Review Article

SURGICAL MANAGEMENT OF BREAST CANCER DIAGNOSED DURING PREGNANCY: A NARRATIVE REVIEW

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ABSTRACT

Background: Breast cancer diagnosed during pregnancy (PrBC) represents a rare but increasingly prevalent clinical scenario, driven by delayed childbearing and increasing breast cancer incidence among premenopausal women. PrBC is characterized by distinct biological features – including a predominance of hormone receptor-negative, poorly differentiated, and lymph node-positive tumors – and poses unique therapeutic constraints. Surgery constitutes the cornerstone of locoregional management; however, evidence-based guidance remains limited to observational data and expert consensus, because randomized controlled trials are ethically precluded in this population.

Methods: A narrative review of the current literature was conducted, incorporating prospective cohort studies, systematic reviews, meta-analyses, and major international guidelines – including the 2023 ESMO Expert Consensus Statements, the 2025 ASCO Sentinel Lymph Node Biopsy Guideline Update, the 2025 RCOG Green-top Guideline No. 12 on Pregnancy and Breast Cancer, and the NCCN Clinical Practice Guidelines in Oncology for Breast Cancer (Version 2.2026) – to synthesize evidence on all aspects of surgical care for breast cancer diagnosed during gestation.

Results: Surgery can be performed safely at any stage of pregnancy. The optimal procedure – breast-conserving surgery (BCS) or mastectomy – is determined by tumor biology, gestational age, and the feasibility of adjuvant radiotherapy, which must be deferred until the postpartum period. Sentinel lymph node biopsy (SLNB) using technetium-99m is considered safe and endorsed by most current guidelines as the standard axillary staging approach in clinically node-negative PrBC, while blue dye agents such as isosulfan blue and methylene blue are discouraged. Venous thromboembolism (VTE) prophylaxis with low-molecular-weight heparin represents a critical yet historically underemphasized component of perioperative care, given the compounded thrombotic risk conferred by pregnancy, malignancy, and surgery.

Conclusion: Definitive surgical treatment of PrBC, delivered within a dedicated multidisciplinary framework, can achieve locoregional control comparable to that in non-pregnant patients.

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Therapeutic conservatism at the expense of oncological adequacy must be avoided. Prospective registry data and validation of novel axillary staging approaches – including targeted axillary dissection – in the PrBC setting remain important research priorities.

Keywords: breast cancer; breast-conserving surgery; mastectomy; pregnancy; PrBC; sentinel lymph node biopsy; targeted axillary dissection; venous thromboembolism.

Introduction

Breast cancer is the most frequently diagnosed invasive malignancy during pregnancy. [1] Breast cancer during pregnancy (PrBC) and postpartum breast cancer were grouped under the umbrella term "pregnancy-associated breast cancer" (PABC). Breast cancer diagnosed during pregnancy (PrBC) is defined as invasive or in-situ breast cancer identified at any gestational age, from conception to delivery. This definition intentionally excludes malignancies diagnosed in the postpartum or lactational periods, which, despite sharing epidemiological and clinical features with PrBC, carry distinct biological microenvironments, metastatic propensities, and therapeutic windows. The clinical and biological differentiation between PrBC and postpartum breast cancer has gained increasing recognition in the literature. [2,3]

The diagnosis and management of PrBC present significant challenges, including delayed recognition, the complexity of therapeutic decisions, ethically sensitive issues such as potential pregnancy termination, and the concurrent care of both mother and fetus. The interval between symptom onset and diagnosis is typically longer compared with non-pregnant controls, suggesting diagnostic delay.[4,5]diagnosis, prognosis, and effective treatment modalities of pregnancy-associated breast cancer (PABC Furthermore, physiological changes of the breast during pregnancy reduce the effectiveness of imaging modalities.[6] The ultimate goal is to provide oncologic management comparable to that of non-PABC breast cancer while ensuring maternal and fetal safety. Moreover, optimal management requires a multidisciplinary approach involving general surgery, medical oncology, obstetrics, radiation oncology, genetics, nursing, and psychosocial support.

The 2023 ESMO Expert Consensus Statements on PrBC management represent a key reference.[7] Crucially, 2025 has seen two landmark guideline publications that substantially advance the formal endorsement of surgical approaches previously supported only by observational evidence: the updated ASCO Sentinel Lymph Node Biopsy Guideline, which includes pregnant patients as a recognized special circumstance and states that clinicians may offer SLNB in this population using technetium-99m;[8] and the Royal College of Obstetricians and Gynecologists (RCOG) Green-top Guideline No.12 on Pregnancy and Breast Cancer, which designates Tc-99m-guided SLNB as the standard of care in clinically node-negative PrBC and recommends LMWH thromboprophylaxis given the risk conferred by pregnancy, cancer, and surgery.[9] We aimed to synthesize the available surgical evidence, incorporating all current guidelines, with attention to TAD, axillary surgery de-escalation, and VTE prophylaxis.

Epidemiology, Risk Factors, and Genetic

The reported incidence of PrBC ranges from 3 to 7,7 per 100.000 deliveries, and this figure is projected to rise as delayed childbearing becomes more prevalent.[10,11] Among women younger than 45 years, PABC accounts for 2.6-6.9% of breast cancer cases.[12]

A 2025 national claims-based analysis of 1,189 PABC patients in the United States reported that the proportion of breast cancer cases meeting the traditional PABC definition rose sig-

nificantly from 2.36% (2007-2009) to 3.94% (2019-2021; p<0.001). It must be noted that this dataset does not stratify intrapartum from postpartum cases, and therefore does not provide PrBC-specific incidence trends.[13]

Risk factors for PrBC are similar to those for breast cancer in general, including early menarche, late menopause, nulliparity, dietary factors, sedentary lifestyle, ethnicity, and family history.[6] The increasing incidence of PrBC is largely attributable to the trend of delayed childbearing into older ages, where breast cancer risk is inherently higher, combined with the overall rising incidence of breast cancer in premenopausal women.[7]

Hormonal surges during pregnancy (particularly estrogen, progesterone, and insulin-like growth factor-1) have been implicated in promoting tumor cell proliferation. Immunological tolerance mechanisms required for fetal survival share overlapping checkpoint pathways with tumor immune evasion, including progestogen-stimulated expression of shared onco-fetal immune checkpoints such as B7-H4.[14-16]

Genetic testing is recommended for patients diagnosed with breast cancer under the age of 40. Since PrBC often occurs in this age group, genetic testing should also be considered.[17] While the optimal timing of testing remains debated, performing it prenatally may aid treatment and prenatal genetic counseling. Most susceptibility genes are inherited in an autosomal dominant pattern, giving a 50% risk of transmission to offspring. Parents may request testing to determine their children's carrier status.[18] Although the association between BRCA1/2 mutations and PABC has not been fully established, these mutations are more frequent in younger patients and have been reported more commonly in PABC cohorts. Several studies also report a higher prevalence of family history in PABC compared with controls.[5,19]

Tamoxifen used for risk reduction is contraindicated during pregnancy and in women planning pregnancy in the near future.[20]

Presentation

The most frequent presenting symptom of PABC is a painless palpable mass. Other common findings include skin thickening, asymmetric breast enlargement, and nipple discharge, which can be mistaken for physiological changes of pregnancy. Accessory breast tissue may also enlarge during pregnancy and mimic a tumor.[21] Although the clinical presentation of breast cancer in pregnant and non-pregnant patients is broadly similar, any suspicious mass persisting for more than one week, unexplained nipple discharge, or erythema warrants further evaluation. Nonetheless, approximately 80% of palpable breast masses during pregnancy are benign.[9,22,23] The interval between symptom onset and diagnosis is longer in PrBC compared with non-pregnancy-related breast cancer, and is significantly associated with overall survival.[4,24]

Pathological Features

Invasive ductal carcinoma accounts for 78-88% of PrBC cases.[25] NCCN guidelines specify that PrBC tumors are more frequently poorly differentiated, more often ER/PR negative, and approximately 30% are HER2 positive.[26] The largest study included 311 pregnant and 865 non-pregnant patients, in which the proportion of ER-negative tumors was almost doubled in pregnant compared to non-pregnant patients (53.4% versus 25.5%). Tumors diagnosed during pregnancy were shown to have a high level of receptor activator of nuclear factor-kappa B ligand (RANKL).[27,28]

Diagnosis and Staging

Accurate preoperative staging directly determines the choice of operative procedure. Breast ultrasound (US) is the first-line imaging modality, achieving sensitivity and specificity of 80.1% and 88.4%, respectively, without ionizing radiation exposure.[29] Mammography is indicated when clinical or sonographic findings raise concern for malignancy; the resulting fetal radiation dose of <3 mGy is well below the threshold of concern. Contrary to prior practice, the American College of Radiology now advises against fetal shielding during mammography, as shielding produces scatter radiation and paradoxically increases rather than reduces fetal dose; without a shield, fetal exposure is negligible, whereas NCCN v2.2026 continues to recommend mammography with shielding.[26,30,31]

Non-contrast breast MRI incorporating diffusion-weighted imaging (DWI) sequences is recommended in selected cases by ESMO 2023, with sensitivities of 72.4-97% for nodal staging and the ability to detect multifocality and contralateral involvement not apparent on US, without the fetal risks associated with gadolinium contrast, which is contraindicated in pregnancy.7,29 Gadolinium agents are associated with stillbirth, neonatal death, and inflammatory skin disorders and must be avoided.[32]

Cumulative fetal radiation exposure exceeding 100 mGy must be avoided as it increases the risk of fetal death, growth restriction, microcephaly, and intellectual disability. Current imaging techniques generally remain below the 50 mGy threshold, which is not associated with increased anomalies or pregnancy loss. However, it is important to mention stochastic effects, which even low-dose exposure carries potential long-term risks of fetal carcinogenesis or genetic damage. Therefore, ionizing radiation should be used only when strictly indicated, at the lowest possible dose.[33]

Ultrasound-guided core needle biopsy is the preferred method for histological diagnosis in pregnancy due to the absence of ionizing radiation and ease of use. Stereotactic biopsy and MMG-guided wire localization can also be safely performed when ultrasound is insufficient. Core biopsy carries a slightly increased risk of bleeding and infection in pregnancy.[34,35]

For axillary staging, ESMO 2023 specifically highlights the role of US-guided core biopsy or fine-needle aspiration cytology (FNAC) of morphologically suspicious lymph nodes. With a specificity of 95.7-100% and a high positive predictive value, a positive FNAC result justifies proceeding directly to primary ALND or, in patients receiving NACT, planning TAD rather than SLNB, thereby avoiding two separate axillary procedures.[7]

For staging clinically node-negative T1-T2 tumors, abdominal ultrasound and chest X-ray with abdominal shielding, liver function and renal function assessment, and a CBC are preferred in pregnancy.[26,36] Non-contrast spinal MRI may be used to detect bone metastases.37 CT scans and PET/CT are generally avoided due to fetal radiation exposure.[38]

Pregnant women with breast cancer require close monitoring with serial ultrasounds and routine prenatal examinations. Continuous fetal assessment is essential and should be overseen by an obstetrician. If developmental anomalies are suspected, more advanced diagnostic evaluations, including amniocentesis, may be warranted.[36]

Surgical Management

Physiological changes during pregnancy- such as rapid PaO2 decline during brief apnea, progesterone- and prostaglandin-induced mucosal changes, and altered hemodynamics can contribute to intubation challenges. Intraoperatively, it is essential to maintain maternal blood

pressure within normal limits and avoid maternal hypoxemia or hypercapnia. Anesthetic agents currently in use have not been associated with teratogenicity when administered for durations of less than three hours.[39]

The modified radical mastectomy has been the most common procedure in PrBC.26 Surgical options for breast cancer in pregnancy include breast-conserving surgery (BCS), mastectomy, and oncoplastic techniques. The choice of procedure depends on multiple factors such as tumor stage, size, and gestational age. The 2025 Seminars in Perinatology practical guidelines confirm that surgery can be performed in any trimester, identifying the second trimester (12-24 weeks) as the optimal window owing to the completion of organogenesis, the lowest risk of spontaneous abortion, and the absence of late-gestational hemodynamic constraints.[6,40] Table 1 summarizes surgical approaches by trimester.

In the first trimester, termination of pregnancy should be discussed with the patient. The patient should be informed that termination of pregnancy has not been shown to improve prognosis; however, the decision belongs to the patient, and her choice should be supported without reservation.[9,26] Mastectomy has traditionally been preferred in the first trimester because adjuvant radiotherapy cannot be initiated during pregnancy without unacceptable fetal exposure, and the interval to delivery is too prolonged to permit safe RT deferral. However, NCCN v2.2026 explicitly states that BCS during the first trimester can be considered in patients who will require adjuvant chemotherapy and can have adjuvant RT delayed until after delivery – a meaningful shift from the prior dogma of routine mastectomy in the first trimester. Immediate reconstruction following mastectomy may be deferred until delivery to limit operation duration.[26,36]

The second trimester offers the most favorable conditions for breast surgery. Both BCS and mastectomy are viable options, and the decision follows the same oncological principles as in non-pregnant patients. Current evidence supports delaying radiotherapy until after delivery without compromise of locoregional control in carefully selected patients.[9,26]

In the third trimester, BCS is particularly well-suited, as adjuvant radiotherapy can begin in the early postpartum period without a clinically significant delay. For patients earlier in the third trimester with larger or more complex tumors, mastectomy remains an appropriate choice.[26] Chemotherapy administered within three weeks of delivery significantly increases the risk of maternal-neonatal myelosuppression. Chemotherapy should be completed at least three weeks before the anticipated delivery date.[26,41]

Axillary staging in PrBC is indispensable for prognostic stratification, planning systemic therapy, and determining the need for regional radiotherapy. In a landmark development, the 2025 ASCO Sentinel Lymph Node Biopsy Guideline Update formally includes pregnant patients as a recognized special circumstance for the first time, explicitly recommending that SLNB can be offered to pregnant patients with clinically node-negative breast cancer.8,42 However, an important discrepancy in guidelines must be acknowledged: the NCCN guideline takes a substantially more cautious position, stating that there are insufficient data to support recommendations for SLNB in pregnant patients and that decisions should be individualized. Furthermore, NCCN cites a review concluding that SLNB should not be offered to pregnant patients before 30 weeks of gestation.[26]

The use of technetium 99m (Tc99m) is considered safe. The ASBrC Oncolactation Resource Guide (2024) recommends same-day administration of the radiotracer to facilitate the use of the lowest possible dose and minimize maternal and fetal exposure.[31] Blue dye is avoided due to the risk of anaphylaxis and other allergic reactions, regardless of the guideline source.[43]

Indocyanine green (ICG), which does not cross the placenta, is emerging as a tracerless alternative but requires prospective validation in pregnancy.[44] To date, only a single case report has described the use of TAD in PrBC, in which a patient with HER2-positive cT2N3a breast cancer diagnosed at 22 weeks of gestation underwent nipple-sparing mastectomy with TAD of clipped nodes following neoadjuvant chemotherapy, achieving complete axillary response and avoiding ALND; prospective validation in the pregnant population is lacking.[45]

Venous thromboembolism (VTE) is potentially a fatal surgical complication in PrBC. A nationwide cohort study of 3,581,214 pregnancies demonstrated that cancer diagnosed during pregnancy is associated with a markedly elevated VTE risk: 75.2 per 10,000 pregnancies in women with cancer versus 10.7 per 10,000 in the no-cancer group, representing an approximately sevenfold increase in risk.[46] Thromboprophylaxis with low-molecular-weight Heparin should be administered.[9]

The safe and effective surgical management of PrBC requires an institutional infrastructure that extends well beyond the operating room. Surgery should occur only in centers with onsite obstetric and neonatal intensive care support, intraoperative fetal monitoring capability, and a dedicated multidisciplinary team meeting (MDT) structure specifically addressing pregnancy-related malignancies.[9]

Conclusion

Breast cancer during pregnancy is a condition that affects both the mother and the fetus and poses serious challenges in diagnosis and treatment management. The primordial principle underpinning this review is that the pregnant context cannot justify therapeutic conservatism at the expense of oncological adequacy. When PrBC is treated with full oncological intent, the pregnancy itself does not independently determine prognosis. Achieving this standard for every patient with PrBC requires institutional commitment, multidisciplinary collaboration, and continued investment in the prospective evidence base.

Declarations

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Table 1. Recommended surgical approaches by gestational trimester in PrBC.

Trimester	Preffered Surgical Approach	Key Considerations
First (≤12 weeks)	Mastectomy preferred; BCS can be considered if adjuvant chemotherapy is planned and RT can be delayed until postpartum(NCCN).	Organogenesis ongoing, RT cannot be given, risk of miscarriage from anesthesia; immediate reconstrution deferred.
Second (13-24 weeks)	BCS or mastectomy; SLNB (Tc99m); neoadjuvant chemotherapy may enable downstaging	Safest anesthetic window; BCS feasible when RT delay until postpartum is clinically acceptable; ALND if SN+; reconstruction deferred.
Third (≥25 weeks)	BCS feasible; mastectomy if BCS margins uncertain	Postpartum RT after delivery without delay; coordinate delivery timing with surgical team; avoid chemo after 35 weeks.

BCS: Breast conserving surgery, RT: radiotherapy, ALND: axillary lymph node dissection.