



# Immediate or delayed breast reconstruction: the aspects of timing, a narrative review

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**Objective:** The objective of this study is to discuss the timing of immediate and delayed breast reconstruction.

**Background:** The evolution of conservative mastectomy surgical techniques and the introduction of acellular dermal matrix (ADM) have paved the road for the increased popularity of immediate reconstruction, and this also includes use of autologous tissue. Immediate reconstruction holds several benefits, the most important being superior aesthetic outcomes and improved levels of psychosocial wellbeing post-mastectomy. Both immediate and delayed breast reconstruction has been found to be oncologically safe, although high-quality studies are still lacking. Potential delay in adjuvant treatment is a significant concern amongst medical and surgical oncologists, and in addition, a few studies have examined complications in cancer surgery and found negative association with the oncological outcome.

**Methods:** Narrative literature review and presentation of the authors practice.

**Conclusions:** Careful patient selection, especially in case of invasive breast cancer is very important. Absolute contraindications for immediate reconstruction include a diagnosis of locally advanced breast cancer or inflammatory breast cancer or active infection in the breast area. Relative contraindications to be carefully considered to keep the risk of complications at a minimum and thus the risk of delaying the adjuvant therapy is: smoking, high BMI, and comorbidities and need of postoperative radiation therapy. Delayed reconstruction should be considered for patients with pressing medical comorbidities, obesity, smoking, inflammatory breast cancer, and for patients distressed regarding their breast cancer diagnosis who are not ready to make treatment decisions. The authors prefer immediate reconstruction if feasible, but it should be remembered that delayed breast reconstruction has been found not to compromise patient-reported outcomes in the long-term. Therefore, the timing and technique of reconstruction should be decided on a case-by-case basis after a thorough discussion with the patient and preferably also in multidisciplinary meetings.

**Keywords:** Breast reconstruction; relative contraindications for breast reconstruction; complications in immediate breast reconstruction; timing of breast reconstruction

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## Introduction

Aside from non-melanoma skin cancers, breast cancer is the most common malignancy affecting women worldwide (1). The last few decades have seen a growth in the number of both immediate and delayed breast reconstruction following mastectomy as breast reconstruction becomes more sought after (2-4). In the United States, the Women's Health and Cancer Rights Act of 1998 compelled payers to provide benefits for mastectomy-related services, including all reconstruction stages and procedures for symmetry (2). These procedures are also covered in tax-funded healthcare systems.

Bilateral mastectomies have become increasingly common, as a risk reduction procedure, often asked by patients (2). As subsequent breast reconstructions also become more popular, choosing when and how to reconstruct the breasts is exceedingly more nuanced. The present study reviews considerations of the aspects of timing when planning breast reconstruction.

Conservative mastectomy, with preservation of the entire skin envelope or nipple sparing procedure, has gained acceptance in recent years, given evidence of comparable prognosis compared to total mastectomy (5-7). Skin preservation allows for optimized reconstructive outcomes by recreating or enhancing breast volume, lower pole contour, symmetry, and appearance (8). By preserving the breast skin envelope, the skin-sparing mastectomy allows for immediate reconstruction closely matched to the preoperative breast's size and shape (9). We present the following article in accordance with the Narrative Review reporting checklist (available at <https://abs.amegroups.com/article/view/10.21037/abs-21-44/rc>).

## Reconstruction options

Breast reconstruction options can be either implant-based or autologous. Implant-based breast reconstruction (IBBR) accounts for approximately 80% of breast reconstructions in the United States, most of which are performed immediately following mastectomy (3,4). IBBR can be completed in either one or two stages following mastectomy. The advent of reconstruction with acellular dermal matrix (ADM) allowed the surgeon to create a breast in one stage immediately. An ideal candidate for single-stage, or direct-to-implant (DTI), reconstruction is a patient undergoing skin-sparing, nipple-sparing mastectomy with small to medium breast size, grade 1 or 2 ptosis, and favorable skin quality (10). Two-stage reconstruction is achieved with tissue

expanders that are exchanged for implants at a later date. In the setting of immediate reconstruction with questionable perfusion to the mastectomy skin flaps, placement of a tissue expander that is partially filled may protect the skin flaps from tension (11). Surgeons began ADM utilization in 2001 to provide coverage for either implants or tissue expanders in breast reconstruction (12). The original description was a submuscular placement of the implant with lower pole ADM supporting the device and obviating the need for tissue expansion. ADM was used to extend the submuscular plane, support the implant in an anatomic position, and define the inferior and lateral breast folds (10).

Autologous breast reconstruction can be achieved with abdominal tissue- pedicled transverse rectus abdominis myocutaneous (TRAM) flap, or most commonly today with perforator microsurgical tissue transfer (free TRAM flap, muscle-sparing TRAM flap, deep inferior epigastric perforator (DIEP) flap, superficial inferior epigastric artery (SIEA) flap- and with non-abdominal tissue- gluteal flap, transverse upper gracilis flap (TUG), PAP (profunda artery perforator flap) or DUG (diagonal upper gracilis flap) varieties, or lumbar artery perforator flap. Additionally, autologous reconstruction can be achieved with a combined autologous and implant reconstruction used in conjunction with any of the above or flaps based on the thoracodorsal artery (the Latissimus Dorsi musculo-cutaneous flap or variants of this) or a perforator from this (the TAP flap). The indications, operative techniques, and patient selection factors relating to these flaps are beyond the present study's scope and are discussed extensively in the literature (11,13).

## Timing considerations and relative contraindications

Historically, less than 25 percent of patients in the U.S. underwent immediate reconstruction (3). The evolution of conservative mastectomy surgical techniques and the introduction of ADM have paved the road for the increased popularity of immediate reconstruction (2,14). In women undergoing mastectomy for early-stage breast cancer, rates of breast reconstruction increased from 11.6% in 1998 to 36.4% in 2011 in the U.S. (15). In Denmark, currently about 20 percent of mastectomized women with invasive breast cancer undergo reconstruction, with a small majority being immediate reconstruction, while most women who undergo mastectomy for in situ cancer are reconstructed immediately (personal message, Hölmich).

Advantages of immediate reconstruction include superior

aesthetic outcomes, improved levels of psychosocial wellbeing post-mastectomy at least short-term, shorter surgical time, fewer surgical procedures, lower costs, and faster social reintegration when compared to delayed reconstruction (16-25). Immediate reconstruction demands better skin flaps than a simple mastectomy followed by a delayed reconstruction and may increase the risk of complications (see below). The main advantages of delayed reconstruction are that potential complications do not compromise adjuvant treatment. In addition, if postmastectomy radiation is needed, it does not compromise the reconstruction site, and it gives patients more time to consider reconstructive options. Disadvantages of delayed breast reconstruction also include more scarring and somewhat less favorable cosmetic outcomes, as well as additional surgical procedures and probably higher cost (19,21,23).

A large multicenter U.S. study found that delayed reconstruction (of all kinds) were associated with a substantial reduction in complications compared with immediate reconstructions (the risk of major complications was halved). Women undergoing delayed reconstruction had significantly worse pre-reconstruction quality of life scores than women with immediate reconstruction; however, 2-year post-reconstruction scores were similar in the two groups (22). Another large register-based U.S. study found a significantly higher incidence of surgical site infection after immediate (8.9%) compared with delayed (6.0%) and secondary (3.3%) implant reconstructions (meaning any secondary procedure), with similar results for noninfectious wound complications. In contrast, the incidence of surgical site infection was similar after immediate (9.8%), delayed (13.9%), and secondary (11.6%) autologous reconstructions. The study concludes that the risks for complications should be carefully balanced with the psychosocial and technical benefits of immediate reconstruction. Selected high-risk patients may benefit from consideration of delayed rather than immediate implant reconstruction to decrease breast complications after mastectomy (26).

Both immediate and delayed breast reconstruction has been found to be oncologically safe, although high-quality studies are still lacking. A meta-analysis including 31 studies (mostly retrospective single-center studies) with almost 140,000 patients compared patients undergoing mastectomy +/- immediate breast reconstruction (27). Most included studies had moderate quality, and selection bias was present; women with reconstruction were younger and had less lymph node metastases than those who only underwent mastectomy, but no difference in tumor size. The pooled

data showed a higher occurrence of post-operative infection among women undergoing reconstruction (risk ratio 1.51, 95% CI: 1.22–1.87;  $P=0.0001$ ); however, no significant difference in total survival or disease-free survival.

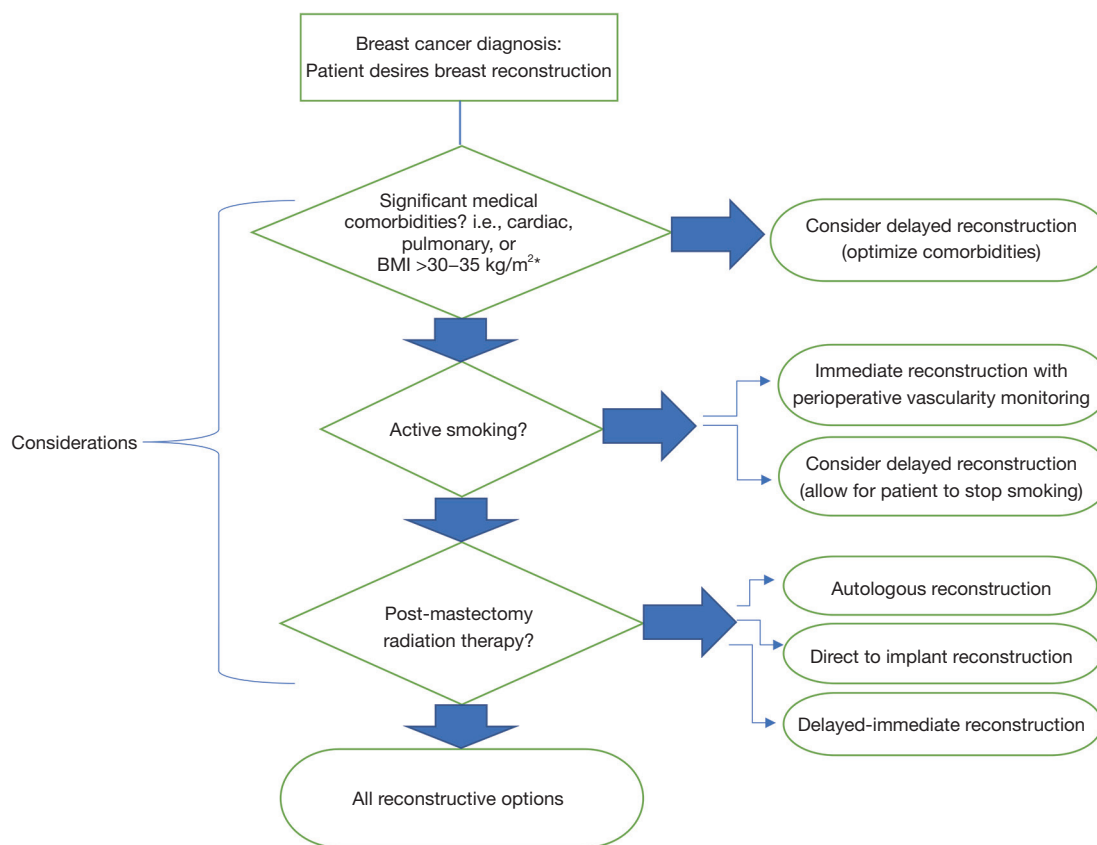
Complications in cancer surgery have been investigated in a few studies and can negatively influence the oncological outcome. The mechanisms involved are unknown but speculated to involve surgical stress, increased inflammatory response with synthesis of growth factors stimulating cancer cells, lowered immune response, and delay of adjuvant treatment (28). These associations have also been found for bowel, lung, and breast cancer surgery (29-32). Of note, two studies evaluated complications in breast reconstruction (33,34). Both studies found more local and distant recurrences in patients with complications compared with those without complications. This is an emerging field; none of the cited studies are large, and the evidence level at best moderate. However, the results call for caution and proper patient selection, in addition to further research protocols.

Potential delay in adjuvant treatment is a significant concern amongst medical and surgical oncologists. A systematic review of 14 studies, including over 5,000 women, of whom about 2,000 had immediate breast reconstruction, evaluated the timing of the adjuvant treatment and found overall that there was no meaningful delay in adjuvant therapy in the reconstruction group (35).

A multicenter prospective cohort study on about 2,500 consecutive patients undergoing mastectomy +/- breast reconstruction (implant-based or autologous) found significantly more complications associated with breast reconstruction than mastectomy alone. However, no overall difference in time to adjuvant therapy was detected. Those with major complications in both groups had their adjuvant therapy significantly later (36). Care should be taken especially in younger women with triple-negative breast cancer, as timely adjuvant therapy has been found to be especially important in this patient group (37,38).

The above allows for the conclusion that immediate breast reconstruction is oncologically safe if adequate precautions are taken; however, care must be taken to avoid complications, and thorough patient selection is therefore critical. If women with risk factors undergo immediate reconstruction, more complications will occur and delay in adjuvant therapy can be expected. Neoadjuvant treatment preoperatively should always be considered.

Despite the numerous benefits, patient selection is therefore critical in evaluating the timing of reconstruction



\*In Denmark, the cutoff is BMI above 30 kg/m<sup>2</sup>; higher in the U.S. presumably due to cultural differences and demographics.

**Figure 1** The authors algorithm for deciding for immediate or delayed breast reconstruction. BMI, body mass index.

as not all patients are suitable candidates for immediate reconstruction. Delayed reconstruction should be considered for patients with pressing medical comorbidities, obesity, smoking, inflammatory breast cancer, patients going to have post-mastectomy radiation therapy, and for patients distressed regarding their breast cancer diagnosis who are not ready to make treatment decisions (22,39,40).

Several absolute and relative contraindications should be considered and discussed in-depth, with the patient and at multidisciplinary tumor board conferences. There is a general consensus that only a few absolute oncologic contraindications for immediate breast reconstruction exist: locally advanced breast cancer and inflammatory breast cancer (9,22). Active infection in the breast area is a surgical contraindication. However, many conditions may present relative contraindications to immediate reconstruction and will be discussed below: increased age, smoking, obesity, comorbidities, risk of delaying adjuvant therapy. *Figure 1* depicts the authors algorithm for deciding for immediate or

delayed breast reconstruction. Some cultural and national differences exist among the authors' practice which is included in the algorithm.

### Age

There has previously been debate about whether increased age is a contraindication to immediate reconstruction. Studies have found increasing age to be associated with infection and skin necrosis, presumably due to decreased vascularity and comorbidity (41-44). Studies have also shown that immediate breast reconstruction is safe in elderly patients if pre-existing medical conditions are optimized pre-operatively, and thus, a patient's age alone is not a contraindication to immediate reconstruction (45-47).

### Smoking

Delaying reconstruction is preferred in patients who are

actively smoking, which will give the patient time to stop. Several studies have found an approximately doubled risk of complications in smokers undergoing breast reconstruction (41-44,48,49). There are also studies indicating that earlier smoking is associated with a higher risk of skin necrosis (48). If reconstruction is performed in an active smoker, peri-operative monitoring of the vascularity of the skin flaps is therefore advisable (50). A large meta-analysis found current smoking and former smoking of 20 pack-years or more to be associated with a significantly increased risk of recurrence and death, both disease-specific and overall (51). Active smoking is therefore considered an important relative contraindication for immediate reconstruction. In Denmark, this also applies to delayed reconstruction. The authors would only consider immediate reconstruction in light smokers without any other risk factors for complications.

## BMI

The risk of complications such as infection, skin necrosis and loss of implant is increased in overweight patients and about double the risk of normal weight (41,44,52,53). Overweight patients often have large and broad-based breasts, which will yield a large wound area during the skin-sparing mastectomy. Larger flaps or implants are generally needed; all of these factors are probably adding to the increased risk of complications. In many national guidelines, BMI above 30 kg/m<sup>2</sup> is considered at least a relative contraindication (44,54). Different countries and cultures have different proportions of obese patients and guidelines often reflect this (55,56). Among the authors, discrepancy exists as BMI 30 is used as cut off in Denmark (and generally so in the Nordic countries), while the upper limit in the US is higher.

## PMRT

In patients requiring PMRT, the optimal timing and method of breast reconstruction are controversial (57). Generally, plastic surgeons and surgical oncologists advise completion of radiation therapy prior to reconstructing the breast to avoid higher rates of complications of the reconstructed breast receiving PMRT (57-59). The traditional approach calls for tissue expander exchange for the permanent breast implant after the conclusion of PMRT however the authors prefer exchange to implant prior to the radiation, if possible, in order to allow surgery in a non-irradiated field. If not possible, the use of a counter incision at the IMF or

outside the field is preferred to one over the central portion of the breast. One study found that nearly 50% of implant-based breast reconstruction patients who underwent radiation may require revisions to their reconstruction (60). A meta-analysis evaluating complications including in pre-mastectomy versus postmastectomy radiation therapy generally in two-staged implant reconstruction and found similar and high complication rates and failures (17% versus 20%) (61). The commonly accepted view is that reconstruction with autologous tissue is superior to implant reconstruction within an irradiated operative field. However, autologous tissue reconstructions can also be negatively affected by PMRT (49,57,58). In contrast, a prospective study demonstrated immediate autologous reconstruction in the setting of PMRT to be a safe option that did not negatively affect breast aesthetics nor the patient's quality of life (62). They attribute their findings to advances in radiation techniques such as three-dimensional planning and simple intensity modulation, which allow for greater dose homogeneity within the treatment field (62). There is an abundance of evidence supporting the oncological safety of immediate reconstruction (27). However, the risk a reconstructed breast may pose on compromising radiation delivery is still a subject of debate (63). The authors generally prefer a delayed autologous reconstruction in case of radiation therapy, but if the patient is not willing to this, an immediate direct-to-implant reconstruction is preferable. We would try to avoid radiation towards an expander, if possible; since it may be more difficult to plan the radiation field in a patient with an expander than with a permanent implant, meaning a potentially higher risk of additional radiation to the lungs and the heart or an insufficient dosage distribution (63). In addition, to overcome expansion during chemotherapy which is often given before radiation therapy and performing exchange before radiation therapy can be demanding.

## Chemotherapy

As discussed previously, post-reconstruction chemotherapy has not been found to be generally compromised by the reconstruction (35,36). Regarding neoadjuvant chemotherapy in the setting of immediate reconstruction, a recent meta-analysis concluded that immediate reconstruction following neoadjuvant chemotherapy is safe with acceptable post-operative complication levels. The meta-analysis found that neoadjuvant therapy may result in slightly increased implant loss levels; however, there was no

delay in commencement of adjuvant therapy (64).

## Conclusions

Patient preference, risk factors and oncologic considerations are always important when planning reconstruction timing. Immediate reconstruction offers many advantages over delayed reconstruction, however, long-term patient-reported outcomes have been found similar, which we should not forget. The authors prefer immediate reconstruction when feasible. The timing and technique of reconstruction should be decided on a case-by-case basis after a thorough discussion with the patient and preferably also in multidisciplinary meetings.

This controversial topic is one that is debated over and over again. Consensus among the surgeons, chemotherapists, and radiation oncologists is the ideal and meetings which encourage this type of dialogue should be routine.

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