Chapter 1

Mastectomy Skin Necrosis: Risk Factors, Prevention, and Management

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First Published **February 17, 2016**

Abstract

In the past decade, there has been an increasing focus on both therapeutic and prophylactic mastectomies in the management of breast disease. It has also become the standard of care to offer patients breast reconstruction for appropriate candidates after mastectomy, which often leads to a multidisciplinary partnership between the oncologic surgeon and the reconstructive plastic surgeon. In most clinical settings, the oncologic surgeon will perform the extirpation of the breast tissue and the reconstructive surgeon will subsequently restore the shape and contour of the native breast through either tissue expander-implant based reconstruction or by autologous tissue transfer. The advent of the skin-sparing mastectomy by the oncologic surgeon has increased the aesthetic potential for reconstructive surgeons by increasing the amount of native skin available for the reconstruction, and therefore offers the most cosmetically appealing reconstruction possible for patients undergoing both unilateral and bilateral mastectomies.

Mastectomy skin flap necrosis is one of the most common complications of both expander-implant and autologous tissue reconstructions, and this leads to challenging problems for both the continued oncologic care of the patient and for the reconstructive surgeon. Treatment may entail prolonged wound care which can have a significant impact on recovery and delay adjuvant therapies while also having a profoundly negative impact on reconstructive outcome. There is thus a large potential gain in terms

of survivability, aesthetics and psychosocial outcome, and a reduction in healthcare costs in minimizing the risk of mastectomy skin flap necrosis and in developing efficient and safe techniques in managing skin flap necrosis should it occur.

In this chapter, we discuss the risk factors associated with mastectomy skin flap necrosis and potential modalities of preventing its occurrence in high risk patients. We will also discuss current methods of managing the challenging problem of skin flap necrosis in post-mastectomy patients.

Introduction

Breast cancer affects one of every eight women and accounts for at least one third of all new cancers yearly [1]. The treatment of early breast cancer has been primarily surgical for over a century, though the operative treatment of breast cancer has undergone substantial changes over time. Halsted's radical operation, described in 1894, included resection of the breast, pectoralis muscle, and the regional lymphatics [2]. Breast surgery has since moved away from Halsted's original paradigm, which stated that successful tumor treatment required wide, en bloc resection of the chest anatomy. In contrast, the modified radical mastectomy, which spares the pectoral muscles, developed by D. H. Patey in the 1930s, was shown to have equivalent outcomes to the Halsted mastectomy for tumors that did not invade the chest wall. Further understanding of the

spread of tumors through lymphatic channels and the use of radiotracer for sentinel node biopsy developed in the 1990s have revolutionized the treatment of breast cancers, leading to the treatment standards of breast conserving therapy or mastectomy for primary breast cancers [3].

As the resection of breast tumors and the breast tissue itself has become more refined over time, so have the techniques for reconstructing the breast after mastectomy. The first true attempt at reconstruction of the breast was in 1895 by Vincent Czerny who utilized a "fist size" lipoma transplanted from the patient's flank. However, as the blood supply to such a volume of fat would be expected to be limited in this rather rudimentary technique, it is not surprising there is no information provided on the long-term outcome of the procedure. The first myocutaneous flap (utilizing a pedicled latissimus dorsi flap with an overlying skin paddle) for breast reconstruction was performed in 1906 by Tanzini, who was having difficulty closing the large wounds left after radical mastectomy. Some other techniques were developed during the first half of the 20th century, including bisection of the contralateral breast as a pedicled flap and the use of tubed abdominal flaps; however, a major limitation was the need for staged operations over several months. Extensive procedures with multiple delays and transfers resulted in significant scars even if flaps were to survive, and disappointing results prevented breast reconstruction from gaining significant popularity during this time period. The teachings of Halsted, which admonished surgeons for attempting to spare tissue for reconstruction, also served to stifle research and innovation in breast reconstruction. The modern era of breast cancer reconstruction began with the introduction of the silicone breast implant by Cronin and Gerow in 1963. Their method was through a staged process following mastectomy, but it was later proved in the 1970s by Snyderman and Guthrie that immediate implant-based reconstruction was also possible. Radovan later introduced the concept of the tissue expander based reconstruction, which allowed patients with more extensive skin deficits to be candidates for reconstruction [4].

In terms of autologous tissue reconstruction, the latissimus dorsi flap was repopularized in the 1970s and 1980s with the development of large skin paddle techniques. In 1979, Robbins reported the use of a vertically oriented skin-muscle flap of the rectus abdominis for breast reconstruction, allowing for a larger volume of tissue to be transferred to recreate the breast mound [4]. Refinements of surgical techniques by multiple surgeons eventually led to the development of the transverse rectus abdominus myocutaneous (TRAM) flap, which has become the workhorse of autologous reconstruction using excess abdominal tissue. Free tissue transfer has also gained increasing popularity, which allows the transfer of a unit of vascularized skin and/or fat from one part of the body (aka, "free flap") to reconstruct a breast mound. Flaps that

have been used include tissue from the abdomen such as the deep inferior epigastric artery perforator (DIEP) flap and the free TRAM. Flaps have also been harvested from the thigh, such as the transverse upper gracilis (TUG) flap, and many other options exist. Truly, the reconstructive surgeon has many options and tools in the modern era of breast reconstruction.

However, despite the large toolbox that reconstructive surgeons have today, a critical factor in determining a patient's reconstructive outcome is the mastectomy technique. Native breast skin may be very difficult to reconstruct even with autologous tissue reconstruction in terms of optimal color match and texture, and optimal cosmesis is best achieved through preserving the actual breast skin itself. The skin-sparing mastectomy (SSM), introduced by Toth and Lappert in 1991, has been shown to be safe and effective with similar recurrence compared to conventional mastectomy by numerous authors for tumors that are remote from the chest wall skin [5-7]. Furthermore, the preservation of the nipple-areola complex (NAC) is also often very attainable (the technique being coined "total skin sparing mastectomy" [tSSM] or "nipple-sparing mastectomy" [NSM] for selected patients [8]. These types of techniques are highly desirable for the reconstructive surgeon as the native skin envelope is preserved, and thus the only challenge for reconstruction is to restore the breast's volume and contour either by implant-based or autologous tissue methods. Preservation of the nipple also obviates the need for further staged surgery and for procedures to reconstruct the nipple. However, one of the dreaded complications of SSM is mastectomy skin flap necrosis, which greatly complicates both the reconstructive process and possibly the completion of oncologic care for patients. Skin flap necrosis may occur after a mastectomy is performed when the overlying breast skin does not have enough blood supply to survive, and over the course of several days postoperatively the skin will progressively become dark and necrotic and form an eschar. Skin flap necrosis increases the cost of care for the reconstruction, necessitating repeated outpatient follow ups, ongoing wound care, and potentially repeat procedures. There is also a psychosocial burden for the patient, who in addition to having just received an oncologic diagnosis, now faces the need for additional treatment as well as an uncertain reconstructive outcome. The rate of mastectomy skin flap necrosis is reported to be up to 30% in some studies [9], and thus there is great incentive to identify patients at risk for skin flap necrosis, to identify mastectomy techniques that minimize risk for this complication, and to determine the most efficient and cost-effective ways to manage this disfiguring outcome.

Incidence, Costs, and Risk Factors

Mastectomy skin flap necrosis is a relatively common problem after skin sparing mastectomy and reconstruction. Review of the literature suggests the rate of skin flap necrosis after reconstruction to be around 15.8% [9]. Some reports cite this rate as high as 30% if partial skin necrosis/desquamation is grouped in this category. The impact of full thickness necrosis of the mastectomy flap can be severe on the recovery of the patient, requiring an average additional 120.6 days of wound care for recovery and average revision surgery occurring 8.9 months after the initial reconstruction [10]. Studies have shown that patients requiring wound care experience a decrease in quality of life with an increased degree of social isolation. The actual cost of wound care is also significant, with dressing changes costing up to $30.92 per square centimeter per change [9].

It is thus imperative to identify which patients are most susceptible to skin flap necrosis. A review of the literature highlights numerous studies showing that age over 65 years, a body mass index (BMI) over 30 kg/m^2, active smoking, a history of preoperative radiation therapy, and higher mastectomy weight are either clinically significant or anecdotally significant factors based on surgeon experience [11-13]. The most prevalent and pervasive risk factor that appears to contribute to mastectomy skin flap necrosis is current smoking status. Smoking contributes to the risk of skin flap necrosis with an odds ratio of up to 3.478 [14-17]. Increased BMI is an independent risk factor for complications, with morbidly obese patients experiencing substantially more risk than their normal, overweight, and obese counterparts. Mastectomy weight is also a strong risk factor for necrosis, with increasing weight correlating with higher risk of necrosis [18].

Several other potential risk factors for the development of mastectomy skin necrosis have also been identified. One of these factors is age, where age over 65 years (or 50 years in some) is reported by multiple studies to be associated with skin necrosis [19]. Wound healing capabilities are compromised with increasing age. Aging also decreases the thickness of the skin, which also may affect viability of the skin flap. However, some studies reported that age was not an independent risk factor for flap necrosis [9,19]. Radiation therapy is another potential risk factor for skin necrosis. While some studies observe that radiation is associated with poor flap outcomes, other studies found no significant association [9,11,19].

Reconstructive technique has also been postulated as a potential risk factor associated with mastectomy skin flap necrosis. However, there remains no clear consensus in the literature. A large meta-analysis conducted by Tsoi et al showed that skin flap necrosis was higher in autologous reconstruction compared to tissue expander-implant based methods (relative risk 2.79), though with a lower risk for other complications such as infection or seroma [20]. However, other studies have showed the opposite finding, with a series by Lee et al actually showing a three

fold increase in mastectomy skin flap necrosis for prosthetic based methods [20]. In terms of excisional technique, there have also been studies comparing the SSM and tSSM; a study by Boneti showed similar rates of skin flap (including nipple) necrosis of 4.6 vs 3.1% respectively [8]. This study also showed similar flap ischemia rates between immediate reconstructions with saline implants versus tissue expanders. In terms of autologous tissue reconstruction, studies have shown an increased amount of mastectomy skin necrosis with higher mass of the transplanted flap, presumably due to higher tension placed on the skin flaps by higher mass of the autograft. However, there was no difference between flap types such as DIEP, super gluteal artery perforator (SGAP), superficial inferior epigastric artery (SIEA), and free TRAM.

Prevention of Skin Flap Necrosis

Several methods have been proposed to prevent the dreaded complication of skin flap necrosis. One obvious strategy is to minimize the risk factors as described in the previous section. However, this may or may not always be feasible for certain risk factors. For instance, the weight of the mastectomy tissue is likely not a factor totally under the surgeon and the patient’s control. Likewise, we would not advocate denying a patient reconstructive surgery due to prior radiotherapy or for advanced patient ages; not only are these risk variables not totally agreed upon in the literature, but it would be unethical to deny the possibility of reconstruction for factors beyond the patient's control. It would be acceptable, however, to encourage patients to quit smoking before proceeding with reconstruction. The risk of mastectomy skin flap necrosis can more than double for smokers versus nonsmokers, and this risk of necrosis can be significantly decreased if the patient ceases smoking four or more weeks pre-procedure. These patients' risk of mastectomy skin flap necrosis is also greatly reduced if done in a delayed reconstruction fashion [21].

Another key factor that has been explored and proposed to reduce mastectomy skin necrosis is maintaining adequate thickness of the mastectomy skin flap. The blood supply to the breast skin is normally derived from the underlying breast tissue; however, when a mastectomy is performed these blood vessels are removed. Therefore, after a skin-sparing mastectomy, the blood supply to the remaining breast skin is from the subdermal plexus, which is derived from blood vessels that originate in the periphery. Understanding the blood supply to the skin is critical and should lead to less skin necrosis and complications. In terms of surgical technique, leaving a thicker mastectomy skin flap with an appropriate amount of subcutaneous fat while also removing all of the breast tissue anatomically makes sense as a thicker flap would preserve more of the subdermal plexus. A flap with a thick, uniform layer of fatty tissue also contributes to a more aesthetically pleasing reconstruction. Some authors have reported mastectomy flap necrosis rates of 16.7% with flap thickness of 4-5 mm [22,23]. This is compared to the rate of 5% reported

for flaps of 1.0 cm in thickness [6,23,24]. Thus, it seems advantageous from a reconstructive standpoint to leave as thick of a flap as feasible, but the oncologic safety of this strategy has been questioned; the goal of the mastectomy is to remove all glandular breast tissue as possible in order to prevent possible cancer development or recurrence. However, even with flaps made meticulously thin (with the thickness of a full thickness skin graft), anatomical studies have shown the presence of residual breast tissue on the pectoralis muscle, periphery of the breast margin, and the skin flaps themselves at the microscopic level [25-27]. Furthermore, in comparing studies of locoregional recurrence for modified radical mastectomies and skin-sparing mastectomies, the reported incidence of locoregional occurrence differs by less than 1% (4.6% for radical and modified radical mastectomies, 5.5% for skin-sparing mastectomies) [28,29]. It can thus be argued that the attempt to meticulously clear the chest wall of all possible breast tissue does not lead to a significant difference in oncologic outcome.

Clinically, it has often been observed that there is a superficial fascial layer separating the subcutaneous layer from the breast parenchyma proper, and some oncologic surgeons strive to find and dissect through this layer. Larson et al examined this layer histologically in patients undergoing reduction mammoplasty. The authors found a range of subcuticular fat between 0 cm to 2.9 cm in the breast samples with a median of 1.0 cm (with >75% of breasts having a fatty layer over 0.5 cm), and interestingly, there was no correlation to BMI, age, or breast weight [23]. They and other authors have noted that the superficial fascial layer of the breast is not always present, and if so is not always visible macroscopically as a reliable plane of dissection [23,30]. However, oncologic surgeons have long noted a plexus at the subcutaneous level where one can separate the subcutaneous tissue from the breast tissue in a relatively avascular plane, and dissection at this plane would allow for optimum preservation of the subdermal plexus to maintain skin perfusion [31]. Thus, if at the time of operation this plane is identifiable, it is the desired potential space for elevation with a goal for subcuticular layer thickness of 1.0 cm. Other techniques advocated in the literature include delicately handling the mastectomy tissue, avoiding deep skin retraction, and using low voltage electrocautery [17].

One method in minimizing the risk of developing mastectomy skin flap necrosis is the use of nitropaste (aka nitroglycerin paste) in the early postoperative period as prophylaxis to prevent mastectomy skin necrosis. In a study by Gdalevitch et al, patients undergoing mastectomy with immediate reconstruction were randomly assigned to receive 45 mg of 2% nitropaste ointment or placebo at the time of surgical dressing, with the ointment being left in place for 48 hours. The trial was stopped early due to the great effect of the nitropaste therapy; 33.8% of patients in the placebo group had some degree of mastectomy skin necrosis, while only 15.3% of patients in the treatment group had this complication [11]. Presumably, the effect we see with the nitroglycerin paste is through the vasodilatory effects on the vascular smooth muscle, leading to dilation of arteries and veins feeding and draining the vulnerable mastectomy skin flaps. Nitropaste is absorbed transdermally and has both local and systemic effects to blood vessels. Nitroglycerin may also induce endothelial cells to produce prostacyclin, inhibiting platelet aggregation and thrombosis [32]. Potential complications of nitroglycerin therapy include headache and hypotension in nitrate sensitive patients, and thus its use may be precluded in some patients. If patients become symptomatic from the use of nitropaste, the treatment is simply to wipe off the nitropaste. However, nitroglycerin therapy is overall a simple, readily available, and cheap ($3 USD for a bottle) prophylactic measure that may mitigate the risk of mastectomy skin flap necrosis [11]. Regardless, in the authors' opinion, such adjunct treatments should not be a substitute for good surgical technique when performing a mastectomy and leaving healthy skin flaps of appropriate thickness.

Assessment of Vascular Supply to Mastectomy Skin

A number of assessment methodologies have been described for the intraoperative assessment of vascular supply to mastectomy skin. These include near-infrared spectroscopy, fluorescein dye administration with inspection by Woods lamp, and indocyanine green dye administration with fluorescent angiography. These methods can help minimize the risk of postoperative mastectomy skin necrosis by identifying areas of skin with relatively poor perfusion intraoperatively, which helps guide the surgeon to avoid leaving behind these high risk areas of skin at the time of surgery.

Near-infrared spectroscopy is a monitoring method that was first described by Jobsis in 1977 [33]. In this method, near-infrared light is delivered to the mastectomy skin via a probe attached directly to the skin flap. Selective absorption of light by oxygen-dependent tissue chromophores, predominantly hemoglobin, results in a reduction in light intensity. The reflected light returns to the probe and is analyzed by a photodiode. Oxygenated and deoxygenated hemoglobin absorb near-infrared light differentially, which allows the system to determine the relative ratios of these two forms of hemoglobin. With this information, the clinician can assess objectively the oxygenation to the mastectomy skin. Rao et al first reported on the use of this assessment method for mastectomy skin necrosis in 2009 [34]. They observed that a reduction in oxygen saturation on the near-infrared spectroscopy probe was significantly associated with the development of skin flap necrosis.

Fluorescein dye is another method that can be used to assess the vascular supply to mastectomy skin. It was

first described in clinical practice in the late 1800s to study fluid in the eye. It has subsequently been developed into a method to assess vascular supply of skin flaps intraoperatively [35]. For mastectomy skin flap assessment, fluorescein dye is injected intravenously at the conclusion of the breast reconstruction. Then, minutes later a Woods lamp is shined on the mastectomy skin with the operating room lights turned off. The Woods lamp is a source of ultraviolet light, which causes the intravenous fluorescein dye to fluoresce, which then allows the surgeon to directly visualize vascularity of the mastectomy skin. In 1978, Singer et al observed that areas of non-fluorescence were more likely to develop skin necrosis postoperatively [36].

Fluorescent angiography has also been described for intraoperative monitoring of mastectomy skin. It was developed in the early 2000s. This method involves intravenous injection of indocyanine green dye, followed immediately by application of a near-infrared light laser to the mastectomy skin that causes excitation of the dye and subsequent emission of infrared energy as the dye travels intravenously through the mastectomy skin. This results in a directly visualized fluorescent image of the vascular system of interest on a charge-coupled device video camera. In some commercial systems, an attempt to quantify the amount of vascularity by measuring pixel intensity through computer analysis has been reported. This method can assist in confirming vascularity in the mastectomy skin flap [37].

Management of Mastectomy Skin Flap Necrosis

The development of mastectomy skin flap necrosis requires prompt identification and management from the reconstructive surgeon. The most common method to tackle this problem is local wound care. For partial-thickness wounds and small full thickness wounds, it is likely appropriate to perform serial dressing changes and office debridements (Figure 1). The management of skin necrosis is also dependent upon whether or not an autologous tissue reconstruction or tissue expander-implant based reconstruction is employed. When there is overlying tissue necrosis a tissue expander-implant based reconstruction is at risk for exposure, extrusion, infection, and need for removal of the expander-implant. Therefore, tissue necrosis in implant-based reconstructions needs to be treated with more caution and, arguably, more aggressively than autologous tissue reconstructions.

Smaller wounds are less likely to lead to large and severe cicatracial deformities, and the healing time may not be so long to delay adjuvant treatment. However, for larger full-thickness wounds, it may be more appropriate to bring the patient back to the operating room soon after presentation of mastectomy skin necrosis for debridement, primary closure, and/or skin grafting. In a retrospective study of patients undergoing autologous reconstruction, Nykiel et al advocate for taking patients

with full thickness wounds greater than 6 cm^2 back to the operating room as soon as feasible as these patients are at risk for a prolonged healing phase (>21 days) that may prevent further adjuvant therapy [9]. This group also advocates harvesting a full thickness skin graft, if necessary, from the lateral flank as often a dog ear is present from the abdominal flap harvest and the prior scar can be extended laterally [9] (Figure 2).

Other authors have advocated a more conservative approach for large areas of skin necrosis with the argument that early operative intervention creates contour and volume abnormalities that are later more difficult to correct. Healing by secondary intention also eliminates the "patchwork" appearance that skin grafts may produce. Maintaining a moist environment for borderline skin, applying an antibiotic ointment that penetrates the eschar and promotes separation, and wet to dry dressings over granulating surfaces are effective strategies for this wound care [10]. However, for large wounds, this process will take many months, and the patient's preference for early intervention versus prolonged wound care as well as the need for adjuvant therapy should be weighed in the management decision.

Figure 1: Small full thickness wounds or partial thickness wounds(such as seen here) may be suitable for outpatient wound care as the desquamated skin re-epithelializes. Debridement should be performed regularly and eschar separated from the wound bed.

Figure 2: Full thickness wound treated with early operative closure with full thickness skin graft. In this case, the skin graft did not have total take and the remaining wound was treated with regular dressing changes with healing by secondary intention.

Another technique that can be used for management of mastectomy skin necrosis in autologous reconstruction is "skin banking." With this technique, the harvested skin paddle of the autograft is not totally trimmed during flap inset and is "banked" underneath closed mastectomy skin. The final trimming of the autograft is planned 4-7 days after the first operation, allowing questionable mastectomy skin flaps to demarcate. The flap can then be tailored to the defect after any necrotic mastectomy skin is debrided. Though this technique requires a subsequent operation, it saves the patient from perhaps a more costly and emotionally distressing period of frequent clinic visits and wound care [11,38].

For implant-based reconstruction, mastectomy skin necrosis can be challenging to manage and may necessitate removal of the expander/implant. Minimal epidermolysis may be observed without compromise of implant stability but may affect overall cosmetic results. In cases of questionable deep skin necrosis, serial office debridements can be done coupled with advanced wound dressings to try to preserve implant coverage with promotion of the deep skin layer to heal. Tissue expansion should be delayed pending healing of necrotic areas. If there is concern for impending expander exposure, options include excision of necrotic areas with primary closure, use of a vascularized flap to bring healthy tissue to the wound to provide coverage (such as a pedicled latissimus dorsi myocutaneous flap), or expander removal with plans for delayed reconstruction with either another implant-based procedure or conversion to complete autologous tissue reconstruction [39].

Conclusion

Mastectomy skin flap necrosis is a common complication after breast reconstruction and can have devastating consequences for a patient's healing, psychosocial health, and final cosmetic outcome. Maintaining a generous mastectomy skin flap thickness to optimize blood supply is important to help reduce the incidence of necrosis. Patients with risk factors for the development of skin necrosis, such as high BMI and active smoking, should

be identified and appropriately counseled preoperatively. Intraoperative assessment of vascular supply to skin flaps can also be obtained to identify potential areas at risk of necrosis. Preemptive measures such as skin banking can also be considered at the time of reconstruction if there is sufficient concern for the patient developing skin necrosis. Postoperatively, the application of nitroglycerin ointment can be utilized to minimize the risk of developing necrosis. In the event of the development of mastectomy skin necrosis, the size of the defect, healing time, type of reconstruction performed, patient preference, and surgeon experience should all be considered in the management of this complication to optimize patient outcomes.

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