Surgical risk factors of breast reconstruction and their clinical implications
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The evolution of reconstructive breast surgery within oncologic boundaries:
A general introduction
Chapter 1

General Introduction

The primary concern in breast cancer treatment is oncologic adequacy and safety and breast reconstruction is justifiable only if it does not restrict the oncologic treatment. Still, reconstruction of the breast reduces the mutilation of oncologic treatment and this helps the patient to cope with her feeling of being betrayed by her body, as well as to cope with the impending loss of integrity of her body. Apart from a restoration of cosmesis, breast reconstruction features psychological benefits such as reduction of emotional stress and a negative post-mastectomy body image. The most important reasons for women to ask for breast reconstruction, however, are the reluctance to wear an external prosthesis that is often dislocated or lost, the ability to wear a greater choice of clothes without being confronted by an emptiness of the décolleté, and the urge to restore body wholeness and self image. Still, an amazingly low 10% of women undergo breast reconstruction after mastectomy. This can mainly be explained by the unawareness of the possibility of reconstruction among these women and their oncologists. Obviously, there is a need to more extensively inform women who face breast cancer treatment about these possibilities, their risks, and their results. Only then, each woman can make a true choice of treatment options open to her. Furthermore, the low percentage may be explained by a lack of facilities to offer such reconstructions. In an optimally staffed and equipped oncologic institute like ours, approximately 50% of women undergo breast reconstruction. This percentage may even be as high as 92% among women who undergo prophylactic mastectomy and who are, consequently, not bound by oncological restrictions.

The principle of reconstructive surgery in the Netherlands Cancer Institute-Antoni van Leeuwenhoek hospital is that reconstruction may only start if, and when, adequate oncologic treatment including possible tumor resection allows it. The oncologic, ablative task of the surgical oncologist is intentionally separated from the reconstructive task of the plastic surgeon. The responsibility of the ablative surgeon extends to the completeness of resection; no more and no less. Reconstructive goals are not to impede with the completeness and safety of the oncologic goals. This does not imply that ablative and reconstructive surgeons cannot cooperate to achieve a superior result for the patient, as together each achieves more. Within the boundaries of safe and adequate oncologic
treatment that are guarded by the oncologist, the plastic surgeon may steer the surgical oncologist to obtain such a superior result. Hence, the requirements and results of breast reconstruction are not only dictated by reconstructive possibilities but, rather, by oncologic requirements, possibilities, and results. This general introduction seeks to illustrate how the evolution of oncologic breast surgery stipulated the evolution of reconstructive breast surgery.

Evolution of surgical treatment of breast cancer

Although breast cancer has been recorded to have been treated surgically as early as the first century A.D., the modern era of oncologic breast surgery started at the end of the nineteenth century when Halsted successfully performed the first radical mastectomies under general anesthesia. Conservation of the pectoralis major muscle during oncologic mastectomy and dissection of the axillary lymph nodes was introduced in 1948 by Patey and Dyson, and popularized by Madden, as of 1965.

It took until the 1980's for breast conservation therapy to become more generally accepted as a valuable treatment of early stage breast cancer, even though this mode of therapy had been pioneered at the Foundation Curie in Paris since the 1930's. Likewise, it took until the late 1980's before skin sparing oncologic mastectomy described by Toth and Lappert and by Kroll became more widely accepted, even though this technique had already been introduced for non-oncologic indications by Freeman, in 1962. These and other advances in surgical, radiological, and chemotherapeutical breast cancer treatment increasingly emphasized tissue conservation and the reconstructive requirements and techniques adapted concurrently.

The modern era of post-mastectomy breast reconstruction started in the 1950's when de Cholnoky successfully transferred a tubed flap from the mid-abdomen to the mastectomy site. With the introduction of the silicone endoprosthesis by Cronin in 1962, it became easier to replace resected breast tissue. Still, it took until 1970 for Hueston and McKenzie to introduce the delayed primary reconstruction, which consisted of a breast reconstruction 2 to 4 days after mastectomy. True immediate breast reconstruction gained popularity in the late 1970's, but immediate breast reconstruction in combination with skin sparing oncologic mastectomy was only introduced in 1984.
Consequently, breast reconstruction after breast cancer treatment currently includes a wide variety of treatment strategies and techniques. These range from delayed to immediate reconstruction, from non-skin sparing to skin sparing techniques, and from prosthetic implantations to microsurgical transplantation of autologous tissues.\textsuperscript{5,24,27-29}

The evolution of breast conservation therapy

Because breast conservation therapy (BCT) and mastectomy proved to feature comparable results in terms of local cancer control and long-term survival, the U.S. National Cancer Institute, in 1990, concluded that breast conserving therapy is an appropriate treatment for stage I and stage II breast cancer.\textsuperscript{15}

Consequently, superior cosmesis became an important secondary goal of BCT. Even though large tumor size alone is not considered a contraindication for BCT in terms of local tumor control,\textsuperscript{30,31} this size plays a major role in the feasibility of BCT in terms of cosmetic results.\textsuperscript{32-34} Therefore, we investigated whether immediate replacement of the lost volume of large T2 tumors (2 – 5 cm) and T3 tumors (> 5 cm) by a deepithelialized latissimus dorsi myocutaneous transposition flap enhanced this cosmesis. This way, it may be possible to equally offer patients with larger breast tumors the opportunity to opt for BCT. The long-term outcome of this study is presented in Chapter 2.

Immediate versus delayed reconstruction after conventional mastectomy

For a variety of reasons, BCT may not be indicated and conventional mastectomy is preferred. As a result, the reconstructive challenge may include the restoration or replacement of both the skin envelope, and the content of the breast. This may be done immediately subsequent to the mastectomy, or delayed. Historically, breast reconstructions were delayed for months or even years after mastectomy because of fear to compromise adjuvant therapy or mask a local recurrence.\textsuperscript{3,16,35} Also, a period of explicit confrontation with the loss of a breast has been suggested to be beneficial for some women to accept that loss.\textsuperscript{36}

The main disadvantage of delayed reconstruction is the intervening period of unrestored mutilation and the implicit need of subsequent operations for secondary breast reconstruction. The remaining mammary skin, then, needs to be expanded which results in even additional operations. Alternatively, a skin flap is added at the cost of an extra scar in its donor area and, more often than not, a difference of quality and color between native mammary skin and the trans-
planted skin. The resulting patchwork-like appearance may be an aesthetic disadvantage.

Immediate breast reconstruction may prevent the use of such flaps, as it may prevent postponement of reconstruction and the need for additional operations. Its overall rate of complication does not significantly differ from that of a delayed procedure. With the increase of knowledge and experience of both ablative and reconstructive breast surgeons, immediate reconstruction has become more accepted and this acceptance may further be increased by more extensive sharing of knowledge between plastic surgeons and surgical oncologists.

Still, there are various reasons for a patient or her doctor to postpone the reconstruction and, consequently, the challenge to restore both the skin envelope and the content of the breast remains. An elegant technique to replace the skin of the amputated breast by the relative surplus of skin of the lateral extension of that breast was introduced by Holmström and Lossing, in 1986. Because this technique apparently was not met with much enthusiasm outside the Scandinavian countries, we prospectively investigated the feasibility and outcome of the use of this lateral thoracodorsal flap. This study is presented in Chapter 3, which also presents some extra indications for the use of this flap. An additional indication for the same flap may be its use as a salvage procedure for partial loss of other flaps used for breast reconstruction. This use of the lateral thoracodorsal flap is illustrated in Chapter 4.

Prosthetic implantation versus autologous transplantation

Whether immediate or delayed, breast reconstruction always involves the replacement of the resected content of the breast. Since silicone breast implants became available in 1962, they have widely been applied for cosmetic or reconstructive restoration of the breast mould. The immediate implantation of such prostheses after skin sparing mastectomy is relative simple and usually allows for a one-stage replacement of the breast content. Although there are various types of filling material of the prosthesis available, silicone-filled prostheses have the advantage of being less permeable and of lacking a fill-nipple that is vulnerable of leakage. So-called biodimensional silicone-filled breast prostheses, furthermore, more closely resemble the natural shape of the breast.
Still, the use of silicone-filled prostheses became controversial because of alleged systemic and proven local complications and this led to their relative ban by the U.S. Food and Drug Administration (FDA), in 1992. Since, multiple studies could not confirm the serological changes or immunological background of these allegedly silicone-related complaints, and this had led to a step-wise revision of the FDA moratorium. Although implant-related local disorders do occur, the majority of women are satisfied after immediate breast reconstruction by use of a subpectorally implanted silicone-filled prosthesis. Still, breast prostheses are mechanical devices and they have a limited expectancy of integrity. Consequently, the appearance of breasts that are reconstructed by use of a prosthesis may deteriorate over time, e.g. as a result of capsular contraction. Moreover, an initially pleasing symmetry to the contralateral non-operated breast may be lost as a result of the aging and natural development of that breast. Finally, a prosthetic breast reconstruction may be contra-indicated because of previous or subsequent radiotherapy of the chest wall. Previous or subsequent adjuvant chemotherapy seems not to feature similar detrimental consequences.

As a result of silicone anxiety, concern of unnatural appearance, or the outcome of previous chest wall radiotherapy, an increasing number of women undergo breast reconstruction by transplantation of autologous tissues. Procedures such as the pedicled transposition of the latissimus dorsi myocutaneous flap (combined with an implant) or a pedicled transposition or microsurgical transplantation of the rectus abdominis myocutaneous (TRAM) flap may be performed secondarily or immediately after the mastectomy. More recently, the microsurgical transplantation of the deep inferior epigastric perforator (DIEP) flap or superior gluteal artery perforator (S-GAP) flap have been introduced as excellent methods of autogenous breast reconstruction with less donor site morbidity.

The advantages of autologous over prosthetic reconstruction include the natural warmth, softness, and suppleness of the reconstructed breast and its long-term symmetry to the contralateral non-operated breast. Also, radiation therapy after autologous tissue reconstruction is usually well tolerated. Disadvantages include the additional scar in the flap donor area, the longer operation time, possible additional operations, and a more severe morbidity of these techniques as compared to prosthetic reconstructions. The need of an abdominal or gluteal
surplus of subcutaneous tissues associated with these autologous techniques implies that not all women may or will choose such reconstruction.

The evolution of prophylactic mastectomy

Advances in genetic testing today allow the identification of women with increased risk of breast cancer. Women with a hereditary increased risk of breast (and ovarian) cancer carry a mutation in either the BRCA1 or BRCA2 gene, in which BRCA stands for Breast Related CAncer. The estimated lifetime risk of breast cancer for these carriers ranges from 55 to 80%. If genetic testing is inconclusive but breast cancer has occurred in multiple generations of a family, this risk is still estimated to be 30 to 50%. Regular surveillance, chemoprevention, or prophylactic bilateral mastectomy and oophoro-tubectomy are options open to these women.

Although the reduction of risk of breast cancer in proven BRCA1 and BRCA2 mutation carriers predictably is 85 to 90%, performing prophylactic mastectomy in these women to reduce their lifetime risk remains controversial. The (surgical) oncologists of the Netherlands Cancer Institute-Antoni van Leeuwenhoek hospital, however, take a liberal stand towards such prophylactic surgery. More than 90% of the women who undergo prophylactic mastectomy in our hospital undergo immediate breast reconstruction and the choice to undergo prophylactic mastectomy seems easier if immediate breast reconstruction is offered.

Skin sparing versus non-skin sparing mastectomy

Historically, the vast majority of oncologic treatment existed of non-skin sparing techniques. Skin sparing oncologic mastectomy was originally introduced by Toth and Lappert in 1991. Excision compromises all of the breast tissue, nipple-areola complex and biopsy site and, sometimes, the skin above a subcutaneously located tumor. The preservation of the natural skin envelope improves the aesthetic outcome of the immediate reconstruction. Many studies have proven that the recurrence rate is correlated with the tumor stage and biological properties of the breast tumor, and that there is no evidence of a higher recurrence rate after skin sparing mastectomy. Combined skin sparing mastectomy and immediate reconstruction seems, furthermore, not to interfere with oncological follow up and the detection of any local recurrence. Hence, skin sparing mastectomy reportedly is a procedure that is oncologically as safe as conventional mastectomy but, contrary to
conventional techniques, offers the possibility to reconstruct a breast in one stage without the need to expand or add skin. Moreover, combined skin sparing mastectomy and immediate reconstruction potentially requires only one operation and hospital admittance. Economic studies documented substantial savings when applying these combined techniques.\textsuperscript{65,66} Still, these savings may be lost in case of complications. We retrospectively investigated which were the evident risk factors for a complicated outcome of such combined procedure. Additionally, we assessed whether this procedure was oncological safe for patients in our hospital. This study is presented in Chapter 5.

Historically, the incision used for the mastectomy evolved from an oblique vertical to a horizontal orientation to enable the surgical oncologist to amputate the breast and to have an adequate exposure of the axilla.\textsuperscript{67} There was not much consideration of the cosmetic outcome of the reconstruction. Furthermore, the prosthesis used for immediate breast reconstruction following a skin sparing mastectomy was usually implanted in a fully submuscular pocket.\textsuperscript{68,69} Such submuscular implantation, however, limits the proper positioning and projection of the prosthesis. The cosmetic outcome of immediate reconstruction may greatly be improved by limitation of the mastectomy scar in the lower lateral part of the breast and by disruption of the origin of the pectoralis major muscle from the ribs and inferior part of the sternum. The combination of these two, however, implies an immediate subcutaneous position of the lower part of the implant and immediate contact between this part and the skin scar. To prevent possibly detriminuous consequences of wound healing problems, we introduced the use of extended deepithelialization of the skin flap to secure the double-breasted closure of the skin. This technique is presented in Chapter 6.

Crucial in performing a skin sparing mastectomy is the avoidance of the use of skin flaps that have been overly filleted to remove all breast tissue, as this increases the risk of skin necrosis. The incidence of skin flap necrosis with subsequent infections has been estimated to be 8 to 15\%.\textsuperscript{27,50,70,71} Such necrosis can lead to exposure of the underlying implant and may result in loss of the implant. We prospectively assessed multiple patient-related and procedure-related characteristics as potential risk factors for these complications to establish selection criteria for potential candidates for immediate reconstruction of the breast. This study is presented in Chapter 7.
A reconstructive surgeon's responsibility toward oncologic follow-up

Working in a cancer institute, even a plastic surgeon develops a sixth sense for the early detection of any form of malignancy. Over the years, this evolved to the routine submission of all scars of previous oncologic treatment during subsequent reconstructive procedures. Hundreds of mastectomy scars, in particular, were excised and sent for patho-histologic examination this way. To assess to what level routine histological examination of clinically unsuspected mastectomy scars benefitted our patients, we retrospectively assessed the oncological gain of such examination of these scars over the last 10 years. This study is presented in Chapter 8.
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