

Rehabilitation Outcomes in Patients with Subclinical Hypothyroidism

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ABSTRACT

Aim: To explore the incidence of subclinical hypothyroidism (SCH) and association between SCH and rehabilitation functional outcome.

Method: Two-year observational retrospective single-centered study was conducted in a tertiary general rehabilitation center.

Results: A total of 653 patients received intensive inpatient rehabilitation treatment. Main outcome measures include Functional Independence Measures (FIM), Length of stay (LOS), FIM gain and FIM efficiency, serum levels of thyroid-stimulating hormone (TSH) and Free Thyroxine (FT4). The incidence of patients discovered with SCH was 12.4% of the sampled population. All patients with SCH displayed an overall FIM gain of 26.9 (± 2.19), compared to patients with normal TSH who had an average FIM gain of 23.8 (± 1.85). The overall FIM efficiency was similar in both groups.

Conclusion: The incidence of SCH is high in tertiary general rehabilitation setting. All patients with SCH have obtained functional gains following rehabilitation treatment. Those with hyperthyroidism have lower FIM scores but the efficiency and length of stay of rehabilitation being similar in all groups.

Keywords

Subclinical hypothyroidism, Thyroid dysfunction, Rehabilitation outcomes, Functional independent measure (FIM).

Introduction

Thyroid dysfunction is a common medical condition characterized by abnormal thyroid stimulation hormone (TSH) level. Previous study showed that 4.6% of the population had hypothyroidism whilst 1.3% population had hyperthyroidism [1]. Hypothyroidism is generally described as an underactive thyroid generating an insufficient number of thyroid hormones leading to a wide range of clinical manifestations. Hypothyroidism is biochemically represented with an elevated serum TSH and decreased thyroid hormones. Subclinical hypothyroidism (SCH), also known as mild thyroid failure, affects 4.3% of the population [1] and is defined

by a mildly elevated serum TSH level but a serum free thyroxine level within the normal reference range [2]. It could also lead to the clinical manifestations similar to hypothyroidism [2].

At the present there are limited studies exploring the relationship between rehabilitation outcomes and thyroid function. A study by Boltzmann et al. suggested that in patients of a mixed brain injury population going through neurosurgical early rehabilitation, all factors, such as triiodothyronine (T3) level, age, duration between injury and admission, and severity of impairment at initial assessment, are independent predictive value for rehabilitation functional outcomes [3]. No associations between thyroid hormones and functional status were found, however, it was noted that patients with higher T3 levels on admission demonstrated favorable functional status on discharge, and there were no clear associations noted with T4 and TSH levels [3]. Although a lower T3

level was associated with poor prognosis on discharge in patients with ischemic stroke, the association was deemed insignificant after adjustments being made in context of other known predictors of stroke outcome [4].

However, Akhoundi et al. examined 73 ischemic stroke patients with SCH and found out that a significant protective association of SCH with better outcomes and lower mortality. This association is possibly due to reduced adrenergic tone and hypometabolic state in the setting of ischemic stroke [5]. Subsequent cross-sectional study of 138 stroke patients by Oshinaike et al. showed similar results that SCH appears to confer a neuroprotective effect in acute ischemic stroke [6]. Another study of 2290 community dwelling older adults with SCH did not demonstrate increased risk of mobility problems and those with mild elevations in TSH showed a slight functional advantage [7].

SCH is a very common finding in the cohort of rehabilitation patients who are usually frail and older following acute illness or injury. However, there is no reported study on how this population progresses in the subacute general rehabilitation setting. The impact of SCH on the functional recovery including cognitive recovery is unknown. It was hypothesized that patients with SCH might have a lower level of rehabilitation improvements compared to their counterparts without thyroid dysfunction.

Methods

This single-centered observational retrospective study was approved by local ethic committee at The Prince Charles Hospital (TPCH) in 2016 (HREC/10/283A215). Participants for this study are those patients receiving subacute inpatient rehabilitation care at TPCH Rehabilitation Unit from January 2015 to December 2016. The inclusion criteria are those who (1) participated in rehabilitation for more than 7 days of duration and (2) had a thyroid function test at admission. Patients were excluded if they (1) had incomplete FIM scores, (2) had no thyroid function test on admission, (3) were transferred back to an acute ward and not returned, or (4) deceased.

Quantitative data collected was based on thyroid function tests

Table 1: Baseline Characteristics of the Participants.

Characteristic	Total (%)	N-TSH (0.3-4.5)	SCH (4.6~19)	H-TSH (≥ 20)	Low-TSH (<0.03)
n	653	553	81	5	14
Female	347 (53.1)	298 (53.9)	38 (46.9)	3 (60)	8 (57.1)
Male	306 (46.8)	255 (46.1)	43 (53)	2 (40)	6 (42.8)
Age (SE)	73.46 (0.50)	73.2 (0.56)	74.2 (1.06)	71.4 (06.45)	80 (2.35)
Major medical conditions n (%)					
IHD	159 (24)	127 (23)	22 (27)	3 (80)	7 (50)
COPD	49 (7.5)	38 (6.8)	7 (8.5)	1 (20)	3 (21.4)
Stoke	41 (6.2)	35 (6.3)	4 (4.9)	1 (20)	1 (7.5)
OA/Osteoporosis	46 (7)	39 (7)	5 (6.1)	1 (20)	1 (7.1)
Residence status n (%)					
Private dwelling	635 (97.2)	539 (97.4)	79 (97.5)	4 (80)	13 (92.9)
Residential facility	18 (2.7)	14 (2.5)	2 (2.4)	1 (20)	1 (7.1)

Data is presented as a mean (percentage). n, total numbers of participants; SE, standard error; N-TSH: normal TSH group, SCH: subclinical hypothyroidism group, H-TSH: high TSH group, Low-TSH: low TSH group.

on admission, chart audits, and recorded Functional Independence Measures (FIM). The serum levels that were measured are TSH and Free Thyroxine (FT4). Some patients have additional tests for Free Triiodothyronine (FT3) and thyroid antibodies in situations of hyperthyroidism or hypothyroidism. The level of TSH was recorded in mm/L. The normal value was 0.3~4.5mm/L. TSH equals or above 20mm/L was considered as profound hypothyroidism and SCH is defined as TSH above normal range but below 20mm/L.

Data was collected pertaining to patient demographics, functional profiles including FIM scores on admission and discharge, Length of Stay (LOS), and FIM efficiency. FIM was applied in this study as the main outcome measure involving motor, cognition, and total FIM scores. FIM gain is calculated by determining the score differences at admission and discharge. FIM efficiency is calculated by the FIM gain divided by the LOS. Besides the abovementioned quantitative figures, the patients' discharge destination, level of care support and services on admission and upon discharge were also collected.

Discrete variables were expressed as counts (percentage) and continuous variables as mean values +/- standard errors (SE). Data were analyzed by descriptive statistics involving an unpaired two sample *t*-test and logistic linear regression. P values of less than 0.05 were considered to indicate statistical significance.

Results

Demography of study population

A total of 707 patients were admitted to TPCH Rehabilitation Unit from January 2015 to December 2016. Of these, 54 patients were excluded from the study as a result of either a lack of thyroid functional test on admission or incomplete FIM data. Overall, 653 patients (306 males and 347 females) were included in this study with a mean age of 73.46 (± 0.5) and range 16 to 98 years old. Based on the thyroid functional tests at admission, the participants were sub-grouped as normal TSH group, SCH group, high TSH group and low TSH group. The baseline demographic data is presented in Table 1. There was no statistic significant difference in age between these subgroups.

Thyroid functional profiles

Of the total 653 patients, 553 (85%) patients had a TSH within normal limits (0.3~4.5 mm/L), 100 patients were found to have an abnormal TSH, of which 81 presented with SCH (TSH 4.6~19.9 mm/L), 5 with profound hypothyroidism (TSH \geq 20mm/L) and 14 with hyperthyroidism (TSH $<$ 0.3 mm/L). The incidence of SCH in this study cohort was 12.4%.

Rehabilitation outcomes and efficiency

Rehabilitation outcomes at admission and discharge are presented in Table 2 and Figures 1 and 2. Figure 1 summarizes the FIM scores at admission and discharge in each subgroup.

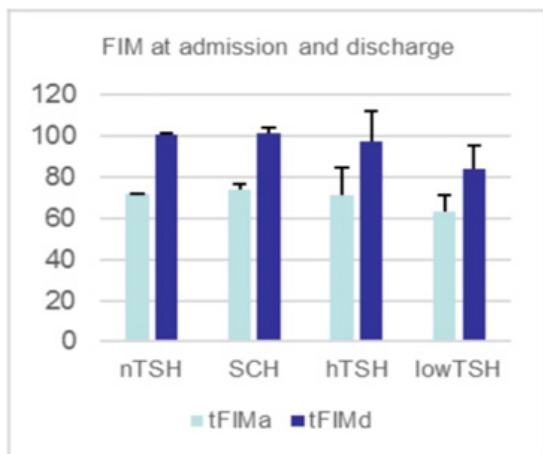


Figure 1: Total FIM scores at admission and discharge. tFIMa: total FIM at admission; tFIMd: total FIM at discharge; nTSH: normal TSH; SCH: subclinical hypothyroidism; hTSH: TSH \geq 20 mm/L, low TSH: TSH $<$ 0.3 mm/L.

All patients with SCH had improvement in function with an FIM gain $26.9 (\pm 2.19)$ compared to $23.8 (\pm 1.85)$ of those patients with normal TSH. Functional profiles (FIM motor, FIM cognition and FIM total) on admission of SCH patients were non-significantly higher than normal TSH patients. Functional profiles on discharge of SCH patients were similar to normal TSH patients. There were no significant differences in FIM efficiencies across two groups. Although both hypothyroidism patients and hyperthyroidism patients experienced a relatively low mean FIM scores at admission and at discharge (Figure 1), there was no significant differences in FIM efficiencies compared to normal TSH and SCH groups (Table 2).

Table 2: Rehabilitation outcomes in subgroups.

Mean (SE)	Normal TSH (0.3~4.5 mm/L)	SCH (TSH 4.6~19.9 mm/L)	Hypothyroidism (TSH \geq 20mm/L)	Hyperthyroidism (TSH $<$ 0.3mm/L)
n	553	81	5	14
Mean FIM gain	23.8 (1.85)	26.9 (2.19)	25.8 (10.43)	27 (5.46)
P value		0.33	0.85	0.73
Mean FIM efficiency	1.16 (0.11)	1.17 (0.18)	1.02 (0.27)	1.7 (0.51)
P value		0.97	0.90	0.52

Data is presented as a mean (standard error). SE, standard error; n, total numbers of participants; SCH: subclinical hypothyroidism group.

The Figure 2 demonstrates the LOS in each subgroup. The mean LOS for patients with SCH was $20.71 (\pm 1.21)$ compared to $21.1 (\pm 0.45)$ of patients with normal TSH. The mean LOS for patients with hypothyroidism was at $27.6 (\pm 5.5)$ compared to patients with hyperthyroidism at $21.07 (\pm 6.3)$. Although the LOS in hypothyroidism was relatively longer than the euthyroid group ($P = 0.6$), there was no statistically significant difference between these two subgroups and across all groups.

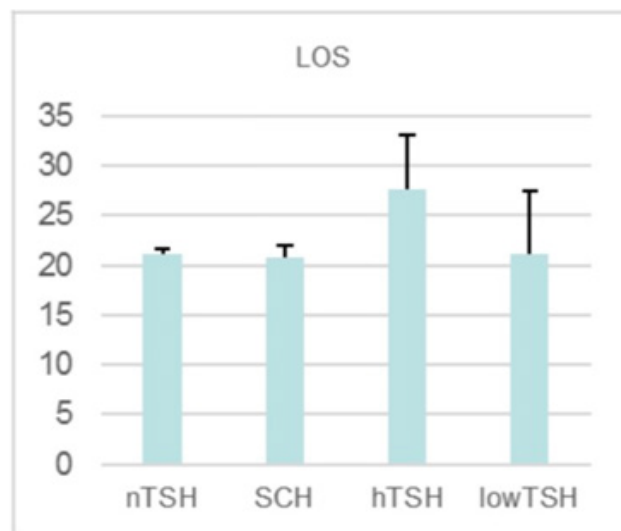


Figure 2: Length of stay of different subgroups. nTSH: normal TSH; SCH: subclinical hypothyroidism; hTSH: TSH \geq 20 mm/L, low TSH: TSH $<$ 0.3 mm/L.

Total 8 out of 81 (9.8%) SCH patients, 2 out of 14 (14.2%) hyperthyroidism patients, and 2 out of 5 (40%) profound hypothyroidism patients were discharged to a nursing home compared to 17 out of 553 (3.1%) normal TSH patients. For the patients returned home, the level of required community support upon discharge was similar across all subgroups.

Discussion

As a mild thyroid dysfunction biochemically, SCH is a common endocrine and metabolic condition. Our study showed all patients with thyroid dysfunction achieved rehabilitation gains comparable to those having normal thyroid function. Therefore, thyroid dysfunction seems not to be a barrier to our rehabilitation expectations.

The association between SCH and adverse clinical outcomes remain unclear and conflicting [8]. The underline biophysiological mechanism or secondary effect of SCH on the impact of functional gains is also poorly understood due to current significant knowledge gap in this area. Several prospective population-based cohort studies showed controversial results in term of correlation between SCH and the incidence of cardiovascular disease and mortality, lipid profiles, mood and cognitive dysfunction [9-14]. The clinical significance of these systemic effects after long term SCH is still unclear. Some findings suggest that these systemic sequelae of SCH are associated with increased disease severity, disease duration, age and individual sensitivity to thyroid hormone deficiency [8]. Recent meta-analysis indicated that SCH is likely associated with an increased risk of coronary heart disease mortality [15]. Large randomized controlled studies are necessary to assess the importance of mood, cognitive and physical function in individuals with mildly elevated TSH.

In our study, all patient with SCH were asymptomatic and, therefore, not requiring Levothyroxine treatment. Results of this study was consistent with a previous report that replacement therapy using levothyroxine to treat SCH is controversial and levothyroxine provided no apparent benefits in older persons with SCH [16].

It was noted that the incidence of patients discovered with SCH is 12.4% of the sampled population. This incidence of SCH is much higher than the general population reported by literature of 4.3% [1]. This is likely due to the case-mix of population in the local hospital setting. TPCH is a tertiary cardiac thoracic hospital with significant complex cardiothoracic patients often requiring longer Intensive Care Unit (ICU) stay with inotropic or extracorporeal membrane oxygenation (ECMO) support. The frail geri-orthopaedic patients with dense cardiac comorbidities might also attribute to the higher incidence of SCH. Further, cardiac polypharmacy (e.g. β -blocker and amiodarone etc.) and acute illness might play a role to the higher incidence. Previous survey studies reported that the prevalence of SCH is higher in older populations [8]. Therefore, the elderly cohort of patients in our study (mean age 73.46) might also lead to this higher incidence.

The SCH patients displayed an overall FIM gain and FIM efficiency comparable to patients with normal TSH level. Although it should be noted that patients with hyperthyroidism had the lowest mean value of admission FIM and discharge FIM, there was no statistically significant difference in rehabilitation efficiency and functional gain compared to the other groups. This retrospective study has provided some information on how people with SCH functioning in the subacute general rehabilitation setting without medical replacement therapy.

Interestingly, it was suggested in the study by Boltzmann (2017) that neurosurgical patients with higher total T3 levels demonstrated more improvements in functional outcome than patients with lower total T3 levels on discharge, and that no association between functional outcome and T4 level or TSH level were noted [3].

However, it was also noted in a meta-analysis evaluating the prognostic value of thyroid hormones in acute ischemic stroke that not only does a low T3 level demonstrate poor prognosis in acute ischemic strokes, it also suggested that there is a reverse association with prognosis of acute ischemic strokes [17]. Unfortunately, it would be difficult to clarify this relationship in our study as T3 level were rarely measured within this studied population.

In this study, there was no significant difference in length of stay across all groups. However, patients with hypothyroidism had the highest mean length of stay of 27.6 days. Further study on a larger cohort of hypothyroidism patients will be very interesting to explore the outcomes of rehabilitation in the future.

Limitations

We acknowledge that there are limitations of this retrospective observational single-centered study, which can be influenced by varying departmental rehabilitation models of care, staffing, and resources. In addition, this study was conducted at a Tertiary hospital with pronounced subspecialties including organ transplant surgery, such as cardiac and pulmonary transplants, which can impact on the case mix accepted into rehabilitation, therefore this can cause discrepancies if this study were to be conducted in another facility.

As this was an observational retrospective study, it is not possible for us to clearly assess the variant rehabilitation exposure for our participants. In this study, the type, frequency and intensity of rehabilitation therapies provided to each individual patient was not specified nor made controlled or consistent. Additionally, those patients whom were on thyroxin supplementation therapies or anti-thyroid medications were not distinguished from other populations. This generates inconsistencies with the selected population which may produce bias in the results. Furthermore, with a sample size above 600 patients in a tertiary hospital, many of them were presented with different medical or surgical conditions. Consequently, bias is then formed by not distinguishing these patients with different medical comorbidities and presenting conditions.

We have noticed limitations of this study that can produce bias and difficulties in interpretations of obtained results. However, this study fills some gap in the literature and prompts us towards the next step for a better and more carefully designed study to further investigate and evaluate the relationship between subclinical hypothyroidism and rehabilitation outcomes.

Conclusion

In conclusion, all patients with subclinical hypothyroidism obtained functional gains following rehabilitation treatment. It was noted that those with hypo- and hyper-thyroidism had lower mean FIM scores with the efficiency of rehabilitation being similar in all groups. We believed that this study has shed light on the functional prognosis of this subclinical hypothyroidism population, who will most likely benefit from ongoing monitoring of their thyroid function to avoid functional disadvantages in the future. It would

be vital to conduct further research and investigation to explore the relationship between thyroid function and rehabilitation outcome in specific case-mix controlled population.

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