)	1	1	1	1	1
Surgical—thyroid cancer	0.1 [0; 0.5]*	0.3 [0.1; 1.1]	2.4 [0.6; 9.5]	0.7 [0.2; 2.6]	0.4 [0.1; 1.7]
Surgical—other reason	0.1 [0; 0.4]*	0.5 [0.1; 1.6]	1.1 [0.3; 4.0]	0.8 [0.2; 3.1]	0.3 [0.1; 0.9]*
Time since diagnosis					
6 months–2 years (ref.)	1	1	1	1	1
2–5 years	1.8 [0.5; 6.1]	1.4 [0.5; 4.5]	2.1 [0.5; 9.7]	1.4 [0.5; 4.3]	1.8 [0.5; 7.2]
More than 5 years	0.9 [0.3; 2.6]	0.6 [0.2; 1.7]	1.8 [0.5; 6.0]	1.0 [0.4; 2.6]	1.3 [0.4; 4.0]
Symptom burden					
None to low	0.1 [0; 0.3]*	0.3 [0.1; 1.0]	0.2 [0.1; 0.4]*	0.04 [0; 0.2]*	0.2 [0.1; 0.6]*
Medium (ref.)	1	1	1	1	1
High	4.3 [2.1; 9.2]*	7.5 [3.6; 16.4]*	7.9 [3.0; 24.2]*	4.9 [2.4; 8.8]*	12.0 [5.3; 29.8]*

Note: OR [95% CI]; (ref.), reference category. Multivariate logistic regression.
*$p < .05$.

explanation that surgical patients did not report lower QOL scores might be that surgical patients are monitored more closely in aftercare and therefore physicians are able to address QOL issues in a better way. Also, our non-surgical group is quite small ($n = 21$), which might make it difficult to find differences. Additionally, our multivariate analysis showed that patients with medium or high symptom burden had higher chances of reporting impairments in QOL across all functioning domains of the EORTC QLQ-C30. These results are not surprising and in line with findings from the literature.[23,24] Even though all patients in our study were currently being treated, around 75% of the patients in our study reported a medium or high symptom burden assessed by the HPQ-28. This finding supports the recommendation of the guideline published by the European Society of Endocrinology in 2015 which describes the general goals of management of hypoPT as being that '[…] treatment targeted to maintain serum calcium level (albumin adjusted total calcium or ionised calcium) in the lower part or slightly below the lower limit of the reference range (target range) with patients being free of symptoms or signs of hypocalcaemia.' They also 'recommend that treatment be personalised and focused on the overall well-being and QOL of the

patient when implementing different therapeutic efforts, aiming to achieve the therapeutic goals'.[1] Findings from our study did not show any association between time since diagnosis and QOL. These findings are in line with results from other studies indicating that impairments in QOL do not disappear over time, potentially affecting patients for the rest of their life.[25,26] Being unable to work (compared to employed/self-employed) was associated with higher odds of reporting impairments in PF (OR: 6.3; 95% CI [2.1; 21.7]), RF (OR: 5.6; 95% CI [2.2; 15.2], and SF (OR: 2.6; 95% CI [1.1; 6.6]). In our study, 17.0% of the patients were not able to work anymore. A study by Hadker et al.[24] reported that 14% of the patients reported 'disabled' as their employment status over the course of their diagnosed lifetime, while Siggelkow et al.[23] reported the percentage of hypoPT patients who are working decreased from 58% before diagnosis to 34% at the time of the survey. The negative effect of being unable to work has been observed in other diseases such as breast cancer[27] or coronary heart disease.[28] One possible explanation for this association might be the loss of income due to loss of work. Studies in cancer patients have shown that financial difficulties are associated with impairments in QOL.[29,30] For example in Germany, the average full disability pension which applies if you are not able to work more than 3 h a day, was €850 in 2019.[31] Such income declines, especially in age groups who were not able to accumulate savings or who had investments might cause financial problems and therefore impairments in QOL.[30] Another possible explanation might be that being able to work may be seen as a return to 'normality'.[28] Third, free text analysis in our study has shown that patients felt that employers and public authorities have no information regarding hypoPT or do not acknowledge the severity of the disease. This has been expressed by authorities and physicians not accepting hypoPT in certain cases as a severe disability, resulting in disability pension and disability pass. This empathy gap related to work might be an explanation for the association of being unable to work and QOL. The aforesaid empathy gap is not only restricted to employers and authorities. Free textes of our survey and other studies[24,32] report that hypoPT patients feel that physicians do not understand hypoPT and its burden the way the patients feel it. In Hadker et al.[24] almost 80% of the hypoPT patients 'strongly agreed' that most physicians do not understand hypoPT. Cho et al.[32] showed that surgeons consistently underestimated the impact of postoperative hypoPTH. This empathy gap and missing knowledge regarding the disease, independently where it occurs, might negatively impact hypoPT patients QOL. 28 patients in the study were treated with PTH replacement. PTH replacement did not have any significant effect on QOL (data not shown) which is in contrast to findings from the literature.[10–12] We do not have any information on how long patients in our study are already receiving PTH replacement. So the duration of the PTH replacement therapy might be too short to provide enough positive effects. Despite all these identified factors, the lack of PTH itself might also have a negative impact on hypoPT patients QOL. PTH receptors have been found in several brain regions, the central nervous system, and in muscle cells. The lack of PTH here may also be a reason for impairments in QOL in hypoPT patients.[33,34]

Our study has several limitations. First, all data provided in this study was obtained personally from the patient and we had no possibility to validate the data by comparing it to patient records. Since we used validated questionnaires and patients were informed by their treating physician or via their self-help organisations, we are confident that all patients included have been diagnosed with hypoPT and their QOL is assessed in a coherent way. Second, this study has a cross-sectional design, making it impossible to detect any longitudinal effects. Third, less than 50% of the patients were able to provide laboratory parameters and comorbidities were not assessed, making it impossible to include these in the analysis. Studies have shown that QOL does not correlate directly with laboratory results[11,21,25,26] and the influence of comorbidities is discussed controversially.[9,21] Our study was a voluntarily online survey which might lead to an inclusion of patients with more severe problems since they are severely affected, but since patients were also recruited through their treating physician we could ensure that the sample was drawn from a representative population. Last, one limitation might be the EORTC QLQ-C30 is a questionnaire developed for cancer patients, but it is also used in various non-cancer populations[35] and shows good correlations in the functioning scales of generic QOL questionnaires in non-cancer populations.[36] Using the QLQ-C30 gives the opportunity to perform comparisons with other thyroid cancer patients (e.g., without hypoPT). Having no control group might be considered as a limitation but not being relevant for identifying factors which influence QOL in hypoPT patients. Additionally, QOL might also be influenced by the COVID 19 pandemic during which the study was performed but this was seldom stated in any of the free text fields. Strengths of our study are the large sample size and the heterogeneity of our study population. Patients were not recruited via one centre or institution but throughout a variety of treating physicians and institutions, therefore resulting in a sample which may be more representative. With a broad set of sociodemographic and clinical variables as well with a disease-specific questionnaire, the HPQ-28,[16] for the assessment of symptoms we were able to identify factors which might impact QOL.

5 | CONCLUSION

High shares of patients with hypoPT report problems of clinical importance in QOL. The occurrence of hypoPT related symptoms is strongly associated with QOL, indicating the need to optimise treatment to reduce of symptoms and not solely rely on laboratory parameters. Additionally, the recognition of hypoPT as a disease which might severely influence daily living and especially the work environment as well as the adoption of supportive opportunities for coping with the disease are of major importance for reducing QOL impairments.

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CONFLICT OF INTERESTS

Matthias Büttner reports speaker fees from Lilly and Takeda outside the submitted work. Dieter Krogh has nothing to disclose. Heide

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ETHICAL APPROVAL

According to the design of the study, no Ethics Committee approval was needed (confirmed by the Ethics-Committee of the Landesärztekammer Rhineland-Palatinate).

AUTHOR CONTRIBUTIONS

All authors participated in critically revising the manuscript and all authors approved the final version of the manuscript for submission. All authors contributed to the conception of the study with Matthias Büttner as principal investigator. Matthias Büttner contributed to the analysis and interpretation of the data and draughted the manuscript. Matthias Büttner will use this paper as part of his PhD thesis. Special thanks go to the Netzwerk Hypopara, the German Society of Endocrinology, Hormones and Metabolism and the German Society of Nuclear Medicine for their support.

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

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