

An Updated Review on Psoriasis and Surgery

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ABSTRACT

Psoriasis is a chronic inflammatory skin disease with a complex pathogenesis involving the interaction between the innate and adaptive immune systems. The release of antimicrobial peptides (AMPs) by keratinocytes, particularly LL-37 peptides, plays a crucial role in the initiation of psoriatic inflammation. The activation of dendritic cells and distinct T-cell subsets, particularly Th1 and Th17, leads to the formation of scaly plaques in psoriasis. Although most cases are treated with topical or systemic medications, severe forms such as pustular psoriasis and psoriatic arthritis may require surgical management. Surgical procedures aim to relieve symptoms, improve function, and minimize scarring and cosmetic deformities. However, psoriatic patients are at higher risk of post-surgical infections and surgical stress may trigger psoriatic flare-ups. Thus, meticulous post-surgical wound care and psychological support are essential for optimal outcomes.

KEYWORDS: psoriasis, inflammation, AMPs, LL-37 peptides, dendritic cells, T-cell subsets, surgical management, post-surgical infections, wound care, psychological support.

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INTRODUCTION

Psoriasis is a chronic inflammatory skin disease with genetic predisposition and autoimmune pathogenic traits as a risk factor.¹ The proposed etiologies of psoriasis include hereditary, immunity system, and environmental. Studies explained the pathogenesis related to the excessive proliferation of keratinocytes or inflammatory activation of synovial cells and chondrocytes within the joints. All the pathogenesis are caused by an immune response that is mainly mediated by T-lymphocytes and various other immune cells.² The histopathology of psoriatic plaques shows acanthosis (hyperplasia of epidermal), which overlies inflammatory infiltrates composed of dermal dendritic cells, macrophages, T-cells, and neutrophils.¹

Studies discovered psoriasis present at any age and has been reported at birth and in older people of advanced age. Several large studies said the mean age of onset for first psoriasis presentation can range from 15 to 20 years old, with a second peak occurring at 55 – 60 years of age.³ People with psoriasis history in their family have an increased risk of developing psoriasis. The prevalence varies significantly worldwide and is associated with race, geographic, and environment. Several studies showed its prevalence in Europe and America is

approximately 1-3%, less than 1% in China, even less percentage in Japan, and may be absent in Australia and South America.^{2,3}

Many treatment methods are available, such as topical therapy, physical therapy, and systemic therapy. The purpose of psoriasis treatment are to control and stabilize the disease activity, delay its widespread progression, relieve the symptoms, avoid risk factor that may trigger the disease, reduce adverse reactions caused by treatment, and improve patient's life quality.² Studies agreed that no specific surgical treatment are available for psoriasis, other than procedures related to psoriasis-related joint and ophthalmic complications.⁴

Due to limited number of references about psoriasis and surgery, we composed this literature review about psoriasis and surgery, based on data from open-access scientific articles that are indexed in Google Scholar, PubMed, Science Direct, and Medscape, and published in the last 30 years, with purpose of updating and refreshing our understandings about psoriasis-related surgical treatment and surgery in a patient with psoriatic comorbidity.

Clinical appearance of psoriasis

An Updated Review on Psoriasis and Surgery

Psoriasis is characterized by local or extensive distribution of scaly erythema or plaques. Psoriasis flares may be triggered by skin trauma, smoking, medication (such as lithium and interferon), infections, and probably stress.⁵ Dermatologic manifestations of psoriasis are varied.¹ Plaque psoriasis is the most common type that representing approximately 80 – 90% of psoriasis cases. This type appears as red, raised skin area, which is commonly located on elbow, knees, hands, feet,



Image 1. Plaque psoriasis

Pathogenesis of psoriasis

Psoriasis is a chronic inflammatory skin disease characterized by the formation of scaly plaques on the skin surface. The pathogenesis of psoriasis is complex, and it involves the interaction between the innate and adaptive immune systems. The initial phase of psoriasis can be triggered by various factors, such as trauma (the Koebner phenomenon), infection, or medication, which cause disturbances in the cutaneous immune systems.⁷

One of the suggested mechanisms for the initiation of psoriatic inflammation is the release of antimicrobial peptides (AMPs) by keratinocytes in response to an injury. LL-37 peptides, β -defensin antimicrobial peptides, and S100 proteins are the most-researched AMPs related to psoriasis,^{8,9} and experts have long linked LL-37 peptides, also known as cathelicidin, to psoriasis.¹⁰ After injured keratinocytes release LL-37 peptides, the peptides form complexes with self-genetic materials and as soon as the peptides attach themselves to DNA, plasmacytoid dendritic cells (pDCs) recognize these complexes, activate toll-like receptor (TLR) 9 and produce type I interferons (IFN- α and IFN- β). This activation of plasmacytoid dendritic cells (pDCs) is crucial for the initiation of the psoriatic plaque.¹¹

Myeloid dendritic cells (mDCs) also play a significant role in the pathogenesis of psoriasis. The phenotypic maturation of myeloid dendritic cells (mDCs) is supported by type I interferon signaling, which has been linked to the differentiation and function of T-helper cells type 1 (Th1) and

scalp, or other areas of body, including nails (see **Image 1**). These plaques often develop on both sides of body and may cause itching or burning sensation.⁵ Other types of psoriasis include guttate psoriasis, inverse psoriasis, erythroderma, generalised pustular psoriasis (see **Image 2**), palmoplantar pustulosis, psoriatic nail disease, and arthropathic psoriasis in which we discover swollen and painful joint, as well as “morning stiffness” phenomenon.³

T-helper cells type 17 (Th17).¹²⁻¹³ Toll-like receptor (TLR) 7 is activated by LL-37 peptide - RNA complexes, whereas LL-37 peptide - DNA complexes stimulate mDCs through TLR 9. Additionally, toll-like receptor (TLR) 8 and LL-37 peptide - RNA complexes also influence mDCs.^{9,10} Activated myeloid dendritic cells (mDCs) secrete cytokines such as tumor necrosis factor (TNF)- α , interleukins 12 and 23 (IL-12, IL-23) as they migrate into draining lymph nodes, and both types of interleukins regulate the differentiation and proliferation of Th17 and Th1 cell subsets, respectively.¹² Monocytes, which are important pro-inflammatory cells found in psoriasis skin lesions, also react to LL-37 peptide - RNA activation by secreting high amounts of tumor necrosis factor (TNF)- α , interleukins 12 and 23 (IL-12, IL-23).¹³

The activation of the adaptive immune response via distinct T cell subsets drives the maintenance phase of psoriatic inflammation. T-helper cells type 17 (Th17) cytokines, namely interleukins 17, 21 and 22 (IL-17, IL-21, IL-22), activate keratinocyte proliferation in the epidermis, leading to the formation of scaly plaques.^{1,14} T-helper cells type 1 (Th1) cells also play a role in the pathogenesis of psoriasis by producing interferon- γ (IFN- γ), which induces keratinocyte apoptosis and exacerbates the inflammatory response.

In summary, the pathogenesis of psoriasis involves the interaction between the innate and adaptive cutaneous immune systems. The release of antimicrobial peptides (AMPs) by keratinocytes in response to injury, particularly LL-37 peptides, plays a crucial role in the initiation of

An Updated Review on Psoriasis and Surgery

psoriatic inflammation. The activation of pDCs and mDCs leads to the production of pro-inflammatory cytokines, which drive the maintenance phase of psoriasis. Distinct T-cell subsets, particularly T-helper type 1 (Th1) and T-helper type 17 (Th17), play a crucial role in the formation of scaly plaques in psoriasis. A better understanding of the pathogenesis of psoriasis could lead to the development of more effective treatments for this chronic inflammatory skin disease.

Psoriasis-related surgical treatment

Psoriasis is a chronic inflammatory skin disorder that can affect the skin, nails, and joints. While most cases of skin psoriasis are managed with topical or systemic medications, in some instances, surgery may be necessary to address certain complications associated with the disease.

A rare form of skin psoriasis that may require surgical intervention is **pustular psoriasis** (see **Image 2**), a rare subtype and a severe form of psoriasis characterized by the formation of pus-filled blisters which can occur anywhere on the human body. The clinical symptoms and signs of pustular psoriasis include the sudden appearance of small, painful pustules on the skin, often accompanied by fever, chills, fatigue, and muscle weakness. In severe cases, the pustules may coalesce, resulting in larger areas of pus-filled blisters and skin erosions. The diagnosis of pustular psoriasis is typically made based on the clinical presentation and confirmed by a skin biopsy.¹⁵

While in most cases, clinicians treat pustular psoriasis with systemic medications, such as retinoids, methotrexate, or

biologic agents, in certain cases clinicians may require surgical management. The indications for surgical management are resistance to medical treatment, functional impairment due to significant pain, or severe cases which may lead to infection or sepsis. The proposed type of surgical procedure for pustular psoriasis depends on the location and severity of the lesions. In general cases, surgeons make simple incision and drainage of the pustules to relieve pain and prevent further infection by supporting it with systemic antibiotic therapy. In more severe cases, surgeons may perform excision of the affected skin, followed by skin grafting or reconstructive surgery to restore function and appearance. The goal of surgical management in pustular psoriasis is to relieve symptoms, improve function, and minimize scarring and cosmetic deformities. However, as with any surgical procedure, there are risks and potential complications associated with surgical management of pustular psoriasis, which include bleeding, infection, wound dehiscence, scarring, and anesthesia-related complications.^{15,16}

The prognosis for patients with pustular psoriasis depends on the severity and extent of the disease, as well as the patient's response to treatment. In some cases, pustular psoriasis may be a chronic and debilitating condition that requires ongoing medical and surgical management. However, with appropriate treatment and management, many patients with pustular psoriasis can achieve long-term remission and improve their quality of life.



Image 2. Pustular psoriasis

Another complication is **psoriatic arthritis** (PsA), a seronegative inflammatory arthritis linked to psoriasis which can affect up to 30% of individuals with psoriasis. The exact cause of psoriatic arthritis is unknown, but experts believe it is due to an autoimmune condition that affects the joints,

causing pain, stiffness, and swelling. The clinical symptoms and signs that lead to the diagnosis of psoriatic arthritis include joint pain and stiffness, swelling, tenderness, and reduced range of motion. Other symptoms may include fatigue, nail changes, co-existing eye inflammation, and

An Updated Review on Psoriasis and Surgery

lower back pain. Contrary to rheumatoid arthritis, psoriatic arthritis is characterized by the formation of new bone and joint remodelling, often leading to joint ankylosis. Another unusual clinical feature of psoriatic arthritis is arthritis mutilans (see Image) due to severe osteolysis. Although current treatment methods, such as TNF antagonists, are effective in controlling inflammation and preventing joint erosions and destruction, joint damage may still occur, leading to the need for surgery to prevent further damage or restore joint function.^{17,18}

Indications for surgical management in psoriatic arthritis cases (see Image 3) are usually limited to cases where conservative non-surgical management strategies such as medication and physical therapy fail to control symptoms or cases where joint damage has progressed significantly and caused dysfunction. Synovectomy is one surgical option for psoriatic arthritis patients with joint involvement. This procedure involves the removal of the inflamed synovial tissue lining the affected joint to alleviate pain and improve mobility. In more severe cases where joint damage is extensive, joint replacement surgery, usually hip and knee

replacements, is the most common procedure to restore joint function and improve the patient's quality of life. The goal of surgical management in psoriatic arthritis is to relieve pain, improve joint function, and increase overall quality of life. This procedure involves removing the damaged joint and replacing it with a prosthetic joint. However, surgical procedures also carry risks, and complications are possible.¹⁸ Patients with psoriatic arthritis may have a higher risk of surgical complications, including wound healing problems, infections, and joint stiffness. Additionally, psoriatic arthritis patients may have a higher risk of developing ankylosing spondylitis, a condition that affects the spine and can cause fusion of the vertebrae.¹⁹

The prognosis for psoriatic arthritis varies, and early diagnosis and treatment are essential to preventing joint damage and disability. With appropriate management, including both medical and surgical interventions, most patients with psoriatic arthritis can lead a full and active life. However, in some cases, joint damage may be irreversible, leading to long-term disability and decreased quality of life.



Image 3. Psoriatic arthritis of the finger joints



Image 4. Arthritis mutilans

In addition to skin and joint involvement, psoriasis may also present with ocular complications. **Psoriatic ocular complications** can affect different structures of the eye and may require surgical management in some cases. One of the most common psoriatic ocular complications is blepharitis, which is inflammation of the eyelid margins. Patients may present with itching, burning, redness, scaling, and swelling near the free edge of the eyelids.²⁰ In severe cases, blepharitis can lead to meibomian gland dysfunction, posterior blepharitis, and even corneal damage. Ectropion of the lower lacrimal point with epiphora, madarosis, trichiasis, and loss of lid tissue may also happen.²¹ Treatment may include topical antibiotics, warm compresses, and lid hygiene. Surgical intervention may be necessary in cases of trichiasis or ectropion,²² which can cause irritation and damage to the ocular surface. The surgical procedure for trichiasis involves removing the misdirected eyelashes, while ectropion correction surgery aims to restore the eyelid position to prevent exposure of the ocular surface. The goal of surgical management in these cases is to improve ocular symptoms and prevent complications such as corneal ulcers.²⁰ The related risks of these surgical procedures are rare but may include bleeding, infection, and recurrence of the condition. The prognosis for patients with blepharitis is generally good with proper management, including surgical intervention when necessary.

Another ocular complication related to psoriasis is uveitis, which is inflammation of the uvea, the middle layer of the eye.²³ Patients may present with redness, pain, and photophobia. Diagnosis is made by a comprehensive eye examination, including dilated fundus examination, and laboratory tests to rule out other systemic causes. Treatment typically involves topical and/or systemic corticosteroids and immunosuppressive agents. Surgical management may be indicated in cases of complicated cataract, glaucoma, or retinal detachment.²⁴⁻²⁶ The goal of surgical management is to improve visual acuity and prevent further ocular damage. The related risks of these surgical procedures are higher than those for blepharitis and may include infection, bleeding, and retinal detachment. The prognosis for patients with uveitis depends on the severity of the inflammation and the presence of other systemic manifestations of psoriasis.

Other less common ocular complications related to psoriasis include conjunctivitis, episcleritis, and scleritis.^{25,27,28} These conditions are characterized by inflammation of the conjunctiva, episclera, or sclera, respectively. Diagnosis is made by a thorough eye examination, and treatment involves topical and/or systemic anti-inflammatory agents. Surgical management may be necessary in cases of severe corneal or scleral thinning, which can lead to perforation. The goal of surgical management is to prevent ocular complications such as infection and vision loss. The related risks of these surgical procedures are similar to those for uveitis and may include

infection, bleeding, and worsening of the condition. The prognosis for patients with these conditions depends on the extent and severity of ocular inflammation and the presence of other systemic manifestations of psoriasis.

Overall, while conservative non-surgical management can effectively treat most cases of psoriasis, certain complications associated with the disease may require surgical management to prevent long-term damage and improve quality of life for affected individuals. A qualified medical professional should provide proper consultation, including the indication, goal, risks and potential complications of the procedure, before an affected patient decide to have a surgical intervention and ensure that the patient receives appropriate post-surgical follow-up care.

Surgery in a patient with psoriatic comorbidity

Psoriasis is not an absolute contraindication to surgery, but there are several precautions and contraindication anticipation that need to be taken when planning surgery for a patient with psoriasis. A surgeon need to evaluate any skin conditions near the surgery site,²⁸ and psoriatic lesions should not be cut since they are more likely to become infected and cause complicated healing. Therefore, surgical procedures should be carefully planned, and the surgeon should avoid the areas with active psoriatic plaques. Working with a dermatologist in the pre-surgical care of patients can better manage skin plaques and reduce the level of bacteria before surgery. During pre-surgical evaluation, a surgeon should also assess patient's current therapy, as some medications may need to be discontinued before surgery to reduce the risk of bleeding or infection.

Studies showed psoriatic patients are at higher risk of post-surgical infections, and some surgical complications may occur in psoriatic patients as surgical stress may trigger psoriatic flare-ups and the isomorphic phenomenon of Koebner on the surgical scar –a psoriasiform pattern that is localized at trauma injury areas, wound, or irritation. The trigger for this Koebner phenomenon is still up for debate, but researchers thought it may be caused by the excessive expression of psychological stress –induced substances P,²⁹ which later release neuromediators, producing interleukins-1 (IL-1), and collagenase. Surgical stress also activate mast cells, which release a number of mediators and preformed cytokines such as TNF and interleukins-4 (IL-4). As surgery can re-activate pre-existing psoriatic arthritis, surgeons should carefully evaluate their patients with psoriatic arthritis and work closely with the rheumatologist to manage the arthritis medications. In orthopaedic cases, an orthopaedic surgeons should anticipate certain complication when having psoriatic patients in need of orthopaedic procedures,, including non-union of fractures, greater rates of wound infection, and intra-articular fibrosis leading to stiffness.

A surgeon must critically consider the effect of disease-modifying treatments and biologic agents during the

An Updated Review on Psoriasis and Surgery

perioperative period. In general, experts agree methotrexate medication can be continued during surgery,¹⁸ however the use of biologic agents and disease-modifying anti-rheumatic drugs (DMARDs) in psoriasis patients undergoing surgery is still unclear. Some recommended to pause treatment three to five half-lives before elective surgery, especially for patients who have diabetes or other conditions that increase their risk of infection,¹⁷ and to resume that biologic medications only after the wound heals properly without drainage or erythema. For surgeries with longer-than-average duration, particularly those involving joint replacement or prosthetic joints, surgeons should administer antibiotic prophylaxis prevent surgical site infections. Studies recommended a third generation cephalosporin, such as cefazolin, as the prophylaxis antibiotic with a dose of 1-2 grams and given within 30 to 60 minutes before a skin incision. If the psoriatic patients have a verified β -lactam allergy, studies advised intravenous vancomycin with a dose of 1 gram and should be given no later than two hours before the incision. A surgeon should anticipate additional dosages for longer duration of surgery and significant blood loss. Surgeons discontinue the prophylactic antibiotics within the post-surgical 24 hours.^{30,31} In summary, clinicians can plan and perform surgeries in psoriatic patients, but careful planning, precautions, management of disease-modifying treatments and biologic agents, application of antibiotic prophylaxis, and pre-surgical care of active skin conditions are necessary to minimize the risk of complications and achieve optimal outcomes. Patients will certainly benefit from meticulous post-surgical wound care and pain management, physical rehabilitation therapy, and last but not least psychological support to manage the stress and anxiety associated with surgery.

SUMMARY

Psoriasis is a chronic inflammatory skin disease with a complex pathogenesis involving both innate and adaptive immune responses. The release of antimicrobial peptides by keratinocytes plays a crucial role in the initiation of psoriatic inflammation, which is further perpetuated by the production of pro-inflammatory cytokines by plasmacytoid and myeloid dendritic cells. T-helper type 1 and T-helper type 17 cells are important contributors to the formation of scaly plaques in psoriasis. While most cases are treated with topical or systemic medications, surgical intervention may be necessary in severe cases, such as pustular psoriasis, psoriatic arthritis, and ocular complications. Psoriasis is not a complete contraindication to surgery procedure, but clinicians should aware that psoriasis, in some cases, may cause higher risk for infection, or causing complicated post-surgical wound healing. There are some pre-surgical precautions such as adjusting psoriatic treatments, proper perioperative antibiotics. Surgeons should carefully plan procedures and avoid areas with active psoriatic plaques, and appropriate treatment and management are necessary to prevent complications and achieve long-term remission.

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An Updated Review on Psoriasis and Surgery

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