

Practical consensus recommendations for gestational breast cancer

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Abstract

This manuscript provides a practical and easy to use consensus recommendation to community oncologists on how to manage gestational breast cancer.

Key words: Anthracycline, blue dye, breast conservative surgery, fetal monitoring, inducing delivery, taxane, trimesters

Introduction

Gestational breast cancer (or pregnancy-associated breast cancer) is defined as breast cancer that is diagnosed during pregnancy, in the first postpartum year, or any time during lactation.^[1] The incidence of pregnancy associated breast cancer is approximately 15 to 35 per 100,000 deliveries.^[2,3] Most pregnancy-associated breast cancers are seen in women under the age of 30, amounting to almost 20% of the population.^[4,5] The diagnosis and management of gestational breast cancer is generally similar to that in nonpregnant patients, with a few changes to account for the maternal and foetal well being. The outcomes of women with gestational breast cancer have been found to be conflicting. One study showed no difference in progression free and overall survival.^[6] Another study showed better disease free survival, and OS.^[7] A meta-analysis carried out in 2012, found a higher risk of death in pregnancy – associated breast cancer, mostly in women diagnosed in the postpartum period.^[8] A retrospective analysis of 26 women from a tertiary care centre in India with a median follow up of 33 months showed a median progression free period of 18 months, and 3 year survival of 50%.^[9] All patients had infiltrating duct carcinoma. The median age of the patients was 26 years, 73% of the patients were diagnosed postpartum. Most of the patients had locally advanced disease at presentation, and 30.7% of the patients had distant metastases at presentation.

The expert group met to discuss and arrive at a consensus statement to provide community oncologists practical guidelines on the management of gestational breast cancer. This manuscript is the outcome of the expert group discussion and consensus arrived at in May 2017.

Defining Clinical Cohort and Practice of Expert Group Panel Members

The primary objective was to provide a consensus statement for community oncologists that could be applicable as ready-to-use practical recommendations. Hence, the applicable setting was outlined by defining the clinical cohort and current practice of the participating delegates and expert group panel members – on the basis of which this document was prepared.

The expert group discussed a hypothetical clinical scenario of a 26 year old lady, primigravida, who was seven months pregnant when diagnosed with nonmetastatic operable, infiltrating duct carcinoma, ER/PR/Her2 neu positive. A series of questions on key practical issues and management challenges were asked, with each question answerable in the form of selection from multiple choice options. The consensus answers were used as the basis of formulating the consensus statement providing community oncologists with ready-to-use practical recommendations. The national and international experts invited to this meeting were also provided the data on the voting by the audience delegates. Members of the panel were also allowed to share their personal experiences, make comments and record dissent while voting for the consensus statements.

Diagnosis and Staging

The panel recommended that breast ultrasound is the imaging test of choice while evaluating breast lumps in pregnant patients. Mammography may be carried out only with appropriate abdominal shielding; however sensitivity may be low in view of increased breast density, increased water content and loss of contrasting fat.^[10-13] The experts recommended that breast magnetic resonance imaging (MRI) without contrast may be considered if ultrasound and mammogram are noncontributory.^[14] Core biopsy is safe and feasible in pregnant patients, and must be carried out in order to confirm diagnosis.^[15,16]

The experts agreed that chest X-ray with abdominal shielding and abdominal ultrasound should be used for staging patients with clinically locally advanced breast cancer. CT scan is not recommended because of concerns of foetal radiation exposure. MRI without contrast may be used, however should be avoided during the first trimester.^[14]

Treatment – Surgery

The experts recommended that surgical resection is the mainstay of treatment in pregnant patients with breast cancer, and is safe in all 3 trimesters of pregnancy.^[3,17-21] The attending oncologists also agreed with the same, as reflected by the poll results. The panel did not recommend inducing premature delivery in case of patients with operable breast cancer. 57% of the oncologists polled agreed with waiting till foetal maturity was achieved [Tables 1 and 2]. The panel also agreed that breast conservation surgery (BCS) is a suitable option for patients with operable breast cancers who are in their 2nd or 3rd trimester of surgery. Breast conservation

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surgery in suitable patients may be considered after proper counselling and discussion with the patient.^[22-24] This was reflected by the poll results as 83.3% of the oncologists polled agreed with the panel [Tables 3 and 4]. Mastectomy is preferred during the first trimester, in view of concerns regarding delaying radiotherapy. At present, axillary nodal dissection is the standard of care in pregnant patients. The role of sentinel lymph node biopsy (SLNB) is still uncertain.^[25-28] One study enrolled 26 pre-menopausal, non-pregnant women who underwent peritumoral injection of ~12 MBq of ^{99m}Tc-HSA nanocolloids. The study showed no radiotracer concentration except in the injection site and in the sentinel node, and concluded that LS and SLNB can be performed safely during pregnancy.^[28] The experts examined the evidence and decided that presently there is insufficient safety data with regard to lymphoscintigraphy (LS). The panel recommends if SLNB is performed, blue dye should be avoided, as it is associated with the risk of an anaphylactic maternal reaction.^[29] The opinion was divided amongst the polled oncologists, as seen in Tables 5-7. The panel also recommended that immediate reconstruction/oncoplastic surgery should be avoided. Reconstruction preferably should be better carried out postpartum, and should be restricted to a prosthetic implant.^[30]

Treatment – Chemotherapy, Targeted Therapy and Hormone Therapy

The experts were of the opinion that chemotherapy may be given during 2nd and 3rd trimesters safely, once the period of organogenesis is over.^[3,31-33] Anthracyclines can be safely used.^[34-38] After examining the current evidence, the panel recommended that taxanes may also be given.^[39] Methotrexate is not recommended during the entire period of pregnancy.^[34,40] Frequent foetal monitoring and ultrasound is important, fetal lung maturity must be carefully determined before delivery. Chemotherapy should be stopped at 33 weeks of pregnancy, so that the delivery and/or, surgery can be safely carried out, giving sufficient time for recovery from chemotherapy induced platelet and neutrophil nadir. Breast feeding is contraindicated during chemotherapy, targeted therapy and hormone therapy. The placenta should also be sent for histo-pathological examination to rule out occult metastases.

The panel does not recommend radiation therapy during pregnancy. Radiation therapy may be given after delivery. The panel agrees with international guidelines that second pregnancy may be feasible two years after completing therapy.^[3]

Take Home Message

- The panel does not recommend inducing premature delivery in case of patients with operable breast cancer
- Surgery is safe in all 3 trimesters of pregnancy and is the treatment of choice in patients being treated with curative intent
- Breast conservation surgery is a suitable option for patients with operable breast cancers who are in their 2nd or 3rd trimester of surgery
- Presently there is insufficient safety data with regard to both LS and SLNB and hence it is not recommended as standard of care. Sentinel node biopsy may be done during pregnancy, however blue die should not be used
- Immediate reconstruction/oncoplastic surgery should be avoided

Table 1: Question categories addressed by the expert panel

Broad question title	Number of sub questions
Optimum treatment of gestational breast cancer	1
Timing of various treatment options	1
Role of surgery in gestational breast cancer	3
Role of chemotherapy/targeted therapy	1

Table 2: Question 1 - In a 7 month pregnant patient with newly diagnosed nonmetastatic breast cancer, is inducing premature delivery recommended before definitive therapy

Options	Yes	No
Percentage of polled oncologists	42.9	57.1

Expert group consensus: Inducing premature delivery not recommended

Table 3: Question 2 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer, what is the optimum treatment option?

Options	Surgery	NACT
Percentage of polled oncologists	75	25

Expert group consensus: Optimal treatment for such a patient is surgery for breast cancer with curative intent. NACT=Neoadjuvant chemotherapy

Table 4: Question 3 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer, is breast conservation surgery a suitable option?

Options	Yes	No
Percentage of polled oncologists	83.3	16.7

Expert group consensus: BCS is a suitable option in pregnant patients provided if feasible - nonpregnancy related contraindications still apply. BCS=Breast conservation surgery

Table 5: Question 4 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer who refuses surgery, is trastuzumab based chemotherapy an option?

Options	Trastuzumab based chemotherapy	No trastuzumab chemotherapy
Percentage of polled oncologists	20	80

Expert group consensus: Targeted therapy with trastuzumab is contraindicated in pregnant patients

Table 6: Question 5 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer is lymphoscintigraphy and sentinel lymph node biopsy safe?

Options	Yes	No
Percentage of polled oncologists	66.7	33.3

Expert group consensus: LS and/or SLNB are not recommended as standard of care in pregnant patients since there is insufficient safety data. LS=Lymphoscintigraphy, SLNB=Sentinel lymph node biopsy

Table 7: Question 6 - In a 7 months pregnant patient with newly diagnosed nonmetastatic breast cancer, can one go for primary surgery followed by oncoplastic surgery?

Options	Yes	No
Percentage of polled oncologists	70	30

Expert group consensus: Immediate reconstruction/oncoplastic surgery should be avoided

- Chemotherapy may be given during 2nd and 3rd trimesters safely. Anthracyclines are safe, and taxanes may also be given. Methotrexate is not recommended

- Chemotherapy should be stopped at 33 weeks of pregnancy
- Frequent fetal monitoring and ultrasound is important, fetal lung maturity must be carefully determined
- Breast feeding is to be avoided while receiving systemic cancer directed therapy
- Trastuzumab is not recommended in pregnant patients
- Placenta should be sent for histopathologic examination to rule out metastasis
- Second pregnancy may be feasible two years after completing therapy
- The panel does not recommend radiation therapy during pregnancy. Radiation therapy may be given after delivery.

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Conflicts of interest

There are no conflicts of interest.

References

1. Asgerisson KS. Pregnancy-associated breast cancer. *Acta Obstet Gynecol Scand* 2011;90:158-66.
2. Smith LH, Danielsen B, Allen ME, Cress R. Cancer associated with obstetric delivery: Results of linkage with the California cancer registry. *Am J Obstet Gynecol* 2003;189:1128-35.
3. Woo JC, Yu T, Hurd TC. Breast cancer in pregnancy: A literature review. *Arch Surg* 2003;138:91-8.
4. Anderson BO, Petrek JA, Byrd DR, Senie RT, Borgen PI. Pregnancy influences breast cancer stage at diagnosis in women 30 years of age and younger. *Ann Surg Oncol* 1996;3:204-11.
5. Wallack MK, Wolf JA Jr., Bedwinek J, Denes AE, Glasgow G, Kumar B, et al. Gestational carcinoma of the female breast. *Curr Probl Cancer* 1983;7:1-58.
6. Amant F, von Minckwitz G, Han SN, Bontenbal M, Ring AE, Giermek J, et al. Prognosis of women with primary breast cancer diagnosed during pregnancy: Results from an international collaborative study. *J Clin Oncol* 2013;31:2532-9.
7. Litton JK, Warneke CL, Hahn KM, Palla SL, Kuerer HM, Perkins GH, et al. Case control study of women treated with chemotherapy for breast cancer during pregnancy as compared with nonpregnant patients with breast cancer. *Oncologist* 2013;18:369-76.
8. Azim HA Jr., Santoro L, Russell-Edu W, Pentheroudakis G, Pavlidis N, Peccatori FA, et al. Prognosis of pregnancy-associated breast cancer: A meta-analysis of 30 studies. *Cancer Treat Rev* 2012;38:834-42.
9. Gogia A, Deo SV, Shukla NK, Mohanti BK, Raina V. Pregnancy associated breast cancer: An institutional experience. *Indian J Cancer* 2014;51:167-9.
10. Liberman L, Giess CS, Dershaw DD, Deutch BM, Petrek JA. Imaging of pregnancy-associated breast cancer. *Radiology* 1994;191:245-8.
11. Yang WT, Dryden MJ, Gwyn K, Whitman GJ, Theriault R. Imaging of breast cancer diagnosed and treated with chemotherapy during pregnancy. *Radiology* 2006;239:52-60.
12. Ahn BY, Kim HH, Moon WK, Pisano ED, Kim HS, Cha ES, et al. Pregnancy- and lactation-associated breast cancer: Mammographic and sonographic findings. *J Ultrasound Med* 2003;22:491-7.
13. Samuels TH, Liu FF, Yaffe M, Haider M. Gestational breast cancer. *Can Assoc Radiol J* 1998;49:172-80.
14. Shellock FG, Cruess JV. MR procedures: Biologic effects, safety, and patient care. *Radiology* 2004;232:635-52.
15. Dominici L, Kuerer H, Babiera G. Wound Complications from Surgery in Pregnancy Associated Breast Cancer. *American Society of Breast Surgeons Annual Meeting*; 2009.
16. Collins JC, Liao S, Wile AG. Surgical management of breast masses in pregnant women. *J Reprod Med* 1995;40:785-8.
17. Mazze RI, Källén B. Reproductive outcome after anesthesia and operation during pregnancy: A registry study of 5405 cases. *Am J Obstet Gynecol* 1989;161:1178-85.
18. Gianopoulos JG. Establishing the criteria for anesthesia and other precautions for surgery during pregnancy. *Surg Clin North Am* 1995;75:33-45.
19. Barron WM. The pregnant surgical patient: Medical evaluation and management. *Ann Intern Med* 1984;101:683-91.
20. Duncan PG, Pope WD, Cohen MM, Greer N. Fetal risk of anesthesia and surgery during pregnancy. *Anesthesiology* 1986;64:790-4.
21. Byrd BF Jr., Bayer DS, Robertson JC, Stephenson SE Jr. Treatment of breast tumors associated with pregnancy and lactation. *Ann Surg* 1962;155:940-7.
22. Kuerer HM, Gwyn K, Ames FC, Theriault RL. Conservative surgery and chemotherapy for breast carcinoma during pregnancy. *Surgery* 2002;131:108-10.
23. Kuerer HM, Cunningham JD, Bleiweiss IJ. Conservative surgery for breast carcinoma associated with pregnancy. *Breast J* 1998;4:171.
24. Annane K, Bellocq JP, Brettes JP, Mathelin C. Infiltrative breast cancer during pregnancy and conservative surgery. *Fetal Diagn Ther* 2005;20:442.
25. Schwartz GF, Giuliano AE, Veronesi U; Consensus Conference Committee. Proceedings of the consensus conference on the role of sentinel lymph node biopsy in carcinoma of the breast, April 1922, 2001, Philadelphia, Pennsylvania. *Cancer* 2002;94:2542.
26. Filippakis GM, Zografos G. Contraindications of sentinel lymph node biopsy: Are there any really? *World J Surg Oncol* 2007;5:10.
27. Lyman GH, Giuliano AE, Somerfield MR, Benson AB 3rd, Bodurka DC, Burstein HJ, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. *J Clin Oncol* 2005;23:7703-20.
28. Gentilini O, Cremonesi M, Trifirò G, Ferrari M, Baio SM, Caracciolo M, et al. Safety of sentinel node biopsy in pregnant patients with breast cancer. *Ann Oncol* 2004;15:1348-51.
29. Khera SY, Kiluk JV, Hasson DM, Meade TL, Meyers MP, Dupont EL, et al. Pregnancy-associated breast cancer patients can safely undergo lymphatic mapping. *Breast J* 2008;14:250-4.
30. Amant F, Deckers S, Van Calsteren K, Loibl S, Halaska M, Brepoels L, et al. Breast cancer in pregnancy: Recommendations of an international consensus meeting. *Eur J Cancer* 2010;46:3158-68.
31. Giacalone PL, Laffargue F, Bénos P. Chemotherapy for breast carcinoma during pregnancy: A French national survey. *Cancer* 1999;86:2266-72.
32. Cardonick E, Gilmandyar D, Somer RA, Maternal Berry DL, Theriault RL, Holmes FA, et al. Management of breast cancer during pregnancy using a standardized protocol. *J Clin Oncol* 1999;17:855.
33. Ring AE, Smith IE, Jones A, Shannon C, Galani E, Ellis PA, et al. Chemotherapy for breast cancer during pregnancy: An 18-year experience from five London teaching hospitals. *J Clin Oncol* 2005;23:4192-7.
34. Ebert U, Löffler H, Kirch W. Cytotoxic therapy and pregnancy. *Pharmacol Ther* 1997;74:207-20.
35. Hahn KM, Johnson PH, Gordon N, Kuerer H, Middleton L, Ramirez M, et al. Treatment of pregnant breast cancer patients and outcomes of children exposed to chemotherapy *in utero*. *Cancer* 2006;107:1219-26.
36. Murray CL, Reichert JA, Anderson J, Twigg LB. Multimodal cancer therapy for breast cancer in the first trimester of pregnancy. A case report. *JAMA* 1984;252:2607-8.
37. Zemlicki D, Lishner M, Degendorfer P, Panzarella T, Sutcliffe SB, Koren G, et al. Fetal outcome after in utero exposure to cancer chemotherapy. *Arch Intern Med* 1992;152:573-6.
38. Turchi JJ, Villasis C. Anthracyclines in the treatment of malignancy in pregnancy. *Cancer* 1988;61:435-40.
39. Mir O, Berveiller P, Goffinet F, Treluyer JM, Serreau R, Goldwasser F, et al. Taxanes for breast cancer during pregnancy: A systematic review. *Ann Oncol* 2010;21:425-6.
40. Doll DC, Ringenberg QS, Yarbro JW. Antineoplastic agents and pregnancy. *Semin Oncol* 1989;16:337-46.

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