

Peer Review File

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Reviewer A Comments

In this original study, the authors aimed to investigate the clinical yield of thyroid function testing in in-patients admitted for delirium. The manuscript is well-written and well-structured. However, the sample size is too small and the results are purely descriptive, resulting in a limited clinical impact.

Thank you for the comments. In response, we have made the following changes:

Comment 1: “The manuscript is well-written and well-structured. However, the sample size is too small and the results are purely descriptive, resulting in a limited clinical impact.”

Reply 1: We have reinforced the limitations associated with the small sample size in our discussion section. We have added additional statistical analysis, including an unpaired t-test comparing number of symptoms reported between patients with TSH tested and those who did not have TSH tested. There was no significant difference between these groups. Additionally, we performed a multivariate regression to analyze which factors were associated with ordering of TSH during admission. We found no association between age, sex, hospital length of stay, known hypothyroidism, pre-existing prescription for levothyroxine, or number of positive symptoms with ordering of TSH. We also performed a multivariate regression to analyze which factors were associated with our primary outcome, reflecting a change in patient management. We found that known hypothyroidism and a pre-existing prescription for levothyroxine were significantly associated with our primary outcome, but age, sex, TSH value, and number of positive symptoms were not associated with the primary outcome.

Changes in the text: Page 8, lines 154-162; Page 9, lines 181-188; Page 10, lines 208-212; Page 13, lines 272-273; Page 18, lines 407-408; Page 19, lines 443-445; Page 21, lines 490-492.

Reviewer B Comments

1. It is better to separate the outcome to 1) in patients investigations 2) in patient treatment. than you can show that almost all of the patients had other indication to TSH testing because of prior thyroid disease, drug treatment or symptoms.
2. In addition, you can add multivariate analysis to show that the factors associate with further analysis. it is interesting the high percentage of hypothyroidism treatment.
3. It is important to say that TSH testing is cheap and maybe in lager sample it will be found

important.

Thank you for the comments. In response, we have made the following changes:

Comment 1: “It is better to separate the outcome to 1) in patients investigations 2) in patient treatment. than you can show that almost all of the patients had other indication to TSH testing because of prior thyroid disease, drug treatment or symptoms.”

Reply 1: We have performed a multivariate regression to analyze for factors which may be associated with ordering of TSH during admission. Independent variables analyzed include age, sex, hospital length of stay, known hypothyroidism, pre-existing prescription for levothyroxine, and number of positive symptoms of thyroid dysfunction. This additional analysis did not find any association between these factors and ordering of TSH during admission.

Changes in the text: Page 8, lines 156-159; Page 9, lines 185-188; Page 19, lines 443-445.

Comment 2: “in addition, you can add multivariate analysis to show that the factors associate with further analysis. it is interesting the high percentage of hypothyroidism treatment.”

Reply 2: We have performed a multivariate regression to analyze for factors associated with our primary outcome. This demonstrated a significant association between known hypothyroidism and pre-existing prescription for levothyroxine with our primary outcome. Age, sex, TSH value, and number of positive symptoms were not associated with our primary outcome.

Changes in the text: Page 8, lines 159-162; Page 10, lines 208-212; Page 21, lines 490-492.

Comment 3: “it is important to say that TSH testing is cheap and maybe in lager sample it will be found important.”

Reply 3: We have reinforced in the limitations the small sample size and inexpensive nature of TSH testing. We have noted that studies with larger sample sizes may find that TSH testing in delirium is clinically important and cost-effective.

Changes in the text: Page 13, lines 272-273 and lines 279-281.

Reviewer C Comments

This study is a well-written paper providing insight into the limited value obtained from ordering thyroid function tests, specifically TSH, in older adults with delirium, especially with low pre-test probability. However, the following concerns will need to be addressed:

1. Grammatical/typographical Errors: The authors repeated free T4 twice on line 135.
2. Statistical analysis: The authors' use of descriptive statistics only to quantify how TSH level alters patient care may be inadequate. Can we consider ANOVA or eta squared statistic to measure the association between a. thyroid disease symptom index and whether or not the

TSH value was ordered? The thyroid symptom index will be a composite score of the number of thyroid symptoms complained by each patient (continuous variable) and whether or not the patient had TSH done (categorical variable).

Thank you for the comments. We have made the following adjustments in response to your concerns:

Comment 1: “Grammatical/typographical Errors: The authors repeated free T4 twice on line 135”

Reply 1: We have removed the repetition of free T4 – this should have read ‘free T3’ instead. We apologize for this error.

Changes in the text: Free T4 changed to Free T3 on page 7, line 136.

Comment 2: “Statistical analysis: The authors' use of descriptive statistics only to quantify how TSH level alters patient care may be inadequate. Can we consider ANOVA or eta squared statistic to measure the association between a. thyroid disease symptom index and whether or not the TSH value was ordered? The thyroid symptom index will be a composite score of the number of thyroid symptoms complained by each patient (continuous variable) and whether or not the patient had TSH done (categorical variable)”

Reply 2: We have completed further statistical analysis. We completed an unpaired t-test to compare the mean number of symptoms reported by patients who had TSH tested during admission and who did not have TSH tested. There was no significant difference between groups. This helps to further support that TSH testing in delirium may not be guided by symptomatology. Furthermore, we performed a multivariate regression to determine which factors were associated with our primary outcome (change in patient management). We found no significant association between age, sex, TSH value, or number of symptoms reported. However, we did find that known hypothyroidism and pre-existing prescription for levothyroxine were associated with our primary outcome.

Changes in the text: Page 8, lines 154-162; Page 9, lines 181-188; Page 10, lines 208-212. Page 18, lines 407-408; Page 21, lines 490-492.