

# THE ROLE OF LYMPHOSCINTIGRAPHY AND SENTINEL LYMPH NODE BIOPSY IN PATIENTS DIAGNOSED AS BREAST CANCER DURING PREGNANCY

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## GEBELİK ESNASINDA MEME KANSERİ TANISI KONAN HASTALARDA LENFOSINTİGRAFI VE SENTİNEL LENF NODU BIYOPSİSİNİN ROLÜ

### ÖZET

Meme kanseri gebelik esnasında en sık tanı konan kanserlerden birisidir. Gebelik ile ilişkili meme kanserinin prevalansının 1:3000 doğumda bir olduğu ve çocuk doğurma yaşının artmasının neden ile giderek daha da artacağı tahmin edilmektedir. Gebelik esnasında tanı konan meme kanserleri genel olarak ileri evre tümörler olsa da tedavi yöntemleri mümkün olduğu kadar gebe olmayan meme kanseri kadınlardaki gibi olmalıdır. Gebe olmayan erken evre meme kanserinde aksiller lenf nodlarının durumu adjuvan tedavinin uygulanmasında en önemli prognostik faktörlerdendir. Aksiller lenf nodu diseksiyonu anlamlı morbidite ile beraber olup mavi boya ve/veya radyokolloid ile sentinel lenf nodu biyopsisi yöntemi aksiller diseksiyon yerine giderek artan şekilde yapılmaktadır. Sentinel lenf nodu biyopsisi için kullanılan mavi boyalar gebelik için class C grubu ilaçlar olup gebelikte sentinel lenf nodu biyopsisi genellikle radyokolloidlerle yapılır. Gebelik esnasında tanı konan meme kanserinde lenfosintigrafi yapmadan önce bazı teknik detayların göz önünde bulundurulması gerekir. Lenfosintigrafi ameliyat ile aynı gün de yapılmalıdır. Sentinel lenf nodu biyopsisi 2-3 saat cerrahi öncesi 3-5 MBq Tc99m ile yapılabilir. Gebelik esnasında görülebilecek konjenital malformasyonları ekarte etmek için detaylı perinatal inceleme yapılmalıdır. Sonuç olarak gebelik esnasında tanı konan meme kanseri hem aile hem de hekimler için zor bir durum olup lenfosintigrafi ve sentinel lenf nodu biyopsisi tedavide optimal bir seçenek olabilir.

**Anahtar sözcükler:** meme kanseri, gebelik, lenfosintigrafi, sentinel lenf nodu biyopsisi

## ABSTRACT

Breast cancer is one of the most diagnosed malignancies during pregnancy. The prevalence of breast cancer associated with pregnancy is estimated at 1:3,000 deliveries and predicted to increase permanently due to the trend to defer childbearing to older ages. Although breast cancer is generally diagnosed in advanced stage during pregnancy, the treatment modality should be as similar as possible with non pregnant women. In non-pregnant women with early stage invasive breast cancer, axillary lymph node status is the most important prognostic factor for determination of accurate adjuvant treatment. Axillary lymph node dissection is associated with significant morbidity and the sentinel lymph node biopsy is performed using blue dye or lymphoscintigraphy with a radiocolloid. Blue dyes are classified as pregnancy class C drugs and lymphoscintigraphy with a radiocolloid is generally used for the sentinel lymph node biopsy during pregnancy in patients diagnosed with breast cancer. Some technical information should be considered before performing lymphoscintigraphy on breast cancer patients during pregnancy. The lymphoscintigraphy should be performed on the same day of intervention. Sentinel lymph node biopsy can be performed within 2-3 h p.i. with 3-5 MBq of 99m Tc radiocolloid. Diligent perinatal diagnostic examinations should be done to exclude any congenital malformations before performing a lymphoscintigraphy during pregnancy. In conclusion, breast cancer diagnosed during pregnancy is a difficult matter for both the families and physicians but lymphoscintigraphy and sentinel lymph node biopsy may result in optimal treatment for the pregnant breast cancer patients.

**Key words:** breast cancer, pregnancy, lymphoscintigraphy, sentinel lymph node biopsy

**B**reast cancer, which is one of the most diagnosed malignancies during pregnancy, is becoming an increasingly common disease in pregnant women. The common description of pregnancy-associated breast cancer is a breast cancer diagnosed during pregnancy, lactation or 1-year postpartum (1). The most challenging and debatable proportion of the disease is cancer diagnosed during pregnancy. The number of breast cancer diagnoses during pregnancy is estimated at 1:3,000 deliveries, and 0.2% of all breast cancers are diagnosed in pregnancy (2). It is predicted that breast cancer diagnosed during pregnancy will increase permanently due to the trend to defer childbearing to older ages (2, 3). Desire to maintain the pregnancy is based on the mother's decision, ethical or religious issues. Different treatment

options which consist of breast conserving surgery, sentinel lymph node biopsy, and adjuvant treatments during pregnancy and the effects of these treatments on the unborn child, complicate and prolong the treatment decisions, and is a difficult and complex situation both for the family and physicians. The majority of breast cancers diagnosed during pregnancy are at a more advanced stage with a delayed diagnosis due to the hypertrophy and engorgement of the breasts in response to the hormonal changes and general comments on the occurrence of breast masses during pregnancy as benign lesions (1). Although coexisting issues such as advanced stage or poor biological features arise in patients diagnosed with breast cancer during pregnancy, the treatment modality should be as similar as possible with non

pregnant women and termination of pregnancy in combination with castration does not seem to improve survival (1-3). In non-pregnant women with early stage invasive breast cancer axillary lymph node status is the most important prognostic factor for determination of accurate adjuvant treatment (4). Axillary lymph node dissection is associated with significant morbidity, including impairment of shoulder movement, neuropathy, pain, seroma, and lymphedema (5). Over the last decade, sentinel lymph node biopsy has become a standard method for the axillary staging of breast cancer in patients with early stage breast carcinoma and has growingly replaced axillary lymph node dissection (6-8). The sentinel lymph node biopsy is currently being performed by many centers in pregnant women with breast cancer, but controversy rose synchronously (9-11). In breast cancer, the sentinel lymph node biopsy has been identified using blue dye, lymphoscintigraphy with a radiocolloid or a combination of both methods. Isosulfan blue and methylene blue are the dyes used in sentinel lymph node dissection but both are classified as pregnancy class C drugs with complications consisting of anaphylactic reactions to placental circulation disorders and vascular accidents causing intestinal atresia (6, 7, 9, 10). The report of International Commission on Radiological Protection published in 2000 has proposed that the most common procedures in diagnostic nuclear medicine has reliable side effects in pregnant women and pregnancy should not be a reason to avoid diagnostic nuclear medicine studies (12). Gentilini et al. (13) published a clinical study of 26 pre-menopausal non-pregnant women with early stage breast cancer who were candidates for lymphoscintigraphy for lymphatic mapping and sentinel lymph node dissection in 2004. The authors performed a single peritumoral injection of Tc labelled human albumin colloid particles in a volume of 0.2 ml as an average of 12.1 MBq. The thermoluminescent dosimeters were placed on the injection site, on two different sites between injection and epigastrium, and on the abdominal surface of the epigastrium, the periumbilical area and the hypogastrium and removed to measure the radiation exposure before operation. The results of the study demonstrated that the total activity excreted within the first 16 h was <2% of the injected activity and in 23 of 26 patients, all absorbed dose measurements over the surface of the abdomen at the supposed levels of the fetus were lower than the sensitivity of the thermoluminescent dosimeters (<10  $\mu$ Gy). The authors claimed that lymphoscintigraphy and sentinel lymph node dissection were safe for patients with breast cancer during pregnancy with negligible risks for the fetus. In another study Keleher et al. (9) measured the absorbed radiation doses to the fetus with two different doses of  $^{99m}$ Tc (0.5 and 2.5 mCi). In their clinical scenario the maximum calculated doses were all within 4.3 mGy and they concluded that the absorbed doses were well below the 50 mGy which is threshold absorbed dose for adverse effects to the fetus. Mondini et al. (10) treated six melanoma and three breast cancer pregnant patients. 78% of the patients underwent lymphoscintigraphy and sentinel lymph node dissection during their first and second trimester. Two patients received isosulfan blue intraoperatively, and four patients were injected with  $^{99}$ Tc-labeled sulfur colloid particles and the three of the patients received both techniques. An

average of 2, 3 sentinel lymph nodes were dissected on this study. Pregnancies were delivered at term and the authors observed no birth defects or discernable malformations in any of the children. The most recent study on sentinel lymph node dissection during pregnancy was published by Gentilini et al. (11) in 2010 reporting on 12 breast cancer patient. Lymphatic mapping was performed by lymphoscintigraphy alone with in the first eight patients with an activity of 10 MBq on average (range 5–12 MBq) on the day before surgery. In the rest of the patients a 3–5 MBq of  $^{99m}$ Tc radiolabelled colloids in a volume of 0.1–0.2 ml was used on the same day of surgery. 11 of 12 pregnancies resulted in the gestational age and no malformation was observed. One baby underwent operation due to perimembranous subaortic ventricular septal defect on the third month. The perinatal ultrasonography on 21 st week retrospectively reevaluated by another observer and a ventricular septal defect suspicion was confirmed. The authors concluded that lymphoscintigraphy which was performed during the 26th week of gestation is not associated with ventricular septal defect. The authors pointed out that lymphoscintigraphy and sentinel lymph node dissection can be safely applied during pregnancy since prenatal doses from this diagnostic procedure, when properly performed, are low enough that they do not significantly increase the risk of radioactive-induced effects such as prenatal death, malformation or mental impairment.

Some technical information should be considered before making a decision on the treatment modality of the pregnant women with breast cancer.

- 100-200 mGy or higher doses of radiation are associated with malformations in central nervous system and reduction of intelligence quotient.
- The dose to the fetus in diagnostic nuclear medicine is usually below 10 mGy, which provides risks well below the threshold for deterministic effects and minimally increases risks of stochastic effects.
- The absorbed doses to the fetus in sentinel lymph node biopsy are mostly below 20  $\mu$ Gy for 10–20 MBq (about 1  $\mu$ Gy/MBq).
- Diligent perinatal diagnostic examinations should be done to exclude any congenital malformations before performing a lymphoscintigraphy during pregnancy.
- The lymphoscintigraphy should be performed on the same day of intervention in order to reduce absorbed doses of radiation to the fetus.
- Sentinel lymph node biopsy can be performed within 2–3 h p.i. with 3–5 MBq of  $^{99m}$ Tc radiocolloid.

In conclusion, breast cancer diagnosed during pregnancy is a complicated matter both for the families and physicians but lymphoscintigraphy and sentinel lymph node biopsy may be an optimal treatment opportunity for the pregnant breast cancer patients. The treatment modalities of breast cancer diagnosed during pregnancy and every scenario should be discussed and re-evaluated due to gestation age, tumor stage, adjuvant treatment options, and patient's demands.

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