PRESSURE ULCERS/INJURIES:

DEFINITION AND ETIOLOGY

Version date: 25 Feb 2025

Suggested Citation

National Pressure Injury Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance. Pressure Ulcers/Injuries: Definition ad Etiology. In: Prevention and Treatment of Pressure Ulcers/Injuries: Clinical Practice Guideline. The International Guideline: Fourth Edition. Emily Haesler (Ed.). 2025. [cited: ***download date***]. Available from: https://internationalguideline.com.

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Definition

Pressure ulcers/injuries are localized damage to the skin and/or underlying tissue, usually over a bony prominences or related to a medical or other devices, resulting from prolonged pressure or pressure in combination with shear.[1] The lesion can present below intact skin or as an open ulcer, which may be painful. Synonyms for this condition include, bedsores, decubitus ulcers, pressure sores and many more.[1] Because most of the English-speaking population, including Australia and the United States of America, prefers the term pressure injury (PI), PI will be used in this International Clinical Practice Guideline (CPG). In the latest version of the Mortality and Morbidity Statistics provided by the WHO (ICD-11), the official terms is 'EH90 Pressure ulceration' including pressure injury, pressure ulcer, and bedsore.[2]

How does a pressure injury occur?

Prolonged mechanical loads on the skin and underlying soft tissues can lead to PIs. These loads cause tissue deformation, which may indirectly result in injury by occluding blood and lymph vessels, leading to necrotic and apoptotic cell death. Alternatively, tissue deformation can cause direct injury by impairing essential cellular functions. Original research from Kosiak[3] and Reswick and Rogers[4] identified a relationship between the magnitude of externally applied pressure, the exposure time, and the likelihood of tissue compromise. This has since been modified to represent a sigmoid curve which provides important insight between the relationship between pressure/tissue deformation, time and tissue tolerance to load.[5] It is of note that this sigmoid relationship may change depending on intrinsic factors such as age, nutrition, skin status (history of wounds) and other comorbidities.[6]

Depending on the body position and posture, damaging loads typically occur at body areas where skin, vessels, subcutaneous fat, or muscle tissue are compressed and sheared between stiff internal structures such as bones or tendon and the adjacent surface such as cushions, mattresses or (medical) devices. Research into the etiology and pathogenesis of PIs can be traced back many decades. However, a modern understanding of the complex PI development emerged approximately 20 years ago[7] through a series of animal and cell model studies. It is not entirely clear and predictable how exactly mechanical loading conditions are transferred to local stresses and strains inside the deformed soft tissues, and how this ultimately leads to cell death. However, there are four main pathophysiological theories: localized ischemia, direct cell deformation damage, reperfusion injury, and impaired lymphatic drainage.[7-9]

Localized ischemia

A huge body of evidence indicates that sustained tissue loading reduces the blood flow and tissue perfusion leading to a shortage of required oxygen and nutrient supply. This causes an accumulation of waste products including carbon dioxide and local acidosis,[10] eventually leading to cell death.[1] However, the actual effects of the reduced blood flow depend on the tissue type. For example, muscle tissue is much more susceptible to ischemia compared to skin, which is much more resistant to reduced perfusion.[1,7] It is also assumed that even at very high deformation, not all vessels are closed, and the degree of ischemia seems to depend on the anatomical location, and loading frequency when cyclical loading is applied.[11,12] In addition, the duration of ischemia that results in tissue damage is not fully understood, although animal models have identified that > 90 minutes maybe required to see cellular changes in tissue.[13]

Direct cell deformation

It has become clear over the last 20 years, that sustained deformation of cells leads directly to cell damage and death.[7,8] Proposed pathways include changes of the cytoskeleton and an increased permeability of cell membranes exceeding the threshold for normal cell homeostasis. Under high tissue deformation when the individual damage threshold is exceeded, this process is believed to be fast, within minutes.[1,9] However, these observations were primarily made in muscle and subcutaneous fat tissue, not in the skin.[8] There has also been research, which, has shown that cellular damage can propagate away from the loaded regions in compression, with subject specific tolerance to mechanical loading which cannot be explained by tissue deformations alone.[14]

Reperfusion injury

When tissues are relieved following periods of loading and ischemia, a physiological reactive hyperemic response occurs to restore the oxygen and carbon dioxide levels in local tissues. There is an association between the magnitude and duration of loading and post loading reactive hyperemia.[11] According to the reperfusion injury theory, the restoration of blood flow also leads to an instant release of accumulated waste products including reactive oxygen species causing inflammation.[7,15] This phenomenon is known in other diseases including myocardial infarction, but a direct extrapolation to the context of PI development is difficult, as PI are not solely caused by complete occlusion of all blood vessels in compressed tissues. There is evidence that tissue injury may increase with a greater number of total ischemia-reperfusion cycles, duration of ischemia, and frequency of ischemia-reperfusion cycles.[16] However, ischemia and reperfusion injury does not explain the rapid onset of deep ulceration undermining intact skin.[8] The physiologic reactive hyperemic response may also be influenced by other factors such as local tissue temperature, with cooling reducing the speed and magnitude of local blood flow back to the tissue.[17]

Impaired lymphatic function

This theory states that sustained mechanical loading may impair lymph flow, reducing the clearance of waste products in soft tissues.[7,18] Similar to perfusion related theories, empirical findings are based on the skin layers and indicate huge interindividual variability.[19,20] Evidence suggests that the level of tissue deformation to occlude lymphatic vessels is lower than that of blood vessels due to their anatomical and physiological characteristics.[21] Lymphatics plays an important role in clearing local oedema and by products of tissue compromise e.g., metabolic waste and inflammatory cytokines, although its relative importance in PI etiology is less well known.

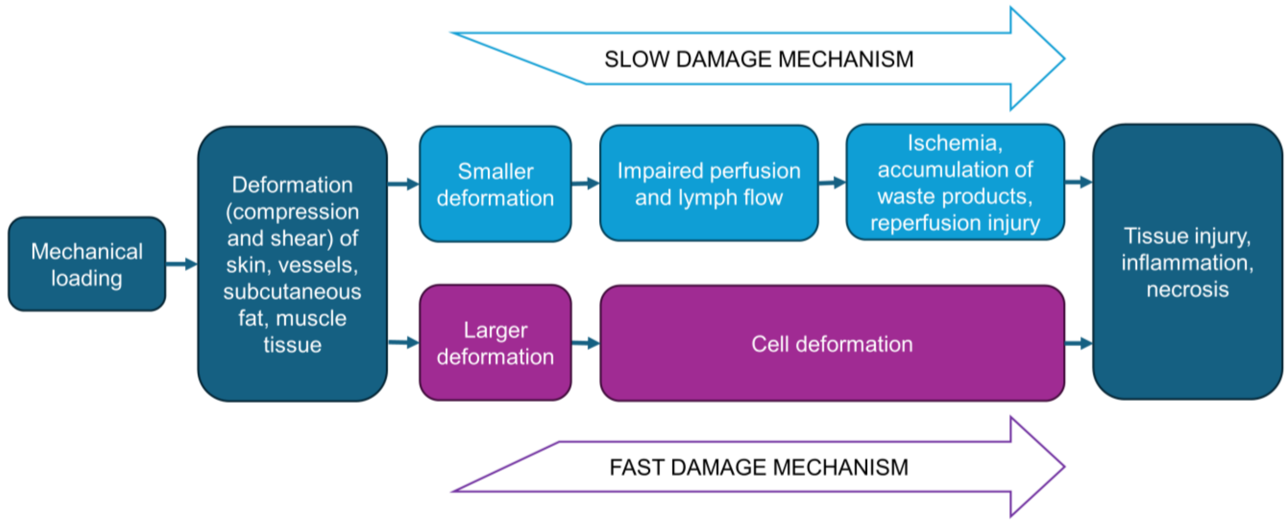

Figure 1. Reported pathophysiological pathways leading to pressure ulceration

Implications for pressure injury development in clinical practice

Animal and human studies, laboratory research, and computer simulations provide evidence that all four pathologic pathways play a role and do this most probably in combination, whereby ischemia and direct cell damage are without doubt very important (Figure 1). The critical threshold and period in which these pathways are active will vary between individuals [22]. In clinical research and practice, it is currently impossible to disentangle these pathways. This is because in loaded tissues all processes act simultaneously and differently at different structural and functional hierarchical levels such as vessels, tissues, and cells [9]. For example, direct cell damage due to loading has been well described in muscle tissues but not for the skin. Direct cell deformation damage seems to be a fast process in muscle tissue leading to deep tissue injuries, whereas ischemia may take much longer to induce pathologic tissue changes [8]. These diverse pathways may explain the difference between the rapid development of deep PI and possibly more friction and shear related superficial PIs [1,8,9]. Taking all loaded tissue layers into account, evidence indicates that signs of PI development might be detectable in all involved tissues including skin, subcutaneous fat, or muscle [23-25]. The anatomical location, morphology (e.g. bone geometry, tissue thickness), properties of soft and stiff tissues, degree of tissue deformation, skin microclimate, individual tolerance, and repair capacity, determine whether damage thresholds are exceeded or not, leading to either deeper or more superficial PIs [1,26,27].

In conclusion, the likelihood of PI development increases with the magnitude and duration of soft tissue loading. Direct deformation damage may occur quickly, whereas perfusion related damage may take much longer to cause local cell death and necrosis. Both major pathways interact and because of the complexity and substantial intra- and inter-individual variability, exact damage thresholds cannot be predicted. Thus, minimizing the magnitude and duration of load on vulnerable tissue sites and applying a personalized prevention approach aligns strongly with our current understanding of pressure injury etiology.

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