IN-DEPTH REVIEW

Pathophysiology, Risk Factors, and Prevention of Wound Dehiscence Following Dermatologic Procedures

Andrew M. Armenta, MD[1], Frank T. Winsett, MD[1], Richard F. Wagner Jr. MD[1]

[1]Department of Dermatology, The University of Texas Medical Branch, Galveston, TX

ABSTRACT

Skin cancer is the most common malignancy in the United States and has been increasing in incidence, affecting approximately one in five Americans. As the number of skin cancers have increased, so have the number of dermatologic procedures including biopsies and excisions. Behind surgical site infection, wound dehiscence is the second most common postoperative complication of dermatologic procedures. There are many preoperative, intraoperative, and postoperative risk factors for wound dehiscence. The current literature on the risk factors of dehiscence within the field of dermatology is scarce. To our knowledge, there have not been any comprehensive reviews on this topic. Our research article aims to serve as a comprehensive and concise review with the goal of educating providers and increasing awareness of the risk factors associated with wound dehiscence.

INTRODUCTION

Skin cancer is the most common malignancy in the United States and has been increasing in incidence, affecting approximately one in five Americans.[1,2] As the number of skin cancers have increased, so have the number of dermatologic procedures including biopsies, excisions and Mohs micrographic surgery.[2] Behind surgical site infection, wound dehiscence is the second most common postoperative complication of dermatologic procedures and often occurs within the first postoperative week.[3-6] There are many preoperative, intraoperative, and postoperative risk factors that must be considered to decrease the risk for this common complication.

REVIEW

PHYSIOLOGY OF WOUND HEALING

Wound healing is separated into four overlapping phases: hemostasis, inflammation, proliferation, and maturation.[7] If any of these stages are impaired, wound healing may be compromised. Hemostasis begins immediately following a break in the skin with bleeding and release of factors that activate the extrinsic and intrinsic coagulation pathways and promote platelet aggregation.[7] The platelet plug is subsequently reinforced with a fibrin network upon which inflammatory cells migrate. During the inflammatory phase, neutrophils and macrophages migrate into the wound and are involved in clearance of pathogens, removal of cellular debris, and the release of various growth factors, setting the stage for the proliferative phase.[8] Within 48 hours the proliferative phase begins with the formation of granulation tissue. During the proliferative phase fibroblasts replace the fibrin network

with collagen, myofibroblasts mediate wound contraction, and angiogenesis with neovascularization occurs. Concurrently, keratinocytes re-epithelialize the wound by migrating from the wound edges and remaining adnexal structures. The fourth and final stage is maturation or remodeling of the wound, which begins 2-3 weeks after wound development and can continue to 1 year. During remodeling, reorganization, degradation and resynthesis of the extracellular matrix occurs and the wound achieves its maximum tensile strength as type III collagen is replaced by type I collagen.[8]

The driving force in wound dehiscence is tension. If the tension applied to the wound is greater than that of the tensile strength of epidermis, dermis, and the wound repair materials, dehiscence will occur. Scar strength increases during the remodeling phase to a maximum tensile strength of approximately 80% of uninjured skin. Depending on anatomic location and surgeon preference, sutures are typically removed between 7-14 days postoperatively. It is important to note, the tensile strength of a postoperative wound is typically less than 5% of normal skin at 1 week and less than 10% at 2 weeks.[9]

RISK FACTORS FOR WOUND DEHISCENCE

Surgical training and experience

Experience, training, and technical ability all play a role in post-operative outcomes of dermatologic procedures. Studies suggest that the experience of the surgeon is more significant than patient-related factors in acute wound failure and dehiscence.[10,11] Two studies have demonstrated that fellowship trained Mohs surgeons have a lower rate of wound dehiscence (0.10% and 0.33%) when compared to non-fellowship trained Mohs surgeons (0.93%).[6,12,13]

Anatomical location

Certain areas of the body are intrinsically more tensile than others. Extra care should be taken in areas of high tension including the scalp, back, proximal upper extremities and over joints.[11,14] These locations have high tension due to movement, stretch and thick dermis. Areas with increased mobility around the joints, legs, lips and eyelids are at increased risk of dehiscence.[15] Additionally, areas prone to trauma such as the distal arms and legs are higher risk for wound dehiscence.

Delayed or slow wound healing, as is often observed on the distal lower extremities, can also be a risk factor for wound dehiscence.[3] Poor perfusion can lead to insufficient oxygen and nutrient delivery needed for proper wound healing.[3] The lower extremities are also at increased risk of venous stasis which can lead to increased tension on the surgical site from swelling.

Method of closure

When performing excisions, the axis of the wound can greatly impact the cosmetic outcome and risk of dehiscence and depends on anatomic location. Langer's lines were first proposed by Karl Langer in 1831 as lines of cleavage oriented parallel to collage fibers in the dermis.[16] Later, Cornelius Kraissl proposed his own set of anatomic skin lines, Kraissl's lines, that run parallel to natural skin creases and perpendicular to underlying muscle fibers.[17] While there is significant overlap between Langer's lines and Kraissl's lines, they differ in certain areas such as the face and abdomen and excisions following Kraissl's lines tend to be under less tension and

result in better cosmetic outcomes.[17] More recently, a set of biodynamic excisional skin tension (BEST) lines have been proposed using a tensiometer to measure tension vectors and determine lines of least tension following circular excisions.[16] Elliptical excisions are preferred over circular excisions, generally in a 3:1 length to width ratio, as they further reduce tension and prevent the formation of standing cones. Of note, vectors of tension may change with changes in position and movement and the axis of elliptical excisions should be decided in a neutral resting position.

Healing wounds have an increased demand for oxygen and nutrients compared to normal skin. When suturing a surgical defect excessive tension on sutures may lead to tearing of tissue or breaking of suture and result in wound dehiscence.[3,18] Additionally, tight suture may strangulate the edges of the wound leading to poor perfusion and necrosis. Adequate undermining is often necessary to relieve tension and prevent dehiscence when approximating edges of a surgical wound.[19]

In areas of high tension, surgical techniques such as layered closure, mattress sutures, “pulley stitch,” “gliding stitch,” “Winch stitch,”, or relaxing skin incisions have proven useful in securely approximating wounds.[20-24] If additional support is needed, adhesive strips or other mechanical devices can be utilized.[25] In some cases, the size and tension of the defect is too great to be closed by primary intention. In these cases, skin grafts and flaps may be used to reduce or redistribute tension on surgical wounds in order to prevent dehiscence.[12,13,19]

Surgical material

Suture material plays an important role in dehiscence rates. One study comparing postoperative dehiscence rates of polyglactin 910 (Vicryl®), polyglecaprone 25 (Monocryl®), and polydioxanon (PDS®) found the rates significantly varied at 10.8%, 12.3%, and 4.7%, respectively. The same study found inflammatory reactions were greatest with polyglactin 910 and least with polydioxanone.[24] Further, too small caliber sutures may break or tear through tissue leading to dehiscence.[11] Removing sutures too soon may also contribute to dehiscence. If prolonged support is needed, sutures may be removed in stages or adhesive strips may be used.[25] Similarly, the application of a pressure bandage immediately postoperatively may help prevent postoperative bleeding as well as hematoma or seroma formation which may lead to dehiscence.[15]

Infection

Infection is a major risk factor for wound dehiscence. A study in Mohs surgery patients found that infection led to a 25% chance of dehiscence.[12] Postoperative wound infection can delay wound healing by prolonging the inflammatory phase and delaying progression of the proliferative and maturation phases.[3] Surgical sites that are high risk for infection and impaired wound healing include the groin, armpits, hands, and lower extremities.[26-28] Skin biopsies performed on hospitalized patients are much higher risk for postoperative infection compared to outpatient dermatologic procedures.[26]

Hematoma Formation

When postoperative bleeding occurs, a collection of blood may form resulting in a hematoma which can increase tension on the wound and lead to dehiscence. Of note, flap and graft repairs are higher risk for hematoma formation when compared to

primary intention.[12] Skin grafts depend on imbibition early on for survival and hematoma development often leads to graft failure, necrosis, and dehiscence.[12,13] Areas of high vascularity such as the face and the scalp are also at increased risk for hematoma formation.

Patient adherence

Patient adherence to postoperative instruction plays an important role in preventing dehiscence. Any significant tension placed on the wound early in the healing process may lead to dehiscence. Therefore, patients should be given clear activity restrictions and instructed to avoid any activities such as heavy lifting, stretching or straining that may increase tension on the surgical site. For lower extremity wounds, patients with congestive heart failure or venous insufficiency are advised to elevate their legs when possible to decrease swelling. Similarly, compressive dressings such as an Unna boot may be used.

Patient demographics that that are associated with an increased risk of dehiscence include young age and male gender, likely due to poor adherence to activity restrictions.[11] Further, propensity for surgical site trauma and poor wound hygiene are also likely to play a role in dehiscence.[29]

Genetic predisposition

Non-modifiable risk factors for dehiscence include genetic diseases, advanced age, and skin site reactions. Genetic disorders with impaired collagen production like Ehlers-Danlos or dystrophic epidermolysis bullosa pose particular challenges during wound repair, as collagen synthesis is required for proper wound healing.[7,30] Patients who have bleeding disorders like hemophilia may also be at increased risks of dehiscence due to postoperative bleeding and hematoma formation.[17]

Although younger age was found to be a risk factor for wound dehiscence, skin atrophy in advanced age can also contribute.[26] With increasing age, collagen production decreases and skin becomes more fragile. Gender may play a role in wound dehiscence behaviorally, but not biologically. Falland-Cheung et al found there were no significant differences when comparing the tensile strength of the scalp in males to females.[14] Allergic reactions to bandages, adhesives, and topical antibiotics may contribute to dehiscence.[15]

Atherosclerosis, Diabetes Mellitus, and Hypertension

Atherosclerosis is the narrowing of an arterial lumen due to abnormalities in the vessel wall.[31] This narrowing limits the delivery of oxygen rich blood and nutrients to peripheral tissue and skin required for wound healing. Impaired blood flow and nutrient delivery result in delayed wound healing and increased risk of dehiscence. The most common causes of atherosclerosis are diabetes, hypertension, smoking, and dyslipidemia.[31] In addition to atherosclerosis, hyperglycemia in diabetics also interferes with nutrient absorption and endothelial function.[32] Similarly, hypertension causes additional oxidative stress, perivascular inflammation and fibrosis that impair wound healing.[33]

Smoking

It is well established that smoking is detrimental to vascular health and affects multiple phases of wound healing. In addition to contributing to atherosclerosis,

during the inflammatory phase smoking can alter cytokines and chemo-attractants and suppress the immune response, leading to an increased risk of infection.[34] Smoking also induces increased amounts of oxidative stress, vascular inflammation, promotes vasoconstriction, and promotes the release of fibrinogen leading to a hypercoagulable state.[35] Furthermore, carbon monoxide from smoking binds to hemoglobin, displacing oxygen impeding its delivery to healing wounds.[35]

Smoking also decreases collagen synthesis and reduces protease inhibition. This blunts tissue formation and accelerates tissue destruction.[35] Overall, the tensile strength of postoperative wounds is weakened by impairing both proliferation and maturation. Smokers who are undergoing dermatologic procedures should be counseled and encouraged to quit smoking prior to, and following surgery.[36] Smoking cessation prior to surgery was reported to decrease wound infection rates, but did not impact dehiscence.[34] Further, flaps and grafts should be avoided in these patients when possible due to higher failure rates.

Obesity

Obesity affects one third of adults in the United States and impairs multiple phases of wound healing leading to an increased risk of dehiscence.[36] An obese body habitus often leads to decreased chest expansion causing hypoxia and decreased oxygen supply.[37] The resultant hypoxia diminishes fibroblast collagen formation and cellular repair mechanisms.[37] Vasculogenic progenitor cells which normally contribute to wound angiogenesis also have impaired migration and proliferation in obese patients.[38] Dysfunctional vasculogenic progenitor cells and avascularity from surrounding adipose tissue decrease oxygen delivery to the wound.[38] Neutrophil and macrophage function are also impaired in obese patients causing a blunted immune response with increased risk of infection and dehiscence.[37]

Malnutrition

Adequate caloric intake is required to support the inflammatory response, cellular activity, angiogenesis, and collagen synthesis required for wound healing.[39,40] Carbohydrates are needed for fibroblast production and migration, leukocyte activity and the secretion of hormones and growth factors.[39] Additionally, proteins like thrombospondin and albumin are essential for normal wound healing.[40] Without a sufficient amount of these macronutrients, wounds are at an increased risk of delayed healing and dehiscence.

Several micronutrients are also integral in would healing. For example, vitamin K is an important factor in the coagulation cascade and hemostasis. Similarly, iron, zinc, and vitamins A, B, C, and D are essential to the inflammatory process and synthesis of collagen.[32] In particular vitamin C (ascorbic acid) is a necessary cofactor in cellular apoptosis, clearance of neutrophils in the inflammatory phase, and collagen synthesis.[41] Impaired collagen production disrupts the proliferative and maturation phases of wound healing and scar formation.

Medications

Some medications have been demonstrated to increase the risk for wound dehiscence. For example, systemic retinoids such as isotretinoin, have been shown to impair collagen and non-collagen protein synthesis in fibroblasts, leading to dehiscence.[42] Further, dehiscence in mature scars (25 to

130 days old) have also been described following the initiation of isotretinoin.[43] Immunosuppressive medications are also problematic. Steroids may impair interleukin signaling, cytoskeletal remodeling, and keratinocyte proliferation during the proliferative phases of wound healing.[44] A retrospective assessment found immunosuppressed patients who underwent Mohs surgery at an increased risk of dehiscence when compared to immunocompetent patients.[4] Similarly, mTOR inhibitors (sirolimus, everolimus) and hedgehog pathway inhibitors (vismodegib, sonidegib) have been shown to increase the incidence of dehiscence.[45,46]

NSAIDs can also slow wound healing, acting mostly in the proliferative phase, thus increasing the risk of dehiscence.[47] NSAIDs inhibit keratinocyte proliferation and angiogenesis through disruption of prostaglandin PGE_2 and PGD_2 synthesis and vascular endothelial growth factor (VEGF) expression, respectively.[47,48] NSAIDs are often used to treat acute postsurgical pain so the benefit of analgesia must be weighed against the risk of dehiscence. Multiple studies have shown that discontinuation of antiplatelet and anticoagulants may not be necessary prior to cutaneous surgery. Significant differences in complications including postoperative bleeding and wound dehiscence have not been demonstrated.[12,49,50]

CONCLUSION

Wound dehiscence is among the most common complications following dermatologic procedures. It can lead to increased healthcare costs, infection, bleeding, need for additional procedures, poor cosmetic outcomes and may affect patient satisfaction. There are many modifiable and non-modifiable risk factors for dehiscence (Table 1) that must be identified in order to prevent this common complication.

Table 1.

Risk Factor	Mechanism	Phase(s) of Wound Healing Affected
Surgical Experience	Personal experience, skill, and knowledge of various surgical techniques	-
Anatomical Location		
Areas with tension	Tension **>** skin + suture tensile strength	Proliferation, Maturation
Areas with ¯ blood flow	¯ oxygen and nutrient delivery to wound	Proliferation
Areas with blood flow	risk of hematoma formation	Hemostasis
Areas with risk of swelling	Edema à tension on wound	Proliferation, Maturation
Areas with close proximity to the ground/structures	risk of trauma	-
Surgical materials		
Suture material	Strength of suture material	-
	Inflammatory reaction from suture material	Inflammation
Suture caliber	¯ caliber à ¯ strength	-
Infection	Persistent inflammatory phase, prevents proliferation and maturation of wound	Inflammation
Setting of procedure	Greater risk of infection in inpatients vs. outpatients	Inflammation

Bleeding		
Active Bleeding	Prevents progression to normal wound healing	Hemostasis
Hematoma	tension on wound	-
Patient adherence	Lifestyle and occupational hazards (increased tension and rates of infection)	-
Gender	Rate of dehiscence: Males > Females	-
Genetic diseases		
Disorders of collagen formation	Impaired collagen production during wound healing	Proliferation, Maturation
Disorders of coagulation	Inability to coagulate à persistent bleeding, risk of hematoma formation	Hemostasis
Patient Age		
Young age	Active lifestyle	-
Old age	¯ Collagen production	Proliferation, Maturation
Atherosclerosis		
Diabetes	Hyperglycemia ® atherosclerosis ® ¯ blood flow	Proliferation
Hypertension	Oxidative stress, perivascular inflammation, fibrosis, and arterial calcification ® atherosclerosis ® ¯ blood flow	Proliferation

Smoking	¯ chemokines, ¯ chemoattractants	Inflammation
	Oxidative stress, perivascular inflammation, ¯ clotting ® ¯ blood flow	Proliferation
	¯ protease inhibition, impaired collagen synthesis ® ¯ collagen	Proliferation, Maturation
Obesity	¯ O_2 supply, O_2 demand ® hypoxia ® impaired immune response, ¯ collagen formation	Inflammation, Proliferation
Malnutrition	¯ nutrient availability ® impaired wound healing	Hemostasis, Inflammation, Proliferation, Maturation
Medications		
Isotretinoin	Impaired collagen and non-collagen protein synthesis ® ¯ collagen	Proliferation, Maturation
Immunosuppressants	Suppression of dermal and epidermal genes ® ¯ IL signaling, cytoskeleton remodeling, keratinocyte proliferation	Proliferation
NSAIDs	¯ PGE_2, PGD_2, VEGF® impaired keratinocyte proliferation, ¯ angiogenesis, ¯ granulation tissue	Inflammation, Proliferation

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Corresponding Author:
Andrew M. Armenta, M.D.
301 University Blvd
4.122, McCullough
Galveston, TX 77550-0783
Email: amarment@utmb.edu

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