Biomechanical Factors in Psoriatic Disease: Defective Repair Exertion as a Potential Cause. Hypothesis Presentation and Literature Review

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Joining main clinical manifestations of psoriatic skin disorder are inflammatory arthritis and nail lesions. Repetitive microdamage has been postulated as a main triggering factor in lesions of psoriatic arthritis. This concept of psoriatic disease might also be admissible for triggering nail lesions because the nail is a frequently traumatized structure. Here, we aimed to describe the conjectural injury mechanisms of nail complex with regard to acting biomechanical factors. Tissue repair response to physical microdamage may be altered in psoriatic disease. It is plausible to consider that a defective repair process in the dysregulated prepsoriatic tissue may lead to innate immune activation and further development of autoinflammatory lesions, although excessive inflammation is known to impair wound healing. Recently published data have revealed the importance of mechanosensitive Wingless-type (Wnt) signaling in the pathophysiology of psoriasis and ankylosing spondylitis. The Wnt signaling system is involved in morphogenesis, repair, and regeneration as a biologic process main regulator. Wnt5a seems to be a dominating mediator in both psoriatic plaques and during the spondylitis process that might also be a linking molecule of psoriatic response to mechanical stress. Future studies should focus on complex responsive interactions of tissue repair regulators regarded in psoriatic disease.

Introduction

Psoriasis is a nonscarring, inflammatory, and hyperproliferative chronic skin disease, likely unique to humans with a varied adult prevalence of 0.9% in the United States to 8.5% in Norway, as it probably depends on geographic factors (1). Interactions between genetic and immunologic variations with certain and unclear affecting environmental factors have supposed to result in psoriatic lesions. Trauma is a well-known triggering factor for psoriatic skin lesions. Development of new lesions in the apparently normal skin secondary to trauma in patients with certain dermatoses has been called Koebner phenomenon after the German dermatologist Heinrich Koebner (2). Although it is typified as true Koebnerization along with lichen planus and vitiligo, psoriasis is most likely to have the highest incidence of the Koebner phenomenon (3,4). Besides, psoriatic lesion development is also a frequent consequence of localized trauma, including friction, shearing, stretching, and pressure (5–7). Therefore, tissue-specific biomechanical triggering factors other than direct external injury should also be considered in terms of lesion development. Psoriatic lesions appear mostly on frequently stretched extensor skin surfaces during daily activities, bony promontories of the knee and elbow, where the joint flexion range of motion is excessive. Friction that occurs during lumbar movements due to waistbands may also traumatize the sacral skin. Another frequently involved site, the scalp is also a stretched skin tissue (8). Flexion of the cervical spine may also lead to an increase in tension, particularly on the occipital skin. All of the aforementioned dermal areas have insufficient subcutaneous support tissue.

Approximately, 20.0% to 30.0% of psoriasis patients are accompanied by psoriatic arthritis (PsA). PsA is classified as seronegative spondyloarthritis (SpA). The prototype disease of SpA is ankylosing spondylitis (AS). Researchers have put forth a role for mechanical stress and repetitive microdamage in triggering musculoskeletal lesions in both PsA and AS (9–13). While axial spinal involvement is much less common and clinically more moderate in PsA, AS is characterized mainly...
by symmetric and ascending spinal involvement. This finding might point to the fact that the spine is exposed to a stronger or perpetual stimulus in AS compared with psoriatic spondylitis but that it might not be segmental. In contrast, PsA is characterized mainly by peripheral manifestations such as inflammatory arthritis, enthesitis, and dactylitis. Even in the presence of psoriatic spondylitis, peripheral involvement is observed more frequently compared with AS (14). Therefore, PsA is an inflammatory disorder of more mobile musculoskeletal structures, unlike AS. This situation might also apply to the axial spine. The cervical spine, probably because of increased mobility during daily activities compared with the lumbosacral region, is more commonly involved in PsA. Mechanical stress–related chronic process of psoriatic lesion development in musculoskeletal structures may substantially be motion dependent (13,15).

Biomechanical factors and nail involvement

The average prevalence of nail lesions in patients with psoriasis can estimated to be more than 50%. The prevalence is much higher among patients with PsA. To date, it has been debated whether trauma is an actual cause of psoriatic nail lesions. Together with the consideration of the physical disuse of nail apparatus in modern humans, applied forces may contribute to the development of specific nail lesions. Pitting, onycholysis, and splinter hemorrhages are the most frequently detected changes in fingernails, whereas onycholysis, crumbling, and subungual hyperkeratosis are the most frequently detected nail changes in toenails (16). It is known that matrix trauma that is due to manicure induces leukonychia (5). Furthermore, injury to the nail matrix in the transverse plane that occurs during nail cutting or nail filing may result in leukonychia, depending on the extent of shearing or the targeted site of applied pressure (17).

While working with hands, friction between the nail plate and nail bed may cause chronic mechanical trauma, leading to onycholysis and thickness. Parts of the nail, including the matrix, can also be repetitively exposed to compressive forces. As a specific injury mechanism of the proximal matrix, impacts between the harder dorsal nail plate layer and solid objects might theoretically lead to development of pitting that is due to Koebnerization by the high-rated mechanical energy transmission (18). However, the density and Young's modulus values of each nail plate layer may not be significantly different, and typewriting typifies this injury mechanism in desk workers, leading to chronic damage of the whole matrix and thereby resulting in the development of crumbling (19,20).

Considering this conjectural injury mechanism may be reasonable because it can explain the co-existence of distal interphalangeal (DIP) joint involvement in patients with nail lesions on the same finger as well as accompanying extensor tendon inflammation because the compressive stress wave may stand on further to the DIP joint–related structures through the fibers of the extensor tendon, which envelopes the nail root, thereby leading to the co-Koebnerization of the nail root and DIP joint (10,11,21,22). The Shearing effect of pulse on the nail matrix and, additionally, the reflection (tensile stress) should also be taken into consideration because the transmitted energy advances in different contiguous tissues with different densities. Impact speed is the main determinant (19,23–28). However applied force during a pinch grip may be a more influential mechanical factor for the development of DIP arthritis overall. Nail involvement in the hand is less common in the little finger compared with other fingers, possibly because it is rarely used during working.

Psoriatic toenail involvement is most frequently detected in the big toe, which lacks the anatomic envelope mechanism of long fingers (21,29). Toes bear much larger mechanical forces compared with fingers. The toenails may be exposed to repetitive mechanical stress during walking, particularly at the end of the stance phase of the gait cycle. As the heel rise starts, the ground reaction force (GRF) vector (center of pressure) moves medially to the big toe, which is forced to an accelerated extension along with the other toes by the lever arm of the ankle propels the body forward. Overload of the big toe concomitant with the generated extension force applied to a repelling force to the extensor side structures leads to displacement toward the nail plate and increased in tissue pressure, particularly in the nail matrix contiguous to the hard nail plate and might result in time-dependent development of crumbling. Toward toe off, the eccentric contraction of the musculus flexor hallucis longus fixes the big toe in full floor contact to undertake the second lever arm function to maintain the forward motion of the body (push-off phase) and thus bears most of the applied forces in comparison with other toes (30). Both lever arms pull the soft tissues to inferoposterior as the toes become hyperextended with a compression of the nail bed by the GRF. Repetitive shearing between the nail bed and the hard nail plate during this phase may cause the development of onycholysis and subungual hyperkeratosis in severe cases. Although individual gait patterns may differ slightly, the human bipedal walking can be considered as an uniform movement. Thus, this biomechanical conjecture may be compatible with the involvement patterns of both toenail lesions and metatarsophalangeal arthritis (16,30–32).

Footwear can alter certain parameters of the gait cycle, such as decreased footspot spreading and increased stance time. Shoes may decrease force dispersion, particularly during the push-off phase, by limiting the natural motion of the barefoot through application of external pressure and additional weight and however, also limits the toe extension range of motion in a variable degree, depending on the rigidity of the footwear. Although the second peak value of vertical GRF in the push-off phase does not differ, the propulsive GRF may be altered (33). Ill-fitted or narrow-toed shoe wearing further decreases the weight bearing area, changes force distribution, and causes impingement of the nail complex. Static shearing of the nail bed occurs in women who wear high-heeled shoes.
Shoes also traumatize the big toenail repetitively by impulsive forefront contact that may result in onycholysis (34). Collectively, all of the aforementioned mechanical factors may explain why the big toenail is exposed to more repetitive microdamage and, consequently, might explain the higher frequency of developing psoriatic nail lesions in the big toe compared with other toes.

Further evidence

It has been revealed by imaging techniques that the main event in PsA may be enthesitis (35). In psoriasis patients without musculoskeletal symptoms, ultrasonographic enthesitis is quite frequent regardless of physical examination (36,37). It has been demonstrated in cadaveric studies that the changes associated with microdamage and inflammation are observed in SpA patients even in their normal joints and entheses (38). As the connections of the skeleton, enthesis-related structures bear excessive tensile load, especially during movement. Overweight is more common in psoriatic patients than in the healthy population, causing higher mechanical stress in both lower limb joints and entheses. This condition is supported by the evidence that species with large body mass have increased incidence of axial SpA (39).

The persistent repair exertion in prepsoriatic tissue under continuous mechanical stress might result in either aberrant innate immune activation or a decreasing ability to terminate inflammation that occurs during the wound healing process, which further develops autoinflammatory lesions, although excessive inflammation is known to impair wound healing (10,40–42). This assumption may point to a vulnerability to chronic physical damage in psoriasis patients, which may also be indicated by disruption of the basement membrane laminin layer as a specific feature, especially at the apex of dermal papillae in both involved and uninvolved skin (43–45). The main function of laminin is to aid anchoring and stabilization of the basal keratinocytes. As the earliest event in the lesion development process, this structural disorder leads to proliferation of unstable keratinocytes before the onset of inflammation and hyperkeratosis (46). Dysfunctionality in tissue laminin synthesis should be taken into consideration (47). Secondly, laminins are the extracellular macromolecules that play a regulatory role during wound healing. Application of laminin-derived peptides promote re-epithelization, angiogenesis, and cell migration during wound healing as well as decrease inflammation and granulation (48).

The defective repair exertion as a potential cause

Cumulative tissue damage that is particularly due to biomechanical factors that may trigger psoriatic lesion development might result from person-specific tissue dysregulation. If this alternative concept of psoriatic disease is true, it is plausible to consider that a defective wound healing process in the dysregulated psoriatic tissue may lead to a vulnerability to chronic damage (13). Psoriatic plaques resemble the wound healing response with regard to many cellular and molecular mediators (41). Furthermore, the wound healing rate may be accelerated in both involved and uninvolved skin (49). Many genes activated during the wound healing process may be differentially involved either similarly or inversely in the molecular pathophysiology of psoriasis. Expressions of late cornified envelope (LCE)-3 genes are upregulated in psoriatic skin which undertake an important role in the epidermal barrier repair following superficial injury of healthy skin (50). Other known psoriasis susceptibility genes consist of upregulated myeloid related protein (MRP) 8 (S100A8), MRP14 (S100A9), MRP8/ MRP14 heterodimer, and nuclear factor-κ-B-inhibitor α (NFKBIA/IκBa) as well as downregulated jun B proto-oncogene and all were demonstrated to be significantly upregulated during a short-term incisional wound model of neonatal mice (51–55). Based on this model, the early growth factor (Egr)-1, c-myc, FOS-like antigen-1 (Fra-1), the mitogen-activated protein kinases (MAP4K4), c-Jun N-terminal kinase (JNK) pathway, retinol binding protein-1, keratins (KRT6), plexins, osteopontin (deep dermal), cathepsin S, ephrin receptor B1 (epha2 in psoriasis), C-X-C motif chemokines (CCL10), C-C motif chemokine ligand family (CCL2/MCP-1, CCL7), and C-C motif chemokine receptors (CCR1) can additionally be listed as expressed genes of wound healing related similarly with psoriasis. However, the notch signaling, C-fos, and mitogen-activated protein kinase phosphatase (MKP)-1 may be down-regulated in psoriatic lesions, contrary to what happens with wounds (56–73). It is worth noting that MRP8, MRP14, and MRP8/MRP14 expression was reported to be higher in the synovial sublining layer of PsA patients compared with rheumatoid arthritis (RA) and SpA (74).

Investigation of the effects of pharmacotherapeutic agents may offer some clues. Systemic treatment with certain drugs, such as β-blockers, statins, corticosteroids, antimalarial drugs, and lithium, may flare or worsen psoriatic skin lesions. These drugs may also affect wound healing. Beta adrenergic blockers delay cutaneous wound healing, whereas propranolol improves wound healing in streptozotocin-induced diabetic rats (75,76). Topical simvastatin improves wound healing in rats by its anti-inflammatory properties, increasing fibroblast proliferation and epithelization (77). Corticosteroids delay repair by affecting proinflammatory cytokines, and they have catabolic effects particularly in the skin and connective tissue. To our knowledge, there is no relevant information in the literature regarding the effects of antimalarial drugs on wound healing. Lithium activates β-catenin signaling through Wingless-type (Wnt) signaling pathway mediated mechanism, enhances tissue healing, increases cutaneous wound strength, and stimulates local mineralization after bone fracture (78–80). It inhibits cell migration as a specific effect.
Wnt signaling system is required in all phases of wound healing. β-Catenin has been shown to inhibit keratinocyte migration and activate fibroblast proliferation in cutaneous healing. It mediates the effects of transforming growth factor (TGF-β) during healing (78). β-Catenin can either inhibit or enhance the wound healing process, indicating the complex interactive responses. A previously published work has revealed a correlation between in vivo β-catenin level and the tensile strength of the wound in mice after irradiation and lithium treatment increases wound strength in those expressing null alleles for β-catenin as well (79). Psoriatic plaques are characterized distinctly with decreased extensibility and elasticity in both uninvolved and involved skin (81). Whether this structural finding might be associated with tissue Wnt system interactions have not yet been investigated. Decreased extensibility may lead to further mechanical stress to the tissues exposed to repetitive stretching. After dithranol treatment, mechanical parameters of psoriatic plaques have improved markedly (81).

Activated Wnt5a signaling in plaques and syndesmophytes

The Wnt signaling molecules are involved in crucial functions, including cellular proliferation and regeneration, tissue regulation, and immune development. The Wnt5a is differentially expressed in psoriatic plaques and is known as a suppressor of notch-1 signaling (82,83). In cultured keratinocytes, Wnt5a can be induced by proinflammatory cytokines interleukin (IL)-1α, tumor necrosis factor (TNF)-α, interferon (IFN)γ, as well as TGF-α (84). Induction of Wnt5a in mesenchymal cells was supposed to adjust the accurate localization and timing of the TGF-β signalization during injury repair (85). TGF-β and nerve growth factor may be the key regulatory molecules of the Koebner phenomenon (42,86). In psoriasis, homeostatic inhibition of Wnt signaling is impaired, and a shift away from canonical Wnt signaling toward noncanonical system driven mainly by interactions of increased Wnt5a may exist. Moreover, circulating Wnt5a was reported to be significantly higher in psoriasis patients than in controls, especially in the obese patients (84,87). Theoretically, chronic injury may cause inappropriately prolonged Wnt signaling (88).

The Wnt signaling is also likely to play an important role in the syndesmophyte formation. Certain cytokines are capable of inducing Wnt proteins (84,89). It was suggested that pro-inflammatory cytokines released during chronic inflammation in SpA may lead to subsequent new bone formation by upregulating β-catenin (90). Recently, Wnt3a, Wnt4, Wnt5a, Wnt7b, and Wnt10b were detected to be highly expressed in spinal ligaments of AS patients with syndesmophytes as osteoinductive Wnts, and their significantly elevated levels in the sera were reported to be correlated with syndesmophyte progression as well (91). Wnt5a seems to be a master regulator of spondylitis response in AS because its serum level increases earlier, along with the Wnt9b and Wnt16b, in the patients without syndesmophytes. As the new bone formation process starts, the Wnt5a level continues to increase in conjunction with the distinct activation of other osteogenic Wnts. However, the process of syndesmophyte formation that could be driven mainly by the Wnt signaling system may be related to the intensity of inflammatory stimulus. In vitro stimulation of a monocyte cell line by low dosage of TNF-α was demonstrated to induce persistent Wnt activity, whereas high dosage stimulation has no effect on Wnts with an increase in expression of canonical Wnt inhibitor dickkopf-related protein (Dkk)-1, also known as a suppressor of bone formation. Thus, excessive release of TNF-α in AS may impair the osteogenic Wnt activity and as well as repair response compatible with the TNF brake hypothesis (41,91,92). Besides that, Wnt5a may also have a role in the augmentation of psoriatic skin inflammation by forming a positive feedback loop with the inflammatory cytokines, thereby enabling the occurrence of cytokine storm (83).

Offering clues of Wnt5a

High circulating levels of Dkk-1 were detected in the patients with axial SpA. Thus, Dkk-1 measurement was suggested to be a good indicator of the presence and severity of osteoprotective radiologic changes of spondylitis in PsA (93). However, capacity of Dkk-1–mediated inhibition of active β-catenin was demonstrated to decrease in AS; this dysfunctionality could be related to the strong activity of Wnt5a, as resembled in psoriatic plaques (82,84,94–96). Wnt5a signaling suppresses keratinocyte proliferation in normal skin, whereas it is required in perichondrium for regulating longitudinal skeletal outgrowth of developing long bones (84,97). However, as similar functions, while Wnt5a likely stimulates the anabolic new bone formation along with the canonical Wnts in axial SpA, it seems to partially suppress canonical Wnts in psoriatic plaques and stimulates keratinocyte proliferation in conjunction with the absence of increased expression of Dkk-1 in psoriatic plaques contrary to the increased expression in the nonlesional psoriatic skin of unknown importance (98,99). However, it was reported that increased expression of Wnt5a alone does not have a psoriasiform effect in transgenic mice, although biologic systems in rodent dermal tissue may differ from humans (100). In contrast with canonical Wnts, activation of Wnt5a signaling also fails to induce cartilage lesions in experimental osteoarthritis induced by collagenase and destabilization of the medial meniscus (101). Therefore, induction of Wnt5a might be related to a compensatory repair process in the aforementioned conditions rather than primary damage. Prolonged activation of noncanonical pathway via Wnt5a signaling was demonstrated to form regenerative changes evidently in cutaneous wound healing (102). Interestingly, despite the absence of frizzled-4 (FZD4) receptor, overexpressed Wnt5a triggering the Wnt/β-catenin signaling pathway may also play an important role in the keloid pathogenesis, which is an aberrant wound healing process that responds to deep skin trauma (103).
Molecular response to mechanical stretching of skin

Interactions of mechanical input with Wnt signaling system may promote tissue regulation. Wnt signaling systems, including the noncanonical pathway, have been revealed as being mechanosensitive (104). Biomechanical stimuli are required for cell behaviors during skeletal, joint, tendon, and ligament development through activating Wnt genes (105). Wnt5a or N-cadherin–mediated β-catenin signaling is essential to mechanically induced mesenchymal stem cell (MSC) osteogenic differentiation in vitro (106).

Mechanical stretching of skin may promote skin tissue regeneration by upregulating the expression of genes related to hypoxia, vascularization, and cell proliferation (107). Mechanical stretching of the expanded skin leads to upregulated mRNA expressions of stromal-derived factor (SDF)-1α, hypoxia-inducible factor (HIF)-1α, and matrix metalloproteinase (MMP)-2 in a rat model of tissue implantation. In vitro mechanical stretching of human MSCs causes upregulation of the genes of Janus kinase/signal transducers and activators of transcription (JAK-STAT), cyclin D2, secreted frizzled-related protein4 (SFRP4), and Wnt5b (107). SDF-1α, HIFs, and MMP-2 are highly expressed in psoriatic lesions (108–110). Upregulated C-X-C chemokine receptor type 4 (CXCR4)/SDF-1α axis may also have potential proinflammatory effects in the pathophysiology of RA and SpA, including PsA (111). JAK1 and JAK3 upregulated in psoriasis are probably concomitant with overexpression of cyclins (82,112). However, expression of Wnt signaling inhibitor SFRP4 is diminished in psoriatic skin, which inhibits excessive keratinocyte proliferation evoked by proinflammatory cytokines in vitro and decreases the severity of psoriasiform lesions in imiquimod-induced mouse model (113). Wnt5b gene expression also tends to be lower in psoriatic plaques (84). Consequently, main molecular behavioral difference that exist in psoriatic skin resulting from mechanical stress may occur in the Wnt signaling system. Thus, the probability that Wnt5a may be an essential regulatory molecule of psoriatic response to mechanical stress has emerged. Whether Wnt5a induction in psoriasis is defective or compensatory should be elucidated (82). A proposed paradigm of the altered repair response to chronic mechanical stress through Wnt5a signaling is shown in Figure 1.

Molecular response to mechanical stretching of tendon

Chronic tendinopathies are characterized with inflammation and matrix destruction. Repetitive mechanical stretching of tendons can change the gene expression and protein synthesis of tenocytes and fibroblasts. Low-magnitude stretching is regarded as anti-inflammatory, whereas high-magnitude stretching is proinflammatory (114). Cyclic stretching or mechanical load can induce gene expressions of IL-1β, bone morphogenetic protein (BMP)-2, cyclooxygenase (COX)-2, MMP-1, and MMP-9 in conjunction with the increase in production of IL-6 and PGE2 (114–118). Apart from mechanical load, the inflammatory cytokine response was suggested as another factor for matrix destruction in overuse tendinopathies (119). Cyclic tensile strain can also induce an immediate but transient stress response by activating the stress-activated protein kinase (SAPK)/JNK pathway and extracellular signal-regulated kinase 2 (ERK2/MAPK-1). The JNK activity is suppressed in a time-dependent manner possibly because of the adaptation of fibroblasts. Therefore, insufficient ability to suppress JNK activity may lead to apoptosis (120–122).

Molecular response to vibration and hypergravity

It should be noted that both changes in gravity and exposure to vibration may cause molecular response. Exposure to long-term whole body vibration (WBV), particularly at low frequencies, is a widely accepted etiologic cause of low back pain and disc herniation (123). Moreover, WBV is also associated with spinal radiographic damage in AS patients (124). Molecular changes secondary to an increase in gravity may also reflect the long-term effects of gravitational acceleration on musculoskeletal system. Short-term hypergravity of 1.8g was reported to induce IL-6 release from chondrocytes and to be capable of regulating genes in vitro related with cartilage integrity including downregulated BMP-4, MMP-3, MMP-10, Wnt5a, and upregulated endothelin (EDN)-1, whereas vibration within a broad spectrum of frequency upregulates IL-6 and IL-8 accompanied with the downregulation of growth factors such as epidermal growth factor (EGF), vascu-

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**Figure 1.** A proposed paradigm of altered repair response to chronic mechanical stress through Wnt5a signaling.
lar endothelial growth factor (VEGF), and fibroblast growth factor (FGF)-17 (125). Low-frequency vibration was demonstrated to cause diffuse cellular neuroimmune response in the rat spinal cord possibly through activating the MAPKs indicated by the decrease in expressions of anti-inflammatory cytokines concomitantly with the increase of some proinflammatory cytokines such as TNF-α and IL-6 (126,127). Besides, higher-frequency WBV may lead to a decrease in systemic IL-17 positive Th cell count counteracted with an increase of forkhead box P3 (FoxP3) positive Treg cells (128). All mentioned factors may be involved in axial SpA pathophysiology (129–133).

**Biomechanical factors in AS**

We think that assessment of AS in terms of biomechanical factors should also be briefly mentioned. The bamboo spine characteristics may not be a frequently encountered feature of axial SpA in nonhuman primates (134,135). The thoracolumbar spinal musculature usually functions in humans with isometric contractions both consciously and unconsciously for balance control and trunk stabilization, rather than intentional motion requiring motor planning. The spinal insertions are exposed to constant stretching in AS, a consequence of axial myofascial hypertonicity that might also point to a subclinical neural disorder (136). Interestingly, the neuropathic pain component was detected in patients with AS and accompanied with cortical thinning in specific areas, including primary somatosensory cortex (perception of proprioception), insula (visceral sensation processing and autonomic regulation, vestibular function), supplementary motor area (learning and planning self-initiated complex movements), and gray matter abnormalities in the putamen (motor learning) and thalamus (sensory signal processing, preparation of voluntary movement, alertness) (137). Available evidence in the literature might not suggest a decrease in postural control of neural origin or a proprioceptive deficit because this impairment is largely attributed to the mechanic changes secondary to the spondylitis process (138,139). As a recent observation, eyes-closed rehabilitation programs were reported to improve more marked balance impairment in AS and therefore might be admissible as a clue for the favorable effect of rehabilitation on proprioceptive acuity (140). Besides, potential significance of the reported vestibular dysfunction in AS patients should additionally be taken into consideration (141,142).

**CONCLUSION**

Biomechanical factors primarily affect musculoskeletal and dermal tissue integrity as well as functions. Lesion-specific injury mechanisms of the nail apparatus should be discussed. While soft-tissue mobility may contribute to the development of nail bed lesions, frequent increases in tissue pressure might result in time-dependent development of crumbling. Offered postulations indicate that psoriatic patients may have a vulnerability to chronic physical damage in both skin and musculoskeletal tissues, particularly to the tissue-specific kinetic factors. However, robust evidence is needed. Investigations regarding disruption of the basement membrane laminin layer or strong activation of mechanosensitive Wnt5a may provide direct evidence to support the concept of mechanical stress in the pathophysiology of psoriatic disease.

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