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The impact of age in the management of hypothyroidism: Results of a nationwide survey

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Abstract

Objective—Evidence exists that TSH increases with age and lowering the TSH goal in older patients on thyroid hormone may cause overtreatment. Risks of overtreatment include cardiac and skeletal events. We assessed practice patterns regarding TSH goals and explored factors influencing physicians' decision making when managing hypothyroidism.

Methods—Members of the American College of Physicians, American Academy of Family Practice and Endocrine Society were surveyed to determine goal TSH when treating hypothyroidism.

Results—Fifty-three percent of physicians reported factoring patient age into their decision making when managing hypothyroidism. Patient age was prioritized third (53%) following patient

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symptoms (69.2%) and cardiac arrhythmias (65.7%). In multivariable analysis, endocrinologists (p 0.002), internists (p 0.049), physicians in academic settings (p 0.003) and high-volume physicians (p 0.021) were more likely to consider patient age when determining goal TSH. When presented with scenarios differing in patient gender and age, 90% of physicians targeted a TSH 3.0 mIU/L in 30-year-old patients. Fifty-three percent of respondents targeted a TSH 3.0 mIU/L in octogenarians, but 90% targeted a TSH>1.5 mIU/L in this group. Regardless of gender, physicians reported TSH goal ranges (0.1–0.5, 0.6–1.5, 1.6–3.0, 3.1–5.0 mIU/L) increased in a direct relationship to patient age (p <0.001).

Conclusion—Just over half of physicians consider patient age when determining TSH goal. When presented with scenarios differing in patient age and gender, physicians targeted a higher TSH goal in octogenarians. This may indicate an attempt to avoid overtreatment in this group. Consensus is needed among physicians regarding the role of patient age in hypothyroidism management.

INTRODUCTION

Hypothyroidism is the most common thyroid disorder in adults in the United States (1). Its prevalence increases with age, with 1.7% of adults over the age of 65 diagnosed with overt hypothyroidism. Prevalence of subclinical hypothyroidism in adults over the age of 65 has been quoted as high as 13.7%, when assuming 4.5 mIU/L as the upper limit of normal for thyroid stimulating hormone (TSH) (1). There is compelling population data to support the theory that the “normal” TSH range, which is the target for treatment, may be higher in older adults and may be associated with longevity and better survival (1–6). Lowering the TSH in these individuals may not be warranted and can pose risk for overtreatment (7–9). Overtreatment with thyroid hormone can lead to detrimental consequences, especially in the elderly. Risks include cardiac arrhythmias, increased cardiovascular mortality, osteoporosis and fractures (10–18).

However, despite convincing evidence that serum TSH increases with age and that overtreatment has implications for patient health, current guidelines do not advocate for specific TSH goals for different age groups with hypothyroidism. Specific TSH ranges are currently only recommended for women of childbearing age interested in conception and for pregnant women (19). Controversy exists regarding the need for age-specific TSH targets in the treatment of adults with hypothyroidism (20–24).

Factors influencing providers’ decision making about goal TSH remain unknown. A recent survey focusing on TSH goals in hypothyroidism was conducted among endocrinologists (25). However, primary care providers are frequently the prescribers of thyroid hormone preparations, and although one other survey included primary care physicians, it was conducted over a decade ago (26). Therefore, we conducted a national physician survey to assess current clinical practice patterns in terms of TSH goals among a diverse group of providers, and to elicit the factors influencing physicians’ decision making in the management of adults with hypothyroidism.

MATERIALS AND METHODS

Data source and study population

Active members of the American College of Physicians, the American Academy of Family Practice and the Endocrine Society were randomly selected and surveyed.

The modified Dillman survey method was used (27). This protocol consists of (i) an initial mailing of an introductory letter, the survey instrument, a postage-paid return envelope, and a small monetary gift, (ii) a postcard reminder 3 weeks later, and (iii) a second survey with a postage-paid return envelope to all non-respondents following 3 more weeks. To enhance survey response rates, follow-up telephone encounters were conducted with non-respondents. Data from the survey were de-identified and entered into a REDCap database (28). The double entry method was used to ensure < 1% error. The study was approved by the University of Michigan Institutional Review Board.

Survey design and measures

The survey instrument was designed and reviewed by a multidisciplinary group of providers, including health services researchers involved in survey methodology, endocrinologists and primary care providers. Prior to administration to the targeted physicians, the survey instrument was piloted in a diverse cohort of providers at the University of Michigan from the fields of endocrinology and primary care. After piloting, minor revisions were made prior to survey administration.

There were two key survey items that addressed provider decision making regarding goal TSH in the management of hypothyroidism (Figure 1). One survey item explored the influence of patient age, patient symptoms (such as racing heart, tremors), patient preference, fatigue, cardiac arrhythmias, heart disease, osteoporosis, fractures, multiple falls and weight, on decision making regarding goal TSH. Another survey item asked about what TSH goal range providers targeted in different clinical scenarios. The scenarios differed in patient gender and age (30, 50, 65 or 85 years old). For the clinical scenarios, TSH goal ranges were set as 0.1–0.5 mIU/L, 0.6–1.5 mIU/L, 1.6–3.0 mIU/L and 3.1–5.0 mIU/L.

Statistical analysis

We initially generated descriptive statistics. To determine the role of patient age influencing decision making regarding goal TSH range in hypothyroid patients (dependent variable), univariate analyses were performed using chi square tests. Subsequently, we performed a multivariable logistic regression analysis controlling for physician gender, specialty, practice setting, years of practice and provider case volume to determine correlates of importance placed on patient's age in deciding TSH goal for treatment of hypothyroidism.

The Cochran-Mantel-Haenszel chi-square statistical test was employed for the provider response distribution results in the clinical scenarios, in order to test the null hypothesis of independence for treatment patterns. Multivariable logistic regression analyses controlling for physician gender, specialty, practice setting, years of practice and provider case volume,

were performed to determine factors associated with specific TSH goals in males and females aged 65 and aged 85 (specifically TSH<1.5 mIU/L or TSH>3.0 mIU/L).

All statistical tests were performed using IBM SPSS Statistics 22. A p value <0.05 was considered as statistically significant.

RESULTS

Of the 1000 physicians surveyed, 118 were ineligible for the survey because they were ill, deceased, retired, having an incorrect mailing address or not treating patients with thyroid disease. Of the 882 response-eligible physicians, 389 physicians who managed thyroid hormone replacement over the past five years completed the survey (44%).

Table 1 shows the respondent characteristics. The majority of the respondents were white (77%) and male (64.5%), and about half had >20 years in practice (48.6%). Endocrinologists were the largest physician group represented (36.2%), followed by family practitioners (35.2%), internists (26.4%) and other (2.2%). The category “other” included geriatricians, hospitalists, emergency medicine physicians, an occupational medicine physician and an endocrine surgeon. Most physicians were in private practice (49%), 19.9% worked at an academic setting, 13.5% at a community-based academic affiliate and 17.6% practiced in other settings. Other practice settings included student health centers, military-based care centers, urgent care establishments, community free clinics, government establishments, a state prison, county primary health centers, Veterans Affairs hospitals, a clinical research center and a pharmaceutical research company.

Figure 2 shows that 53% of physicians reported patient age as an important factor influencing decision making regarding goal TSH in treating hypothyroid patients. Patient age was third only to patient symptoms (such as racing heartbeat, tremors) (69.2%) and cardiac arrhythmias (65.7%). Skeletal health issues, such as osteoporosis (43.4%), fractures (27.2%) and multiple falls (7.7%) were less commonly considered in decision making. Pregnancy was cited as important by 40.6% and interest in conception by only 27.2%. Approximately 12% of physicians reported that none of the above factors were important in their decision making regarding goal TSH when treating adults with hypothyroidism.

In univariate analyses using patient age as a dependent variable, physician gender (p 0.017), physician specialty (p<0.001), practice setting (p 0.010) and patient volume (p<0.001) were all significant factors associated with importance placed on patient age when determining goal TSH in hypothyroidism (Table 2). After controlling for physician gender, years in practice and practice setting, endocrinologists (p 0.002), internal medicine physicians (p 0.049), physicians practicing in an academic setting (p 0.003) and high patient volume physicians (p 0.021) were significantly more likely to place importance on patient age when determining goal TSH in hypothyroidism in multivariable analyses. Notably, a total of 75% of endocrinologists as compared to only 43.8% of internists and 35.6% of family physicians consider age when determining TSH goal in the management of hypothyroid patients (Table 2).

Table 3 shows the distribution of the respondents' answers to clinical scenarios differing in patient age and gender in terms of goal TSH range in hypothyroid patients. It is shown that 90% of providers aim for a TSH ≤ 3.0 mIU/L in a 30 year-old patient regardless of gender. This proportion decreases with age such that a slight majority of respondents (53%) continue to target a TSH ≤ 3 mIU/L even in octogenarians. Additionally, 80% of respondents who selected a 0.6–1.5 mIU/L TSH goal for a 30-year-old also selected a higher TSH goal for the 85-year-old (>1.5 mIU/L). Overall, 90% of providers do target a TSH >1.5 mIU/L in the octogenarian age group. Multivariable logistic regression analyses failed to yield significant correlates associated with targeting specific TSH goals in males and females aged 65 and aged 85 (specifically TSH <1.5 mIU/L or TSH >3.0 mIU/L).

Patterns were similar when comparing the TSH goals in female and male patients differing by age. Age and TSH goal were conditionally dependent for both genders (females: M^2 47.519, df 1.0, $p < 0.001$; males: M^2 34.996, df 1.0, $p < 0.001$). The reported TSH goals in female patients aged 30, 65, and 85 years old are shown as an example in Figure 3.

DISCUSSION

Our study found that only 53% of providers report patient age as an important factor contributing to their decision making when determining TSH goal in hypothyroid patients. Even though endocrinologists and internists were both significantly more likely to incorporate patient age into their decision making as compared with family medicine practitioners, the proportion of internists who do this (43.8%) was far less than the endocrinologists (75%). However, when presented with more granular clinical scenarios that incorporated patient gender and age, physicians' reported TSH goals shifted with age but not gender. Even though in our survey we found that a slight majority (53%) aim for a TSH ≤ 3.0 mIU/L in octogenarians, those highest at risk for adverse outcomes with excess thyroid hormone replacement, approximately 90% of respondents aim for a TSH >1.5 mIU/L in the 85-year-old category, which may suggest an attempt to avoid overtreatment in this age group. A similar pattern is not seen in the 30-year-old group, the cohort at lowest risk for adverse effects from thyroid hormone overtreatment. Close to 15 years ago, a survey of primary care physicians and thyroid specialists regarding the management of hypothyroidism showed that only 30% of primary care physicians and 19% of thyroidologists aimed for a higher TSH range (2.0–5.0 mIU/L) for a 73 year-old patient with hypothyroidism (26). Another recent study that exclusively surveyed clinical endocrinologists showed that 29.5% would target a TSH range of 3.0–3.9 mIU/L and 22.5% would target a TSH range of 4.0–4.9 mIU/L in an octogenarian (25). Similarly, our study shows that there is currently no consensus among physicians regarding TSH goals depending on patient age.

Convincing evidence exists that TSH in the population increases with age (1–6) and lowering this with thyroid hormone therapy may predispose to overtreatment (7–9,18). Previous population studies have shown that increasing patient age is associated with shifts in the TSH distribution curve to higher concentrations presumably due to changes in TSH bioactivity, changes in negative feedback relationships between TSH and free T₄, or influences from medications (2,20–24). Additionally, several other studies have

demonstrated an association between longevity and higher TSH levels in several different patient populations (3,4), which raises the possibility that a mildly elevated TSH may be beneficial in certain elderly patients.

Current guidelines recognize that the normal TSH reference range changes with age (19) but do not currently recommend targeting specific TSH goals based on patient age. A question is raised as to whether age-specific TSH ranges should be implemented to avoid overtreatment in vulnerable populations, such as the elderly. A study performed in the general population demonstrated that only 60% of adults taking thyroid hormone have TSH levels in the euthyroid range with up to 20% being overtreated (8). In a cohort of men and women aged 65 years and older enrolled in the Cardiovascular Health Study, 41% of thyroid hormone users were found to be overtreated (9). The Framingham Heart Study showed that an alarming 48% of older adults aged 60 years and over on thyroid hormone replacement have low TSH levels, also indicating overtreatment (10). The deleterious effects of excess thyroid hormone on the cardiac system, including cardiac arrhythmias and increased cardiovascular mortality, and skeletal systems, including osteoporosis, have been widely described (10–18). In addition, higher TSH and lower free T4 concentrations within the euthyroid range in older patients (age ≥ 65 years) not taking thyroid hormone medications have been recently shown to be associated with lower risk of multiple adverse events in older adults, including mortality (29).

In this current study, in addition to evaluating the role of age, we investigated other reasons for modifying TSH goal. Interestingly, patient symptoms (such as tremors, racing heartbeat) were considered the most important factor influencing goal TSH for patients with hypothyroidism. This may be appropriate as symptoms such as tremors and racing heartbeat may indicate overtreatment with thyroid hormone replacement and dose adjustments may be necessary. Interestingly, fatigue was quoted as an important factor influencing decision-making by almost half of the treating physicians. This is discordant with current guidelines, which do not recommend adjusting the TSH goal in hypothyroid patients according to symptoms such as fatigue (19). Finally, despite known deleterious effects of a low TSH on both the cardiac and skeletal systems (10–18), physicians were more likely to consider cardiac arrhythmias and heart disease rather than osteoporosis, fractures and falls in their decision-making process in treating hypothyroidism. More physician education is needed to highlight the importance of thyroid hormone overtreatment on skeletal risks in addition to cardiac risks, especially in older adults.

This study has several strengths including the inclusion of primary care providers in addition to specialists, the sampling at a national level, and the large set of independent variables included in the analysis. However, this study also has several limitations. First, as with survey studies in general, there is a risk for non-response bias. Second, even though the survey included an extensive set of factors that may influence physician decision making in the management of hypothyroidism, there may be other factors that were not included in our survey. Third, it is possible that the provider report to the survey questions is not consistent with provider treatment behavior. Finally, this study focuses only on the physician, but the patient is also involved in the decision-making process.

In conclusion, this study has implications for both patients and physicians. Failure to recognize the relationship between age and thyroid hormone requirements may lead to overtreatment, especially in the elderly. Overtreatment with thyroid hormone replacement is common and it can have negative effects, especially in older adults (7–9,18). We found that close to half of all physicians do not report patient age as an important factor when determining TSH goal, thus potentially placing older patients at risk for overtreatment. Paradoxically, when presented with clinical scenarios differing by patient gender and age, 90% of respondents reported aiming for a TSH >1.5 mIU/L in octogenarians, which may indicate an attempt to avoid overtreatment in this specific age group. The inclusion of internists and family practitioners among the surveyed physicians is critical to understanding clinical practice patterns in the management of hypothyroidism, as a large number of hypothyroid patients are managed in primary care settings. Understanding differences in practice patterns based on specialty may also have implications for targeting physician education.

In order to streamline practice patterns, there is a need to reach a consensus among treating physicians across specialties. There is also a need for further investigation into the role of patient preference in determining TSH goals in the management of hypothyroidism.

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- What factors influence your decision making regarding goal TSH range when treating patients with thyroid hormone replacement therapy? **Please check ALL that apply.**

☐ Cardiac arrhythmia	☐ Fractures	☐ Pregnancy
☐ Heart disease	☐ Multiple falls	☐ Interest in conception
☐ Patient preference	☐ Osteoporosis	☐ None of the above
☐ Patient symptoms
(such as racing heart,
tremors)	☐ Fatigue	
	☐ Age	
	☐ Weight	

- For the following questions please select the answer that best describes your experience.

For the patients you have treated in the last 5 years, what serum TSH range did you aim for in...

(Please select ONE answer for each item)

	TSH 0.1-0.5 mIU/L	TSH 0.6-1.5 mIU/L	TSH 1.6-3.0 mIU/L	TSH 3.1-5.0 mIU/L
...Female, Age 30	☐	☐	☐	☐
...Female, Age 50	☐	☐	☐	☐
...Female, Age 65	☐	☐	☐	☐
...Female, Age 85	☐	☐	☐	☐
...Male, Age 30	☐	☐	☐	☐
...Male, Age 50	☐	☐	☐	☐
...Male, Age 65	☐	☐	☐	☐
...Male, Age 85	☐	☐	☐	☐

FIGURE 1.

Some items from the provider survey are shown.

FIGURE 2.
Factors influencing physicians' decision-making regarding goal TSH in hypothyroidism.

FIGURE 3.
Trends of TSH goals for hypothyroid female patients by age.

TABLE 1

PROVIDER CHARACTERISTICS *

	N (%)
Gender	
Male	247 (64.5)
Female	136 (35.5)
Race/Ethnicity	
White	292 (77.0)
African-American	10 (2.6)
American Indian/Alaskan Native	3 (0.8)
Asian	64 (16.9)
Native Hawaiian/Pacific Islander	3 (0.8)
Hispanic/Latino	15 (4.2)
Other	10 (2.6)
Years in practice	
0–5 years	46 (12.0)
6–10 years	48 (12.5)
11–20 years	103 (26.9)
>20 years	186 (48.6)
Specialty	
Endocrinology	140 (36.2)
Family Practice	136 (35.2)
Internal Medicine	102 (26.4)
Other	8 (2.2)
Primary practice setting	
Private practice	189 (49.0)
Academic tertiary care center	77 (19.9)
Community-based academic affiliate	52 (13.5)
Other	68 (17.6)
Insurance covering majority of patients	
Medicare	141 (36.8)
Medicaid	63 (16.4)
Private Insurance	204 (53.3)
Uninsured	15 (3.9)
Other	28 (7.3)
Percentage of patients over the age of 65	
0–10%	44 (11.5)
11–25%	76 (19.8)
26–50%	147 (38.4)
51–75%	97 (25.3)
76–100%	19 (5.0)
Number of patients on thyroid hormone replacement therapy physician saw in the last year	

	N (%)
0–15	43 (11.9)
16–50	119 (32.9)
>50	200 (55.2)

* Missing data not included

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TABLE 2

UNIVARIATE AND MULTIVARIABLE ANALYSES OF PHYSICIAN CHARACTERISTICS ASSOCIATED WITH IMPORTANCE PLACED ON PATIENT AGE IN DETERMINING GOAL TSH IN HYPOTHYROIDISM*

	Physicians reporting age as important for decision on goal TSH [n (%)]	Univariate p value	Multivariable p value
Gender		0.017	0.199
Male	112 (48.3)		
Female	79 (58.1)		
Specialty		<0.001	
Family Practice	47 (35.6)		Ref
Endocrinology	90 (75.0)		0.002
Internal Medicine	42 (43.8)		0.049
Other	14 (58.3)		0.999
Practice setting		0.010	
Private practice	102 (54.0)		Ref
Community-based affiliate	23 (44.2)		0.246
Academic tertiary care center	45 (58.4)		0.003
Other	23 (33.8)		0.009
Number of patients on thyroid hormone replacement seen in 1 year		<0.001	0.021
0–15	12 (27.9)		
16–50	54 (45.4)		
>50	126 (63.0)		
Years in practice		0.061	0.926
0–5	29 (63.0)		
6–10	29 (60.4)		
11–20	47 (45.6)		
>20	85 (45.7)		

* Missing data not included.

TABLE 3

RESPONSE DISTRIBUTION FOR GOAL TSH IN HYPOTHYROID PATIENTS *

	Target TSH Range			
	TSH 0.1–0.5 mIU/L	TSH 0.6–1.5 mIU/L	TSH 1.6–3.0 mIU/L	TSH 3.1–5.0 mIU/L
Female, Age 30	10 (3.0)	152 (46.2)	134 (40.7)	33 (10.0)
Female, Age 50	4 (1.2)	104 (31.4)	182 (55.0)	41 (12.4)
Female, Age 65	1 (0.3)	53 (16.0)	203 (61.1)	75 (22.6)
Female, Age 85	1 (0.3)	33 (10.1)	139 (42.6)	153 (46.9)
Male, Age 30	8 (2.5)	134 (41.2)	148 (45.5)	35 (10.8)
Male, Age 50	4 (1.2)	99 (30.3)	184 (56.3)	40 (12.2)
Male, Age 65	1 (0.3)	54 (16.6)	189 (58.0)	82 (25.2)
Male, Age 85	2 (0.6)	29 (9.0)	141 (43.5)	152 (46.9)

* Missing data not included. Data are n (%).