# Evidence-Based Medicine: Pressure Sores

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**Learning Objectives:** After studying this article, the participant should be able to: 1. Cite risk factors for pressure sore development. 2. Detail the pathophysiology of pressure sores. 3. List the types and classification of pressure sores. 4. Consider the various nonsurgical conservative wound management strategies. 5. Describe the appropriate surgical interventions for each pressure sore type. 6. Understand the causes of recurrent pressure sores and methods of avoiding recurrence.

**Summary:** Pressure sores are the result of unrelieved pressure, usually over a bony prominence. With an estimated 2.5 million pressure ulcers treated annually in the United States at a cost of $11 billion, pressure sores represent a costly and labor-intensive challenge to the health care system. A comprehensive team approach can address both prevention and treatment of these recalcitrant wounds. Consideration must be given to the patient's medical and socioeconomic condition, as these factors are significantly related to outcomes. Mechanical prophylaxis, nutritional optimization, treatment of underlying infection, and spasm control are essential in management. A variety of pressure sore patterns exist, with surgical approaches directed to maximize future coverage options. A comprehensive approach is detailed in this article to provide the reader with the range of treatment options available. (*Plast. Reconstr. Surg.* 132: 1720, 2013.)

With an estimated 2.5 million pressure ulcers treated annually in the United States at a cost of $11 billion, pressure sores represent a costly and labor-intensive challenge to the health care system. Although numerous and widely disseminated preventative guidelines exist, the elderly, acutely ill, and spinal cord–injured remain vulnerable. These wounds contribute to a prolonged and complicated path to recovery that may derail into chronic disability and premature mortality in some patients.[1] In 2009, the Centers for Medicare & Medicaid Services deemed pressure sores reasonably preventable and halted additional reimbursement for the treatment of hospital-acquired pressure ulcers, even if clinicians deem them unavoidable.[2] Failure to prevent pressure ulcers may present a substantial liability, with 87 percent of lawsuits favoring long-term care patients (**Level of Evidence: Therapeutic, II**).[1]

Plastic surgeons are often consulted in the acute care setting. These patients may be recently injured or ill with a pressure sore caused by immobility or have an exacerbation of a chronic condition that causes or worsens an existing ulcer. Among those conditions associated with pressure sores are neurovascular disease, orthopedic or neurologic injury, chronic deconditioning, malnutrition, and cardiovascular disease. Independent risk factors for pressure sores are found in age, male sex, altered sensorium, moisture, immobility, malnutrition, and friction/shear injury.[3]

Patients with existing pressure sores may enter the emergency room with evidence of infection or sepsis, but the source is rarely the ulcer itself. Therefore, it is important for all infectious sources to be investigated and the patient pan-cultured, particularly with regard to the genitourinary

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system. Special attention should also be paid to the risk factors associated with spinal cord injury patients. These patients often present as younger, male patients with a history of malnutrition, tobacco use, and narcotic or recreational drug use/abuse.[4]

Once the wound is evaluated in the context of the patient's medical and social condition, the plan of action can be established. A consultation with a specialized wound care team can help to optimize conservative management, whether for surgical preparation or a comprehensive nonsurgical approach.

## PATHOPHYSIOLOGY

Pressure sores, as the name suggests, are caused by unrelieved pressure to the soft tissue over a bony prominence. Evidence dating to the 1930s shows the temporal relationship between an external compression force and capillary perfusion pressure-induced ischemia (Fig. 1). Animal models have shown ischemic changes at 2 hours with pressure as low as 70 mmHg and muscle necrosis at 500 mmHg.[5] Skin is much more ischemia resistant than muscle and therefore may mask a much larger, deeper wound. This phenomenon is the "tip of the iceberg" and must be accounted for in the assessment (Fig. 2).

Additional important factors in the progression of pressure sores are the presence of infection, inflammation, and edema. It has been demonstrated that pressure in combination with infection resulted in a 100-fold increase in bacterial counts.[6]

The role of inflammation in wound healing has been widely investigated.[6] General markers of inflammation such as elevated C-reactive protein and erythrocyte sedimentation rate are noted but not yet incorporated into biological assays to guide management.[7] Matrix metalloproteinases, particularly matrix metalloproteinase-8 and matrix metalloproteinase-9, have been found to be elevated in chronic wounds. These proinflammatory markers aid in cellular recruitment and breakdown of extracellular matrix. A homeostatic balance between matrix metalloproteinases and their counterregulatory tissue inhibitors of metalloproteinases is disrupted in chronic wounds. Ladwig et al.[8] found a higher ratio of matrix metalloproteinase-9 to tissue inhibitor of metalloproteinase-1 in chronic pressure sores that improved with wound healing. Reduction in matrix metalloproteinase

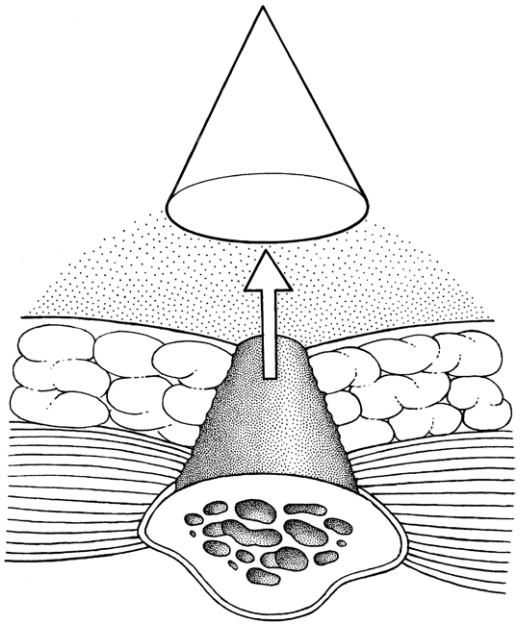


**Fig. 2.** Tip-of-the-iceberg phenomenon.

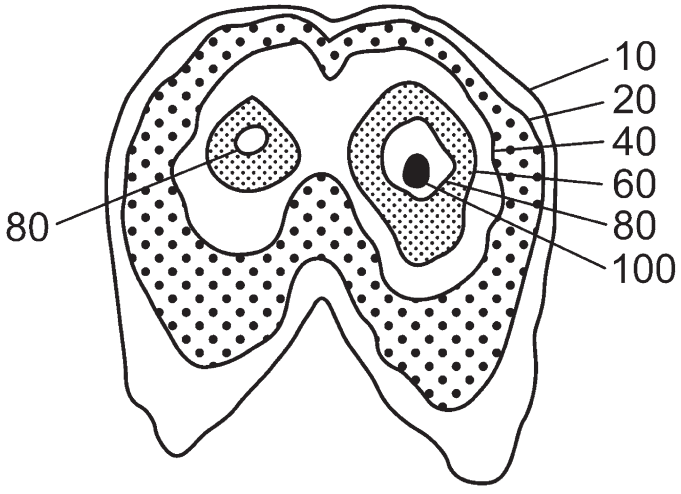



**Fig. 1.** Pressure distribution in a sitting position.

levels has been hypothesized to be the likely source of improvement.[9] Wound vacuum-assisted closure studies have similarly found elevated matrix metalloproteinases in nonhealing wounds.[10] Pilot studies have found some correlation between delayed healing and elevated serum procalcitonin and decreased RANTES (regulation on activation, normal T-cell expressed and secreted) and interleukin-13 levels.[11] To date, no standardized analysis exists in clinical practice, although the data are promising for future developments.

Edema becomes particularly important in denervated, compressed skin. Spinal cord–injured patients experience concomitant vasodilation in dependent areas, which exacerbates the pressure sore and may slow healing. Trauma may also cause the release of inflammatory mediators such as prostaglandins that further compromise the tissue.[6]

### Staging

One of the most widely recognized staging classifications is that developed in 1989 by the National Pressure Sore Advisory Panel Consensus Development Conference. This is a four-stage scoring system based on the clinical appearance of the wound. Defining stages in the presence of significant eschar and/or infection may prove complicated and shift on débridement.[6]

## CONSERVATIVE MANAGEMENT

Conservative management of pressure sores is a significant and innovative aspect in these wounds. In all patients, obtaining a healthy wound bed and stabilization or improvement of the pressure sore is essential. For those in whom surgical intervention is contraindicated or nonbeneficial, this approach may be an optimal long-term strategy.

Multiple factors must be accounted for in the care of pressure sores and reflect the risk factors listed above. These factors are often coincident with preoperative optimization of the patient and generalized pressure sore prevention guidelines. Offloading of pressure points with turning protocols (every 2 to 4 hours), specialized mattresses/beds, and adequate cushions for transportation devices apply to all at-risk patients. A tremendous number of both static (e.g., mattresses or foam) and dynamic (e.g., alternating-pressure beds) exist, but no definitive data have proven any one method superior.[1] In addition, care must be taken to keep the skin moisturized without oversaturation.[12–14]

Infection of the pressure sore complicates management. Débridement may be performed at the bedside sharply or with the use of agents as detailed below. Quantitative and qualitative biopsy of the wound should be performed sharply and expeditiously to aid in the establishment of treatment regimens. Broad-spectrum antibiotics can then be tailored based on the microbiology. Common skin flora (*Staphylococcus* and *Streptococcus* species) and enteric bacteria (*Proteus*, *Escherichia coli*, and *Pseudomonas*) are most often found. Sources of infection vary depending on the patient's medical status, including respiratory, bowel, and bladder function and diversion status. The original wet-to-dry dressings have been replaced with moisture-preserving ones. In a marginal or infected wound, Dakin's solution (0.025% hypochlorite) is an inexpensive, easily prepared option. Other choices in infected wounds include Silvadene (King Pharmaceuticals, Inc., Bristol, Tenn.) and Sulfamylon (UDL Laboratories, Inc., Rockford, Ill.), if eschar is present.[6] More expensive, silver-ion dressings lack high-quality supportive evidence.[15]

Dressings to the wound exist in two general categories with a spectrum of therapeutic goals. Passive dressings primarily control wound exudate, whereas active ones alter the local biochemical environment. Moisture, in moderation, is preferred in wound healing. Occlusive dressings may facilitate painless enzymatic autolytic débridement, but evidence from meta-analyses is mixed.[15] None of the active dressings, such as collagenase, hydrocolloids, and alginates, has been found to be superior to the others (**Level of Evidence: Therapeutic, II**).[16]

A relatively clean, minimally exudative wound may be well served by films, hydrogels, or other occlusive dressings. A larger amount of exudate may benefit from the addition of hydrocolloids or alginates. Although not a replacement for surgical débridement, small amounts of necrotic tissue may be treated with enzymatic débriding agents and antimicrobials.[17] Negative-pressure wound therapy has an important role in pressure sore management as a bridge to future surgery. Through deformational forces and edema reduction, among other properties, they allow for the treatment of variable sizes and depths of wounds. Bony exposure and poorly vascularized tissue still require expeditious surgical coverage to preempt deep-space infection. Some evidence shows improved circulation and reduced edema and bacterial load with wound contraction, whereas other studies are more equivocal. Two recent reviews could not show clinical benefit to

hyperbaric oxygen therapy.[16] At supranormal oxygen concentration, the treatment induces angiogenesis and fibroblast proliferation. Although it has shown benefit in carbon monoxide poisoning and in chronic wounds in animal models, the need for specialized equipment, the presence of complications, and the absence of human data are substantial barriers. Topical growth factors (e.g., platelet-derived ones) have been reported to have broad efficacy; however, the cost and the large volume of these wounds limit their application.[17]

Bioengineered skin constructs have also found application in nonexudative pressure ulcers. Despite their depth, the bilayered skin construct is able to stimulate tissue regrowth throughout the wound and not just from the edges.[18] As with the topical growth factors, wound size limits their practicality.

Nutrition in the context of wound healing has produced few clear recommendations in well-designed studies. Evidence supports a serum albumin goal of greater than 2.0 g/dl to promote adequate healing.[8] Protein intake should target a goal of 1.5 to 3.0 g/kg/day, with oral or intravenous supplementation as needed.[19] In one study, albumin levels below 3.5 g/dl were associated with ulcer recurrence within 12 months. Although not clinically malnourished, these patients appear to have dysfunctional wound healing.[20] The use of vitamin supplements has been reported with variable impacts on wound healing. Vitamin C has shown some benefit when given at 500 mg twice daily.[21] Supradietary additions of zinc, arginine, and antioxidants have failed to produce clinically significant benefits.[21–26] A well-balanced diet is likely sufficient to provide the vitamins and minerals (including trace minerals) that have been shown to be important in wound healing. Many practitioners believe the low-cost and low-risk nature of a daily multivitamin makes it worthwhile. Keys et al.[20] found a significant association between poorly controlled diabetes (hemoglobin A1C value >6 percent), indicating the importance of glycemic control in at-risk patients (**Level of Evidence: Risk, III**). To achieve dietary goals, consultation with a dietician and coordination of patient resources may be beneficial.

In the face of an infected wound, culture and biopsy are essential to identify the target organisms for antibiotic therapy. Osteomyelitis must also be assessed and treated as indicated. Diagnostic imaging may be performed by means of plain radiographs, magnetic resonance imaging, or bone scan. Combining these modalities with erythrocyte sedimentation rate and leukocyte count increases their value. Bone biopsy is considered the criterion standard in diagnosis. Antibiotic therapy may be required for 6 to 8 weeks before wound closure, and up to 3 weeks thereafter.[6]

Muscle spasm is a significant consideration, particularly in the spinal cord–injured patient, and may worsen in the patient or appear de novo in those without a known history during the operative course and sabotage the repair. Medical management is first line. Pharmacologic agents include diazepam, baclofen, and dantrolene. Failure of these agents may require more significant interventions and coordination with anesthesia or pain-management teams. These include nerve blocks, epidural stimulators, and baclofen pumps. Interruption of the spinal cord roots (rhizotomy) can be performed surgically (often by neurosurgery) or chemically with phenol.[19]

## PREOPERATIVE CARE

As detailed above, the conservative management serves to prepare the patient for surgical treatment of the wound. General risk factors for wound healing include age, smoking, diabetes, renal insufficiency, infection, malnutrition, and immunosuppression.[27]

Before a significant procedure, the patient must be nutritionally optimized (assessed with serum prealbumin and albumin) and have control of muscle spasms. In addition, distant sources of infection should be treated appropriately.[6] Nicotine cessation for several weeks before the operation is important and can be confirmed with a urine cotinine test (Fig. 3).

## ANESTHESIA

Anesthesia and pain management are important considerations in patient care. Insensate patients may tolerate more aggressive bedside débridement, although control of bleeding is a limiting factor. Once in the operative suite, the dorsal location of these wounds requires the attendant resources of prone positioning. Those patients with an acute cardiovascular or neurologic insult may require delayed repair. American Society of Anesthesiologists classification is particularly challenging in spinal cord–injured patients. The prevalence of tobacco and other substance abuse increases this risk.[19]

Induction of anesthesia may produce variable responses, depending on the level of spinal injury and anesthetic maneuver. Yoo et al.[28] suggested altered catecholamine responses with position changes, endotracheal suctioning, and Valsalva

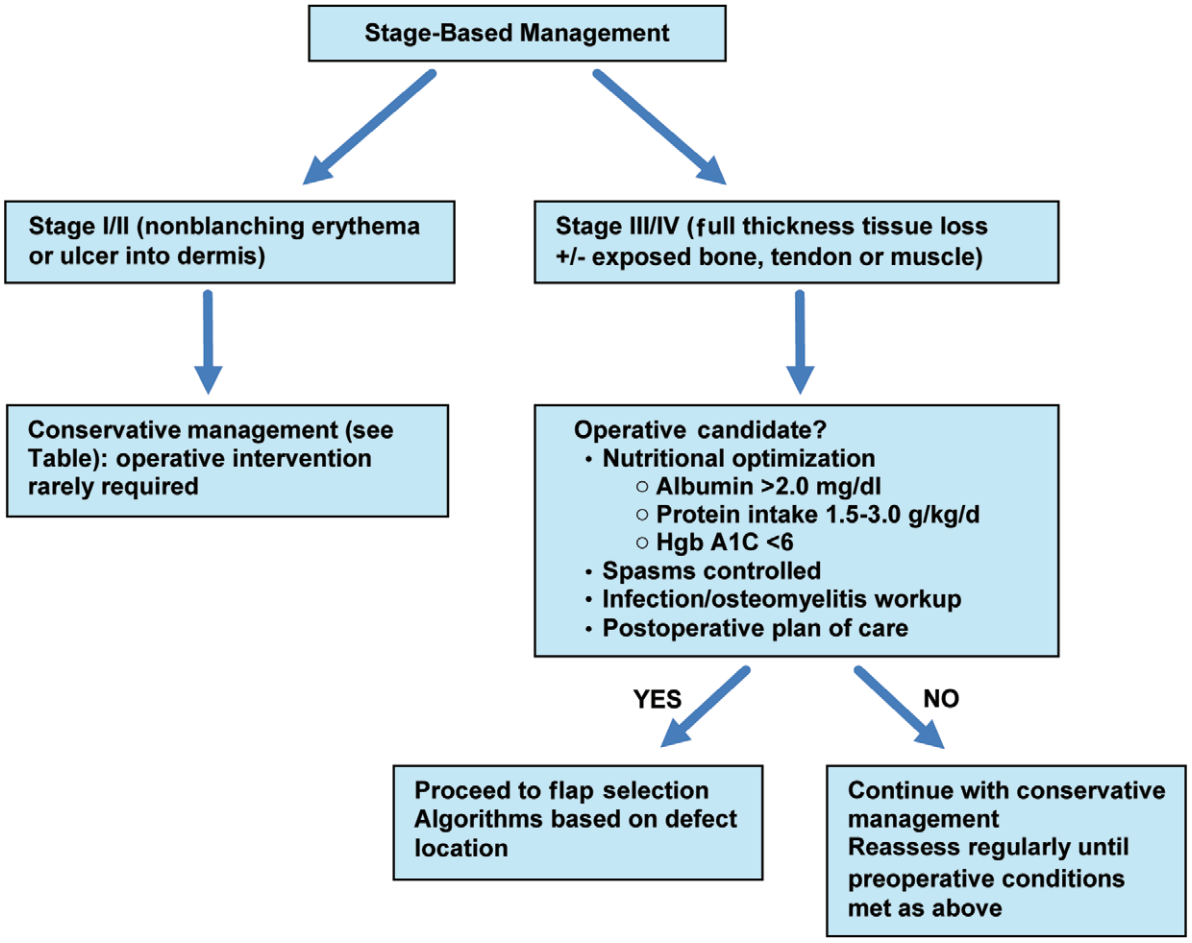



**Fig. 3.** Stage-based management.

maneuvers. Spinal cord injuries with intact vagal responses and interrupted sympathetic tone may show bradycardia and hypotension. Paraplegic patients often demonstrate hypertension and tachycardia.[28] The use of succinylcholine is contraindicated in these patients because of the lifetime risk of hyperkalemia from acetylcholine-receptor up-regulation in denervated muscle.[29] Prior coordination with experienced anesthesia personnel should be sought.[19]

## OPERATIVE MANAGEMENT

Initial treatment of pressure sores often begins with débridement of the affected area, with or without immediate flap coverage. Thorough removal of the bursa is important, as it can be a pressure point in itself (Fig. 4). Removal of the necrotic tissue, including bone, should include specimens sent for Gram stain, wound culture, and quantitative and qualitative biopsy. Obtaining specimens before and after débridement may be beneficial. Removal of the bone should be limited, to prevent pressure (with subsequent ulceration), excessive bleeding, and dysfunction.[30] Heterotopic bone is usually excised. (**See Video, Supplemental Digital Content 1**, which demonstrates the excision of a heterotopic bone, available in the "Related Videos" section of the full-text article on PRSJournal.com or, for Ovid users, at ***http://links.lww.com/PRS/A918***.)

Wound closure techniques depend on the location, size, and depth of the pressure sore. The specific nature of the patient's medical comorbidities and the previous surgical interventions or scarring in the area must be considered. Although the wound may appear to reapproximate well, primary closure is usually contraindicated. Skin grafting lacks sufficient bulk or strength to cover the wound, with failure rates of approximately 70 percent. Local tissue rearrangement may consist of skin and fascia with or without muscle (Fig. 5). Fasciocutaneous flaps are durable, well-vascularized flaps that spare significant functional deformity. The flaps may provide good bony prominence coverage,

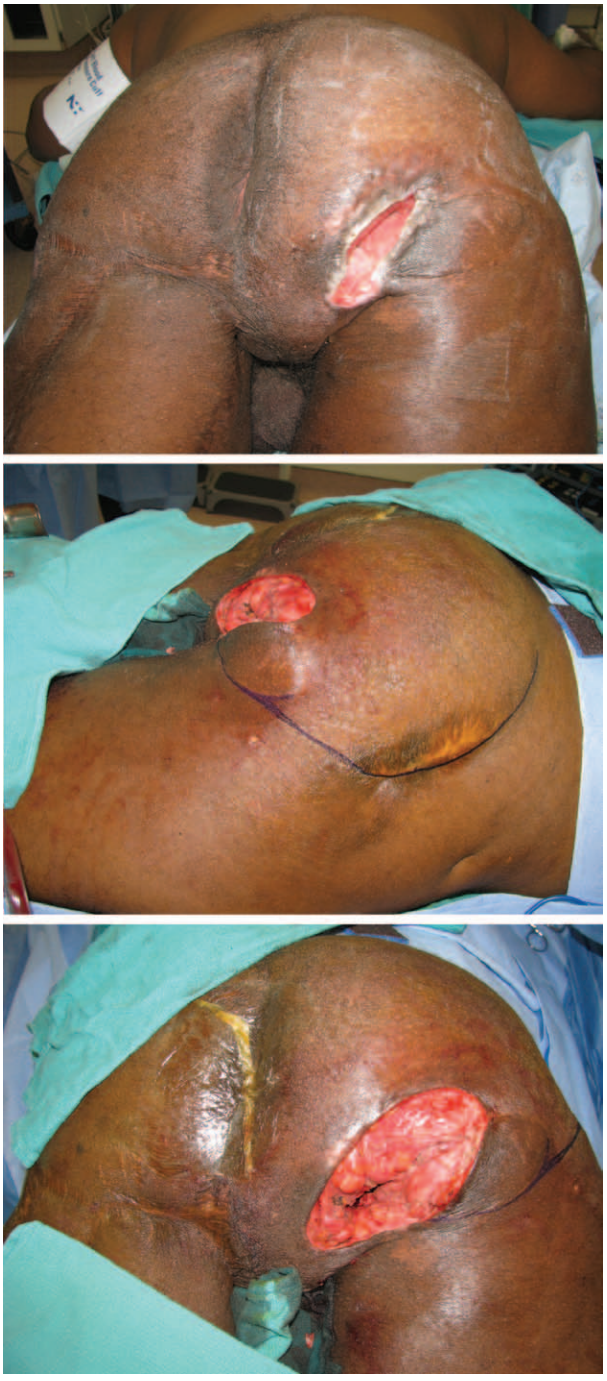
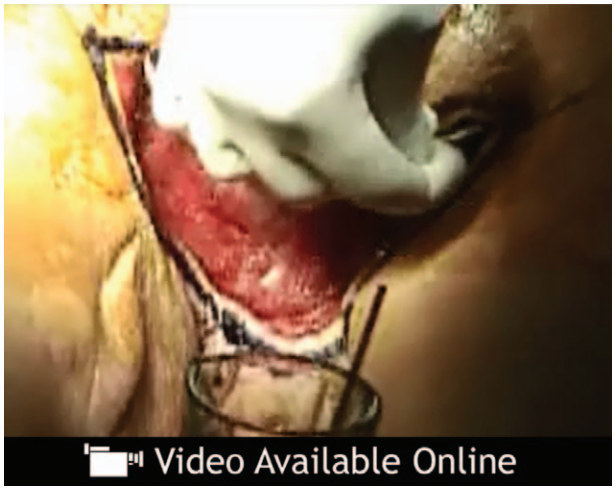


**Fig. 4.** Adequate débridement of a sacral pressure sore with bursectomy.

but the limited bulk may be insufficient for large or deep wounds (Fig. 6). Musculocutaneous flaps provide more depth of coverage with the same benefits of the fasciocutaneous flaps at a cost of functional deformity. Muscle flaps are also a good choice in an infected wound. The better local blood supply provides improved tissue oxygenation, improved antibiotic delivery, and enhanced lymphocytic function that




**Video 1.** Supplemental Digital Content 1, which demonstrates the excision of a heterotopic bone, is available in the "Related Videos" section of the full-text article on PRSJournal.com or, for Ovid users, at ***http://links.lww.com/PRS/A918***.

improves bacterial killing. Free tissue transfer has also been performed, particularly in recurrent wounds. Flaps such as the latissimus dorsi, serratus anterior, and lower extremity–based fillet flaps have been described (Fig. 7).[31] Drains are placed routinely and a strong multilayer suture closure is important.[6]

## ISCHIUM

The bilateral ischia present a significant source of pressure ulceration for patients in the sitting position. Patients often return to their preoperative sitting habits, making these likely to recur. Choices in muscle flap coverage of ischial defects are most commonly the gluteus maximus flap, V-to-Y hamstring advancement, and medial thigh and gracilis flap. Fasciocutaneous flaps, such as the tensor fascia lata and gluteal thigh flap, often lack sufficient bulk (Fig. 8). The gluteal flap can be raised as a myocutaneous or muscle-only flap that may be designed as an advancement, rotation, or island flap (Fig. 9). A split flap may be raised on the superior or inferior gluteal artery. The inferiorly based flap provides the most bulk of the muscle flaps.[22]

The hamstring advancement provides adequate bulk with incorporation of the rectus femoris, semitendinosus, and semimembranosus muscles. (**See Video, Supplemental Digital Content 2**, which demonstrates hamstring advancement, available in the "Related Videos" section of the full-text article on PRSJournal.com or, for

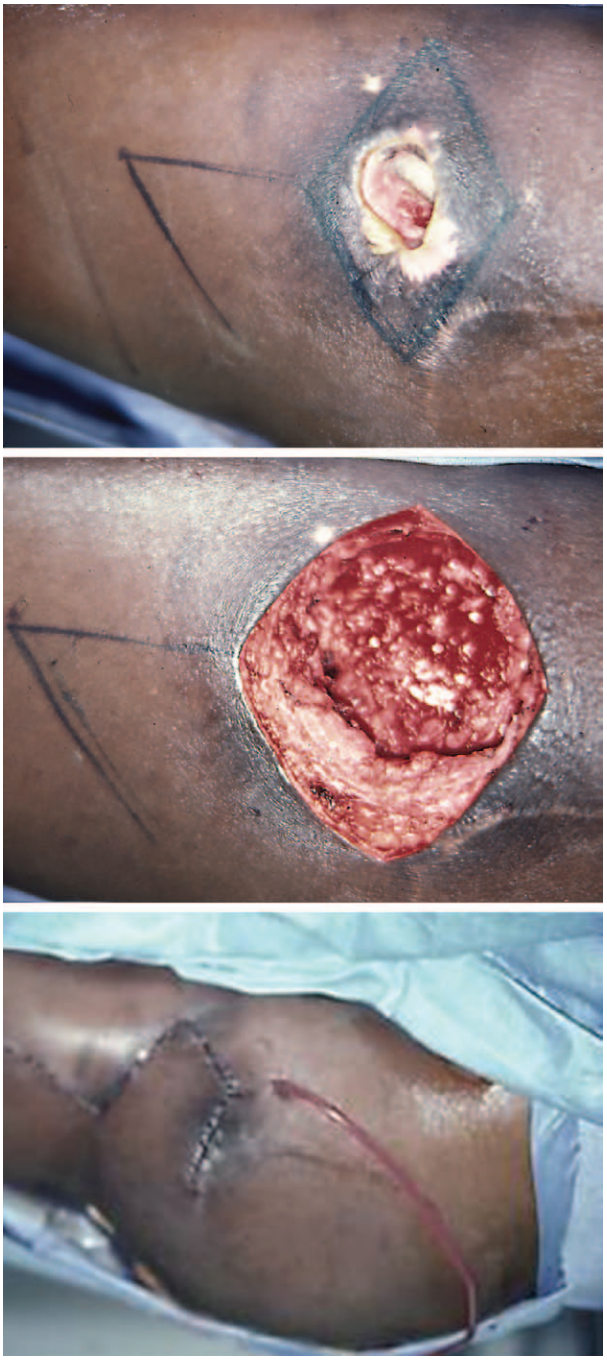


**Fig. 5.** Rhomboid flap for a small pressure sore.

Ovid users, at ***http://links.lww.com/PRS/A919***.) Disadvantages include tension at closure, incision lines at the prime pressure point, and flexion-induced dehiscence. Given their recurrence, the fundamental principle is to minimize local tissue disruption to allow future flap design. The gluteal and hamstring flaps can be readvanced multiple times. For more complex, deeper, or larger wounds, a combination of flaps may be necessary.[32]

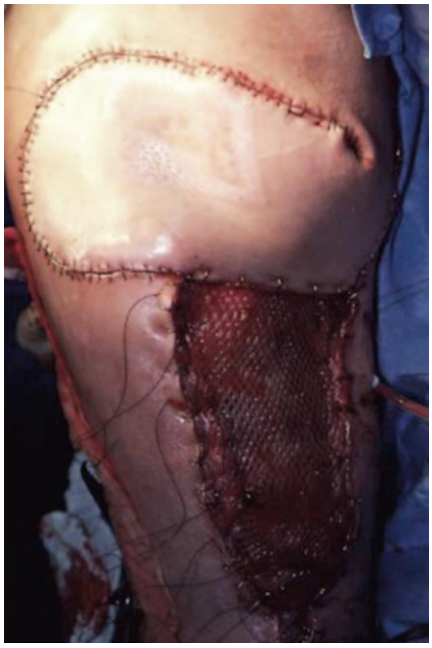


**Fig. 6.** Hamstring fasciocutaneous flap.

## SACRUM

Supine patients are at risk for sacral pressure sores, which are operatively managed much like ischial defects (Fig. 10). Gluteal flaps are predominant. Unilateral V-to-Y advancement flaps are reliable and can be readvanced. Larger defects may require bilateral pedicles. Careful dissection in ambulatory patients can preserve sensation. Less-common alternatives include the transverse and vertical lumbosacral flap, based on lumbar-perforating vessels. These flaps lack significant bulk and are not useful in deeper wounds.

## TROCHANTER

These ulcers are more common among those who stay in the lateral decubitus position, often as result of significant hip flexion contractures. The mobility of this region, especially in spastic patients, worsens the "iceberg" effect. Any gains in contracture management will aid in reconstruction. First-choice flap coverage is the reliable tensor fasciae latae perforator flap (Fig. 11). The T12 to L3 sensory input may allow postoperative sensation in lower level spinal cord injury/myelomeningocele patients. These flaps may be raised in a classic manner or as a V-to-Y flap. The donor site is usually skin grafted. The arc of rotation of the flap may risk dehiscence. Other flap choices include vastus lateralis, rectus femoris, and gluteal thigh flaps (Fig. 12).[6,32]

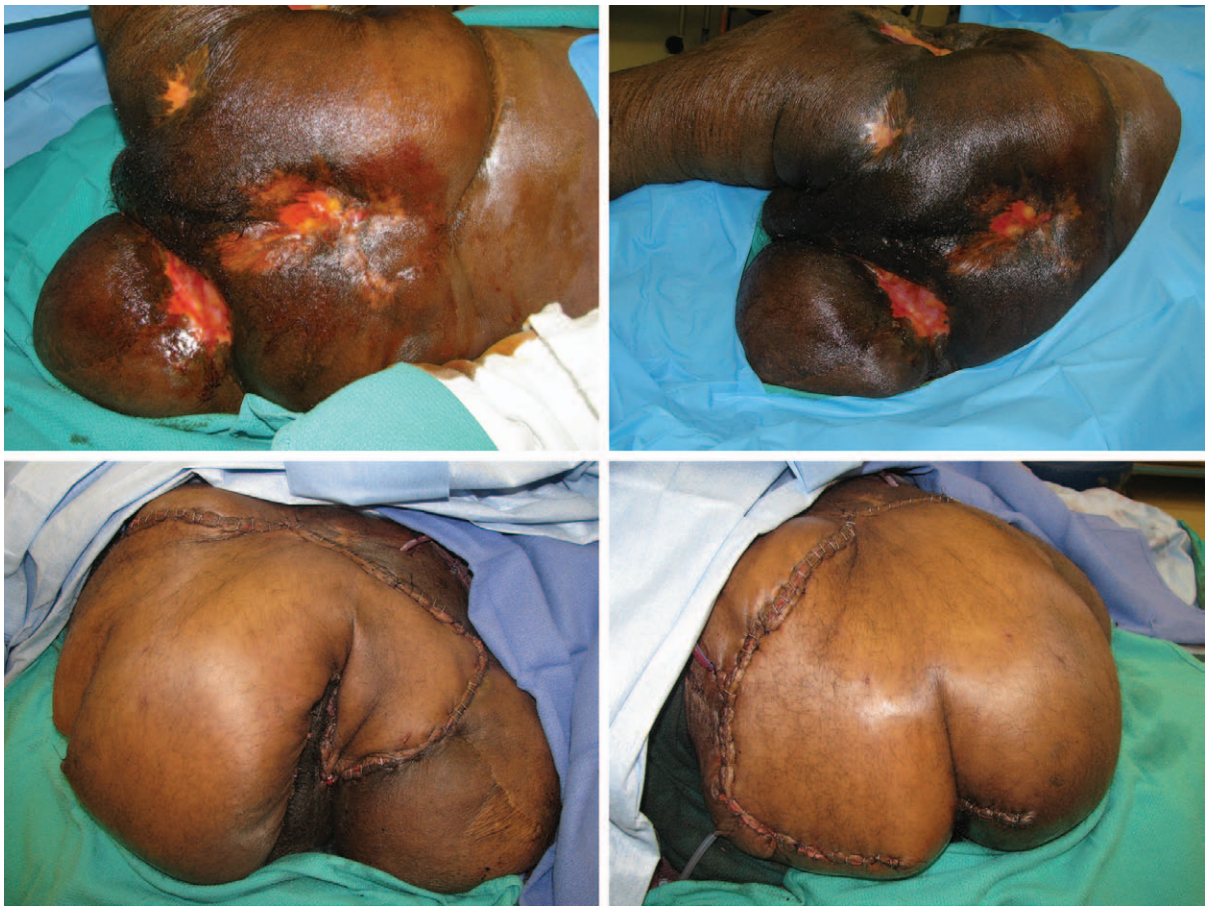


**Fig. 7.** Total thigh flap.

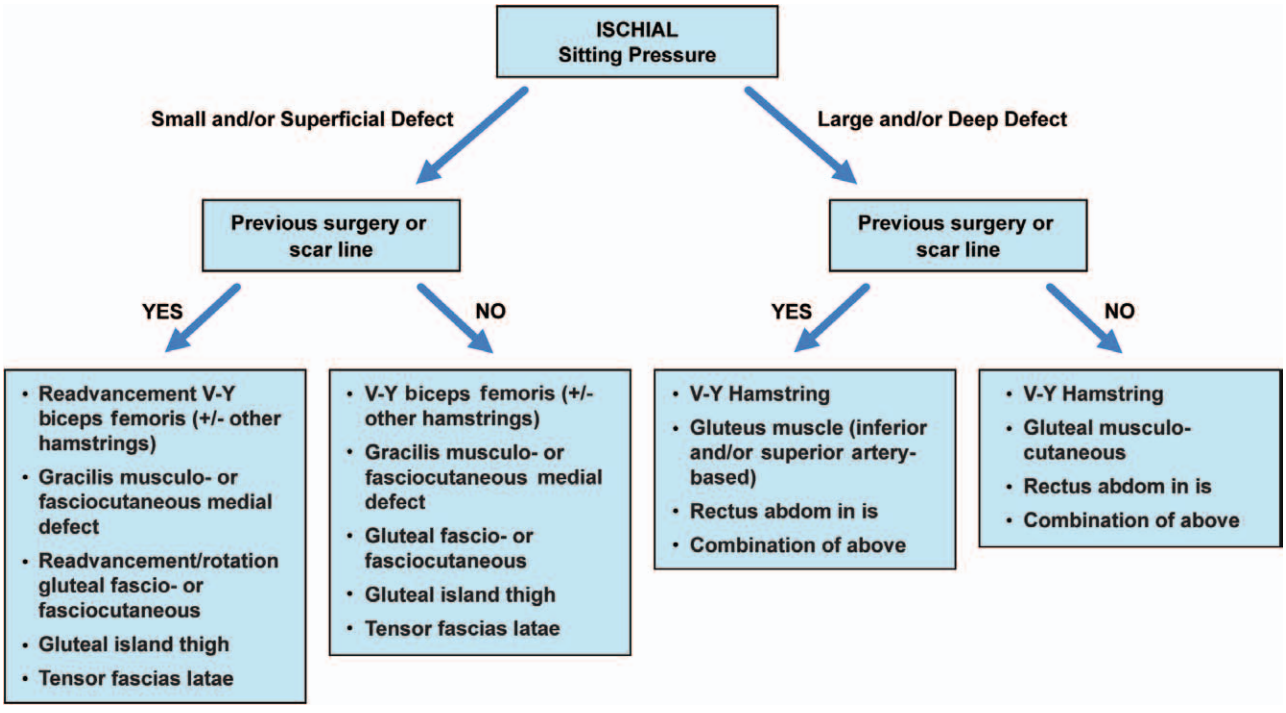



**Fig. 8.** Sources of flaps for ischial pressure sores. Leg flaps are preferred to preserve superior-based flaps for other defect sites.

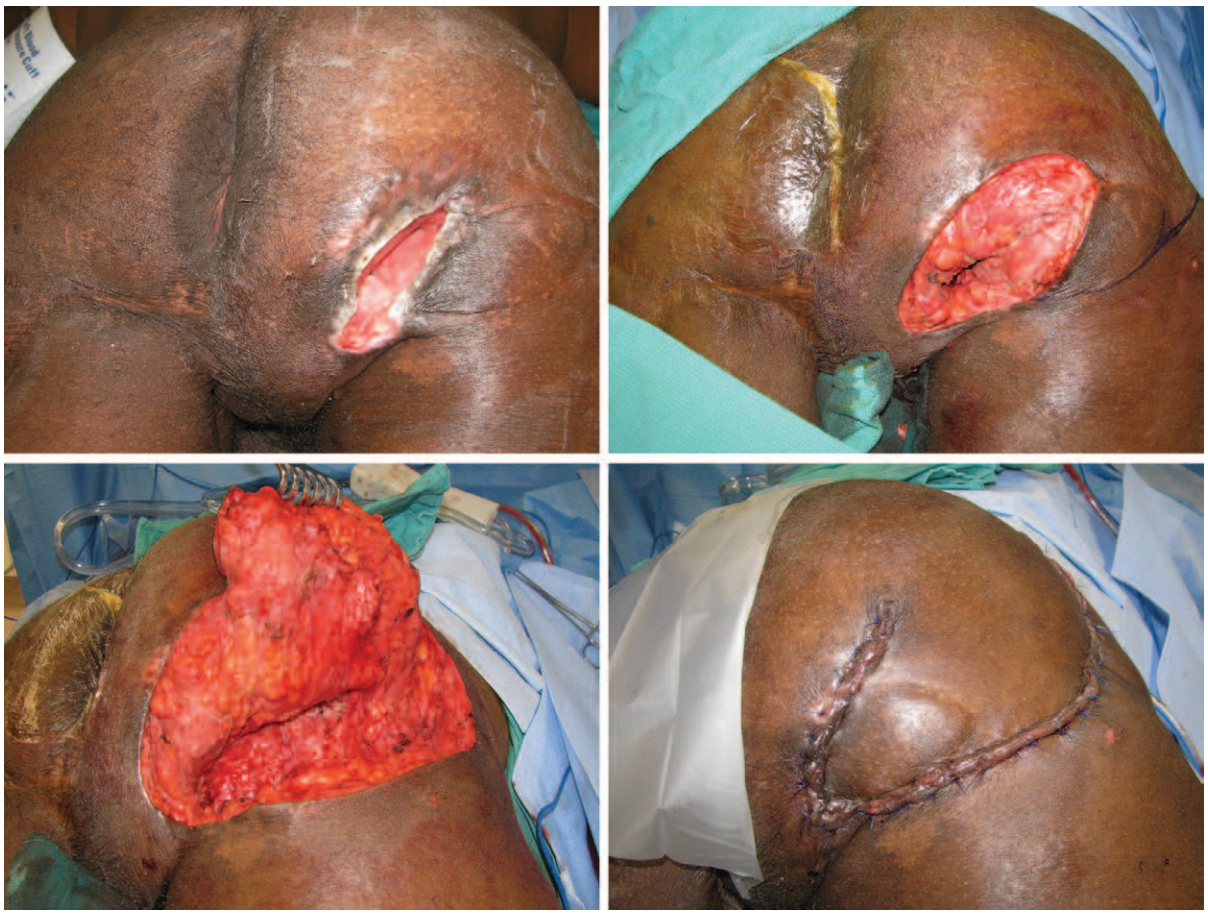
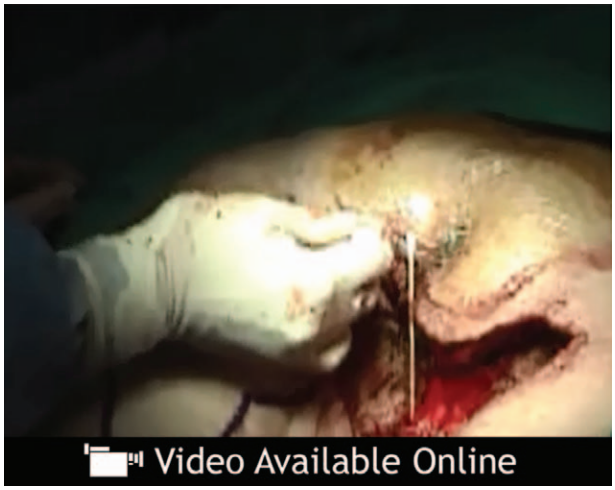


**Fig. 9.** Gluteal rotation flap for ischial pressure sore.




**Video 2.** Supplemental Digital Content 2, which demonstrates hamstring advancement, is available in the "Related Videos" section of the full-text article on PRSJournal.com or, for Ovid users, at ***http://links.lww.com/PRS/A919***.

## POSTOPERATIVE CARE

Postoperative management is based on the preoperative protocols established for a particular patient. Offloading in a tension-free position for 3 to 4 weeks postoperatively is critical. Inpatient admission is usually necessary to achieve this, sometimes for several weeks if there is not adequate physical or social support at home or a care facility. As discussed for preoperative management, it is essential that the entire team be in agreement on the course of action and all coordinating services on board. Patient positioning, nutritional support, and spasm control are essential. Bowel and bladder control should be established before intervention and managed aggressively to prevent wound contamination. Important considerations include the use of a low-air-loss mattress and turning every 2 hours. Early rehabilitation may be used to minimize deconditioning while protecting the flap.[29,30]

Nutritional supplementation, in addition to a balanced diet, may benefit the patient, with little downside in this setting. All preoperative spasm management must be followed dutifully because of the increased frequency of spasm postoperatively, even in those without a reported history.

Antibiotics are continued in the perioperative period, as the surgical procedure may cause intraoperative bacteremia. Whether continuing

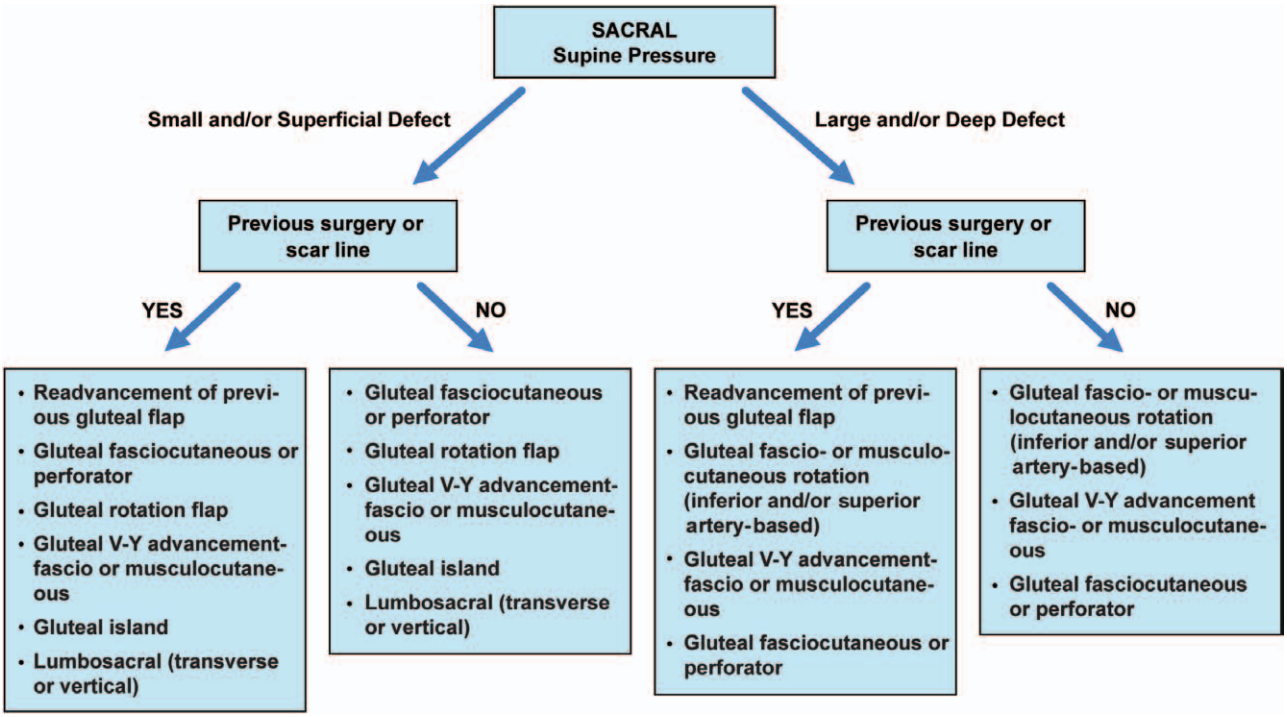



**Fig. 10.** Sources of flaps for sacral pressure sores. Gluteal flaps are the primary source in variable configurations.

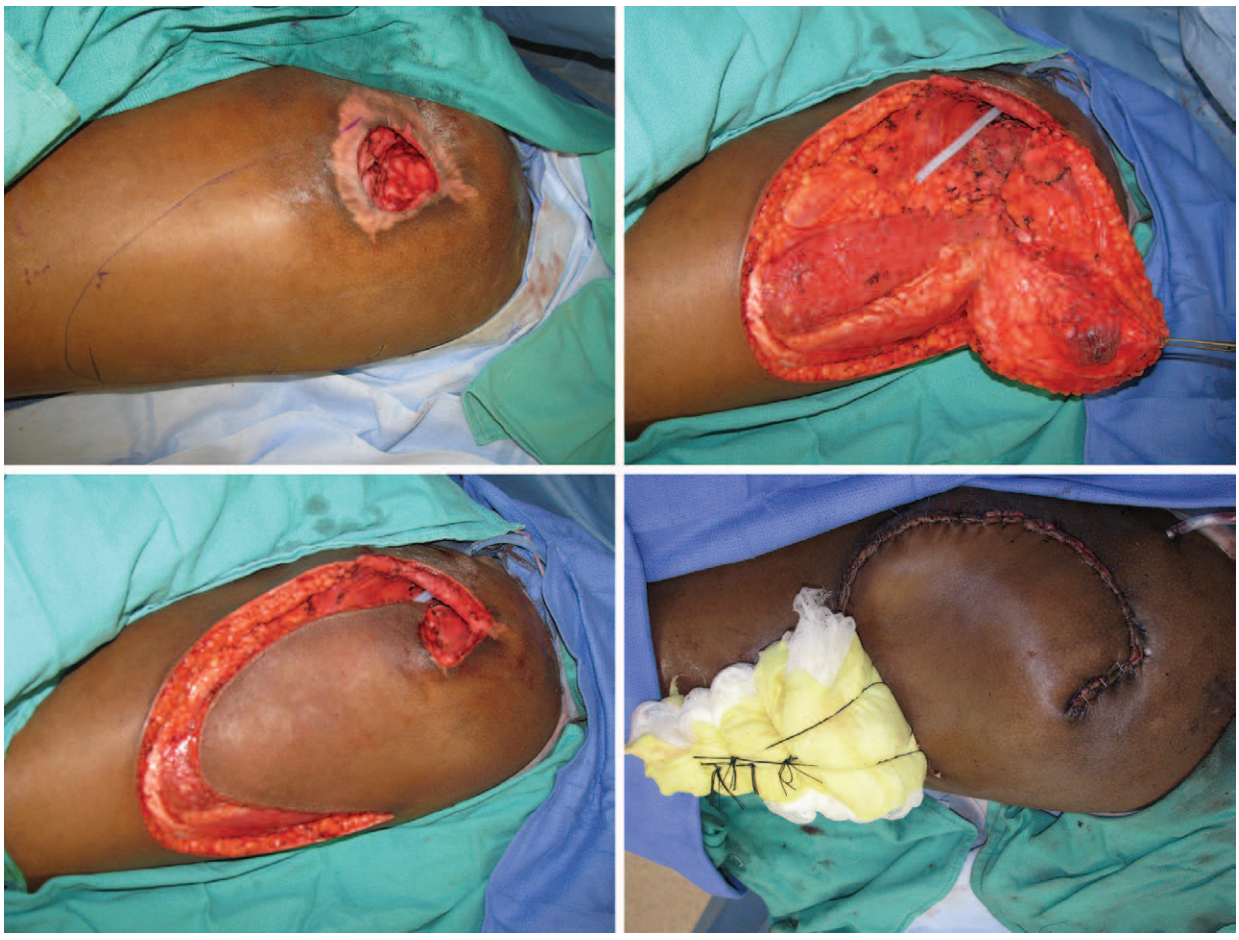


**Fig. 11.** Tensor fasciae latae flap.

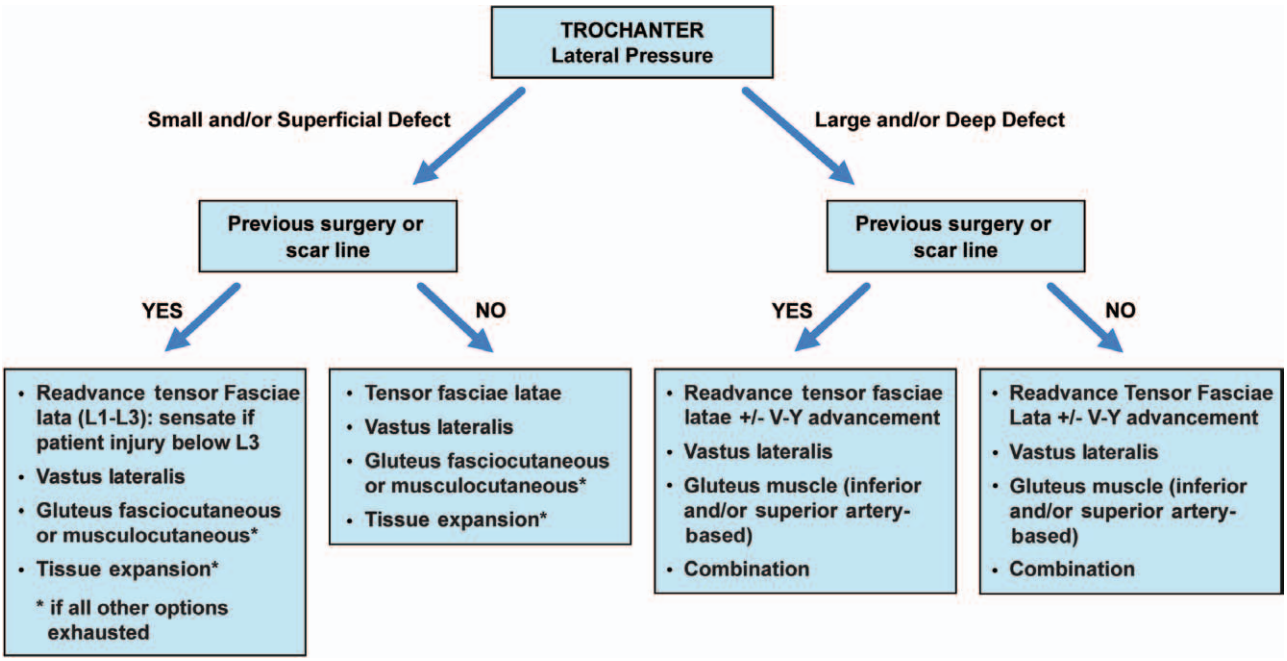



**Fig. 12.** Sources of flaps for trochanteric pressure sores.

treatment for a preexisting infection or osteomyelitis, based on recent cultures or empiric coverage, a broad-spectrum therapy is an important consideration. As culture data are obtained, the regimen is tailored.

Institutional sitting protocols are begun after approximately 2 to 3 weeks of complete flap offloading. The process is begun after the patient has healed enough to tolerate pressure on the flap, usually in 15- to 30-minute intervals to a goal of 2 hours at 6 weeks. Adjustments are made if the patient does not tolerate the protocol to protect the site. Drains are often left in place for a significant period to allow better flap apposition and may remain in place at discharge from the inpatient setting.[31,33]

## OUTCOMES

Surgical outcomes of pressure sore reconstruction have been an area of considerable research. Because of their recurrent nature, allocation of increasingly limited resources should target those patients most likely to benefit from surgical intervention. Recurrence rates have been reported between 3 and 82 percent, depending on endpoint definition and length of follow-up. An approximation of 70 percent is reported in the literature.[26] Predictors of pressure sore recurrence have been suggested, but clinical evidence is lacking. A recent retrospective review by Keys et al.[20] found a recurrence rate of 49 percent among spinal cord–injured patients. Defined as early recurrence or dehiscence requiring reoperation, significant risk factors were found to be poorly controlled diabetes, albumin levels less than 3.5 g/dl, age younger than 45 years, previous same-site surgery, and ischial wound location.[20]

Assessment of these risk factors in a structured algorithm may provide a potent resource in patient stratification. Given that one-third of spinal cord–injured patients have a pressure ulcer, with the majority having multiple wounds, understanding these recurrence risks is critical.

## CONCLUSIONS

Management of the pressure sore patient is multifaceted, with the outcomes related to the patient's comorbidities. Patients predisposed to pressure sores are also at significant risk of cardiovascular, pulmonary, renal/urologic, and bleeding disorders, among others. Concomitant infection, whether systemic or local, can worsen these conditions and, when added to the altered local tissue environment, risks further damage to adjacent structures. Bladder and bowel diversion can mitigate some of these dysfunctions, but damage to the organs themselves can be significant. Chronic wounds are also risk factors for Marjolin ulcer (Fig. 13), a type of squamous cell carcinoma. Social factors such as accessibility to supportive care, compliance, and substance abuse are also important considerations with considerable impact on definitive treatment.[22]

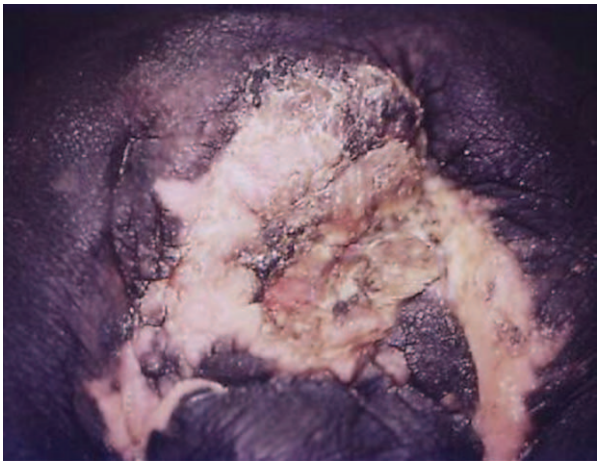


**Fig. 13.** Marjolin ulcer.

Given these concerns and the high recurrence rate, conservative management of the ulcers continues to be a well-traveled path. Preventative strategies and local wound care coordinated with a knowledgeable team are essential. The risks of surgery and recurrence must be balanced with the risk of infection, attention to wound care, and possible malignant degeneration. Further research into optimum wound care continues with an increased number of randomized controlled studies and systematic literature reviews. Once surgical intervention is decided on, the flap choice is determined as detailed above. As evidence-based medicine and limitations in health care spending continue to evolve, the holistic approach to the patient is crucial.

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## REFERENCES

1. Reddy M, Gill SS, Rochon PA. Preventing pressure ulcers: A systematic review. *JAMA* 2006;296:974–984.
2. Department of Health and Human Services. Centers for Medicare & Medicaid Services Program. Changes to the hospital Services Medicare Program. Changes to the hospital inpatient prospective payment systems and fiscal year 2009 rates. *Fed Reg.* 2008;73:48472.
3. Fisher AR, Wells G, Harrison MB. Factors associated with pressure ulcers in adults in acute care hospitals. *Adv Skin Wound Care* 2004;17:80–90.
4. Krause JS, Vines CL, Farley TL, Sniezek J, Coker J. An exploratory study of pressure ulcers after spinal cord injury: Relationship to protective behaviors and risk factors. *Arch Phys Med Rehabil.* 2001;82:107–113.
5. Daniel RK, Wheatley D, Priest D. Pressure sores and paraplegia: An experimental model. *Ann Plast Surg.* 1985;15:41–49.
6. Bauer J, Mancoll S, Phillips L. Pressure sores. In: Thorne CH, Beasley RW, Aston SJ, Bartlett SP, Gurtner GC, Spear SL, eds. *Grabb and Smith's Plastic Surgery.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2007:722–729.
7. Hahm G, Glaser JJ, Elster EA. Biomarkers to predict wound healing: The future of complex war wound management. *Plast Reconstr Surg.* 2011;127(Suppl 1):21S–26S.
8. Ladwig GP, Robson MC, Liu R, Kuhn MA, Muir DF, Schultz GS. Ratios of activated matrix metalloproteinase-9 to tissue inhibitor of matrix metalloproteinase-1 in wound fluids are inversely correlated with healing of pressure ulcers. *Wound Repair Regen.* 2002;10:26–37.
9. Beidler SK, Douillet CD, Berndt DF, Keagy BA, Rich PB, Marston WA. Multiplexed analysis of matrix metalloproteinases in leg ulcer tissue of patients with chronic venous insufficiency before and after compression therapy. *Wound Repair Regen.* 2008;16:642–648.
10. Utz ER, Elster EA, Tadaki DK, et al. Metalloproteinase expression is associated with traumatic wound failure. *J Surg Res.* 2010;159:633–639.
11. Forsberg JA, Elster EA, Andersen RC, et al. Correlation of procalcitonin and cytokine expression with dehiscence of wartime extremity wounds. *J Bone Joint Surg Am.* 2008;90:580–588.
12. Torra i Bou JE, Segovia Gomez T, Verdu Soriano J, et al. The effectiveness of a hyperoxygenated fatty acid compound in preventing pressure ulcers. *J Wound Care* 2005;14:117–121.
13. van der Cammen TJ, O'Callaghan U, Whitefield M. Prevention of pressure sores: A comparison of new and old pressure sore treatments. *Br J Clin Pract.* 1987;41:1009–1011.
14. Green MF, Exton-Smith AN, Helps EP, et al. Prophylaxis of pressure sores using a new lotion. *Modern Geriatr.* 1974;4:376–382.
15. Fan K, Tang J, Escandon J, Kirsner RS. State of the art in topical wound healing products. *Plast Reconstr Surg.* 2011;127(Suppl 1):44S–59S.
16. Reddy M, Gill SS, Kalkar SR, Wu W, Anderson PJ, Rochon PA. Treatment of pressure ulcers: A systematic review. *JAMA* 2008;300:2647–2662.
17. Janis JE, Kwon RK, Lalonde DH. A practical guide to wound healing. *Plast Reconstr Surg.* 2010;125:230e–244e.
18. Falanga V, Faria K. Bioengineered skin constructs. In: Lanza R, Langer R, Vacanti J, eds. *Principles of Tissue Engineering.* 3rd ed. Amsterdam: Elsevier Academic Press; 2007:1167–1185.
19. Bauer J, Phillips LG. MOC-PSSM CME article: Pressure sores. *Plast Reconstr Surg.* 2008;121(Suppl):1–10.
20. Keys KA, Daniali LN, Warner KJ, Mathes DW. Multivariate predictors of failure after flap coverage of pressure ulcers. *Plast Reconstr Surg.* 2010;125:1725–1734.
21. ter Riet G, Kessels AG, Knipschild PG. Randomized clinical trial of ascorbic acid in the treatment of pressure ulcers. *J Clin Epidemiol.* 1995;48:1453–1460.
22. Desneves KJ, Todorovic BE, Cassar A, Crowe TC. Treatment with supplementary arginine, vitamin C and zinc in patients with pressure ulcers: A randomised controlled trial. *Clin Nutr.* 2005;24:979–987.
23. Benati G, Delvecchio S, Cilla D, Pedone V. Impact on pressure ulcer healing of an arginine-enriched nutritional solution in patients with severe cognitive impairment. *Arch Gerontol Geriatr Suppl.* 2001;7:43–47.
24. Myers SA, Takiguchi S, Slavish S, Rose CL. Consistent wound care and nutritional support in treatment. *Decubitus* 1990;3:16–28.
25. Taylor TV, Rimmer S, Day B, Butcher J, Dymock IW. Ascorbic acid supplementation in the treatment of pressure-sores. *Lancet* 1974;2:544–546.
26. Norris JR, Reynolds RE. The effect of oral zinc sulfate therapy on decubitus ulcers. *J Am Geriatr Soc.* 1971;19:793–797.

27. Parry SW, Mathes SJ. Bilateral gluteus maximus myocutaneous advancement flaps: Sacral coverage for ambulatory patients. *Ann Plast Surg.* 1982;8:443–445.
28. Yoo KY, Jeong SW, Kim SJ, Ha IH, Lee J. Cardiovascular responses to endotracheal intubation in patients with acute and chronic spinal cord injuries. *Anesth Analg.* 2003;97:1162–1167.
29. Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: Etiologic factors and molecular mechanisms. *Anesthesiology* 2006;104:158–169.
30. Vasconez LO, Schneider WJ, Jurkiewicz MJ. Pressure sores. *Curr Probl Surg.* 1977;14:1–62.
31. Whitney J, Phillips L, Aslam R, et al. Guidelines for the treatment of pressure ulcers. *Wound Repair Regen.* 2006;14:663–679.
32. Foster RD. Pressure sores. In: Mathes S, Hentz V, eds. *Plastic Surgery.* Philadelphia: Saunders; 2006:1317–1311.
33. European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel. *Prevention and Treatment of Pressure Ulcers: Quick Reference Guide.* Washington DC: National Pressure Ulcer Advisory Panel; 2009.