

## SURGICAL TREATMENT OF THYROID DISORDERS AND THYROID NODULES IN PREGNANT PATIENTS

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### Summary

The incidence of thyroid nodules and thyroid disorders is more common in women. Thyroid nodules are more prevalent with increasing age. It is proven that thyroid nodules and thyroid cancer incidence have been increased in the last three decades. The same period has registered the increase in average age at which women are getting pregnant rising the probability to develop thyroid cancer in pregnancy. Surgery during pregnancy can have a negative impact on both mother and unborn child causing changes in decision making for surgical procedure in pregnant patients with a low risk thyroid cancer. The aim of this review is to identify indications for surgical treatment of the thyroid nodules and thyroid disorders in pregnancy and to establish the most appropriate period of pregnancy to schedule surgery.

KEYWORDS: *thyroid cancer, thyroid nodules, hyperthyroidism, hypothyroidism, pregnancy, surgery*

### EVALUACIJA POTREBE KIRURŠKOG LIJEČENJA TRUDNICA SA ČVOROVIMA U ŠTITNJAČI I POREMEĆAJIMA RADA ŠTITNJAČE

#### Sažetak

Čvorovi u štitnjači i poremećaji rada štitnjače učestaliji su u žena. Učestalost pojave čvorova u štitnjači raste sa životnom dobi. Posljednja tri desetljeća porasla je incidencija čvorova u štitnjači kao i karcinoma štitnjače. Istovremeno povećana je i prosječna životna dob u kojoj žene planiraju trudnoću pa je time povećana i incidencija karcinoma štitnjače u trudnoći. Kirurško liječenje za vrijeme trudnoće negativno utječe i na majku i na plod, što potiče mijenjanje strategije u donošenju odluke o operativnom zahvatu u trudnih pacijentica s karcinomom štitnjače. Cilj je ovog pregleda utvrditi apsolutne indikacije za kirurško liječenje čvorova štitnjače u trudnoći i poremećaja rada štitnjače u trudnoći te utvrditi idealno vrijeme u tijeku trudnoće za potreban operativni zahvat.

KLJUČNE RIJEČI: *karcinom štitnjače, čvorovi štitnjače, hipertireoza, hipotireoza, trudnoća, operativno liječenje*

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### INTRODUCTION

Indications for thyroid surgery have been well investigated and identified. There are absolute and relative indications for thyroid surgery in pregnancy. Absolute indications include malignant thyroid tumor, large goiter causing compres-

sive symptoms and FNAB (fine needle aspiration biopsy) validated follicular neoplasm. Relative indications for thyroid surgery involve hyperthyroidism (caused by solitary toxic nodule, multinodular toxic goiter or Grave's disease) and FNAB-proven benign thyroid nodules without extensive compressive symptoms (1-2). The preg-

nant woman undergoes significant physiological changes that affect almost every organ system and whose magnitude of derangement increases as the gestation progresses relative to the nonpregnant state (3). Randall et al. reported that there are ethical dilemmas the clinician and the patient face when dealing with the question of surgery during pregnancy. The first consideration is to compare the risk for the disease in the mother and the possible postponed treatment with the risk of surgery to the fetus. Risk to the fetus includes the possible teratogenesis, fetal damage and even fetal loss. These issues should be identified and discussed to enable the patient to fully understand and consider the ramification of surgery versus postponement (4).

## METHODS

We have performed a literature review based on articles found in PubMed up to 2012. All of the articles were found electronically searching PubMed database. MeSH (Medical Subjected Headings) search engine was used to identify the influential and important articles about unavoidable need for thyroid surgery in pregnancy as well as feasibility of surgery. Original research papers were included in the present review. The keywords and the keywords combination used in this search included: pregnancy, surgery, thyroid surgery, thyroid nodule, hyperthyroidism, Grave's disease, toxic adenoma, multinodular toxic goiter, papillary thyroid cancer, follicular thyroid cancer, medullary thyroid cancer, anaplastic thyroid cancer, hypothyroidism.

## DISCUSSION

Thyroid tumors and thyroid disorders requiring surgical procedure are performed in our institution on daily basis with extensively low incidence of complications. Pregnancy is a condition that obliges us to special care when planning surgery in particular period of pregnancy. If an absolute indication for surgery exists it should be done in second trimester after the organogenesis (4-8). Because of the complexity of pregnancy and malignant disease a team of specialists (surgeon, endocrinologist, nuclear medicine specialist, obstetrician and primary care physician) should be

involved in decision making process and follow up (6).

Endocrine society (which one? Croatian Society for Endocrinology?) proposed guidelines for care of pregnant patients diagnosed with thyroid nodules or thyroid cancer. They advocate thyroid nodule measure 1 cm or larger should be evaluated by FNAB. For patients with malignant nodules or in case of their rapid growth surgery should be offered in the second trimester of pregnancy. Patients with follicular neoplasm wait until postpartum for thyroidectomy, patients with known thyroid cancer should maintain low but measurable thyroid stimulating hormone (TSH) and normal thyroxine (T4) values on levothyroxine while pregnant, RAI therapy should not be provided to women who are pregnant and breastfeeding and women should wait 6-12 months before getting pregnant after RAI therapy (8). It is known that aggressive subtypes of micro papillary cancer (tall cell, columnar cell, diffuse sclerosing, solid/trabecular, and insular variants) can develop central and lateral neck metastases even if the tumor is less than 5 mm in size. Special attention should be provided to all thyroid nodules with suspected ultrasound features: irregular borders, micro calcification and hyper vascularity even if the nodules are smaller than 1 cm, perform FNAB and central and lateral neck ultrasound (9,10). Well-differentiated thyroid cancer first metastasizes to central and lateral compartment of cervical lymph nodes;. In the presence of positive cervical lymph node metastasis the need for surgery is not questionable. All the pregnant women with lymph node metastasis have to undergo surgery regardless of size of the primary thyroid cancer. Randall et al. suggest indications for surgery of thyroid cancer during pregnancy. They state as generally accepted that almost any cancer discovered in the third trimester may be observed until after delivery. Second trimester surgical intervention may be considered for aggressive variants of cancer and, in particular, for medullary cancer. Many reviews of thyroid cancer in pregnancy generally advise postponing surgery for well-differentiated thyroid cancer, but suggest that a more aggressive surgical approach may be warranted when medullary cancer is diagnosed (4,11,12,13,14). Management of medullary carcinoma during pregnancy is a complex subject. Even though patients with thyroid nodules and proven medullary carcinoma

can be observed, the general tendency is to consider surgical intervention unless the tumor is very small and the calcitonin level is quite low, as cure is dependent on surgical treatment and delay could decrease the chance of cure (4,15). Medullary cancer can induce early regional metastasis with high frequency. When medullary cancer is diagnosed, the surgery is the key to locoregional control and surgery should not be postponed, if possible (11).

The question with unanimous answer in reviewed literature is the importance of the thyroid cancer size (16). Doherty et al. suggest that newly diagnosed thyroid nodules in pregnancy should not be investigated until delivery because potential malignancy might cause stress and anxiety in patient, finally even leading to premature delivery. Therefore, this group generally postpones FNAB until delivery in patients who are discovered to have a thyroid nodule after 20 weeks of gestation (4,17). Because of potential aggressive papillary, medullary and anaplastic subtypes of cancer we highly recommend a complete work up including ultrasound, ultrasound-guided FNAB and thyroid hormones' level check to exclude aggressive subtypes of thyroid cancer. Postponing investigation of a newly discovered thyroid nodule after 20 weeks of pregnancy to avoid unnecessary anxiety may be feasible in some countries and cultures. In our patient population anxiety can be more potentiated by not clarifying the true nature of the discovered thyroid nodule. Mazzaferri suggests postponing thyroid cancer surgery after the delivery and proposes ultrasound controls during each trimester with thyroid hormone level control every 4 weeks (6,18). Surgery should be considered in case of 50% or more growth rate, in ultrasound evidence of extra capsular invasion or when lymph node metastasis bigger than 1 cm appear (6). Yasmeen et al. validated that pregnancy had no significant effect on mortality after diagnosis of thyroid cancer. Thyroidectomy during pregnancy was not associated with adverse maternal or neonatal outcomes (19).

Treatment options for hyperthyroidism include surgery, radioactive iodine ablation and medication. Radioactive iodine ablation is not an option in pregnancy because of potential teratogenesis. Surgery in pregnancy is usually not recommended since medication treatment with propylthiouracil in the first trimester and methima-

zole in the last two trimesters obtains euthyroidism and causes no severe adverse effects (20). Malignancy in hyperthyroidism has been observed but in not so many cases. Occult malignancies are found in 2-3% of thyroidectomy specimens for Plummer's disease (multinodular toxic goiter) (1). Hyperthyroidism and synchronous thyroid cancer should be treated as two different diseases.

## CONCLUSION

Well-differentiated thyroid cancer is a malignant disease with overall good prognosis. Our attitude is that all the pregnant women with ultrasound-guided FNAB-proven well-differentiated thyroid cancer 1 cm or less in size (micro cancer) and without suspected lymph nodes should be followed up on monthly basis. If the thyroid cancer is less than 1 cm in size with FNAB-positive lymph nodes in central or lateral neck, the patient has to be referred for surgery. All the patients with well-differentiated thyroid cancer larger than 1 cm have to be operated if the pregnancy is normal. The ideal moment for surgery is the second trimester. All patients with medullary and anaplastic cancer should undergo surgery. Hyperthyroidism in pregnancy should be treated with propylthiouracil in the first trimester and with methimazol until the delivery with fT4 level at 10% above the referent value range of the laboratory.

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