Surgery on breast cancer in pregnancy

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Abstract: Pregnancy-associated breast cancer (PABC) is defined as breast cancer develops either during or within 1 year after pregnancy, it is a rare disease arising in 1:3,000 to 1:10,000 pregnant women. Prognosis of this tumor is influenced by local or systemic treatment, which might be conditioned by gestational age and limited by the concern on potential adverse impact on fetus. The aim of this literature review is to analyze the main topics regarding surgical treatment of patients diagnosed with breast cancer in pregnancy: anesthesia and maternal-fetal monitoring, type of breast surgery, immediate breast reconstruction after radical surgery and management of the axilla. Some important topics remain controversial since the relative rarity of PABC precludes the feasibility of large studies leading to a lack of literature data. Multi-institutional collaboration is warranted to collect women with PABC, in order to best define surgical treatment in view of associated maternal and fetal risks.

Keywords: Pregnancy-associated breast cancer (PABC); breast cancer; pregnancy; breast surgery; axillary surgery

Introduction

Pregnancy-associated breast cancer (PABC) is defined as breast cancer develops either during or within 1 year after pregnancy. It's a rare disease arising in in 1:3,000 to 1:10,000 pregnant women and represents 0.2–3.8% of the total number of diagnosed breast cancers (1-3). This clinical situation expected to become even more common, since women tend to delay pregnancy at a later age, when breast cancer rates increase (4). Despite its low incidence, it is the most frequent pregnancy-associated cancer, before melanoma, cervical cancer and malignant hemopathies (5). Based on the European data, the average age of PABC onset is 33 years, and the average gestational age is 21 weeks (6).

Women with PABC often present more advanced tumours at diagnosis, because of increased breast density, making clinical examinations and mammography more difficult to interpret (7-9). This rare entity usually presents with high rates of hormone-receptor negativity and

HER2 overexpression (10,11) leading to a bad prognosis and poorer outcomes compared to other young women with breast cancer (6,7,12-17). In large recent Korean study, Bae reviewed and compared clinical-pathological features of 2,770 non-pregnant patients with breast cancer diagnosed under 40 years of age with 40 cases of PABC. The study confirmed lower expression of ER/PR, higher overexpression of HER2, fewer luminal A subtype, and more triple negative subtype cases compared to breast cancer in young patients. The series showed worse breast cancer-specific survival, especially luminal B subtype, compared to young non-pregnant cases (18).

Prognosis of this tumor is influenced by local or systemic treatment, which might be conditioned by gestational age and limited by the concern on potential adverse impact on fetus (4,7,19,20).

The aim of this literature review is to analyze the main topics regarding surgical treatment of patients diagnosed with PABC (anesthesia and maternal-fetal monitoring, type

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breast surgery, immediate reconstruction after mastectomy and management of the axilla) in order to shed light on this concerning topic. The focus is on women with breast cancer diagnosed and treated during pregnancy until delivery since the puerperium does not cause limitation on any kind of surgical treatment.

Anesthesia and fetal management during surgery in pregnancy women

Pregnant women undergoing non-obstetric surgery are almost 2% of all pregnancies (21). Because of the lack of large-scale randomized clinical trials in this population, there are no specific recommendations on anesthesia and fetal monitoring during surgery (22). The American College of Obstetricians and Gynecologists (ACOG), in 2017 review its guidelines, stated that: "*A pregnant woman should never be denied medically necessary surgery or have that surgery delayed regardless of trimester because this can adversely affect the pregnant woman and her fetus.*" (22).

Both fetal and mother conditions should be monitoring during pregnancy surgery, according to physiological changes, adaptations and possible drugs teratogenicity.

Maternal management

One of the most important changes in a pregnant woman affects respiratory system, with a 20% increase in oxygen consumption and a 20% decrease in pulmonary functional residual capacity both of which contribute to the rapid decrease in maternal PaO_2 that is observed even during brief apnoea (23). Airway changes also interest a reduction in the cross-sectional area of the pharynx, while minimal and mean tracheal cross-sectional areas remained unaffected (21). A review published by Kinsella *et al.* in 2015 describes an obstetric failed intubation incidence of 2.6 (95% CI: 2.0 to 3.2) per 1,000 general anesthetics (24). Increased levels of progesterone and prostaglandins result in maternal mucosal capillary engorgement with a more friable airway (24), while hemodynamic changes during pregnancy include a 40–50% increase in blood volume and cardiac output and a 20% reduction in hematocrit due to dilution (23). These changes could result in a bloody, difficult-to-visualize glottis, particularly in the context of instrumentation (25).

Although gastric emptying has been shown to be normal during pregnancy, the risk of aspiration is increased because of reduced pressure at the level of the lower esophageal sphincter (23). Acid aspiration prophylaxis is recommended

to reduce gastric content and increase gastric pH, to reduce morbidity and mortality when accidental aspiration occurs (26). Prophylaxis of choice should be an H2-receptor antagonist and non-particulate antacid and should be employed after 16 weeks of pregnancy (25).

Venous thromboembolic (VTE) disease is a major risk in pregnancy and has been shown to complicate 0.5 to 2.2 of every 1,000 pregnancies, especially in postpartum period (25). Prophylaxis with low molecular weight heparins should be used.

During surgery, maintenance of normal maternal blood pressure is of great importance because of the relative passive dependence of the uteroplacental circulation (27).

Fetal management

Regarding fetal monitoring, pre- and post-operatively monitoring is indicated, while there is no agreement about intraoperative fetal heart rate monitoring (iFHRM). SAGE (Society of American Gastrointestinal Endoscopic Surgeons) guidelines, published in 2017, stated that "fetal heart monitoring of a fetus considered viable should occur preoperatively and postoperatively in the setting of urgent abdominal surgery during pregnancy" (28) with the current lower limit of viability fixed between 22 weeks and 24 weeks. ACOG as well expresses the importance of post-operatively monitoring, by simultaneous electronic fetal heart rate and contraction monitoring to assess fetal well-being and the absence of contractions, when the fetus is considered viable (22).

Regarding iFHRM, a recent review published by Po' *et al.* concluded that in pregnancy women ≥22 weeks, non-reassuring fetal heart patterns were limited to fetal tachycardia due to maternal fever (29).

Finally, no teratogenic effects have been associated to current anesthetic agents, when they used at standard concentrations, either no evidence that in utero human exposure to anesthetic or sedative drugs has any effect on the developing fetal brain (22). Furthermore, Food and Drugs Administration (FDA) raise concern about inhalational agents and intravenous propofol and midazolam use, the common agents administered during pregnancy for general anesthesia and sedation, for potential risks to fetal development, minimizing fetal exposure to these agents is important and advisable (30). Also, maternal hypoxemia/ hypercapnia and maternal hypotension, that could lead to fetal asphyxia, are possibly related to teratogenic effects (25). Prolonged or serious maternal hypoxemia causes utero-

placental vasoconstriction and reduce the utero-placental perfusion, resulting in fetal hypoxemia, acidosis and, finally, fetal death (26). Similarly, maternal hypercapnia should be avoided, related to uterine artery vasoconstriction and reduced uterine blood flow (26).

In conclusion, anesthesia during pregnancy for non-obstetric surgery is possible but it should be reserved to necessary surgery. Anesthetic drugs are not apparently related to fetal neurotoxicity, especially if exposure is limited (<3 hours) (22). No agreement about iFHRM, but many authors recommended it (27,29) to evaluate the need of an urgent cesarean delivery.

Breast surgery

Mastectomy versus breast conserving therapy (BCT)

Breast surgery is considered safe in all trimesters of pregnancy without any risk to the fetus. Mastectomy was the standard surgical approach in PABC patients during past decades (4,16), although the presence of the pregnancy nowadays, does not justify a radical surgery itself. The optimal surgical approach is not well established, but recent analysis suggests the non-superiority of mastectomy versus other type of surgery in survival outcome, adjusting data for tumour stage (31,32). To be taken into account is the anatomical difference of pregnant breast from the nonpregnant one's highlights by Beriwal in his paper, making BCT in pregnancy more complex due to the increased of the anastomosing network of ducts and vessels (33).

In a series conducted by Gentilini *et al*, all first trimester-pregnancy patients who had diagnosis of breast cancer terminated the pregnancy, although alternatives were discussed, due to the concern about the possible different schedule of treatments. Conservative surgery was performed in 15 of 21 patients during pregnancy with no local reappearance after 24 months of follow-up (34).

A preliminary clinical report by Kuerer *et al*. reported on the outcomes of four pregnant patients treated with neoadjuvant chemotherapy followed by BCT finding no local recurrences after a 44 months follow-up. Nevertheless, the small sample, the authors found no contraindication in offering conservative surgery in operable breast cancer pregnant women (35).

In contrast, a study with a wide sample of patients designed to compare locoregional recurrence (LRR) in PABC treated with different surgical approach, found a 5 years actuarial rates of LRR of 37% in BCT group and 10% in mastectomy group (P=0.04). This difference was not significant on multivariate analysis in which anyhow no tumour or patients' characteristics were associated with a significant increased risk of relapse (33).

Modified radical mastectomy is not mandatory for PABC in the paper by Rodriguez *et al*. In the multivariable analysis, controlling for tumour and patients' characteristics, the risk of death is equivalent for women treated with radical surgery compared with other surgical procedures (32).

The diagnosis of breast cancer during the first trimester, in patients who wish not to terminate the pregnancy, represents the most difficult scenario due to the few treatment options available. According to the National Comprehensive Cancer Network (NCCN) guidelines (36), and Adult Treatment Editorial Board (PDQ) (37) breast conserving surgery is feasible, if radiotherapy can be delayed to postpartum period, because it is contraindicated due to the well-known deleterious effects of ionizing radiation on the developing fetus. The last version of AIOM (Associazione Italiana di Oncologia Medica) suggest that BCT can be performed in second and third trimester and radiotherapy postponed after delivery, without significant impact on recurrence rate or survival compared to radical surgery. During first trimester BCT may cause excessive delay in postoperative radiotherapy, so mastectomy is preferable or neoadjuvant chemotherapy should be offered (38).

There are some recent series about the recurrence rate related to delayed radiotherapy after breast conserving treatment in non-pregnant breast cancer patients. A retrospective study on 747 women affected by breast cancer who underwent BCT and radiotherapy, reported a significant decrease in disease free survival with HR =2.29 (95% CI: 1.16–4.54) in delaying adjuvant radiotherapy more than 65 days (39). Flores-Balcázar in 2018 performed a retrospective study about the relationship between waiting time for radiotherapy and the relapse-free survival/disease-specific survival in 1,000 patients diagnosed with breast cancer. The authors divided all the patients into five groups according to the timing of radiotherapy and found a decrease in disease-specific survival in the subgroup of patients with locally advanced breast cancer (TNM stages IIIA–IIIB) (40) receiving radiotherapy after 60 days or more after surgery (P>0.001), whilst no difference was found in women with early breast cancer (41). Toesca *et al*. concluded to consider all the alternative treatments in case of surgery performed at a very early gestational age for the risk of recurrence linked to long delay radiotherapy (4).

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Mastectomy and reconstruction surgery

Mastectomy is one of the viable surgical options to manage breast cancer during pregnancy. After adjusting data for tumour stage, hormone receptor status and patients' age, there is no survival advantage for pregnant patients undergoing radical surgery versus BCT (31). A body of evidence in literature demonstrates that breast cancer during pregnancy is diagnosed in more advanced stage compared to breast cancer in nonpregnant women (17,42). The reason for this data can be deduced from many elements: on the one hand, diagnosis at an early stage is more difficult due to physiological changes during gestation, e.g, growing of mammary glands and milk ducts; at the other hand young women, pregnant or non-pregnant, have higher breast density and are not routinely screened by mammography (42-44).

Breast reconstruction after mastectomy is a critical element in breast cancer treatment, mostly at a young age (45). Immediate breast reconstruction reduces the emotional impact of injury, affords better aesthetic result and improved woman and surgeon satisfaction (46,47).

In 2010, a European Consensus on the management of PABC not recommend immediate breast reconstruction for the lack of evidence of literature and suggest reconstruction after delivery (48). But the consensus defined surgery of PABC as safe anytime throughout any trimesters of pregnancy given the absence of considerable maternal and/ or fetal complications (43).

Lohsiriwat *et al.* retrospectively analysed all PABC patients who were subjected to mastectomy and immediate breast reconstruction at the European Institute of Oncology between 2002 and 2012. On 78 women with PABC subjected to a surgical procedure during pregnancy, 22 patients had mastectomy; of whom 13 were subjected to immediate breast reconstruction. Twelve of these women had a two-stage procedure with tissue expander insertion. Median gestational age was 16 weeks. No major surgical or pregnancy complications, either major congenital malformation were reported. Only one patient had a miscarriage. The authors concluded that tissue expander seems to guarantee a quick surgery time and does not appear to be related with significant morbidity to the fetus and the woman (43).

Caragacianu *et al.* performed a retrospective study of women who underwent immediate reconstruction after mastectomy within a PABC cohort. On 82 pregnant patients with PABC, 29 of them (35%) had mastectomy:

10 (34%) had immediate reconstruction with tissue expander placement. Mean gestational age at surgery was 16.2 weeks. Mean surgery duration was higher in reconstruction group (198 versus 157 minutes). No fetal or major obstetrical complications were documented and all infants are born on term, or close to. All patients transitioned to permanent implant. In summary, the authors state that immediate reconstruction in PABC was not correlated to harmful obstetrical consequences, and all babies had adequate indicators at birth (44).

Despite the low relevance of the studies conducted and the low levels of evidence, in patients with PABC presenting with operable breast cancer, immediate reconstruction appears to be a safe option after a meticulous case selection. Multidisciplinary strategy is the key in treatment of these women.

Axilla staging

State of art

For almost a century, axillary lymph node dissection (ALND) has been the standard technique in the axillary staging and treatment, but during the last years, axillary surgery has undergone significant changes towards an increasingly conservative approach, based on the introduction of the sentinel lymph node (SLN) biopsy in the 1990s, limiting lymphedema and other debilitating morbidities (2-4). This technique has quickly become the gold standard for the assessment of the axilla in early breast cancer patients with clinically and ultrasound negative axillary lymph nodes, thus limiting ALND to patients with metastatic sentinel nodes (45-47).

Between 2011 and 2013, two studies have significantly changed the management of the axilla: the ACOSOG Z0011 trial and the IBCSG 23-01 trial (48,49). The ACOSOG Z0011 trial demonstrated that ALND can be omitted without affecting both overall survival and disease-free survival, in selected patients with early breast cancer (cT1–T2), clinically and ultrasound negative axilla (cN0) and 1 or 2 micro- or macro-metastatic sentinel nodes, receiving breast conserving surgery followed by total breast irradiation. Two years later, the IBCSG 23-01 trial confirmed these findings in patients with the same clinical T and N characteristics and 1 or 2 micro-metastatic sentinel nodes, undergoing either breast conserving surgery followed by total breast irradiation or mastectomy not followed by radiotherapy. Unfortunately, the mastectomy

group only accounted for 9% of the cohort; therefore, to date, the omission of ALND in the patients undergoing mastectomy can't be accepted as a standard procedure.

The results of the EORTC group study (AMAROS) define whether axillary radiation therapy provides regional control with fewer side effects than ALND (50) and concluded that axillary RT is an adequate alternative to axillary dissection in patients with positive SLNB, with a lower rate of lymphoedema. Unfortunately, the study has important limitations: the small sample and the short follow up, that do not allow drawing therapeutic directions.

According to NCCN, the ALND level I–II indication is limited to patients with a positive biopsy. Traditional level I–II axillary dissection requires at least 10 lymph nodes to be removed to allow pathological evaluation to accurately stage the axilla (51,52). Axillary dissection should be extended to level III in case of macroscopic disease clinically detected at level II or III.

If axillary lymph nodes are clinically negative at diagnosis or if fine need aspiration/core biopsy of suspected lymph nodes are negative, NCCN recommends SLNB (36).

Based on the results of the ACOSOG Z0011 study, for patients with T1 and T2 tumours with 1 or 2 sentinel lymph nodes positive, treated with BCT without systemic pre-surgical treatment, candidate to whole breast RT, NCCN recommends nop to perform ALND (36). If any of these criteria are not met, NCCN recommends axillary dissection.

In the 2019 version of the NCCN guidelines, based on the results of the IBCSG 23-01 study, NCCN does not recommend ALND for patients with micrometastasis in sentinel node. If SLN is not identified, NCCN recommends ALND for axillary staging. For patients undergoing mastectomy with clinically negative axilla but a positivity of SLN for metastasis, NCCN establishes that axillary radiotherapy may replace axillary dissection for regional disease control.

SLN in pregnancy

The axillary staging technique is not yet validated as a routine procedure for pregnant women in international guidelines (53,54) for lack of literature data. The indication of sentinel node biopsy in pregnant women affected by breast cancer, concerns about 28% of patients due to the low incidence of early stages of breast cancer in pregnancy (55).

In addition, the reliability of this technique is limited by hormonal changes involving breast during pregnancy and not clear consequences on lymphatic drainage pathways, and thus on tracer migration, which could result in a higher rate of false negatives. The use of radioactive tracers in pregnant women also raises questions about fetal irradiation. The guidelines of the American Society of Clinical Oncology on SLNB in the early stages of breast cancer published in 2005 do not validate the use of the SLN technique in pregnant patients, due to the lack of literature data available (56). The statement was confirmed in 2014 (57) and 2017 (53) due to the same limitations, with low strength of recommendation.

The 2018 AIOM guidelines on the management of PABC supporting the feasibility of SLNB with radionuclides according to the results of studies demonstrating that the dose absorbed by the fetus is lower than the risk-dose of 0.1–0.2 Gy (38).

In 2013, the ESMO guidelines on tumour management in pregnant women, also underlined the limited data in the literature, but do not contraindicate the SLN procedure in this subgroup of patients in oncological centres which long-standing experience (54).

NCCN guideline 2019 contraindicates the procedure of SLN in pregnant women: the feasibility should be decided case-by-case and is not recommended under 30 weeks of gestation. NCCN stresses the lack of data on radioactive tracers with regard to fetal irradiation and advises against the use of isosulfan blue or methylene blue dye for SLN procedure (36).

A recent complete review (5) analyzed all issues related to SLN and pregnancy. Balaya *et al*, found five series published in the literature evaluating breast cancer in pregnant women, including 3 (58), 10 (59), 12 (60), 25 (61), and 145 patients (including 12 cases already published) respectively (62). In 21 patients out of 183 (11.5%) was used the combined technique (assumption of colorimetric and isotopic technique). The colorimetric technique alone was used in 23 cases (12.6%) and the isotopic technique with technetium 99 m (Tc99m) in 116 cases (63.4%). Fluorescin is associated with isotopic technique with Tc99m in only one case. In the large series of Han *et al.* SLN was identified in 99% of cases using radiolabelled colloids and therefore the colorimetric technique appeared unnecessary (62). Balaya *et al.* concluded that axillary dissection was not necessary for these patients who were exposed to potential side effects of this procedure (lymphoedema, nerve lesions, shoulder dysfunction) (5,63).

The colorimetric technique is based on the periareolar or intratumoral injection of blue patent. No animal studies have been conducted to test the safety of this tincture on

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pregnant women (64). In the 1980s methylene blue was used for the early diagnosis of membrane rupture with a single intramniotic injection of 2.5 mg methylene blue, but adverse events were reported as fetal bowel atresia, phototoxicity and respiratory distress (65). The pharmacokinetics of methylene blue was studied in 10 non-pregnant women and after a subareolar injection of 5 mg of methylene blue and the maximum estimated dose to the fetus was 0.25 mg, corresponding to 5% of the administered dose (66). In a series of 10 pregnant women in which SLNB for breast cancer was performed, Khera *et al.* used blue patent in 8 patients (6 with Tc99m and 2 with blue only) without significant complications and the SLN was identified in all cases (59). Similarly, in a series of 25 patients, Gropper *et al.* used exclusively methylene blue in 7 patients without reporting side effects, identifying SLN in all 7 cases (61). However, there is a theoretical 2% risk of anaphylactic shock related to the injection of a blue (67), therefore this technique is not recommended by international guideline.

Regarding the use of radioisotopes in pregnant women, the potential risk of radiation exposure of the fetus is the main reason to avoid SLN biopsy in pregnancy, although the established threshold dose of fetal irradiation is 50 mSv (68). As a reminder, one millegray (mGy) dose corresponds to one milliSievert (mSv) effective dose of Tc99m. In SLN technique, the first dosimetry study was conducted in non-pregnant women. In a series of 26 non-pregnant women with breast cancer, Gentilini *et al*, reported that a peritumoral injection of 0.2 mL of Tc99m coupled with nanocolloids, corresponded to an average activity of 12.1 MFq. The scintigraphic images showed the radiomarcant only at the injection site and at the same level in the SLN. The radioactivity measured in the urine, 16 hours after injection, was 2% lower than the injected dose and the measured radioactivity of the blood after 4 and 6 hours the injection was 1% lower than the injected dose (69). Keleher *et al.* calculated the theoretical dose absorbed by the fetus in 2 doses of Tc99 m at 18.5 MBq and 92.5 MBq. According to 3 different models of bio-distribution and pharmacokinetic, they demonstrated that the maximum dose theoretically absorbed by the fetus was 4.3 mGy. This dose is much more based than recommended thresholds and it is equivalent to an injection of Tc99m with an activity of 92.5 MBq, corresponding to 8 times higher the dose usually used in the SLN procedure (70). In a retrospective data, obtained from 1,021 non-pregnant patients, who received a Tc99m injection of 3.7 MBq on the day of surgery or 18.5 MBq on the day before surgery, Pandit-Taskar *et al.*

demonstrated that the maximum dose of radioactivity that a fetus at 9 months of pregnancy is theoretically exposed was 0.014 mGy for an injection of 18.5 MBq. The estimated effective dose was 0.245 mSv in women of childbearing age, much lower than the 50 mSv threshold set by the National Council on Radiation Protection for pregnant women (68,71). These data were confirmed in a prospective series of 14 non-pregnant women who received an injection of Tc99m of 39±20 Mbq on average and for whom the absorbed dose at uterine level was estimated to be around 0.11 mGy (72).

In addition, as evidenced by lymphoscintigraphy images, the injected dose of Tc99m is localized in the injection site and in the SLN, which are both removed during surgery, making the fetal risk of potential residual activity negligible. Fetal prognosis is rather related to the duration of general anaesthesia, which is shorter in the case of SLNB procedure than in the case of ALND. The identification of SLN with the fluorescence technique using green indocyanine has not yet been evaluated in pregnant women. However, the incidence of severe anaphylactic reaction is very low (0.05%) (73), and no fetal consequences and teratogenicity have been reported in pregnant women in the past 50 years (74). In PABC, Tc99m-associated fluorescine was used in only one uncomplicated patient (5). The SLN technique does not seem to have an impact on fetus and obstetrical story. Balaya's review data from 182 single pregnancies and one twin pregnancy: two patients (1.1%) had a spontaneous abortion (correlation with SLNB procedure unknown), six patients requested termination of pregnancy (3.3%), of which one for a prenatal diagnosis of trisomy 21. On 165 patients, only 3 babies were premature, all 166 children were healthy (including 2 twins). The study not showed obstetrical complications occurred after the SLN procedure or fetal malformation (reported 2 not related cases) (5).

Studies that attest to the risk induced by using radioisotopes in the SNL procedure in pregnant women with breast cancer seem quite reassuring. Preliminary studies showed acceptable oncological results, without compromising the fetal and obstetrical prognosis. Studies involving large cohorts are needed to confirm these data and to recommend this technique in pregnant women. SLNB procedure should not be indicated to pregnant patients under 30 weeks of gestation (period for fetal organogenesis) (36). However, considering the benefit to the patient and the low risk on fetal and obstetrical outcomes, it seems reasonable to discuss the SLN indication case-by-case in multidisciplinary teams.

Conclusions

Breast cancer diagnosed during pregnancy is a rare disease and requires multi disciplinal collaboration and careful counseling with the patient. The surgical treatment should be based on gestational age at diagnosis, the stage of the disease and possible maternal and fetal risk. Both fetal and mother conditions should be monitored during pregnancy surgery. According to physiological pregnancy changes, more attention should be paid during intubation, prophylaxis with gastric anti-acids (H2 receptors antagonist) and low molecular weight heparins should be performed and appropriate level of blood pressure should be maintained to preserve the uterus-placental circulation. Some Authors recommended pre- and post-operatively fetal monitoring by simultaneous electronic fetal heart-rate in order to assess fetal well-being as well as the absence of uterine contractions. Anesthetic drugs are not apparently related to fetal neurotoxicity or teratogenic effect, especially if exposure is limited (<3 hours). Regarding surgical options, breast surgery is considered safe in all trimesters of pregnancy without any risk to the fetus and the most recent recommendations allow BCT in second and third trimester with radiotherapy treatment delayed after delivery; the first trimester represents the most difficult scenario due to the few treatment options available linked to a long delay radiotherapy. International guidelines do not recommend immediate breast reconstruction after radical surgery for the lack of evidence and suggest reconstruction after delivery, whilst some recent studies demonstrated that immediate reconstruction with expander appears to be a safe option in selected cases. Sentinel lymph node biopsy to stage the axilla remain a controversial issue, some guidelines propose this technique despite the limited data of literature, since preliminary studies showed acceptable oncological results, without compromising the fetal and obstetrical prognosis.

The relative rarity of PABC precludes the feasibility of large studies. There is a need of multi-institutional collaboration and a central registry in order to gather and track a larger number of women with PABC. This will lead to a better surgical management of the disease and its associated maternal and fetal risks.

Acknowledgments

Footnote

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