Original Article

Comparison of Two Guidelines on Management of Thyroid Nodules and Thyroid Cancer during Pregnancy

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Abstract

Background: Some hormonal and metabolic changes may stimuli normal or neoplastic thyroid cells. Thyroid tumors discovered during pregnancy present unique challenges to both the clinician and the mother. The aim of this article is to compare American Thyroid Association (ATA) guidelines to Endocrine Society guidelines for management of thyroid tumors during pregnancy.

Method: We reviewed the section of thyroid nodules and cancer of ATA and Endocrine Society guidelines which have been published recently. Both organizations have discussed and given recommendations related to maternal and fetal aspects of thyroid nodules and cancer. Each topic from either guidelines was compared together and that recommendation which was more complete included in 4 tables.

Results: There is a high degree of similarity between these two guidelines. Both organizations have discussed and given recommendations related to maternal and fetal aspects of thyroid tumors. Regarding their similarity any of these two guidelines can be used for safe and proper management of women with thyroid tumors during pregnancy.

Conclusion: Regarding their similarity any of these two guidelines can be used by clinicians for safe and proper management of pregnant women with thyroid nodules and cancer.

Keywords: Guideline, pregnancy, thyroid cancer, thyroid nodule

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Introduction

Thyroid nodules are extremely common and their incidence varies among different populations and geographic regions. Palpable thyroid nodules are found in about 4–7% of the general population.[1–3] The prevalence of is greater in individuals living in countries affected by iodine deficiency.[4] With the frequent use of imaging especially carotid and neck ultrasound study, many thyroid nodules are found in asymptomatic patients.[3,5] The prevalence of thyroid nodules on ultrasonography may exceed 50%. Despite the high prevalence of thyroid nodules in the general population, thyroid cancer is relatively uncommon, and only one in 20 palpable nodules is malignant.

Some hormonal and metabolic changes affect the thyroid gland during pregnancy.[6] Some of these changes may give rise to growth stimuli for normal or neoplastic thyroid cells.[7–10] Whether pregnancy is associated with a higher incidence of thyroid nodules and thyroid cancer is controversial. Women seek medical care more often during their pregnancy, so thyroid nodules are relatively common in pregnant women, and this is frequently a source of major anxiety. The incidence of thyroid cancer during pregnancy varies among different studies, probably due to detection biases, but is likely to be similar rate observed in general population. According to previous studies, differentiated thyroid carcinoma is the second most common malignancy, after breast cancer, diagnosed during pregnancy.[11]

The management of thyroid nodules and cancer poses a number of diagnostic dilemmas. The most significant challenge is to find thyroid cancer while distinguishing it from benign nodules that require little or no treatment.[12–13] Management of thyroid cancer during pregnancy poses distinct challenges because certain diagnostic and therapeutic options such as radioisotope scanning, radiological investigation, ablative therapy with radioactive iodine and in some cases anesthesia or operation are strictly contraindicated.[14–15] The diagnostic evaluation of a thyroid nodule during pregnancy is similar to that applied to non-pregnant women.[1,2,16–20] However, avoiding interventions that may adversely impact the mother and pregnancy outcomes is mandatory. Recently ATA,[21] American Association of Clinical Endocrinologist (AACE)[22] and Korean Society of Thyroid Radiologist[23] have published three sets of guidelines regarding management of thyroid nodules in the general population, which have many similarities. Two guidelines on thyroid and pregnancy have been also developed in October 2011[24] and August 2012[25] from ATA and Endocrine Society, respectively. These two guidelines have recommendations regarding management of thyroid nodules and thyroid cancer in pregnant women. The aim of this article is to compare recommendations of these two guidelines.

Material and Methods

We reviewed the section of thyroid nodules and thyroid cancer in both guidelines (pages 1100–1105 of the American Thyroid Association[15] and pages 2546 and 2554–2555 of the Endocrine Society Clinical Practices).[16] Each topic from either guideline was

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Table 1. Comparison of recommendations of American Thyroid Association and Endocrine Society on the characteristics of thyroid nodules during pregnancy.

Topic	Recommendations	
	American Thyroid Association (2011)	**Endocrine Society (2012)**
Nodular prevalence	The prevalence of thyroid nodules varied between 3% and 21%	Thyroid nodules may be more prevalent in pregnant women
Impact of parity on nodular prevalence	The prevalence of thyroid nodules increases with increasing parity: 9.4% without a prior pregnancy, 20.7% with one prior pregnancy, 20.7% with two prior pregnancies, and 33.9% with three or more prior pregnancies	Pregnancy could promote the onset of growth of a benign or malignant nodule due to a pregnancy-induced relative iodine deficiency, the thyroid-stimulating effect of hCG, and high estrogen levels.
Nodular size	An increase in nodular volume has reported during pregnancy.	The volume of thyroid nodules may increase in gestation.
Family history	Obtaining a family history of benign or malignant thyroid disease, familial medullary thyroid carcinoma, multiple endocrine neoplasia type 2 (MEN 2), familial papillary thyroid carcinoma, and familial polyposi coli.	None

Table 2. Comparison of recommendations of American Thyroid Association and Endocrine Society on the diagnostic methods for evaluation of thyroid

Topic	Recommendations	
	American Thyroid Association (2011)	**Endocrine Society (2012)**
Thyroid function test	All women with a thyroid nodule should have a TSH and FT4 performed. Thyroid function tests are usually normal in women with thyroid cancer.	The diagnostic evaluation of a single thyroid nodule or a nodule found in a multinodular goiter discovered during pregnancy should be similar to that of non-pregnant patients.
Calcitonin	The utility of measuring calcitonin in pregnant women with thyroid nodules is unknown. Calcitonin measurement should be performed in pregnant women with a family history of medullary thyroid carcinoma or MEN 2. However, the utility of measuring calcitonin in all pregnant women with thyroid nodules has not been evaluated in the literature. The pentagastrin stimulation test is contraindicated in pregnancy	None
Ultrasound	. Thyroid ultrasound is the most accurate tool for detecting thyroid nodules, determining their features, monitoring their growth, and evaluating cervical lymph nodes.	Same recommendation
Fine needle aspiration biopsy (FNA)	Thyroid nodules discovered during pregnancy that have suspicious ultrasound features, as delineated by the 2009 ATA guidelines, should be considered for FNA. In instances in which nodules are likely benign, FNA may be deferred until after delivery based on patients' preference.	FNA cytology should be performed for predominantly solid thyroid nodules greater than 1 cm, complex nodules 1.5–2 cm or larger and for nodules 5 mm to 1 cm in size with high-risk history or suspicious findings on ultrasound.
Radionuclide scanning	The use of radioiodine imaging and/or uptake determination or therapeutic dosing is contraindicated during pregnancy. Inadvertent use of radioiodine prior to 12 weeks of gestation does not appear to damage the fetal thyroid.	Same recommendation

reviewed and compared together. Then, the more completed recommendation was selected and included in Tables 1 to 4. Different or additive recommendations of other organizations was cited, otherwise the word "same" was placed. If similar information regarding a recommendation of one organization was present in the recommendation or text of guidelines of other organization word same recommendation was added.

Results

In the Endocrine Society Clinical Practice Guideline, a total of four recommendations for performing FNA cytology, time of surgery for malignant nodules, administration of thyroid hormone to achieve a suppressed TSH and avoidance the use of radioactive iodine were given for the management of thyroid nodules and thyroid cancer during pregnancy. ATA guideline has presented 12 questions including number 58 to 69, and their appropriate answers. This guideline also presents17 recommendations including number 46 to 62 on the optimal diagnostic strategy, management and time of surgery for malignant nodules, administration of thyroid hormone to achieve a suppressed TSH, avoidance the use of radioactive iodine and monitoring previously treated differentiated thyroid cancer during pregnancy. Comparison of recommendations of both organizations is summarized in Tables 1 to 4. There is a minor difference between these two guidelines regarding the characteristics and the detection methods for evaluation of thyroid nodules (Tables 1 and 2) and also management of benign and suspicious thyroid nodules during pregnancy (Table 3). Endocrine Society guideline has not included family history and calcitonin measurement in diagnostic strategy and also no recommendation has been presented regarding the management of benign and suspicious thyroid nodules during pregnancy.

Table 3. Comparison of recommendations of American Thyroid Association and Endocrine Society on the management of benign and suspicious thyroid nodules during pregnancy.

Topic	Recommendations	
	American Thyroid Association (2011)	**Endocrine Society (2012)**
Management of benign thyroid nodules	Pregnant women with thyroid nodules that are read benign on FNA cytology do not require surgery during pregnancy except in cases of rapid nodule growth and/or if severe compressive symptoms develop. Postpartum, nodules should be managed according to the 2009 ATA guidelines.	None
Management of suspicious thyroid nodules	Pregnant patients with an FNA sample that is suspicious for thyroid cancer do not require surgery, except in cases of rapid nodular growth and/or the appearance of lymph node metastases. Thyroid hormone therapy is not recommended.	None

Table 4. Comparison of recommendations of American Thyroid Association and Endocrine Society on the management of thyroid cancer during pregnancy.

Topic	Recommendations	
	American Thyroid Association (2011)	**Endocrine Society (2012)**
Cancer prevalence	A population-based retrospective analysis of all obstetrical deliveries in California between the years 1991 through 1999 has reported a prevalence of thyroid cancer in pregnancy of 14.4/100,000, with papillary cancer being the most frequent pathological type	The malignancy rate is either similar to or possibly greater than that seen in the general population.
Prognosis	The majority of studies indicate that pregnancy does not worsen the prognosis in women diagnosed with DTC.	There is no clear evidence that pregnancy worsens the survival from well-differentiated thyroid cancer found during an existing pregnancy.
Treatment of thyroid cancer	Same recommendation	If the result of FNA is consistent with or highly suggestive of papillary, follicular, anaplastic, or medullary carcinoma, or has suspicious sonographic characteristics, surgery should be offered.
Time of surgery	Surgery for thyroid carcinoma during the second trimester of pregnancy has not been demonstrated to be associated with increased maternal or fetal risk. Surgery in women with well-differentiated thyroid carcinoma may be deferred until postpartum without adversely affecting the patient's prognosis. However, if substantial growth of the well-differentiated thyroid carcinoma occurs or the emergence of lymph node metastases prior to mid gestation occurs, then surgery is recommend.	Same recommendation
Management of DTC during pregnancy	If surgery is deferred until postpartum, thyroid hormone suppression therapy may be considered for patients with an FNA biopsy diagnostic of a DTC. When a decision has been made to defer surgery for well differentiated thyroid carcinoma until after delivery, neck ultrasounds should be performed during each trimester to assess for rapid tumor growth, which may indicate the need for surgery.	Same recommendation
Thyroid Hormone	Thyroid hormone therapy may be considered in pregnant women who have deferred surgery for well differentiated thyroid carcinoma until postpartum. The goal of LT4 therapy is a serum TSH level of 0.1–1.5mIU/L.	It is appropriate to administer thyroid hormone to achieve a suppressed but detectable TSH in pregnant women with a previously treated thyroid cancer, in those with an FNA positive for or suspicious for cancer, or in those who elect to delay surgical treatment until postpartum. The free T4 or total T4 levels should ideally not be increased above the normal range for pregnancy.
Monitoring of previously treated DTC	Ultrasound and Tg monitoring during pregnancy in patients with a history of previously treated DTC is not required for low-risk patients with no Tg or structural evidence of disease prior to pregnancy. Ultrasound monitoring should be performed each trimester during pregnancy in patients with previously treated DTC and who have high levels of Tg or evidence of persistent structural disease prior to pregnancy	Monitoring with TG is recommended for women who have received RAI, and women may be maintained on suppressive doses of T4 that do not cause overt hyperthyroidism
Radioactive iodine	There is no evidence that previous exposure to radioiodine affects the outcomes of subsequent pregnancies and offspring. Pregnancy should be deferred for 6 months following RAI treatment. LT4 dosing should be stabilized following RAI treatment before pregnancy is attempted.	RAI with ^{131}I should not be given to women who are breastfeeding or for at least four weeks after nursing has ceased. Furthermore, pregnancy should be avoided for six months to one year in women with thyroid cancer who receive therapeutic RAI doses to ensure stability of thyroid function and confirm remission of thyroid cancer.
DTC recurrence	Pregnancy does not pose a risk for tumor recurrence in women without structural or biochemical disease present prior to the pregnancy. However, pregnancy may represent a stimulus to thyroid cancer growth in patients with known structural or biochemical disease present at the time of conception.	Several series have examined the natural history of cancer recurrence in women who became pregnant after receiving successful treatment for thyroid cancer, and in all studies there was no evidence that thyroid cancer was adversely influenced by the pregnancy.

DTC = differentiated thyroid carcinoma; Tg = thyroglobulin.

Discussion

The prevalence of thyroid nodules is high in women and thyroid cancer is among the five most frequent cancers that occur during reproductive life. As pregnancy imposes several limitations on thyroid cancer management, special considerations should be paid in this regard to prevent any adverse effects on the mother, fetus or neonate. Two new guidelines of ATA (2011) and Endocrine Society (2012) on thyroid and pregnancy have considered the issue of thyroid nodule and cancer management during pregnancy without major disagreement or controversy. Both organizations have discussed and given recommendations related to maternal and fetal aspects of thyroid nodules and cancer. The aim of this manuscript is to give guidance to clinicians for optimal management of pregnant women. Regarding their similarity any of these two guidelines can be used by clinicians for safe and proper management of pregnant women with thyroid nodules and cancer.

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