Impaired Quality of Life and Muscle Function in Patients with Hypoparathyroidism/Hypothyroidism Compared with only Hypothyroidism and Controls.

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BACKGROUND / AIM / POPULATION

Background: Hypoparathyroidism (HypoPT) is often a complication to total thyroidectomy. Accordingly, patients with postsurgical HypoPT are often also suffering from postsurgical hypothyroidism (HypoT+PT) and are often on substitution therapy with levothyroxine. Hence, the question is whether the previously shown impaired quality of life (QoL) and muscle strength in HypoPT (1,2) are mainly due to disturbances in calcium homeostasis or thyroid function.

Aim: The aim of the study was to assess QoL, muscle function, bone indices, and postural stability in patients with postsurgical HypoT+PT as compared to patients with postsurgical HypoT and healthy controls.

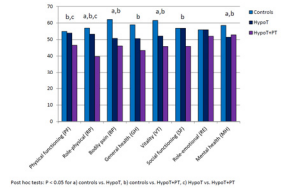
Population: Using a cross-sectional study design, we included 66 subjects.
HypoT+PT:22 patients with chronic postsurgical HypoPT and well-substituted hypothyroidism
HypoT: 22 patients with postsurgical well-substituted hypothyroidism without HypoPT
Controls: 22 healthy controls without abnormalities in their thyroid or parathyroid function.
The three groups were matched on gender, age at time of testing (± 2 years) and the first two groups were also matched on time of thyroid surgery (± 2 years).

(1) Sikjaer T, Rolighed L, Hess A, Fuglsang-Frederiksen A, Mosekilde L, Rejnmark L 6/2014 Effects of PTH(1-84) therapy on muscle function and quality of life in hypoparathyroidism: results from a randomized controlled trial. Osteoporos Int 25,1717-1726.
(2) Sikjaer T, Amstrup AK, Rolighed L, Rejnmark L, Mosekilde L 6/2010 Reduced muscle strength in patients with long-standing hypoparathyroidism compared to healthy controls. Bone 47, Supplement 1:S235-S236.

QUALITY OF LIFE

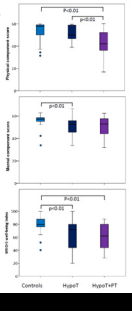
Methods: QoL was measured by the two questionnaires;
Short Form questionnaire 36 version 2 (SF-36v2): *Results shown in fig. 1 and 2*
WHO-Five Well-Being Index survey (WHO-5): *Results shown in fig. 2*

Figure 1
Findings on the eight subscales of quality of life as measured by the Short Form questionnaire 36 version 2 in patients on treatment for postsurgical hypothyroidism (HypoT), postsurgical hypothyroidism and hypoparathyroidism (HypoT+PT) and healthy controls.



Post hoc tests: P < 0.05 for a) controls vs. HypoT, b) controls vs. HypoT+PT, c) HypoT vs. HypoT+PT

Figure 2
Box and whisker plots showing the physical component score (top) and mental component score (middle) as assessed by the Short Form questionnaire 36 version 2 (SF-36v2), as well as findings from the WHO-5 well-being index (bottom) in patients on treatment for postsurgical hypothyroidism (HypoT), postsurgical hypothyroidism and hypoparathyroidism (HypoT+PT) and healthy controls.



DEMOGRAPHICS / BIOCHEMESTRY

Table 1. Characteristics of included participants in the control group and in the groups of patients on treatment for postsurgical hypothyroidism (HypoT) and postsurgical hypothyroidism plus hypoparathyroidism (HypoT+PT). Number with percentages or medias with interquartile (25 - 75 percentile) range.

	Controls (n=22)	HypoT (n=22)	HypoT+PT (n=22)	p-value
Gender, M/F	18/3	18/3	18/3	
Age, years	55 (45 - 63)	52 (41 - 62)	52 (40 - 60)	0.71
Height, cm	168 (165 - 177)	166 (164 - 174)	170 (164 - 174)	0.79
Weight, Kg	69.7 (65.9 - 79.5)	74.4 (65.0 - 90.1)	80.4 (72.7 - 96.2)	0.17
BMI, Kg/m^2	25.2 (22.8 - 28.4)	27.4 (23.2 - 28.5)	27.7 (25.1 - 32.6)	0.12
ALMI, Kg/m^2	7.5 (6.9 - 8.3)	7.7 (7.2 - 8.7)	7.9 (7.1 - 9.1)	0.74
FMI, Kg/m^2	8.2 (5.4 - 10.6)	8.1 (5.7 - 9.8)	9.4 (7.5 - 13.8)	0.09
Total SM, Kg	24.3 (21.7 - 28.5)	24.6 (21.8 – 29.2)	24.7 (21.9 – 31.4)	0.94
Diseases necessitating surgery, N (%)				0.16
Thyroid cancer	NA	2 (9%)	5 (23%)	
Atoxic goiter	NA	7 (32%)	10 (45%)	
Toxic goiter	NA	13 (59%)	7 (32%)	
Time since surgery, years	NA	8 (6 - 14)	5 (4 - 12)	0.18
Medical treatments				
Levothyroxine, N (%)	0	22 (100%)	22 (100%)	NA
Dose, mcg/d	0	133 (100 - 159)	173 (143 - 206)	**0.01**
Alfacalcidol, N (%)	0	0	22 (100%)	NA
Dose, mcg/d	0	0	2.0 (1.4 - 3.0)	NA
Use of calcium supplements, N (%)	2 (9%) [b,c]	8 (36%) [a,c]	22 (100%) [a,b]	**<0.01**
Dose (users only), mg/d	900 (600-900) [c]	800 (433 - 1400)	1600 (950 - 2000) [c]	**0.01**
Use of vitamin D3 supplements, N (%)	5 (23%) [b,c]	13 (59%) [a,c]	22 (100%) [a,b]	**<0.01**
Dose (users only), IU/d	400 (400 - 1500)	800 (400 - 1500)	800 (800 - 1600)	0.17

ALMI: Appendicular Lean Mass Index (Kg/m^2), FMI: Fat Mass Index (Kg/m^2), and Total SM: Total Skeletal Muscle Mass (Kg).
Post hoc tests: p<0.05 compared with a) the control group, b) the HypoT group, and c) the HypoT+PT group.
After adjusting for body weight, daily dose of levothyroxine did no longer differ between HypoT+PT- and HypoT (2.1 [1.6 – 2.7] vs. 1.7 [1.5 – 2.1] µg/Kg/day, p = 0.11).

Table 2. Biochemistry on included participants in the control group and in the groups of patients on treatment for postsurgical hypothyroidism (HypoT) and postsurgical hypothyroidism plus hypoparathyroidism (HypoT+PT). Number with percentages or median with interquartile (25 - 75 percentile) range.

	Controls (n=22)	HypoT (n=22)	HypoT+PT (n=22)	p-value
Creatine kinase	118 (82 - 175)	99 (78 - 150)	89 (73 - 120)	0.29
Thyroid stimulating hormone	2.10 (1.45 - 5.57) [c]	2.59 (1.65 - 3.56) [c]	0.64 (0.19 - 2.08) [a,b]	**<0.01**
Calcium, ionized, mmol/L	1.22 (1.18 - 1.23) [b,c]	1.18 (1.16 - 1.21) [a,c]	1.15 (1.08 - 1.20) [a,b]	**<0.01**
Phosphat, mmol/L	0.95 (0.83 - 1.11) [c]	1.00 (0.89 - 1.09) [c]	1.09 (1.00 - 1.22) [a,b]	**0.02**
Magnesium, mmol/L	0.84 (0.82 - 0.86) [c]	0.86 (0.84 - 0.88)	0.89 (0.86 - 0.92) [a]	**<0.01**
Estimated Glomerular Filtration Rate (eGFR), mL/min	83 (76 - 95)	84 (73 - 97)	74 (63 - 88)	0.06
eGFR < 60 mL/min, N (%)	0	1 (5%)	4 (18%)	0.06
Parathyroid hormone, pmol/L	4.4 (3.2 - 4.9) [c]	3.5 (3.1 - 4.5) [c]	1.1 (0.9 - 2.1) [a,b]	**<0.01**
25-hydroxyvitamin D, nmol/L	66 (55 - 88)	78 (54 - 100)	76 (67 - 94)	0.25

Post hoc tests: p<0.05 compared with a) the control group, b) the HypoT group, and c) the HypoT+PT group.

BONE

Methods: Using DXA , we measured BMD and TBS: *Results shown in table 4*

Table 4. Bone indices of included participants in the control group and in the groups of patients on treatment for postsurgical hypothyroidism (HypoT) and postsurgical hypothyroidism plus hypoparathyroidism (HypoT+PT). Median with interquartile (25 - 75 percentile) range.

	Controls (n=22)	HypoT (n=22)	HypoT+PT (n=22)
Bone Mineral density (BMD), g/cm^2			
Lumbar spine	1.05 (0.96 - 1.11)	1.06 (1.00 - 1.15)	1.14 (1.03 - 1.35) [a,b]
Total hip	0.93 (0.80 - 1.08)	0.92 (0.86 - 1.02)	1.03 (0.88 - 1.09)
Femoral neck	0.73 (0.66 - 0.92)	0.78 (0.71 - 0.85)	0.90 (0.74 - 0.94)
Total forearm	0.54 (0.50 - 0.60)	0.55 (0.50 - 0.61)	0.55 (0.51 - 0.60)
Ultradistal forearm	0.39 (0.35 - 0.43)	0.39 (0.38 - 0.45)	0.43 (0.36 - 0.47)
Whole Body	1.18 (1.04 - 1.30)	1.17 (1.12 - 1.24)	1.19 (1.07 - 1.27)
Trabecular bone score (TBS)			
Lumbar spine (L1-L4)	1.37 (1.23 - 1.49)	1.39 (1.32 - 1.46)	1.37 (1.31 - 1.46)
Biochemical markers of bone turnover			
Bone specific alkaline phosphatase	23.8 (19.2 - 26.7) [c]	22.1 (17.3 - 26.1)	18.4 (16.1 - 21.6) [a]
Procollagen I, N-terminal propeptide	38.6 (30.4 - 56.5) [c]	41.4 (33.6 - 52.6) [c]	25.1 (17.1 - 35.2) [a,b]
Osteocalcin	20.8 (16.9 - 25.1) [c]	19.5 (17.4 - 25.0) [c]	14.2 (10.2 - 19.2) [a,b]
C-terminal telopeptide of type I collagen	0.29 (0.24 - 0.55) [c]	0.31 (0.25 - 0.49) [c]	0.14 (0.07 - 0.23) [a,b]

Post hoc tests: p<0.05 compared with a) the control group, b) the HypoT group, and c) the HypoTPT group.

MUSCLE AND BALANCE

Methods: Muscle strength was measured by a dynamometer as illustrated below and by two functional tests; Repeated Chair Stands and Timed Up and Go: *Results shown in table 3 and fig. 3*
Postural stability was measured by a stadiometer as illustrated below : *Results shown in table 3*

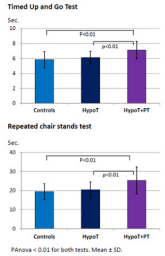
Muscle strength

Maximal voluntary force were performed on the dominant leg and arm using a dynamometer. (Meititur Ltd, Finland). Max Force (MF) and Max Force Production (MFP).

Postural stability

Postural stability was assessed by measuring dynamic stability using a stadiometer. (Meititur Ltd, Finland)

Figure 3
The Timed Up and Go Test and Repeated chair stands test in patients on treatment for postsurgical hypothyroidism (HypoT), postsurgical hypothyroidism and hypo-parathyroidism (HypoT+PT) and healthy controls.



PAnova < 0.01 for both tests. Mean ± SD.

Table 3. Muscle strength and postural stability in included participants in the control group and in the groups of patients on treatment for postsurgical hypothyroidism (HypoT) and postsurgical hypothyroidism plus hypoparathyroidism (HypoT+PT). Median with interquartile (25 - 75 percentile) range.

	Controls (n=22)	HypoT (n=22)	HypoT+PT (n=22)
Muscle strength			
Elbow extension			
Max force, N	140 (124 - 178)	140 (101 - 187)	144 (115 - 184)
Max force production, N/s	431 (278 - 697)	527 (249 - 641)	340 (192 - 522)
Elbow flexion			
Max force, N	221 (182 - 267)	199 (158 - 247)	204 (144 - 253)
Max force production, N/s	824 (484 - 1269) [c]	699 (390 - 1147) [c]	364 (244 - 632) [a,b]
Hand grip			
Max force, N	338 (272 - 434)	346 (294 - 407)	309 (249 - 410)
Max force production, N/s	1360 (1138 - 2704) [c]	1586 (1229 - 1930) [c]	781 (501 - 1051) [a,b]
Knee extension 60°			
Max force, N	414 (339 - 468)	393 (315 - 427)	350 (290 - 432)
Max force production, N/s	1217 (829 - 1818) [c]	1130 (757 - 1681) [c]	742 (582 - 982) [a,b]
Knee flexion 60°			
Max force, N	205 (165 - 242) [c]	210 (145 - 260) [c]	145 (106 - 196) [a,b]
Max force production, N/s	556 (345 - 903) [c]	570 (316 - 663) [c]	263 (149 - 438) [a,b]
Knee extension 90°			
Max force, N	382 (316 - 445) [c]	347 (287 - 470)	314 (231 - 377) [a]
Max force production, N/s	1341 (869 - 1815) [c]	1169 (695 - 1595) [c]	776 (560 - 1039) [a,b]
Knee flexion 90°			
Max force, N	188 (166 - 245) [c]	198 (154 - 241) [c]	151 (114 - 201) [a,b]
Max force production, N/s	656 (486 - 771) [c]	537 (417 - 719) [c]	340 (247 - 491) [a,b]
Postural stability			
Normal stand eyes open, mm^2/s	3.1 (2.1 - 4.7)	3.5 (2.3 - 4.7)	4.0 (2.7 - 6.2)
Normal stand eyes closed, mm^2/s	5.5 (3.1 - 10.0)	5.9 (4.0 - 8.0)	7.9 (5.3 - 10.9)
Semi-tandem stand, mm^2/s	18.0 (16.0 - 24.8)	21.3 (13.0 - 31.0)	25.4 (15.8 - 34.4)
Tandem stand, mm^2/s	31.3 (23.5 - 40.9) [c]	30.8 (22.0 - 46.9)	40.6 (25.7 - 71.0) [c]

Post hoc tests: p<0.05 compared with a) the control group, b) the HypoT group, and c) the HypoTPT group.

DISCUSSION AND CONCLUSION

Discussion: Compared with controls, HypoT was associated with a significantly lower mental summary score (SF36v2) and lower scores in four subdomains. Whereas patients with HypoT+PT had a significantly lower physical summary score compared to both controls and HypoT along with lower scores in seven out of eight subdomains compared to controls.
WHO-5 well-being index was significantly lower in both groups of patients compared with controls, but did not differ between groups of patients.
Compared with controls, muscle strength and maximal force production were significantly reduced in HypoT+PT, but not in HypoT. In HypoT+PT, the time spend on the *timed up and go test* and the *repeated chair stands test* were significantly longer than in the HypoT- and the control-group.
Biochemical markers of bone turnover were decreased in HypoT+PT and bone mineral density was increased at the lumbar spine. However, trabecular bone score (TBS) did not differ between groups.
Adjusting for differences in body weight and plasma levels of TSH, ionized calcium, phosphate, 25OHD and eGFR did not change results to any major degree.

Conclusion: Compared with the general background population, QoL is moderately reduced in patients on treatment for postsurgical hypothyroidism, but patients do not have impairment of their muscle function. Patients on treatment for both postsurgical hypothyroidism and hypoparathyroidism are more severely affected, as they have reduced QoL as well as impaired muscle function. Studies on how to improve well-being and muscle function in HypoT+PT patients are warranted

Keywords: Hypoparathyroidism, Hypothyroidism, Quality of life, Muscle function, BMD, and TBS