The Pathophysiology of Skin Failure vs. Pressure Injury: Conditions That Cause Integument Destruction and Their Associated Implications

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ABSTRACT

Introduction. Although integument failure commonly is attributed to pressure alone, especially when a wound develops over a bony prominence (pressure injury), all skin failure should not be attributed to pressure injuries. **Objective.** A systematic review of the literature was conducted to: (1) differentiate the types of integument injury and etiology; (2) describe the anatomic and pathophysiologic factors affecting integument failure; (3) differentiate avoidable vs. unavoidable integumentary injury of nonpressure-related sources; (4) describe factors leading to integument injury, including comorbid and risk factors; and (5) briefly discuss clinical and economic importance of delineating pressure injuries from integument failure and associated risk factors in order to determine the pathophysiology underlying wound development and multiple factors capable of interacting with pressure to synergistically influence integumentary failure. **Methods.** The PubMed database was searched for English-language studies during March 2020 using the key words *pathophysiology*, *etiology*, *pressure ulcers*, *pressure injury*, *pressure wounds*, and *risk factors*. **Results.** The PubMed search yielded 1561 publications in total; of these, 59 were selected for review based on their relevance, timeliness, and subject matter, including 50 original studies of any study design, 5 review articles, and 4 public agency reports that addressed the 5 study purpose components. **Conclusions.** Clinicians need to better understand the pathophysiology and classification of integument injuries by underlying etiologies both avoidable and unavoidable. A more accurate diagnosis would lead to more appropriate treatment strategies, an improved quality of care for affected patients, less wasted resources and reduced financial penalties for healthcare providers, and decreased medicolegal claims.

KEY WORDS

integument failure, pressure injury, pressure ulcer, pathophysiology, skin failure

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With the medical advancements in past decades, patients frequently survive acute and/or chronic conditions that once relegated them to immediate death. Consequently, medical conditions, such as integument failure, once without time to manifest, are now commonly observed.

Skin is the largest organ in the body, and like other organ systems can fail.[1,2] Integument failure of various etiologies is a significant issue for severely ill patients in both acute and chronic care settings.[2] Indeed, of the more than 5 million patients treated annually in intensive care units (ICUs) in the United States, 12% to 42% will suffer from skin breakdown.[3,4] Yet, the pathophysiology and anatomic etiology underlying integument failure are not clearly described.

In 2014, the Centers for Medicare and Medicaid Services (CMS) set a goal to reduce the number of hospital-acquired conditions (including pressure injuries) by 20%.[5] The most recent Agency for Healthcare Research and Quality report[6] indicates that, while the number of hospital-acquired cases were improved from 2014 to 2016, conditions such as pressure injuries can (and should) be further reduced.

Since the CMS initiative,[5] the reported incidence of hospital-acquired pressure injuries (HAPIs) has increased from 2014 to 2016 by 10% in ICUs in the United States.[3,4] However, whether this increase is due to higher awareness about HAPIs or a combination of increased awareness and/or misidentification of the primary cause of injury is not clear.

Because of the complexity of the underlying mechanism leading to integument failure, it is imperative not only to better understand its underlying pathophysiology, but also to accurately classify integument injury by the avoidable and unavoidable factors responsible for injury (primary cause), including pressure. This may lead to better

and more appropriate treatment strategies, an improved quality of care, and better outcomes for affected patients, while potentially reducing wasted health care resources (eg, prolonged hospital stays, repeated emergency room visits), financial penalties for health care providers, and medicolegal claims.

The purpose of this study was to review existing studies and case reports to systematically present the (1) different types of integument injury and etiology; (2) anatomic and pathophysiologic factors affecting integument failure; (3) various ways to differentiate avoidable versus unavoidable integumentary injury regarding nonpressure-related sources; (4) factors leading to integument injury, including comorbid and risk factors; and (5) clinical and economic importance of delineating pressure injury from integument failure and associated risk factors.

METHODS

During March 2020, the PubMed database was searched for English-language studies using the keywords *pathophysiology*, *etiology*, or *risk factor*, in conjunction with any of the following terms, *pressure ulcers*, *pressure injury*, *pressure wounds*, and *skin failure*. The filters used were clinical trial, randomized controlled trials, review, and systematic review. The PubMed search yielded 1561 publications in total; of these, 59 were selected for review based on their relevance, timeliness, and subject matter, including 50 original studies of any study design, 5 review articles, and 4 public agency reports that addressed the 5 study purpose components. Although some of the articles are more than 5 years old, they were included for consideration because of their importance in this field. In addition, both of the terms *pressure ulcer* and *pressure injury* appear in the current study as they utilized in the cited publications. However, it is important to acknowledge that the National Pressure Ulcer Advisory Panel, now the National Pressure Injury Advisory Panel, released a document in 2016, that replaced the term *pressure ulcer* with *pressure injury* and presented the new definitions for the stages of pressure injury.[7]

RESULTS

Pathophysiology of integument failure

As the largest organ system in the body, integument failure leads to consequences that can be varied and severe. Despite the research conducted to date, the relevant anatomic pathophysiology has yet to be fully elucidated. Additionally, the terminology of various end-of-life integument injuries is not consistent and lacks consensus.

To better understand pathophysiology of integument failure, it is important to better understand its anatomy. In 1987, Taylor and Palmer[8] introduced the concept of *angiosomes* when describing the arterial anatomy. This 3D description of blood supply to the integument and underlying tissue laid the foundation for composite flap reconstruction. Taylor and Palmer[8] found that angiosomes are linked at every tissue level either by a true (simple) anastomotic arterial connection with no caliber change or by reduced-caliber choke anastomosis. The authors also found junctional zones between adjacent angiosomes at all levels of tissue. The muscles provide an important anastomotic detour (bypass shunt) when the main source artery is obstructed. This has recently led to the development of the concept of *functional angiosomes* as defined by Taylor et al[9]; they describe separate "islands" of skin (and underlying tissue) that are vascularly supplied by a single-source vessel. Connections between these islands called *anastomotic perforators* are true anastomosis and choke vessels that have the potential to dilate in response to ischemia, if time permits.[9] To date, no data have shown how vascular delay affects wound healing in areas of tissue loss and whether recruitment of surrounding choke vessels in the skin adjacent to integument injuries occurs. Taylor et al[9] describe the pathology that occurs when the perforating vessel of the angiosome is damaged. Keeping in mind that muscle is more prone to ischemia than skin, this seems particularly relevant.

Types of integument injury

Various types of injuries can damage skin. Pressure is the most commonly diagnosed injury in hospitals and nursing homes and is often avoidable. However, skin can break down and pressure is *not* the primary factor instigating necrosis; these causes are unavoidable. The following section will discuss different types of common injuries.

Pressure injury. The Joint Commission defines pressure injuries as localized damage to skin and/or underlying soft tissue, typically over a bony prominence.[7,10] They are at times painful, and skin may or may not lose integrity.[7] The injury occurs due to pressure alone or pressure in combination with shear. The tolerance of soft tissue for pressure and shear is thought to be affected by numerous factors, including nutrition, perfusion, hydration, and other medical comorbidities.[11]

Skin failure. Skin failure was first described in 1991 by Irvine[12] as a loss of normal temperature control with an inability to maintain core body temperature; failure to prevent percutaneous loss of fluid, electrolytes, and protein with resulting imbalance; and failure of the mechanical barrier to prevent penetration of foreign materials.

Acute skin failure. Acute skin failure describes the cause of integumentary loss in association with hemodynamic instability and/or organ system compromise in critically ill patients. In 2005, Inamadar and Palit[13] described acute skin failure as a state of total dysfunction of the skin resulting from varying dermatologic conditions, including erythroderma, Stevens-Johnson syndrome, and immunologic conditions. Many of these conditions lead to unavoidable integumentary failure. The authors[13] concluded that acute skin failure constitutes a dermatologic emergency requiring a multidisciplinary approach.

The term *skin failure* also was used by Delmore et al[2] to differentiate pressure injuries from acute skin failure in ICU patients. In their study of 552 ICU patients, acute skin failure was associated with peripheral arterial disease (PAD), mechanical ventilation, respiratory failure, liver failure, and severe sepsis/septic shock, with an odds ratio of these factors varying from 1.9 to 3.8.

Etiology of integument failure

Various etiologies lead to integument failure. These are affected by different factors

requiring thorough assessments and different treatments even though presenting symptoms may be similar. Therefore, it is important to understand the contributing factors to each etiology.

Functional angiosomes and integument failure. These conditions, specifically identified in critically ill patients, are associated with poor integumentary perfusion. The multifactorial interplay between cardiac output/ejection fraction, peripheral vascular disease, hypotension, sepsis, and various shock states affects the integument via the sympathetic portion of the autonomic nervous system and alpha receptors.[14] Additionally, distributive shock, which arises from abnormalities of the peripheral circulation (sepsis and anaphylaxis), further implicates perfusion of the tissues to integument failure.[14] When there is a significant reduction in perfusion, the risk of integumentary injury increases. Exactly at what point this occurs is multifactorial, affected by chronic conditions impacting the arterial vessels, varies by patient, and still to be understood.

Taylor et al[8] describe a pediatric patient with severe, full-thickness skin loss of the lower extremities from a meningococcal sepsis infection and associated 3D loss of entire angiosome secondary to associated perforator destruction. An association between the cutaneous perforators and tissue loss is evident from Taylor et al's photographs (**Figure 1**), which show full-thickness dermal loss as well as the loss of the entire 3D structure of an angiosome. This demonstrates a real-life consequence of damage to the perforator and associated angiosome.

The complexity of differentiating causes of integumentary injury is much greater when adjoining perforator anatomy and choke vessels are taken into consideration. In the presence of arterial disease, chronic microvascular calcifications, and contributing pathology such as uncontrolled diabetes, the effects on the vascular anatomy are even more complex. No current data are available to define increased or decreased relative risk between what could be considered watershed areas of perforator intensity in the event of ischemia or relative ischemia (areas with higher and lower perforator density). Areas such as the sacral midline lack musculature; the extent to which gluteal perforators connect with the sacral angiosome, as well as the extent of midline crossover, appears uncertain. Saint-Syr et al further described the theory of perforasomes, or the vascular territory that a perforating vessel supplies.[15] These perforasomes are shown to be linked via both direct and indirect linking vessels (**Figure 2**).

Additionally, as muscles are more prone to ischemic events from pressure, it is unclear if the temporal nature of the underlying compromise always happens at the time of noted integument breakdown. This suggests that an interval lag exists between each insult, as evidenced

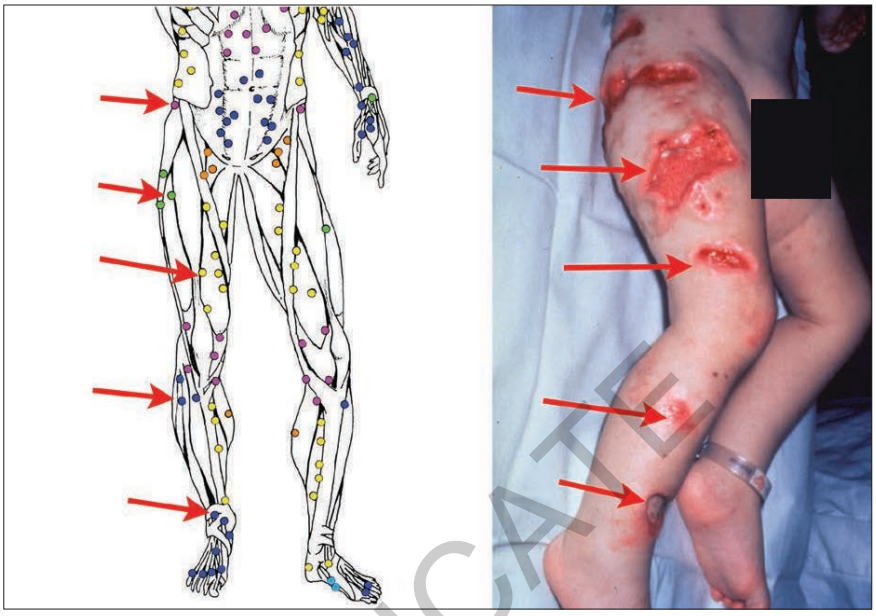


Figure 1. Integument failure corresponding to the cutaneous perforators. This relationship was described by Taylor et al's functional angiosome.[8]
Used with permission; Figure 11 from Taylor et al, *Plast Reconstr Surg,* 2017.

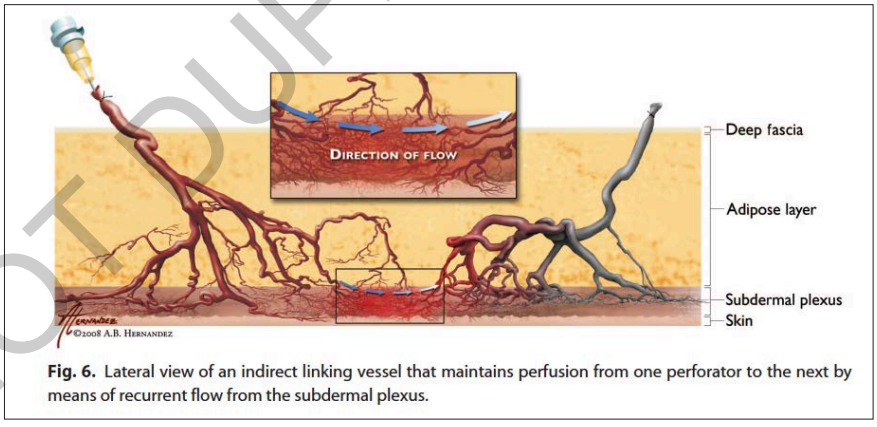
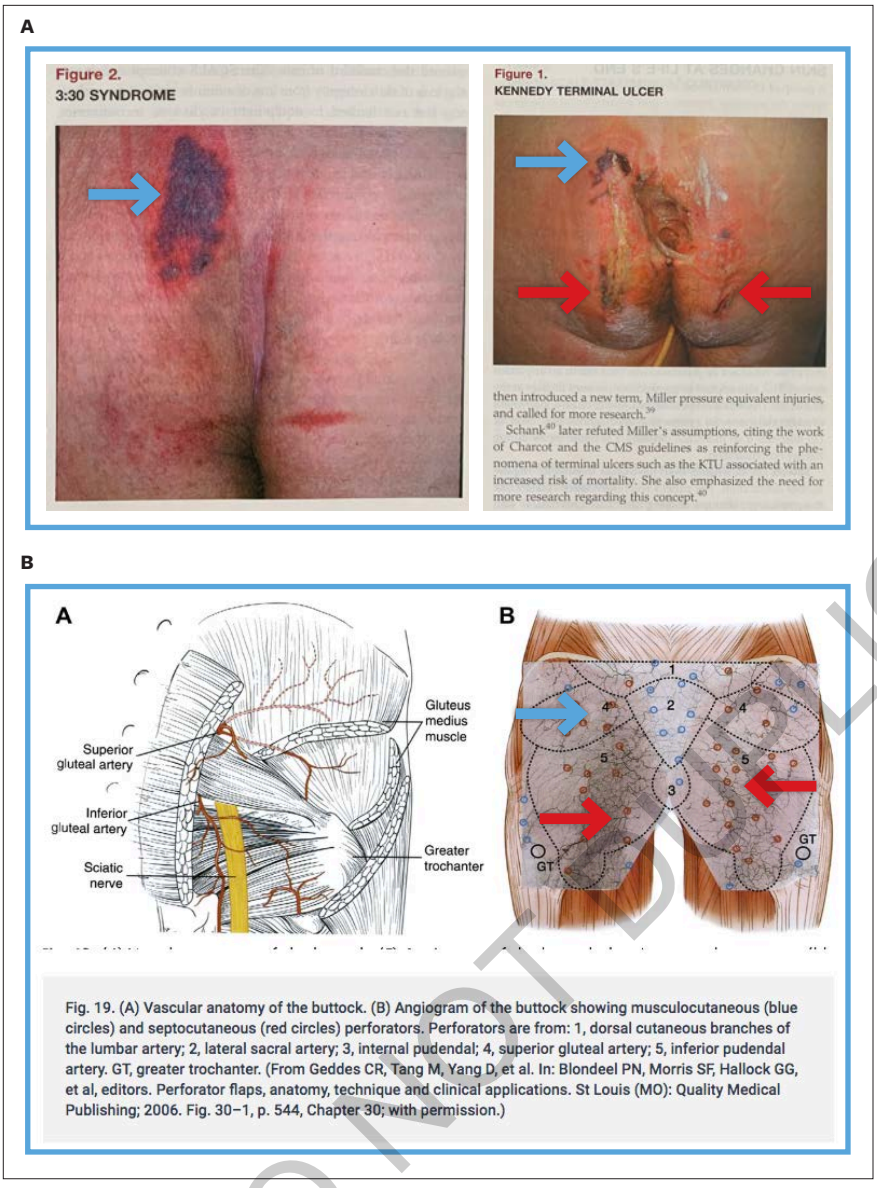


Fig. 6. Lateral view of an indirect linking vessel that maintains perfusion from one perforator to the next by means of recurrent flow from the subdermal plexus.

Figure 2. Lateral view of an indirect linking vessel. Vascular perforators are linked via direct vascular connections in the suprafascial and adipose layer and indirect linking vessels via the subdermal plexus. Communicating branches in the coronal, sagittal, and transverse planes provide a protective mechanism to ensure blood flow to the skin. This figure shows recurrent flow in indirect linking subdermal vessels. Both sets of vessels are prone to insult from multiple sources despite bidirectional and recurrent flow. Source: Saint-Cyr et al, 2009.[15]
Used with permission; Figure 6 from Saint-Cyr et al, *Plast Reconstr Surg,* 2009.



Figures 3. Example of misclassification. Kennedy ulcer and 3:30 syndrome (A)[16] with associated anatomic arterial perforators (B)[17] are shown in this figure. The blue arrow corresponds to the location of a clotted septocutaneous perforator of the superior gluteal artery and corresponding occlusion. The red arrow corresponds to location of clotted inferior pudendal artery. The photo at top right may truly represent an ischemic process often brought on by pressure, however both superior gluteal compromise and inferior pudendal compromise are easily identified. The photo at top left is compatible with superior gluteal artery compromise for which the corresponding anatomy is well shown in the 2 schematics.
Used with permission; Figures 1 and 2 from Ayello et al, *Adv Skin Wound Care*, 2019. Figure 19 from Morris et al, *Clin Plast Surg*, 2010.

when considering deep tissue injury while further research is needed.

Delmore et al[2] conclude that the "concept of acute skin failure remains an enigma," and that much of what is classified currently as *pressure injury* might be better categorized as *acute skin failure*. The pathophysiology of *acute skin failure* results from decreased perfusion within a functional angiosome via the cutaneous arterial perforators, inability of arterial anastomotic connections to augment flow, lack of time for choke vessels to respond and vasodilate followed by tissue ischemia, and eventually associated tissue loss. The initiating events leading to this destruction vary (**Figure 3**).

End-of-life integument failure

Integument failure at the end of life has been described in a number of ways.[18-20] Thrombley et al[20] noted and named terminal tissue injuries (TTI)—spontaneously appearing skin alterations found in end-of-life patients (**Figure 4**). Terminal tissue injuries are characterized as rapidly evolving and enlarging areas of stained skin in non-pressure areas. This phenomenon was further validated by a recent study by Brennan et al.[21] Terminal tissue injuries correspond to arterial perforators, as described by Taylor et al,[8] that occur in the absence of pressure (as described previously).

Terminal ulcers as described by Kennedy[18] typically occur between 1 day and 6 weeks before end of life. These terminal ulcerations have subsequently been characterized as skin failure as a result of ischemia.[22] Hypotension and shock states alone will not cause spontaneous failure of the integument. Tissue perfusion, skin surface pressure, and comorbid conditions all seem to act differently on the underlying angiosome in each patient. Photos of the terminal ulcerations show that the necrotic area appears to correlate with the sacral angiosome and destruction of the arterial perforators and the lateral areas of the adjoining angiosomes (**Figure 5**). A component can be observed of direct pressure injury as well as injury to the underlying arterial and adjoining perforators between the sacral and gluteal angiosomes. The adjoining choke vessels are not able to dilate and additionally perfuse the necrotic area owing to the acute nature of the injury. However, this may be a factor in the healing of marginally injured areas. This ultimately may explain why pressure injuries typically do not cause systemic sepsis; the choke vessels and anastomotic vessels are permanently damaged.

Research does not suggest that end-of-life integument injuries do not have a component of pressure. The associated comorbidities that cause hypoperfusion, exacerbated at the end of life within the

sacral angiosome itself, explain the etiology of these integumentary injuries. The sacrum and heels are not an anatomically privileged area. During times of hypotension, blood is shunted from the periphery and gastrointestinal tract and to the head, neck, and other major organs, making integumentary breakdown in those areas more likely.

Moisture-associated skin damage

Moisture-associated skin damage (MASD) is a type of contact dermatitis caused by prolonged exposure to various sources of moisture and is characterized by inflammation and erosion of the epidermis.[23,24] Pathologic studies have shown distinct differences between superficial pressure (stage 1) injuries and moisture.[25] Moisture-associated skin damage inflicts these superficial tissue injuries; they are distinguishable from those caused by pressure, but both activate pathways that can stimulate cell death and increase the skin's sensitivity to further integument failure.

Moisture-associated skin damage is influenced both by intrinsic factors (ie, perspiration, skin pH, psychological stress) and extrinsic factors (ie, chemical or biological irritants, medication metabolites, and infections). Woo et al[24] reported that patients with bowel or bladder incontinence are 5 times more likely to develop pressure injuries (5.6%–50%), with the highest percentage found among critically ill patients. However, the pathways that damage the stratum corneum of the sacrum due to the presence of chronic urine and stool and ultimately lead to an increased risk of pressure injury (per Woo et al's description[24]) are far more complex; as such, tissue destruction cannot always be attributed to pressure injury alone. Excess ammonia from incontinence creates an alkaline environment that promotes integumentary damage and potentiates the effect of fecal enzymes on the skin.[24] Independently, medical conditions such as neurological issues can augment urologic spasticity, increasing incontinence and its downstream effects. Drugs and their stool or urine metabolites can further exacerbate skin breakdown.[2]

Biofilm and infection in MASD injuries facilitate frank integumentary failures. Biofilm degrades epithelium, utilizing the ceramidase enzyme, initiating integumentary breakdown, and permitting subsequent bacterial colonization and infection.[26] Once present, bacteria compete for oxygen within the tissue, impairing perfusion and leading to integumentary death.

Moisture-associated skin damage tissue injury can closely mimic pressure, but it requires different treatment and prevention pathways. As more experience with MASD accumulates, its role as a factor acting synergistically with pressure during wound development becomes more evident.

Vasopressors and integument failure

Critically ill patients are recognized as at risk for integument breakdown over the torso.[27,28] Mean arterial pressure (MAP) has long been used to measure tissue perfusion[29,30]; a MAP less than 80 independently results in delayed wound healing and chronic wounds.[31] Additionally, end-organ perfusion is determined to be compromised if MAP is less than 60, but the overall effect on the skin has yet to be elucidated.[29,30] A MAP of less than 60 alone is not enough to cause acute integumentary failure throughout the body, underscoring acknowledgment that a complex interplay of factors must be present.

Multiple studies report inconsistent results regarding the risk of skin breakdown and the use of vasopressors. Vasopressors are known to act via various mechanisms at different dosages. Most have alpha agonists effects and cause vasoconstriction of the integument's perforators and choke vessels. A 2015 retrospective study by Cox and Roche[3] of 306 patients requiring vasopressor use in the ICU found a direct correlation between the use of 2 agents (norepinephrine with added vasopressin) and pressure ulcer development. These agents synergistically create an additive risk for skin breakdown by lowering perfusion to skin throughout the body. Presumably, the threshold integumentary failure, due to decreased arterial flow, becomes more pronounced with decreased perfusion (alpha agonist) effects of these medications with any risk factor.

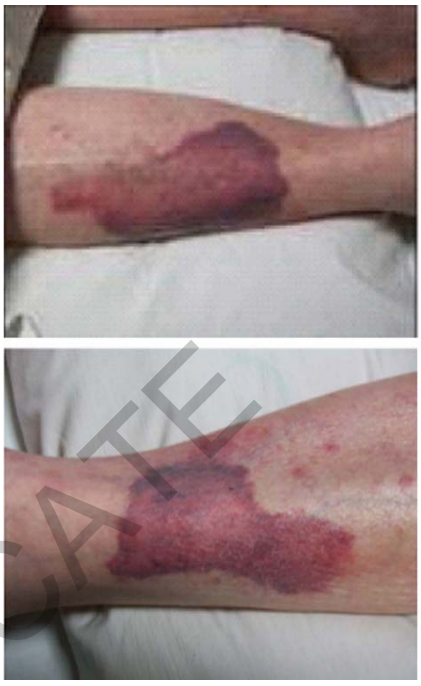


Figure 4. Terminal tissue injuries on lateral calf. The tissue injuries shown by Thrombley show cutaneous perforators as described by Taylor's functional angiosome (Figure 1), which shows ecchymosis arising from the cutaneous perforator.[20] Whether this is poor arterial perfusion leading to coagulation has yet to be elucidated. Used with permission; Figure 3 from Trombley K et al, *Am J Hosp Palliative Med*, 2012.

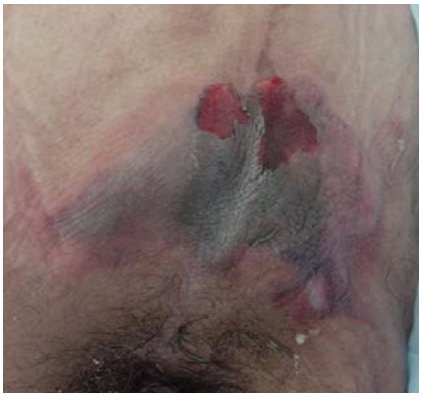


Figure 5. Terminal ulceration. Terminal ulcerations seem to be ischemic events at the end of life associated with arterial compromise, combined with a variable pressure component. Photo courtesy of Dot Weir, RN.

No single factor leads to integument breakdown. It appears that the multifactorial interplay among hypotension/shock, MAP less than 60, and vasopressor use increases the risk of integument breakdown.

Other factors, including smoking,[32] diabetes, immobility, nutrition, and PAD, further increase this risk.

Most common sites of integumentary failure

Sacrum. Breakdown of sacral integument is commonly observed both in acute and chronic care settings. The sacrum is more prone to ischemic insult in times of shock than is the lateral portion of the buttocks that lies directly over musculature. This difference is likely due to the paucity of cutaneous perforators from the superior and inferior branches of the lateral sacral artery that supply the single sacral angiosome compared with the relatively large number of vessels supplying the multiple buttock angiosomes.[33]

The 2017 research by Yamada et al[34] investigated the conditions associated with microvessel occlusion, a condition known to contribute to sacral integument failure. The authors hypothesized that even red blood cells stacked within sacral microvessels may cause enough pressure within the vessel to decrease perfusion into the sacral angiosome and promote integument failure. Their study[34] concluded that the interaction among external pressures, intrinsic comorbid factors (lower back anatomy, tissue elasticity, microvasculature stiffness, and pressure within vessels), and extrinsic comorbid factors (patient weight and posture) influence vascular occlusion, which result in sacral integument failure.

Extrapolating from the results of the Yamada et al study,[34] the pathophysiology of sacral integument failure is likely multifactorial and a result of external pressure, internal pressure, and comorbid factors on the angiosome microvasculature and the angiosome itself. No single factor causes sacral integument breakdown; when pressure and comorbid factors are present and interact synergistically, integument failure can result. If this is the case, integument breakdown in the sacrum continues to be a risk in health care settings.[27]

Heel. The heel of the foot is another common site of integument failure. The skin of the foot and ankle are comprised of 6 angiosomes supplied by 3 major arteries, creating significant vascular redundancy within a normally perfused foot.[35] In contrast, the plantar heel is comprised of a single angiosome supplied by 2 arteries: the calcaneal branch of the posterior tibial artery and the calcaneal branch of the peroneal artery.[36] Similar to the rest of the foot and ankle, perforator crossover is substantial in the heel of the foot.[29,33]

Other comorbid factors influencing angiosome perfusion, such as chronic hypoxia/reperfusion injury, impaired nutrient supply, growth factor abnormalities, and chronic inflammation, also affect tissue sensitivity to pressure.[35] Furthermore, a history of uncontrolled diabetes, which destroys the microvascular circulation, is a confounding factor not easily measured, especially when coupled with loss of major perforators.

Integument failure in the heel is most commonly associated with pressure. Many patients who develop heel pressure ulcers have undiagnosed arterial insufficiency or PAD because there is no way to identify the loss of the lateral peroneal artery branches by physical examination.[29,33]

In patients with either microvascular disease or gross vascular disease, small dermal breaks eventually develop into chronic wounds and can be exacerbated by factors other than pressure. For example, translocation of bacteria biofilm production with subsequent translocation across the heel stratum corneum promotes further integumentary breakdown and permits bacterial colonization and infection.[26] These bacteria compete with living tissue for oxygen, resulting in relative ischemia and leading to integumentary compromise and death of the skin in the heel. Researchers and clinicians are seeking to determine whether this lowers the threshold by which pressure can cause skin breakdown or, in the presence of arterial disease and active offloading, it increases the risk of integumentary comprise due to lack of perfusion.

Risk factors for integument failure

Multiple comorbid or risk factors influence integument breakdown, affecting patients' quality of life while increasing medical expenses. These risk factors usually overlap between integument failure and pressure injury; therefore, identifying which patients are at high risk for skin breakdown is critical.[37] Major risk factors include the following.

Body mass index. Body mass index (BMI) has a complicated effect on pressure injuries in ICU patients. Patients who are underweight (BMI < 19) and those who are morbidly obese (BMI ≥ 40) appear to have an increased risk of pressure injury.[38] Yet, obese patients with a BMI between 25 and 40 seem to be protected from pressure injury. Hyun and others[38-40] found that, although extremely obese patients had lower Braden scores upon ICU admission ($P < .001$), they presented with a significantly higher incidence of pressure ulcers ($P < .001$). The interplay among all of these factors was found to affect the avoidability or unavoidability of integumentary loss, unanticipated results that are likely due to the multifactorial etiology of integument breakdown.

Stress. Choe et al[41] recently identified psychological stress as a factor that influences the severity of MASD. Psychological stress increases integumentary production of endogenous glucocorticoids that destabilize skin barrier function.[41,42] These study authors also noted marked improvement in skin barrier function following administration of selective serotonin reuptake inhibitors (SSRIs).[41] Although stress is an important aspect of patient recovery, few studies are available and more research effort is warranted.

Uncontrolled diabetes mellitus. Uncontrolled diabetes mellitus (DM) often presents with hypertension and associated renal problems. These conditions can lead to calcified blood vessels and microvascular damage, resulting in decreased perfusion of flow through blood vessels to the skin and causing various skin problems and breakdowns, regardless of the types of DM.[43] Due to the high prevalence of DM, especially in elderly patients, it should be taken into consideration when evaluating integument failures.

Malnutrition and hydration. Malnutrition and hydration have long been associated with wound development and impaired healing, including pressure ulcers.[44,45] Chronic wounds are usually seen among the elderly with comorbidities and,

frequently, with malnutrition.[46,47] Malnutrition has been suggested to double the risk of developing pressure ulcers.[48] Although more research is needed, evaluations of malnutrition in patients at high risk of either skin breakdown or chronic wounds is warranted due to its possible role in integument breakdown.

Assessing for integument failure

Multiple scales have been designed to assess the risk of integument breakdown, including the Braden, Norton, and Risk Assessment Pressure Sore (RAPS) scales.[39,49,50] The Braden Scale is one of the most commonly used scales in the United States and is clinically validated with a high capacity to predict skin failure.[39,49,51,52] This scale consists of 6 subscales measuring 6 risk factors (Sensory Perception, Moisture, Activity, Mobility, Nutrition, and Friction/Shear).[49] A lower Braden score indicates a reduced level of functioning and, therefore, a higher risk for integument failure.[53]

Although other scales can be utilized to assess the risk of skin breakdown (pressure injury), the Braden Scale is among the risk assessment instruments that are balanced between sensitivity and specificity[50] and can be applied to more than pressure injury. More importantly, the Braden Scale is a proxy for many of the comorbidities known to contribute to causes of acute integument failure. Taking comorbidities into account while treating critically ill patients is crucial because they may render a patient's tissue unable to tolerate even the briefest time of ischemia without negative consequences.

DISCUSSION

The significance of integument failure in both acute and chronic settings is exemplified by its inclusion as a condition subject to the CMS Deficit Reduction Act.[54] This directive requires hospitals to report secondary diagnoses that are present on patient admission and is reserved for high-cost, high-volume conditions thought preventable using evidence-based guidelines. The CMS emphasizes the importance of identifying pre-existing "pressure injuries" with appropriate documentation as the only mechanism by which facilities can maintain treatment reimbursement. Thus, addressing pressure injuries, unavoidable or otherwise, has become a direct financial responsibility of the care facility where the condition was not present on admission.

In reality, the etiology of *pressure injuries* is multifactorial and should be attributed to the interplay between pressure and comorbid factors including vascular disease, nutrition, hydration, infections, medication, and medical conditions; all influence tissue perfusion and oxygenation and ultimately affect skin stability. In the authors' opinion, pressure is only one facet of integument failure. If a person with DM and PAD developed a foot wound, the integument breakdown would most likely be attributed to DM and PAD. However, if the same person developed a heel wound, it would likely be called a pressure injury, despite presenting the same etiology. In both cases, DM with chronic calcification and microvascular loss, PAD, and pressure all play a role, and these etiologies ultimately act synergistically. Therefore, current institutional protocols designed to reduce skin breakdown, such as every 2-hour (q2h) turning, are likely destined to fail in patients with multiple risk factors and associated conditions.

Identification of the comorbid factor(s) that contribute to or exacerbate the development of both acute and chronic integument failure is a challenge in all medical care facilities, affecting both the quality of individual health outcomes and the economic resources of health care infrastructures.[35] From 2014 to 2016, the incidence of HAPI rose by 10%, despite increased awareness of skin injuries and the implementation of increasingly aggressive wound prevention protocols in medical facilities.[6] Because integument breakdown is multifactorial, failure can occur despite the implementation of interventions designed to address pressure alone (turning q2h, pressure-redistribution mattresses, and pressure-reduction dressings).

If skin injuries were correctly classified by the comorbid factors acting in conjunction with pressure, the number of HAPIs for which nursing homes and hospitals are financially responsible, would significantly decrease.[55] It is important to identify patients with significant MASD and associated conditions so that appropriate care and prevention of integumentary failure in these cases can be addressed. Likely, many end-of-life integumentary failures are not avoidable. Integument failure in the ICU, when the patient is turned q2h and cared for appropriately while on vasopressors, would be correctly identified as a complication of a medication with an open wound of the appropriate body part. These are not avoidable pressure injuries and should not be identified as such.

In the authors' opinion, available scientific evidence indicates integument failure is multifactorial and due to comorbid factors that can reduce angiosome perfusion. The diagnosis of skin breakdown as a pressure injury should be a diagnosis of exclusion rather than an automatic conclusion despite the high likelihood of being the actual diagnosis. This directly challenges the time-honored assumption that all integument failure is preventable. In the authors' opinion, a patient's attendant comorbidities may render their tissues unable to tolerate even the briefest ischemia without consequence, regardless of current hospital or nursing home protocols.

Care should be taken to accurately identify the pathophysiologic causes of integument breakdown because they play a significant role in determining the best long-term treatment strategies for patients with skin wounds.

How a patient's chronic disease is diagnosed and managed substantially impacts the cost of care.[56] For example, hospitals are ultimately responsible for the cost of HAPIs, because payer local coverage determinations (LCDs) and other Medicare quality initiatives are based on the faulty premise that all pressure injuries are preventable.[57] In the United States, a further complication is being able to determine when a HAPI occurred, particularly during the transfer of a patient from another facility to a hospital setting and which may be inaccurate due to inadequate administrative claims and reporting methods.[58] New approaches, such as digital wound care management in conjunction with data analytics, can reduce the

incidence of *preventable* pressure injuries and the associated burden of care and litigation,[59] but it could also be potentially harnessed as an avenue to identify other causes of integument failure if the paradigm on pressure focus is changed. Most importantly, the cost of skin failure in any setting attributable to causes other than pressure is not known because no coding mechanism exists to facilitate data collection. If providers and payers recognize that certain kinds of integument failure are being misdiagnosed as preventable pressure injuries, this could lead to new evidence-based guidelines that would employ better algorithms to identify those patients at risk for various modes of failure. In turn, this could pave the way for cost-effectiveness analysis of treatments that not only would benefit payers and providers in terms of cost, but also the patients who could receive more appropriate care.

LIMITATIONS

This review is limited by the depth of the literature view and focus on specific issues, in particular by the difficulty in assessment of the anatomic changes that occur in ill patients, the focus of studies in different anatomical areas, and the difference between living tissue and cadaver research.

CONCLUSIONS

It is imperative not only to better understand the pathophysiology, but also to accurately classify integument injuries by factors responsible for the injuries (primary cause) both avoidable and unavoidable, including pressure. A more accurate diagnosis, which could be formalized by Medicare in terms of claims and amended directives, could result in more appropriate treatment strategies, an improved quality of care for affected patients, fewer wasted resources and reduced financial penalties for health care providers, and decreased medicolegal claims.

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