The pathophysiological links between pressure ulcers and pain and the role of the support surface in mitigating both


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This article reviews the reported associations between the alleviation of sustained or excessive tissue deformation and mitigation of pressure ulcer (PU) risk or associated pain, with a specific focus on the role of the support surface. Three patient case studies are used to analyse relevant literature and demonstrate important links between aetiological factors for PUs, background diseases, perceptions of discomfort and pain, and the ability of an adequate support surface to provide relief. Taken together, the literature and case studies indicate that alleviation of sustained or excessive soft tissue deformation caused by weight-bearing forces — through adequate envelopment of the support surface — protects from PUs and also effectively relieves chronic pain.

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Pressure ulcers (PUs), or pressure injuries, result from sustained cell and tissue deformations (Gefen 2018, 2019; Gefen et al, 2019). Primary deformation-inflicted damage progresses over time and exacerbated by secondary inflammatory damage and tertiary ischaemic damage (Gefen 2018, 2019; Gefen et al, 2019). Tissue damage in PUs does not appear instantaneously but develops gradually from the cellular to the tissue level. It ultimately presents as skin breakdown or discolouration (typically purple or maroon marks) due to underlying tissue necrosis.

When lying in bed, the transfer of body weight forces to the support surface cause sustained soft tissue distortion and high concentrations of tissue stress, particularly under bony prominences where rigid and highly curved (almost 'sharp') bone surfaces come into contact with easily deformable soft (muscle, adipose or skin) tissues. High levels of tissue stress progressively damage the cytoskeleton, the complex protein scaffold that forms the structural framework of cells and supports the plasma membrane. Damage to the cytoskeleton leads to plasma membrane poration, which in turn compromises molecular transport across the cell membrane. The inability of a large number of cells to control molecular traffic causes collective loss of homeostasis, resulting in massive apoptotic cell death within minutes (Gefen 2008; Gefen and Weihs, 2016; Gefen et al, 2019, 2020). This triggers damaged and dead cells and nearby immune cells to release pro-inflammatory cytokines, such as interleukin-1α (IL-1α) and tumour necrosis factor-α (TNF-α), which activate and attract additional immune and tissue-repairing cells such as mast cells and fibroblasts (Soetens et al, 2019). The recruitment of immune and tissue-repairing cells is a normal phase in the body's response to localised cell and tissue damage and is primarily aimed at clearing cellular debris, neutralising potential pathogens and preparing for tissue regeneration.

However, in the context of PU aetiology, pro-inflammatory signalling can contribute to injury as local vasodilation and increased blood vessel permeability facilitate leukocyte extravasation, enabling immune cells to migrate from the circulatory system to the site of initial damage and resulting in leaky vasculature, causing plasma to build-up in the interstitial spaces, resulting in oedema (Traa et al, 2019). When constrained between a bony prominence and a support surface, which is often the case for bed-bound patients, the soft tissues cannot sufficiently expand in volume. This causes a

sharp rise in interstitial pressure, leading to further cell deformation and additional cell death (Gefen 2018, 2019; Gefen et al, 2019, 2020). In an effort to relieve rising interstitial pressure, reactive oxygen and nitrogen species may be released. These degrade and damage the extracellular matrix. Growing interstitial pressure may eventually obstruct the vasculature, inducing additional ischaemic damage. The three key aetiological factors that contribute to PUs — direct deformation damage (primary), inflammatory damage (secondary) and ischaemic damage (tertiary) — degrade and exacerbate the state of the cells and tissues (Gefen 2018, 2019; Gefen et al, 2019, 2020). Each is activated successively at a time and rate specific to the individual. A person's anatomy (bony prominences, soft tissue mass and composition) affects the extent of deformation-inflicted tissue damage. Their immune system function affects the extent and rate of accumulated inflammation-related damage and their cardiovascular system determines the magnitude and rate of ischaemic damage (Gefen 2018, 2019; Gefen et al, 2019, 2020). Exposure to sustained cell and tissue deformation is always the triggering event and driving factor in this cycle. The most effective intervention is to reduce exposure to sustained tissue deformation and high concentrations of tissue stress.

What makes a support surface effective in PU prevention?

The two most important biomechanical features determining the effectiveness of a support surface in reducing the risk of PUs for patients with impaired movement or sensory functions are immersion and envelopment (Levy et al, 2018; Call and Cheney, 2020; Call et al, 2020):

- Immersion is the depth to which a patient's body penetrates when placed on a support surface
- Envelopment is the ability of a support surface to conform around the patient's body.

Good envelopment is associated with low interface pressures and shear, since more of the body surface area is in contact with the support surface and the body weight loads are transferred more uniformly (Call and Cheney, 2020; Call et al, 2020). The larger the contact area for load transfer, the smaller the localised cell and tissue deformations and tissue stress concentrations. A support surface that continuously provides good envelopment regardless of patient body characteristics and position fulfils the primary requirement for being effective in PU prevention (Levy et al, 2018). Additional features affecting the sustained tissue loading conditions of a patient positioned on a mattress are the frictional properties of the skin-facing layer (which could potentially be the bedsheets or the mattress cover) and thermal properties of the support surface, which determine the microclimate at the body–mattress interface. Elevated skin temperatures may lead to perspiration, which causes adhesive friction resulting in elevated frictional forces on the skin and sustained shearing in underlying tissues (Schwartz et al, 2018; Zeevi et al, 2018). Skin temperature rise will also increase the metabolic rate and demands on skin and underlying tissues, making tissues more susceptible to ischaemic damage. Each 1°C rise in tissue temperature is associated with a 10–13% increment in oxygen consumption by the tissue's cells (Landsberg et al, 2009).

The links between PUs and pain

In contrast to measurable physiological signals – such as heart rate, blood pressure or core body temperature – pain is subjective and cannot be quantified in a strict sense. While noxious pain stimuli and the associated neural responses can be assessed from an electrophysiological (laboratory) perspective, the pain sensation itself ('the pain experience') is multifaceted and includes mental, psychological, emotional, cognitive and social elements, all of which are characteristic to the individual and specific to the time and circumstances (Upton and Solowiej, 2010). Accordingly, the pain experience can only be evaluated with a patient's cooperation and requires a patient-centred approach for interpretation (Crowe et al, 2019). Little information has been published on the relationship between PUs and pain and the role of the support surface in this regard. Studies have mentioned anecdotally that the type of support surface may be associated with improvement in reported discomfort or pain levels in patients at risk of PUs (Girouard et al, 2008; Gouin and Kiecolt-Glaser, 2011; Gleeson, 2016). However, individualised multifactorial subjective elements — including learned behaviours to cope with chronic pain — limit the validity of such work. Given the subjective nature of pain perception and need for a patient-centred approach, case reports reviewing the conditions and quality of life of individuals and documenting their relevant experience is useful, despite being qualitative rather than quantitative (Gefen and Soppi, 2020).

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Although the pain experienced by bed-bound individuals has non-physical elements, it typically includes noxious physical stimuli. Sustained tissue deformation activates peripheral sensory neurons (nociceptors) in the skin as well as the adipose, ligament, tendon and skeletal muscle tissues; these nociceptors transmit signals to the spinal and supra-spinal nuclei and, from there, to the medulla oblongata in the brainstem (Bechert and Abraham, 2009; Gold and Gebhart, 2020). Once nociceptive stimuli reach the brain, a process of pain modulation is activated: the body may decrease pain intensity by inhibiting the ascending transmission of pain impulses from the primary afferent neurons to the second-order neurons in the spinal cord (Bechert and Abraham, 2009). Pharmaceutical opioids that bind to receptors at the dorsal horn of the spinal cord can mimic or enhance pain modulation (Bechert and Abraham, 2009). The brain's primary somatosensory cortex is highly involved in the sensory aspects of pain, including localisation and discrimination of pain intensity (Bushnell et al, 1999). Damage to this specific region, eg due to a brain trauma or cerebrovascular accident, may impact the body's ability to modulate pain and cause somatosensory symptoms.

The central nervous system picks up and delivers pain signals, indicating potentially tissue-damaging events through nociceptors. This sensory perception is the first line of defence against PUs. Motor ability is needed to respond to discomfort or pain stimuli in a timely manner (through postural changes including micro-movements). These sensory and motor abilities distinguish healthy people from those at risk of developing PUs. Susceptibility to deformation-inflicted tissue damage can be due to high-level nerve injury, eg stroke or peripheral neuropathy.

Inflammation — a key factor in PU development — is very strongly related to pain. Pro-inflammatory cytokines contribute not only to the onset and maintenance of inflammation after localised mass cell death events but also to the development of pain by stimulating nociceptors (Kulmatycki and Jamali, 2007). IL-6 and TNF-α, which are associated with PU formation (Jiang et al, 2014; Kurose et al, 2015; Krishnan et al, 2017), also play important roles in pathological pain (Hess et al, 2011; Zhou et al, 2016; Gefen and Soppi, 2020). Inflammation lowers the threshold for pain perception in the central nervous system, leading to hyperalgesia (Reinold et al, 2005) and elevated concentrations of pro-inflammatory cytokines are neurotoxic (Czirr and Wyss-Coray, 2012; Brambilla, 2019), hence, PU-related inflammation aggravates the neural system.

'Inflammatory pain' is one of three primary contributors to the general pain sensation associated with exposure to sustained tissue deformation. The second is mechanical irritation resulting from increasing interstitial pressure on nociceptors as inflammatory oedema builds, causing direct 'nociceptive pain' (Fleckenstein et al, 2017; Gefen and Soppi, 2020). Direct mechanical loading on primary nerve endings when the skin breaks down, as occurs in category 2 or deeper PUs, also causes nociceptive pain (Bechert and Abraham, 2009). The third contributor to general pain is ischaemic (and acidotic) biochemical conditions in the soft tissues at and adjacent to the site of damage. These conditions may develop once oedema compromises blood perfusion, inducing 'ischaemic pain' (Gefen and Soppi, 2020). Nociceptors are further stimulated by the accumulation of lactic acid in ischaemic tissue regions, as hypoxic cells shift to an anaerobic metabolic pathway, lowering tissue pH, and by a rise in extracellular adenosine triphosphate (Inoue et al, 2005; Melani et al, 2005; Birdsong et al, 2010; Anitescu, 2018). Ischaemic pain can be amplified by the presence of sustained shear stresses in soft tissues distorted due to the force of body weight or an externally applied medical device. Such stresses may further obstruct the vasculature and aggravate biochemical tissue conditions (Linder-Ganz and Gefen, 2007). Multifactorial general pain, consisting of inflammatory, nociceptive and ischemic pain components, is therefore strongly coupled with PU development, in which inflammatory and ischaemic damage play a key role (Gefen, 2018, 2019; Gefen et al, 2019; Gefen and Soppi, 2020).

Reducing general pain typically improves the overall mental and physical conditions of at-risk patients, allowing them to better respond to (physically) or communicate (verbally) any changes or sensations that may indicate a PU is forming. With reductions in general pain, patients become more sensitive and responsive to localised discomfort or pain sensations relating to tissue damage and are able to sleep better, so they have greater stamina and coping ability. They are also likely to need lower doses of pain and sleep medications (which improves their cognitive state), as well as less strenuous care regimens. Reducing general pain is therefore pivotal in the treatment of patients at risk of PUs.

Box 1: Patient A case history.

Clinical background

Presentation: A 74-year-old female was admitted to the emergency department with right upper quadrant pain, nausea, vomiting and fever (39ºC). She was drowsy and unable to remain seated in bed. She had a flare up of long-standing psoriasis that was causing considerable pain. Oozing from the psoriasis and faecal incontinence resulted in her skin being constantly moist.
Blood cultures confirmed septicaemia.
Medical history: Hypothyroidism, myelodysplastic syndrome, cholecystectomy, psoriatic arthritis, obesity (110 kg) and limited mobility due to arthritis.

Interventions and clinical outcomes

Day 0: The patient had a high risk of skin breakdown based on a Waterlow score of 24 and clinical judgement. She was placed on an alternating pressure (three-cell cycle) mattress but complained about general discomfort and pain.
Day 3: Three areas of broken skin appeared on the right buttock/sacrum. These were assessed and identified as Category 2 pressure ulcers.
Day 6: The patient was transferred to a minimum tissue deformation (MTD) mattress with the aim of improving/maintaining current skin conditions. While on the MTD mattress, the patient felt comfortable and her pain was relieved.
Weeks 1–6: The patient continued to be nursed on the MTD mattress. Her general condition improved and the pressure ulcers begun to granulate, allowing her transfer to another hospital.

Case studies: a patient-centred approach

The case studies presented here were documented in interviews and clinical examinations; all three patients eventually used a powered, non-alternating, minimum tissue deformation (MTD) mattress (Thompson et al, 2008; Ahtiala et al, 2020; Gefen and Soppi, 2020). The MTD mattress has a double-cell structure and reactive air pressure adjustment technology that automatically maximises patient-specific body envelopment at all times. The case studies focus on patient perspectives, particularly in an aetiological context and in light of analysis of PU formation and pain pathways.

Patient A *[Box 1]*

Patient A had a number of factors that contributed to inflammation, and so her patient's risk of developing PUs.

Psoriasis is an inflammatory disease. Increased levels of IL-6 and TNF-α occur in the blood plasma of patients with active psoriasis (Grossman et al, 1989; Castells-Rodellas et al, 1992; Goodman et al, 2009; Yost and Gudjonsson, 2009; Kyriakou et al, 2014). These cytokines also induce inflammatory pathological pain (Hess et al, 2011; Zhou et al, 2016; Gefen and Soppi, 2020) and are associated with inflamation-related damage in PUs (Jiang et al, 2014; Kurose et al, 2015; Krishnan et al, 2017). Psoriasis flare ups are often associated with hyperalgesia; affected individuals are more sensitive to experimentally applied somatosensory stimuli than healthy controls (van Laarhoven et al, 2013).

Obesity causes low-grade inflammation. It results in the recruitment and activation of immune cell subsets in adipose tissues, which systemically increase IL-6 and TNF-α levels (Eder et al, 2009; Kern et al, 2018). Hypothyroidism and myelodysplastic syndrome are also associated with low-grade inflammation and overexpression of IL-6 and TNF-α (Taddei et al, 2006; Marchiori et al, 2015; Shi et al, 2019).

Patient A's psoriasis, obesity, hypothyroidism and myelodysplastic syndrome may have contributed to her inflammatory pain. Moreover, hypothyroidism is associated with impaired endothelium dysfunction and vasodilatation (Taddei et al, 2006; Marchiori et al, 2015), making her more susceptible to localised oedema during early-stage PU damage, leading to a considerable rise in interstitial pressures that would cause nociceptive pain.

The cyclic action of an alternating pressure mattress may have caused waves of high stress concentration in soft tissue under bony prominences in Patient A, stimulating local nociceptors to signal increases in inflammatory pain. This likely explains the general discomfort and pain she reported when placed on the alternating pressure mattress. The development of PUs must have aggravated her pain, as PUs activate both inflammatory and nociceptive pain pathways. MTD air-float technology does not induce the cyclic increases in localised interface pressures and shear caused by alternating pressure systems and MTD mattresses may therefore be advantageous in patients with inflammatory conditions that predispose to oedema.

Patient B *[Box 2]*

Patient B had herpes zoster. The most common complication of this condition — which is caused by reactivation of varicella-zoster virus — is postherpetic neuralgia, a neuropathic burning pain that occurs due to peripheral nerve damage. Neuropathic pain may mask localised sensations indicating PU formation, theoretically increasing PU risk. Tissue culture models of skin infected by varicella-zoster revealed >30-fold increased IL-6 levels compared to uninfected skin (Jarosinski et al, 2018). The virus also causes rapid and transient expression of TNF-α by macrophages (Paludan et al, 2001). Elevated IL-6 and TNF-α levels can generate or aggravate inflammatory pain, in turn inducing nociceptive pain.

Elastic solid support (spring-based or foam-based) surfaces, such as the spring mattress

Box 2: Patient B case history.

Clinical background

Presentation: A 78-year-old male with a body mass index of 16.6 admitted due to deterioration of underlying diseases, in particular herpes zoster that resulted in painful neuralgia. The patient also had a painful spontaneous compression fracture of the spine at his L1 vertebra.
Medical history: Severe chronic obstructive pulmonary disease with cardiac involvement, muscle atrophy and osteoporosis.

Interventions and clinical outcomes

Post discharge: The patient's wife was solely responsible for the care of her husband, who was completely bed-bound. The patient was nursed at home on a standard spring mattress. In addition to chronic pain, he suffered from disturbed and intermittent sleep, which affected his wife's sleep and overall quality of life. The patient was drowsy due to nighttime sedatives and pain management medications (delivered via drug-releasing patches), however his cognitive status was not impaired.
2 months: A minimum tissue deformation mattress was made available and the patient's general pain and pain due to the compression fracture diminished. The pain due to postherpetic neuralgia was still present. The patient's sleep improved as a result of his reduced pain levels, and his wife's sleep improved as a consequence.
6 months: The patient and his wife were very satisfied with the MDT mattress. The patient reported that the pain relief was persistent, which resulted in better quality of life and easier care, as moving in bed was not as painful as previously.

initially used by Patient B, are inherently inferior to air-cell-based support surfaces as they provide lower body envelopment, resulting in greater concentrations of tissue stress when compared to air-cell-based mattresses (Moysidis et al, 2011; Levy et al, 2014, 2015). The increase in body envelopment provided by the MTD mattress and associated decrease in localised soft tissue stress, therefore substantially reduced the inflammatory and nociceptive pain experienced by Patient B.

Patient C *[Box 3]*

Patient C is a classic example of a cerebrovascular accident damaging the primary somatosensory cortex in the brain, leading to loss of pain modulation capacity by the central nervous system. This damage explains her somatosensory symptoms and tactile hypersensitivity complaints.

As with Patient B, envelopment was lower and tissue deformations and stress concentrations greater on the commodity mattress than on the MTD mattress. Generally, the intensity and frequency of the trains of action potentials fired by stimulated nociceptors are proportional to tissue distortion levels (Eilers and Schumacher, 2005; Djouhri et al, 2006, 2012). Hence, the greater envelopment and reduced localised tissue distortions provided by the MTD air-float mattress translate to less chronic pain, especially in conditions where pain modulation is impaired, as in Patient C's case.

Summary and conclusions

Reducing general pain is a central objective in the management of patients at risk of developing PUs. The aetiological links between the PU cycle, which is triggered and driven by exposure to sustained cell and tissue deformation, and experience of pain, which is fed by inflammatory oedema and ischaemia (secondary and tertiary factors in PU aetiology), need to be considered. This article has analysed the complex interactions between PU aetiology and pain pathways, applying known and theoretical knowledge to the case histories of patients with inflammatory disease or neural damage, which are risk factors for PUs and chronic pain. Alleviation of sustained tissue deformation through good immersion and envelopment by the support surface, as with MTD air-float technology, therefore appears to protect against PUs and relieve chronic or general pain. WINT

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Box 3: Patient C case history.

Background and underlying conditions

Patient C had cerebral palsy from birth that resulted in weakness on the left side of her body but was otherwise independent and able to walk. At the age of 21, she had a cerebrovascular accident with no known cause, which resulted in the need to use a wheelchair as she was unable to move her legs. After the stroke, the patient began to experience aching sensations in her lower extremities and numerous pain relievers were prescribed. She reported electric shock-like sensations below her knees that were triggered by objects in contact with her skin. These sensations were resistant to all treatments.
For 9 years the patient woke up tens of times each night, causing extreme exhaustion and fatigue. She slept in the same position at night on a commodity mattress for conventional home use.

Interventions and clinical outcomes

Patient C had the opportunity to test a minimum tissue deformation mattress. She has now used this mattress for the past 8 years, reporting that her pain levels have decreased and her quality of sleep is satisfactory. In particular, she has reported that she no longer wakes up during the night because of pain. The patient, who is currently 39 years old with a body mass index of 22.9, has never suffered from pressure ulcers.

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