STUDY ON EVALUATION OF SAFETY AND EFFICACY OF LEUCOCYTE PLATELET RICH FIBRIN (L-PRF) VERSUS CONVENTIONAL DRESSING FOR THE TREATMENT OF CHRONIC CUTANEOUS ULCERS

By

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DISSERTATION SUBMITTED TO

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In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY

IN

GENERAL SURGERY

Under the guidance of

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ABBREVIATIONS

ANOVA - Analysis of Variance

ATP - Adenosine Triphosphate

BMI - Body Mass Index

CD - Cluster of Differentiation

CECT - Contrast-Enhanced Computed Tomography

CI - Confidence Interval

CONSORT - Consolidated Standards of Reporting Trials

CRP - C-Reactive Protein

CTGF - Connective Tissue Growth Factor

DFU - Diabetic Foot Ulcer

ECM - Extracellular Matrix

EGF - Epidermal Growth Factor

ESR - Erythrocyte Sedimentation Rate

FGF - Fibroblast Growth Factor

G-CSF - Granulocyte Colony-Stimulating Factor

GF - Growth Factor

GM-CSF - Granulocyte-Macrophage Colony-Stimulating Factor

Hb - Hemoglobin

HGF - Hepatocyte Growth Factor

IGF - Insulin-like Growth Factor

IL - Interleukin

IQR - Interquartile Range

IRB - Institutional Review Board

ABSTRACT

Introduction: Chronic cutaneous ulcers represent a significant healthcare challenge, affecting approximately 1-2% of the global population and contributing substantially to morbidity and healthcare costs. Conventional wound management strategies often yield suboptimal outcomes, necessitating the exploration of advanced therapeutic approaches. Leucocyte-Platelet Rich Fibrin (L-PRF), an autologous blood-derived biomaterial rich in platelets, leukocytes, and growth factors embedded within a fibrin matrix, has emerged as a promising regenerative medicine strategy for tissue repair. This study aimed to evaluate the efficacy and safety of L-PRF compared to conventional dressings in the management of chronic cutaneous ulcers.

Methods: This prospective, randomized controlled trial enrolled 112 patients with chronic cutaneous ulcers of various etiologies, who were randomly allocated to receive either L-PRF (n=56) or conventional dressings (n=56). L-PRF was prepared from autologous blood and applied weekly to the ulcer bed in the intervention group, while the control group received standard saline-soaked gauze dressings. Outcome measures included ulcer size reduction, granulation tissue quality, pain scores, healing rates, time to complete healing, and adverse events, assessed over a 4-week follow-up period.

Results: Demographic characteristics and baseline ulcer parameters were comparable between groups. The L-PRF group demonstrated significantly greater ulcer size reduction at 2 weeks ($p=0.02$) and 4 weeks ($p<0.001$), superior granulation tissue quality ($p<0.001$), and lower pain scores ($p<0.001$) compared to the conventional dressing group. Most notably, 100% of ulcers in the L-PRF group achieved complete healing versus 26.8% in the conventional group ($p<0.001$), with a significantly shorter healing time (4.25 ± 0.83 vs. 5.4 ± 0.5 weeks, $p<0.001$). The L-PRF group exhibited a lower incidence of minor infections

(5.4% vs. 12.5%), although this difference was not statistically significant (p=0.18). No serious adverse events were reported in either group.

Conclusion: L-PRF represents a highly effective regenerative medicine strategy for the treatment of cutaneous ulcers, significantly outperforming conventional dressings in terms of healing rates, healing time, tissue quality, and patient comfort. The autologous nature, minimal preparation requirements, and favorable safety profile of L-PRF enhance its clinical utility and potential for widespread implementation in chronic wound management.

Keywords: Leucocyte-Platelet Rich Fibrin, L-PRF, chronic ulcers, wound healing, regenerative medicine, autologous blood products, growth factors, tissue regeneration, wound management, cutaneous ulcers.

INTRODUCTION

Because of their intricate wound-healing mechanisms, cutaneous ulcers provide a serious clinical problem that necessitates creative treatment approaches. One These difficult wound situations have significant medical and financial ramifications for healthcare systems around the world and arise from a variety of etiological reasons, such as diabetes, vascular insufficiency, chronic inflammatory disorders, and traumatic traumas.[1]

Global epidemiology data show that managing chronic wounds is a significant burden. Chronic wound complications affect about 1% to 2% of people worldwide, with notable differences among various clinical and demographic groups. [2] With yearly healthcare costs associated with wound care projected to surpass billions of dollars, the economic effect is significant and emphasizes the urgent need for cutting-edge regenerative treatment techniques.

Healing chronic wounds requires intricate relationships between:

- Cellular mechanisms of inflammation
- The processes of tissue regeneration, extracellular matrix remodeling, and growth factor signalling
- Delays in wound healing, elevated risks of infection, and possible long-term problems are all consequences of disruptions in these complex biochemical cascades. [3]

Regenerative medicine is a cutting-edge method of managing wounds that emphasizes harnessing biological processes to improve tissue restoration and healing. Leucocyte-Platelet Rich Fibrin (L-PRF) is a highly advanced treatment approach that

uses concentrated autologous biological components to maximize the body's natural healing capability. [4]

Concentrated platelets, leucocytes, growth factors, and cellular signaling components make up the complex matrix that is L-PRF. Together, these elements support improved tissue reconstruction, decreased inflammatory responses, increased wound healing, and accelerated tissue regeneration. By moving away from conventional wound care techniques and toward more complex, biology-driven therapies, the creation of L-PRF marks a substantial technological breakthrough in regenerative medicine.[5] By avoiding outside interventions and optimizing natural regenerating processes, this technology allows for the precise concentration and selective deployment of autologous healing components.

L-PRF exhibits significant benefits over traditional wound care techniques:

•Autologous origin lowers the chance of immunological rejection

•Techniques for minimally invasive preparation

Increased capacity for tissue regeneration; sustained release of growth factors; and improved cellular recruitment.[6]

Numerous medical specialties, such as chronic wound care, diabetic ulcer treatment, reconstructive surgery, dermatological therapies, and trauma wound rehabilitation, may be affected clinically by L-PRF.

The current study intends to thoroughly examine: The effectiveness of L-PRF in treating cutaneous ulcers; the molecular principles underlying tissue regeneration; a comparison with traditional wound care techniques; long-term clinical results; and the possibility of standardizing regenerative regimens. [7]

Modern methods for preparing L-PRF need complex protocols:

Accurate blood centrifugation; consistent membrane production; regulated growth factor concentration; and methodical clinical application techniques

These developments mark important breakthroughs in the application of laboratory research to clinical settings. [8]

The results of the study could significantly aid in: • Better wound healing procedures • Tailored regenerative medicine strategies • Lower medical costs • Better patient recovery outcomes . The study intends to enhance medical knowledge of tissue restoration mechanisms by offering comprehensive insights into L-PRF's regeneration potential. [9] Molecular characterization of L-PRF components, sophisticated imaging methods for evaluating healing, customized regenerative medicine procedures, and integration with complementary therapeutic approaches are some examples of emerging research fields. [10]

AIM & OBJECTIVES

Aim:

To compare the conventional dressing and L-PRF membrane dressing in wound healing

Objective:

1. To assess the duration for L-PRF membrane dressing in wound healing.
2. To assess the efficacy of L-PRFmembrane dressing in wound healing.

PHYSIOLOGY OF WOUND HEALING

Hemostasis, inflammation, proliferation, and tissue remodeling or resolution are the four highly interconnected and overlapping stages of the wound-healing process.[11] These stages and their biophysiological processes need to take place in the right order, at the right time, and continue for a predetermined amount of time at the best possible intensity.[12]

FUNCTION

Restoring the protective epithelium barrier is one of the main purposes of wound healing. Without this barrier, we lose our first line of defense against infection, making us more susceptible to external infections and fluid loss. Regaining tissue strength and volume requires later phases of wound healing.[13]

ISSUES OF CONCERN

The tissue is returned to a state that is comparatively close to what it was prior to the injury if the healing process proceeds as planned and encounters no issues. Infections or persistent wounds can arise when this mechanism is disrupted. Chronic wounds are those that do not heal after three months. Patients with chronic wounds may be more susceptible to subsequent problems like amputation, infection, deformity, or loss of function.

In some cases, the healing process could be too rapid and produce too much scar tissue, leading to issues like keloids and hypertrophic scars. Itching, burning, or discomfort may be linked to either hypertrophic scars or keloids.[14]

THE WOUND-HEALING PROCESS

Four continuous, overlapping, and carefully planned phases make up the dynamic process of wound healing. Every phase's events must take place precisely and under strict

control. A chronic wound that doesn't heal or one that heals slowly can result from process disruptions, anomalies, or prolonging.

MECHANISM

Tissue reconstitution is the outcome of an ordered series of overlapping processes that characterize wound healing. Hemostasis, inflammation, proliferation, and the development of mature scar tissue are all steps in this process.

Hemostasis

Hemostasis starts as soon as the injury occurs. Vascular constriction, platelet thrombus development, coagulation cascade propagation, clotting termination, and fibrinolysis are the methods used to control bleeding from wounds. [15.]

"Blood flows to the wound site when the vascular endothelium is damaged, exposing the basal lamina. After activated platelets attach to the exposed collagen, a variety of growth factors, inflammatory mediators, and cytokines are released. In order to stop additional blood loss, a fibrin clot forms a seal and the intrinsic and extrinsic coagulation pathways are triggered". [16]

Following their release during the hemostasis phase, cytokines contribute to angiogenesis, chemotaxis, extracellular matrix deposition, and epithelialization. These consist of "platelet-derived growth factor, fibroblast growth factor, epidermal growth factor, transforming growth factor-beta, and vascular endothelial growth factor". [15]

Inflammation

In the initial days after injury, platelet activation is followed by the migration of inflammatory cells to the wound site. "In order to facilitate migration, mast cells emit vasoactive cytokines including prostaglandins and histamine, which raise capillary permeability and encourage local dilatation".

The majority at first are neutrophils, which are drawn to the wound bed by bacterial products. After the first 48 to 72 hours, neutrophils absorb the bacteria and any dead tissue, resulting in the pus that is visible in wounds. “Monocytes then develop into macrophages, which further debride the wound by removing fibrin, wasted neutrophils, and other cell debris from the matrix. The majority of inflammatory cytokines, including fibroblast growth factor, platelet-derived growth factor, epidermal growth factor, and transforming growth factor-beta, are also released by macrophages. Because of these functions, macrophages are necessary for effective wound healing; when their function is inhibited, wound healing is delayed. [15, 16] The inflammatory phase establishes a clean wound bed through these mechanisms, which serve as the foundation for subsequent repair mechanisms”.

Proliferation

Angiogenesis, granulation tissue creation, collagen deposition, and epithelialization are all processes that take place during the proliferative phase, which lasts from three to twenty-one days following damage. The filling of the wound defect is the main result of this phase. Endothelial cells in the wound bed produce nitric oxide (NO) in response to hypoxic conditions, which triggers the production of vascular endothelial growth factor and encourages angiogenesis.[16]

“Angiogenesis, which provides the new wound with oxygen, glucose, and other elements required for appropriate healing, is also triggered by the release of fibroblast growth factor and platelet-derived growth factor”. Here, the freshly produced extracellular matrix serves as the foundation for the thin-walled endothelium, which branches off of existing arteries. Oxygen saturation returns to normal as blood flow resumes, and vascular endothelial growth factor and NO levels fall to limit the angiogenesis process. The prevention of

excessive collagen synthesis and aberrant scar formation is aided by this autoregulatory process.

Elastin and collagen are produced by migrating fibroblasts to provide the new extracellular matrix required for granulation tissue and vascular support. The last phases of wound healing, maturation, and remodeling depend on granulation tissue, a highly vascular connective tissue.[15,16]

Maturation

Collagen cross-linking, remodeling, and wound contraction are all part of the maturation phase, "which is the last stage of wound healing. Type 1 collagen, which is widely distributed in healthy skin, is thicker than type 3 collagen, which is first produced by fibroblasts. A scar develops as type 1 collagen takes the place of type 3 collagen in granulation tissue during the maturation phase". The enhanced strength of wounds observed 4–5 weeks after healing is correlated with this rise in type 1 collagen. Three months following an accident, a wound will return to 80% of its initial strength. Regretfully, it is difficult to restore the skin to its pre-injury strength. [15]

In open wounds, wound contraction reduces the quantity of connective tissue needed to fill the wound bed. According to one hypothesis, myofibroblasts' production of alpha-smooth muscle actin facilitates contraction. [17] How well the wound contracts depends on the position and mobility of the tissue around the wound bed. Contraction can be problematic in places with limited movement, but it can be prevented by a skin transplant or other flaps. On the inside, epithelial cells migrate inward from the borders of the incision to produce a new protective layer. In order to restore the proper thickness of the epithelium, different migration rates enable "both stratification of the epithelial layer and increasing tissue depth. [18] A wound leaves a scar after it has healed". Due to enhanced vascularity and excessive

collagen deposition, the scar tissue will be red, hard, and somewhat elevated. For the first six to nine months, this would usually remain this way before starting to soften, flatten, and becoming whiter. [19]

FACTORS AFFECTING WOUND HEALING

"Impaired wound healing can result from a number of circumstances. In general, there are two types of elements that affect repair: systemic and local. Local factors are those that directly affect the wound's features, whereas systemic factors are those that affect an individual's ability to heal based on their general health or illness status (Table 1). Numerous elements are interrelated, and the systemic factors influence wound healing through local consequences".

Table 1: Factors Affecting Wound Healing

"Local Factors	**Systemic Factors**
Oxygenation Infection Foreign body Venous sufficiency	Age and gender Sex hormones Stress Ischemia Diseases: diabetes, keloids, fibrosis, hereditary healing disorders, jaundice, uremia Obesity Medications: glucocorticoid steroids, non-steroidal anti-inflammatory drugs, chemotherapy Alcoholism and smoking

	Immunocompromised conditions: cancer, radiation therapy, AIDS Nutrition”

ULCER

An ulcer is a surface discontinuity of the epithelium. It is distinguished by a granulating base and the breakdown of the surface epithelium. There are two types of ulcers: non-specific and specific malignant. “Chronic leg ulcers (CLUs), sometimes called chronic lower limb ulcers, are persistent wounds on the leg that either do not heal at all after three months of appropriate therapy or do not heal completely after twelve months”. [20]

Epidemiology:

Between 0.6 and 3% of people over 60 have chronic leg ulcers, while over 5% of people over 80 have them. The frequency of CLU in the community varies from 1.9% to 13.1%, making it a common source of illness. [21] “The aging population and increased risk factors for atherosclerotic occlusion, such as obesity, diabetes, and smoking, are regarded to be the main causes of the rising incidence of ulceration. Nearly 10% of people will get a chronic wound during their lives, and the fatality rate from wounds is 2.5%. [22] About 15% of older persons in the US have chronic wounds, such as diabetic (neuropathic) foot ulcers, pressure ulcers (bedsores), and primarily venous stasis ulcers, according to the Wound

Healing Society. An additional 2 to 3 million Americans receive a diagnosis of a chronic wound each year. According to estimates, the yearly incidence of leg ulcers is 3.5 per 1000 people in the UK and 0.2 per 1000 people in Switzerland. Vascular ulcers are thought to affect between 500,000 and 600,000 people in the US, and their prevalence rises with age. [23] Although research on the epidemiology of chronic wounds is scarce in India, one study calculated that the frequency was 4.5 per 1000 people. At 10.5 per 1000 people, the incidence of acute wounds was more than doubled". [24]

Aetiopathogenesis

According to reports, 70% of leg ulcer presentations are caused by venous insufficiency, 10% are caused by arterial disease, and 15% are caused by ulcers of mixed origin. [25] Less prevalent pathophysiological factors account for the other 5% of leg ulcers, and diagnosing, evaluating, and treating these patients can be quite difficult. [26] Venous insufficiency, arterial insufficiency, neuropathy, diabetes, or a combination of these conditions are the primary causes of leg ulcers in the Western world. About 70% of leg ulcer cases are venous ulcers, making them the most prevalent kind. An additional 5% to 10% of leg ulcers are caused by arterial disease; the majority are caused by neuropathy (often diabetic) or a combination of both conditions. [27]

According to the Indian study, systemic diseases like diabetes, atherosclerosis, tuberculosis, and leprosy were among the causes of chronic wounds. Vasculitis, pressure ulcers, venous ulcers, and trauma were other significant causes. According to the study findings, the most frequent cause of chronic wounds was improper management of acute traumatic injuries. [24] According to a Chinese study, trauma or traumatic wounds exacerbated by infection are the primary cause of ulceration (67%). The percentages of pressure ulcers,

venous ulcers, and diabetic ulcers were 9.2%, 6.5%, and 4.9%, respectively. Farmers and other agricultural workers suffered the majority of these injuries. [28]

Since the aetiologies of leg ulcers in the gaiter area and the forefoot differ, it is helpful to separate them into these two categories. One-third of all lower leg ulcers have at least two identifiable aetiological causes. Most frequently, venous ulcers develop above the lateral or medial malleoli. Arterial ulcers frequently develop on pressure sites or on the toes or shin. Neuropathic ulcers typically develop on pressure sites or on the sole of the foot. Due to venous pressure brought on by insufficient calf muscle pump function, patients who are obese or have limited movement may develop ulceration in the gaiter area. Systemic lupus, polyarteritis nodosa, and rheumatoid arthritis are the most frequent causes of vasculitis ulcers. Thrombocythaemia, polycythaemia rubra vera, sickle-cell disease, and thalassaemia are the blood dyscrasias that most frequently cause leg ulcers. [29]

Leukemia, polyclonal dysproteinemia, granulocytopenia, thrombotic thrombocytopenic purpura, and hereditary spherocytosis are further hematological conditions linked to the development of leg ulcers. “Microcirculatory obstruction is typically the cause of leg ulcers associated with hematological diseases. [21] Raynaud's phenomenon, Martorell's ulcers, and cutaneous vasculitis are examples of microcirculatory and vascular conditions that can cause atypical leg ulceration”. Many conditions, such as leprosy, alcoholic neuropathy, and tabes dorsalis, can cause neuropathy of the lower legs and the ulceration that goes along with it because of insensate damage, burns, or pressure ulcers.[21]

A recent study found that myocardial ischemia, hypertension, and chronic kidney disease (CKD) may also raise the incidence of foot ulcers, particularly serious ulcers that require amputation. In addition, compared to the general population, patients with chronic

venous leg ulcers have been found to have greater rates of malnutrition and vitamin and mineral deficiencies, including zinc. [30]

Venous Ulcers

For almost two millennia, the connection between lower limb venous problems and ankle ulcers has been recognized. The lower limbs' venous circulation develops from superficial to perforating to deep veins, each of which has valves to guarantee unidirectional blood flow. “Blood flows from the deep veins into the inferior vena cava as a result of the pumping action of the calf muscles contracting”. Venous insufficiency is the result of disease of these routes. Nearly 80% of lower leg ulcer cases are caused by venous insufficiency, making it the most frequent cause. About 1 million of the 7 million Americans who suffer from venous insufficiency go on to get venous leg ulcers. [31]

“Around one percent of people will experience leg ulcers at some point in their lives. In the UK, the prevalence of chronic venous leg ulcers is thought to be between 0.1% and 0.3%. As people age, the prevalence rises. Venous ulcers are present in about 1% of the US population overall. Older adults and women are more likely to develop venous ulcers. Older age, obesity, prior leg injuries, deep vein thrombosis”, and phlebitis are the main risk factors. Open ulcers can last anywhere from a few weeks to several years, while venous ulcers frequently repeat. Cellulitis, osteomyelitis, and malignant transformation are examples of severe consequences. [32] In terms of aetiology, natural history, and prognosis, patients who get chronic venous ulcers before turning 50 seem to be a unique group.

Ulcers in venous illness are typically found on the medial surface of the leg, “in the gaiter area between the ankle and the calf”. Venous valve incompetence is the cause of venous ulcers. The vessels enlarge and stretch to accommodate the increased blood flow when there is valve incompetence in the deep veins. Venous hypertension and retrograde

blood flow are caused by the valves' ineffective closure. [33] A brownish-red pigment is deposited in the leg's gaiter area as a result of venous hypertension, which causes fluid to flow from the stretched veins into the tissues. Ninety-five percent of venous ulcers form in the gaiter area, particularly in the area surrounding the malleolar (the rounded protuberances on the ankle). [34]

Surgery, trauma, or DVT can all harm veins, resulting in blood flowing backward through the venous system where the injury occurred. Varicose veins, obesity, congenital vein anomalies, and repeated pregnancies are other contributing factors. Failure of the calf muscle pump is another factor that affects the development of venous leg ulcers. Paralysis, immobility, prolonged leg dependence when sleeping in a chair, and fixed ankle joints are the causes of calf pump failure. By contracting and relaxing, the calf muscle facilitates the veins' return of blood to the heart. Increased venous pressure and blood stasis result from this mechanism's failure. [35]

The development of ulceration is explained by three main ideas. (1) Fibrin cuff theory: a pericapillary fibrin cuff is created when fibrinogen seeps from the epidermis's dilated capillaries. Ulceration results from a decreased diffusion of oxygenated blood to the tissues, which is caused by this. (2) “According to the leukocyte entrapment theory, venous hypertension lessens the pressure differential between the capillaries' venular and arteriolar ends”. This causes the blood to flow slowly through these capillaries and makes blood cells more likely to stick to the endothelium. Reactive oxygen species and inflammatory mediators (ICAM-1, VCAM-1) are then released, obliterating functional capillary loops, exacerbating ischemia, and ultimately leading to ulceration. (3) Microangiopathy theory: it has been shown that patients with venous leg ulcers have lengthy intracapillary stasis or microthrombi obstructing some of their capillaries. As a result, the skin may receive less oxygen and

nourishment, making ulceration more likely.[26] The chronic condition known as venous ulceration is marked by flare-ups and remissions. Venous ulcers frequently take a long time to heal, which impairs a patient's functional status and causes them to experience physical and psychological distress.

Arterial Ulcers

Reduced arterial blood flow and consequent tissue perfusion lead to arterial leg ulcers.[37] "Any type of arterial or arteriolar blockage may cause ischemia of the skin and subcutaneous tissues, which may result in ulceration. Atherosclerosis-related peripheral vascular disease, diabetes with microvascular or macrovascular disease, and/or vasculitis may cause ischemic leg ulceration". [36, 37] Tissue in the region that the artery is supplying dies when the blood flow is reduced. Ulcers frequently develop quickly and cause extensive tissue damage.

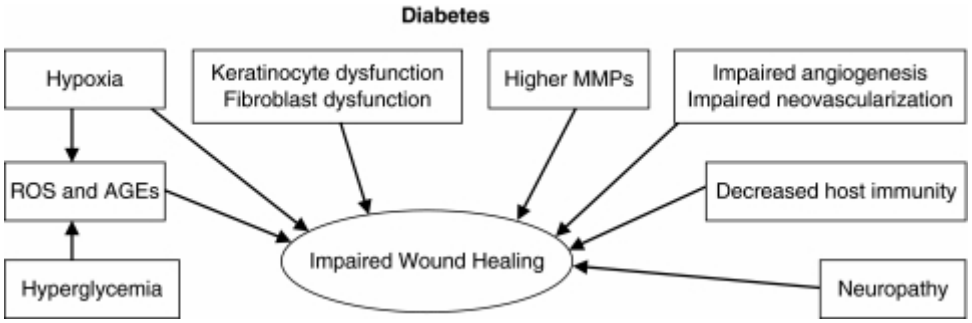
There is a notable lack of hair and the limb appears pallid. The pathogenesis of ischemic leg ulcers involves three mechanisms: intramural blood flow restriction, mural thickening or accretion, and extramural strangling. The precise pathogenesis is not often well characterized, and there is sometimes a great deal of overlap. Leg ulcers are likely to result from tissue hypoxia and the exudation of fibrin-like substances in the majority of acute types of vasculitis as well as some subacute and chronic forms. [28] Usually, arterial ulceration develops across the foot's toes, heels, and bony prominences. The ulcer has a pale, nongranulating, necrotic base and well-defined margins, giving the appearance of being "punched out." [37]

Diabetic Foot Ulcer

15% of people with diabetes are thought to develop diabetic foot ulcers at some point in their lives. For example, nonhealing foot ulcers are thought to affect 18% of diabetic individuals over 65 in the United States. The fact that 15–20% of individuals with these foot

sores eventually require amputation is now recognized. Diabetic foot ulcers precede about 85% of amputations. According to estimates, diabetic wound infections cause the loss of a lower leg every 30 seconds worldwide.[38] Patients with diabetes are more likely to develop ulcers as a result of both neuropathy and vascular disorders. “Furthermore, neuropathic impairment of sensory, motor, and autonomic function, usually in the hand and foot, or "stocking and glove" distributions, increases the risk of ulcers due to hyperglycemia. Diabetic foot ulcers typically have a complex etiology”. Peripheral neuropathy and ischemia from peripheral vascular disease are identified as the main underlying causes. Edema, callus development, trauma, and deformity are additional variables that contribute to ulceration.[39]

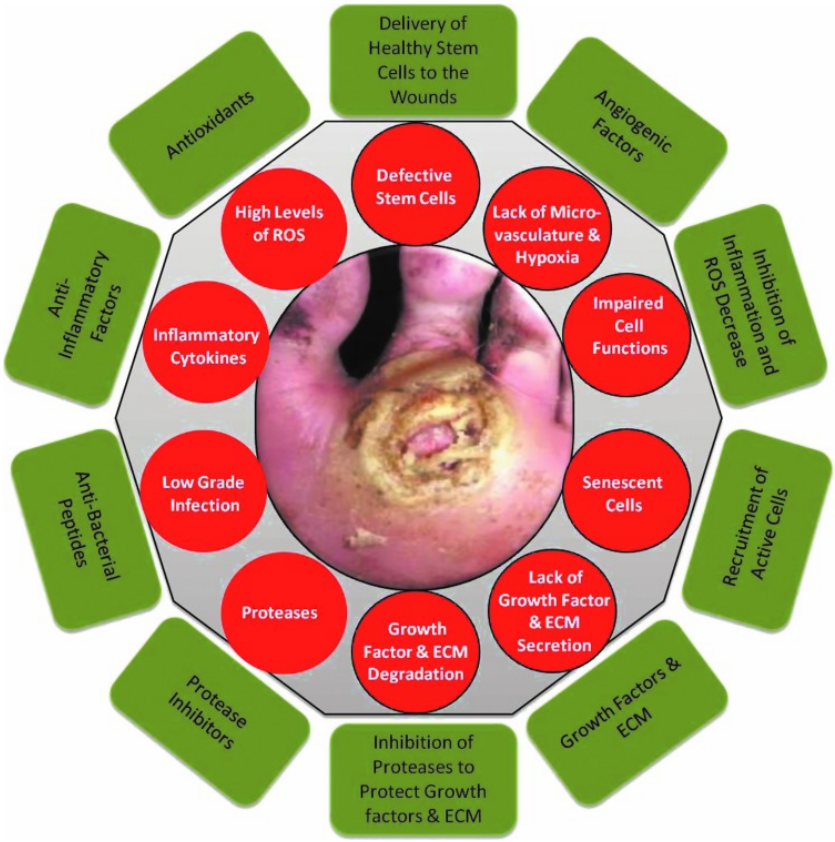
Figure 1: “The potential effects of diabetes on wound healing. MMPs, matrix metalloproteases; ROS, reactive oxygen species; AGEs, advanced glycation end-products”.



Pressure Ulcer

As the name suggests, unrelieved pressure is the main cause of pressure ulcers. They can happen on any region of the body that is under strain, although they typically happen over bony prominences like the sacrum or the heel. Age-related pressure ulcers account for about 70% of all cases. In addition to being a significant source of infection, pressure ulcers can result in consequences like osteomyelitis, septicemia, and even death. For patients who are at risk, preventing pressure injury to the skin and underlying tissue is a crucial component of treatment.[20]

Figure 2: “Molecular and cellular deficiencies in chronic wounds (red circles) and factors required to overcome them (green rectangles)”.



Clinical Assessment

History

Compiling a thorough history and evaluation of the patient is the first step in diagnosing any leg ulcer. “General health status, social and occupational circumstances,

medical history of pertinent diseases (e.g., diabetes, autoimmune diseases, inflammatory bowel disease, connective tissue disease, and deep vein thrombosis), skin condition, current vascular status, limb size and shape, and ulcer history and status should all be included". [40]

"Ask the patient about claudication, anesthesia, paresthesia, and lower extremity pain. Determining the length of ulceration and whether it is a first episode or recurrent is crucial. Unless there is a neuropathic component, leg ulcer sufferers have significant pain. Therefore, the absence of pain points to a neuropathic cause. Asking patients about their mobility is also a good idea. The ulcer's cause can be inferred from its clinical course. Diabetes, hypertension, hyperlipidemia, coronary artery disease, alcohol and tobacco use, thyroid, pulmonary, renal, neurologic, and rheumatic diseases, peripheral vascular disease, deep vein thrombosis, and cutaneous factors like cellulitis, trauma, and recent surgery are among the conditions that may need to be ruled out. [41] Analysis Palpating the pulses and looking for symptoms of venous hypertension, such as varicose veins, haemosiderin pigmentation, varicose eczema, atrophie blanche, and lipodermatosclerosis, should be included of the leg examination. To rule out a peripheral neuropathy, the range of motion in the hip, knee, and ankle should be assessed, and sensory testing should be done. [42] The site, size, look, wound base, level of exudates, and surrounding skin should all be examined when examining an ulcer. [39] Pain, edema, erythema, warmth, induration, discoloration, maceration, dryness, scarring from prior wounds, hair pattern, gangrenous fingers, clubbing, cyanosis, capillary refill, and varicose veins should all be checked in the surrounding area. It is crucial to remember that a patient may have both arterial and venous illness. [41] Venous ulcers are significantly different from arterial ulcers and other lower extremity ulcers. Vasculitis-related ulcers are indicated by an uneven ulcer border, erythema, black necrosis, or bluish or purple discolorations of the

surrounding skin. A leg ulcer that is painful and with violaceous edges may indicate pyoderma gangrenosum".

Investigations:

(1) For a more precise evaluation of arterial perfusion, the Ankle Brachial Pressure Index (ABPI) can be performed with a handheld Doppler ultrasonography and sphygmomanometer. "The findings can help direct the treatment strategy and are used to assess the probability of arterial insufficiency. [43] Arterial duplex ultrasonography can (noninvasively) offer precise anatomical and hemodynamic information on the location and severity of arterial disease when Doppler tests reveal arterial insufficiency. When necessary, digital subtraction angiography, computer tomographic angiography, or magnetic resonance angiography can provide more precise anatomical data for treatment planning".[44]

(2) To provide an unbiased evaluation of the efficacy of the present management strategy, it is critical to monitor the wound accurately and consistently. A validated instrument for measuring leg ulcer assessment, the Leg Ulcer Measurement Tool (LUMT) can be used to monitor changes in wound health over time. [45]

(3) Patients with chronic leg ulcers require blood testing, including "complete blood counts, erythrocyte sedimentation rates, blood sugar, lipid profiles, renal function tests, and liver function tests.

(4) The following are laboratory screening tests for vasculitis: "routine and immunohistopathology of skin biopsies, antinuclear antibodies, rheumatoid factor, complement C4, circulating immune complexes, paraproteins, immunoglobulin fractions, antineutrophil cytoplasmic antibodies, serological testing, cultures for underlying infections, and urine analysis for proteinuria, hematuria, and cylindruria".

Activated partial thromboplastin time, prothrombin time, thrombin time, factor V (Leiden)

mutation (506R fi 506Q), factor II (prothrombin) mutation (20210G fi 20210A), antithrombin III, protein C and protein S, and lupus anticoagulant anticardiolipin are the five laboratory screening tests for clotting disorders. [46]

(6) Before valvular surgery, venography may be carried out as an investigative measure. Patients experiencing ischemic rest discomfort, unbearable claudication, imminent gangrene, or nonhealing ulcers of probable arterial origin should have lower extremity arteriography.

(7) The location and severity of reflux in venous ulcers are also evaluated using "color duplex ultrasound scanning, which is quickly becoming the de facto standard for evaluating venous blockage".

(8) Data from venous pressure and plethysmography are crucial in assessing whether a surgical bypass or valve replacement is necessary. "Air plethysmography provides quantitative information on reflux, calf muscle pump ejection fraction, and venous obstruction, while venous pressure studies evaluate the physiological significance of anatomic obstruction because collaterals may or may not adequately compensate for an obstructed pathway".

(9) "As soon as a wound infection is detected, a quantitative bacterial culture should be conducted because it is more specific. Curetting or biopsying the ulcer's bed is how this is done. The gold standard for determining the type and amount of microbial infections in a wound is now a quantitative biopsy. Systemic antibiotic therapy should be taken into consideration if quantitative biopsies show more than 105 organisms per gram of tissue, which is deemed significant. Representative cultures from the bone or deepest tissue layers must be acquired if osteomyelitis is suspected". [47]

(10) "Due to their propensity for malignant development, ulcer biopsies are crucial for accurate diagnosis and for ruling out cancer. This may typically be done under local

anesthetic and involves removing a deep wedge of tissue from the ulcer edge. Biopsies of chronic ulcers are occasionally performed for experimental protocols: (A) to gather data about the wound bed or the wound edge. (B) to cultivate nonhealing wound cells in vitro.[48] (11). A straightforward blood test that would serve as a genetic screening tool might be used to identify the high-risk minority of patients beforehand, according to the clinical application of gene variant analysis and evaluation in patients with venous leg ulcers".

Treatments

One therapeutic difficulty is the management of lower extremity chronic ulcers. There is ample evidence to support the idea that causative therapy ought to come first. At the beginning of treatment, a thorough diagnostic evaluation that takes into account the vascular, metabolic, and physical components outlined above is crucial. "Current treatments for CLU include surgery, sclerotherapy, compressive therapy (conventional therapy), and adjuvant pharmacotherapy. The basic principles of treatment include removing or treating the precipitating cause (e.g., surgical intervention), promoting circulation and improving venous return (e.g., compression therapy), promoting healing (e.g., wound care, lifestyle changes, symptom management), and promoting preventative care (e.g., health education). When surgery is not an option, Vowden has described four fundamental treatment approaches that can be used separately or in combination to promote recovery and improve results. Additionally, he has talked about neurovascular procedures like spinal cord stimulation or lumbar sympathectomy; hyperbaric oxygen systemic therapy or prostaglandin-based intervenive therapy; local mechanical treatments like electromagnetic stimulation, negative pressure wound therapy (NPWT), or enhanced local oxygen therapy; and, lastly, topical treatments using vaso-active growth factors or tissue-engineered skin products".[49]

Table 2: Treatment options for common leg ulcers.[32]

"Ulcer type	**Treatment options**
Venous	Leg elevation Compression therapy Aspirin Pentoxifylline (Trental) Surgical management
Arterial	Revascularization, Antiplatelet medications, Management of risk factors
Neuropathic	Off-loading of pressure, Topical growth factors; Tissue-engineered skin
Pressure	Off-loading of pressure; Reduction of excessive moisture, Sheer, and friction; Adequate nutrition"

WOUND DRESSINGS

"Before applying any wound dressing, it is important to assess for the following factors that may influence the type of dressing chosen. All of these should be addressed, if present:

- Mechanism of injury
- Risk of contamination
- Potential injury to deeper structures
- Underlying nerve or tissue damage
- Presence of perfusion deficits
- Presence of tissue edema
- Tetanus status
- Amount of tissue loss
- Presence of infection"

"To get rid of any debris from the initial inspection, the wound should be thoroughly irrigated with a neutral solution, like sterile water or regular saline, after the initial evaluation. It is not advised to use irritating or toxic treatments, like hydrogen peroxide, as they can cause discomfort and hinder the healing of wounds. To maximize bacterial clearance, current research recommends applying at least 50 to 100 milliliters of irrigant per centimeter of the wound". [50] However, depending on the wound, modifications should be made. Since necrotic tissue does not undergo re-epithelization, devitalized tissue can be removed with a sharp edge. Persistent bacteria will form biofilm, however modest bacterial loads aid in wound healing by producing proteolytic enzymes. They ought to be eliminated since they may cause chronic inflammation, which would postpone healing. [51] Dry wounds were thought to promote better healing in the past. Recent studies, however,

have shown that a moist wound environment promotes wound healing more effectively. In many ways, a properly wet wound bed can improve healing. In addition to providing a pathway for epithelial cell migration to enable effective re-epithelization, the secretion of relevant growth factors and signaling molecules facilitates cell communication, promotes collagen synthesis, and fosters an environment conducive to necrotic tissue autolysis. [52]

However, an exudate-rich wound bed can impede the “healing process. Therefore, it is essential to choose a dressing that will regulate the exudate in order to prevent the surrounding tissue from macerating. The depth of the wound, the volume of exudate, the chronicity, and the presence of infection are some common considerations when selecting a dressing”. Numerous essential qualities are present in the perfect wound dressing. In addition to minimizing pain, the dressing would shield the wound from the elements and not stick to it. Additionally, the dressing should control exudate, prevent maceration of the surrounding skin, and provide a moist wound bed to encourage autolytic debridement. Lastly, the dressing should be selected to maximize function, minimize cost, and maximize patient compliance in order to improve the patient's quality of life. [51]

“The several types of contemporary wound dressings, together with their benefits and drawbacks, therapeutic uses, and general dressing change guidelines, are listed below. A sales person or the manufacturer's website may provide more details regarding the indications for a particular dressing”.

“Gauze: When removed, moistened gauze offers mechanical debridement.

• Benefits: Gauze is widely accessible and reasonably priced.

• Drawbacks: Gauze does not retain moisture. Because of the non-selective debridement this dressing does, fresh granulation tissue may be removed when the dressing is changed. A secondary dressing is necessary since this dressing is prone to bacterial contamination.

• Clinical Application: This covers the initial phases of more extensive wounds that need to be packed.

• Dressing Change Frequency: If the dressing is being used for packing, change it several times throughout the day".[53]

Films: "Films are translucent, thin dressings.

• Benefits: Films hold moisture and are pliable. They make it possible to visually monitor wounds. Because films are semi-permeable, gases can exchange while outside microorganisms cannot enter the wound. They stick to themselves.

• Drawbacks: Because films are impermeable to fluid and non-absorbent, they may result in maceration.

• Clinical Uses: Apply films to minor wounds, intravenous access sites, shallow wounds, split-thickness skin transplant donor sites, and secondary dressings.

Moderate to severe exudative or septic wounds are among the contraindications.

• The frequency of dressing changes might vary from a few times per week to a weekly schedule".[54]

Foams

• "Bilayer dressing: This type of dressing has a hydrophobic, porous outer layer and an inside layer made of silicone or polyurethane.

• Benefits: Exudate is absorbed by foams. They are both semi-permeable and semi-occlusive. They provide additional defense against external injuries because of their thickness.

• Drawbacks: These include drying out a wound and not being able to see wounds.

• Clinical Use: Apply foam to pressure injuries, chronic wounds, and mild to severe exudative wounds.

• How often should you change your clothes? Every day or a few times a week". [54]

Hydrogels: “Hydrogels are starch polymers that are hydrophilic, meaning they are mostly made of water. These come as gauze, sheets, and amorphous gels.

• Benefits include the ability to absorb water and produce a cooling sensation, both of which can lessen discomfort. In general, hydrogels are clear or translucent. They promote autolytic debridement by creating a wet environment.

• Drawbacks: Hydrogels need a second dressing because of their poor absorption ability.

• Clinical Applications: Hydrogels are used to treat surgical wounds, venous or arterial ulcers, and tissue desiccation.

• Restrictions: Heavy exudative wounds should not be treated with them.

• You should change your clothes every one to three days”.[55]

Hydrocolloids: “Hydrophilic polymers that are cross-linked with cellulose, gelatin, or pectin exist. Hydrocolloids can be in the form of sheets, paste, or powder; one type of dressing that is accessible is hydrofiber.

• Benefits: They absorb water gradually, becoming increasingly porous and gelling, after initially being impenetrable to it. Hydrocolloids prevent germs from growing by lowering the pH of wounds. These can be applied to wound cavities or across joints.

The inability to visualize wounds is a drawback.

• Clinical Uses: Apply them to mild to moderate exudative wounds and pressure wounds.

• Contraindications: Necrotic or infected wounds are not suitable for them.

• Dressing Change Frequency: Replace dressings every two to four days”.[54]

Alginate: “This seaweed polysaccharide dressing turns into a gel by exchanging calcium ions for sodium ions.

• Benefits: Calcium ions have hemostatic qualities, while alginate is extremely porous.

• Drawbacks: When this dressing dries, it may stick to the wound bed and turn yellow or

brown, which could be confused with purulence. Alginate needs a secondary dressing to prevent drying and has an unpleasant smell.

• Clinical Uses: Moderate to severe exudative wounds are treated with this treatment.

• Contraindications: mildly exudative wounds are not suitable for them.

• Dressing Change Frequency: Change your clothes every one to three days".[54]

Antimicrobial: In addition to deactivating bacterial enzymes, silver ions also interfere with DNA synthesis and bacterial cell walls. There are other dressings that are infused with iodine.

• Benefits: They possess broad-spectrum antibacterial qualities.

• Drawbacks: Skin discoloration may result from oxidized silver. Deep wounds cannot be penetrated by silver ions, and long-term use of iodine-based products raises the possibility of systemic side effects.

• Clinical Applications: These can be applied to wounds that are at high risk of infection or that are only superficially affected.

• Restrictions: Deep wounds should not be treated with them.

• Dressing Change Frequency: Depending on dressing saturation, change every day or every few days. [53]

Another option for a treatment for wounds is honey. Because honey is hypertonic, it dehydrates the wound and produces an acidic environment, which inhibits the growth of bacteria. 50 Not every wound will heal well with the traditional coverings listed above. Beyond the purview of this activity, some wounds can call for more specialist wound dressings, such as biological skin products, skin substitutes, and other complicated wound dressing treatments.[56]

"An Alternative Perspective of Wound Types and Their Appropriate Treatment":

1. Infection: Local infections can be treated with topical antimicrobials and antimicrobial dressings. However, if there are indications of a systemic illness, antibiotics ought to be taken into account.

2. Dryness: Hydrogel has the ability to hydrate the wound. Collagenase and other enzymatic debridement agents can also help dry eschars.

3. Exudate: Alginate, foam, or hydrocolloid dressings can be used to control high exudate. Film dressings, hydrogel, or hydrocolloid can be used to control low exudate.

4. Odor: Topical metronidazole or activated charcoal dressings can be used to reduce excessive odor.

5. Deep wounds: For deep wounds, apply wound packing or negative pressure therapy.[57]

Platelet Concentrates in Non - Healing Ulcers

The majority of medical specialties, including orthopaedic surgery and sports medicine, use platelet concentrates. “Pure platelet-rich plasma (PRP), leucocyte and platelet-rich plasma (LPRP), pure platelet-rich fibrin (PRF), and leucocyte and platelet-rich fibrin (L-PRF) are the four categories into which platelet concentrates are divided based on the amount of leucocyte and fibrin they contain. A cheap and immunologically safe source of several growth factors, PRP gel is a coagulated mixture of PRP with calcium or thrombin that is thought to hasten the healing process of wounds. In addition to PRP gel, PRF/L-PRF gel is a second-generation platelet concentrate that includes leucocytes, which may offer antibacterial action and other growth factors”. [58]

Brief history of various platelet concentrates

Over 40 years ago, several blood-derived compounds were first used to promote the healing process. Platelet concentrates were initially solely used to stop bleeding in cases of severe thrombopenia. “The adhesive qualities of fibrin matrix, which is the end product of

coagulation cascade, and the massive numbers of growth factors stored inside the platelets led to an increase in the use of platelet concentrates for the regeneration of hard and soft tissues. Initially, fibrin glue or sealant was used to develop platelet concentrations to promote tissue repair. Donor plasma is used to create this first bioactive surgical adjuvant, and the polymerization process is started by adding calcium and thrombin. Originally made from donor plasma, these adhesives can either be purchased commercially or obtained from the patient (autologously). However, the use of fibrin adhesives in contemporary regenerative medicine is restricted because of the risk of disease transmission, the expense of their manufacturing, and the varying quantities of fibrinogen in plasma".

In order to assist the "healing process and replace fibrin sealants, autologous blood products with high platelet concentrations, such PRP, have been created over the past 20 years. The first generation of platelet concentrate, known as PRP, was initially made available in 1998. PRP's functional qualities are primarily dependent on combining the effects of growth factors—which platelets actively secrete—with fibrin glue characteristics, which promote tissue regeneration and healing".

The protocol for preparing PRP is not consistent, despite the fact that it has been used extensively for a long time. There are currently over 40 distinct technologies available for producing PRP from autologous whole blood. In order to prevent platelet activation and degranulation, "20–80 mL of venous blood are drawn from patients and put in an anticoagulant tube in the majority of existing protocols. Centrifugation and activation comprise the two main components of the PRP extraction technique".

Two centrifugations are advised in the initial step, and they are typically finished in an hour. Using various density gradients, the first centrifugation separates the blood into three separate layers. Platelets are found just above the "buffy coat of white blood cells, which

forms above the erythrocyte layer (at the bottom of the centrifuge tube). Aspiration, pulling, and transfer of the buffy coat and plasma to a different centrifuge tube (without anticoagulant) for a second centrifugation (hard spin) are performed". Concentrated platelets in plasma suspension are easily evacuated from the tube's bottom after the last centrifugation stage concentrates them there. Lastly, at the time of application, the produced PRP is combined with activators (calcium chloride and thrombin). Platelet gel is formed and different growth factors are realized as a result of the activators utilized, which cause platelets to degranulate and fibrin to polymerize.

Human platelet counts typically range from 1,50,000 to 3,50,000 cells/μL of blood. The final PRP's total platelet count varies from 2 to 5 times or more than the physiological level and is mostly determined by the PRP preparation procedure. "95% platelets, 4% erythrocytes, and 1% white blood cells are often present in PRP blood clots". Growth factors are actively secreted by concentrated platelets, which also stimulate the need for, growth, and differentiation of different cells involved in the regeneration process. However, PRP will not have any therapeutic benefit if the final platelet concentrate has fewer platelets. Autologous PRP removes any worries about immunogenic reactions and transmissible diseases because it is stable for eight hours after production.

Within the first ten minutes after PRP activation, the platelets begin to produce growth factors. It is suggested that PRP must be "administered during the first 10 minutes of activation because the majority of growth factors (95%) are produced within the first hour. But over the past ten years, a number of PRP disadvantages" have been documented. Specifically, the anticoagulant added to the PRP preparation routine inhibits coagulation and fibrin clot formation, interfering with the body's natural healing process. Following PRP administration, coagulopathies and bleeding problems may result from a "reaction to cow

thrombin and antibodies to bovine factor V a. Due to the rapid release of growth factors and the lack of consistency in the PRP preparation process, a novel platelet concentrate was created that can get past the aforementioned restrictions". [58]

Choukroun et al. presented PRF for the first time in France in 2001 because to legislative restrictions regarding the replantation of blood-derived products. An autologous platelet and leukocyte-rich fibrin biomaterial, this second generation of platelet concentrate aims to build up platelets, immunity-promoting factors, and released cytokines in the fibrin clot. Since anticoagulants are not needed for the PRF preparation procedure, clot formation happens spontaneously and the wound healing cascade is not impeded by them. The risk associated with the use of bovine thrombin is eliminated because PFR can be obtained without the use of bovine thrombin, calcium chloride, or other activators. PRF has a number of advantages to PRP, including a high concentration of leukocytes that aid in wound healing in addition to immunological and antimicrobial responses. During wound healing, the PRF naturally creates a dense network of fibrin, which slows down the pace of "degradation and, consequently, delays the release of growth factors into the surrounding tissue".

Growth factors have been known to be released from PRF for as long as seven days for most of them and longer for some. Additionally, the benefits of PRF over PRP include a straightforward manufacturing process, lower costs, and standard protocol production. In short, 10-mL glass-coated plastic tubes are used to collect blood samples without anticoagulants. "The samples are then centrifuged for 10–12 minutes at 2,700–3,000 rpm (around 400 g). Erythrocytes are found at the bottom of the centrifuge tube after centrifugation, whereas platelet-poor plasma (PPP) is found at the top. In the center of the tube, between the PPP and erythrocyte layer, a PRP clot forms that massively entraps platelets, leukocytes, and growth factors. The overlying PPP layer can be removed to simply

collect the obtained PRF. The basic idea is to allow fibrin polymerization and platelet activation as they would occur naturally".

As soon as the platelets come into contact with the centrifuge tube wall, they begin to activate, forming a thick fibrin network and a viable PRF clot. As a result, blood must be drawn and transferred to centrifuge tubes as quickly as possible—at most, within two minutes and thirty seconds. If this time is extended, fibrin will diffusely polymerize and the resulting PRF will not be suitable for therapeutic usage. [59]

Biologic effects of PRF[59]

The composition of PRF is determined to be fibrin clot-enriched with circulating stem cells, platelets, leukocytes, and immune cytokines. "The fibrin matrix plays a significant part in the therapeutic impact of this platelet concentrate, despite the fact that leukocytes and platelets are the primary cells that give PRF its biologic activity. With the help of the available thrombin in the blood sample, soluble fibrinogen is transformed into insoluble fibrin that polymerizes".

The final fibrin matrix's biologic properties are significantly influenced by the polymerization process. Bovine thrombin and calcium chloride are used during PRP preparation to facilitate rapid fibrin polymerization. However, because of the physiological levels of thrombin in the blood sample, PRF processing causes fibrin to polymerize slowly and naturally. Bilateral and equilateral connections are the two possible configurations for fibrin polymerization. Bilateral connections and the creation of a stiff fibrin network are induced by high thrombin concentrations (during PRP preparation). "Growth factors and cytokines can be extrinsically trapped in colloidal suspension between the fibrin network due to this abrupt polymerization, and they are released in large quantities within the first hour".

Conversely, during PRF processing, equilateral connections and a flexible fibrin matrix are formed when thrombin concentrations are low. Increased trapping of circulating (intrinsic) cytokines in the fibrin matrix is made possible by slow fibrin polymerization. These molecules, which provide the long-term action of cytokines at the injury site, will only "be used when cicatricial matrix remodeling takes place and is released gradually.
The primary cells in charge of PRF's biologic action are platelets", which make up the majority of the protein. These cells carry a variety of platelet-derived protein molecules that are engaged in the wound-healing signaling cascade, despite their critical involvement in blood clot formation. Three different kinds of granules—alpha, delta, and lambda—found inside platelets store all of these chemicals. The most prevalent platelet granule and the primary source of growth factors are alpha granules. When the platelets are triggered, the growth factors found in these granules—"which are crucial for the regeneration of both soft and hard tissue following injury—are released through exocytosis. vascular endothelial growth factor (VEGF), insulin-like growth factor 1 (IGF1), platelet-derived growth factor (PDGF), transforming growth factor β (TGF-β), and epidermal growth factor (EGF). Additionally, the PRF contains immune cytokines such tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6, and IL-4, which are among the growth factors released from platelets".

One of the more than thirty members of the TGF-β superfamily, TGF-β is a multifunctional cytokine. TGF-β1 is the most prevalent of the three isoforms (TGF-β1, TGF-β2, and TGF-β3). Activated platelets release the active form of TGF-β1, which promotes fibroblast chemotaxis, collagen and fibronectin synthesis, and inhibits the degradation of collagen. Furthermore, TGF-β1 stimulates immune cell chemotaxis and angiogenesis.

Additionally, it inhibits the production of osteoclasts and bone deterioration while promoting osteoblast proliferation and deposition.

One of the first growth factors that seem to be present at the site of injury is PDGF. There are three distinct isoforms of it, AA, BB, and AB, and it is made up of two subunits, A and B. The mesenchymatous cell lineage migrates, proliferates, and survives thanks to the PDGF that platelets produce. Additionally, angiogenesis, macrophage chemotaxis, activation, and TGF-β release from macrophages are all made possible by this growth factor. A high concentration of PDGF in PRF may have a more significant impact on bone regeneration and wound healing since each platelet contains about 1,200 PDGF molecules.
Somatomedin C, or IGF1, is a polypeptide hormone that is widely distributed in the bloodstream but can also be released when platelets degranulate. In addition to inducing survival signals to shield cells from distinct apoptotic stimuli, it promotes mesenchymal cell development and mitogenesis. Furthermore, IGF1 promotes osteoblast activation and chemotaxis, which improves bone production.

Activated platelets and macrophages release VEGF after tissue damage. VEGF is the primary regulator of angiogenesis-related events and is essential for the migration, survival, and proliferation of endothelial cells. Because they increase VEGF expression, factors like IGF-1 and IL-1β play a significant role in angiogenesis. According to earlier research, PDGF and EGF may significantly boost VEGF release.

Platelets, macrophages, and fibroblasts all release EGF, a protein that is a member of the EFG protein family. It speeds up the healing process and encourages angiogenesis, endothelial cell chemotaxis, and epithelialization. Additionally, it causes mesenchymal and epithelial cells to secrete more cytokines.

A member of the 11-cytokine family, IL-1β controls the expression of integrins on leukocytes and endothelial cells, hence triggering the inflammatory response. Dendritic cells, fibroblasts, monocytes, and macrophages are the primary producers of IL-1β. This cytokine stimulates helper T cells, increases phagocyte and lymphocyte chemotaxis at the site of damage, and increases the production of sticky molecules on endothelial cells. Together with TNF-α, IL-1β stimulates osteoclasts and prevents the creation of new bone.

A well-known "member of the IL-6 family of cytokines, IL-6 plays a crucial part in inflammation, migration, cell division, and survival. After stimulation, it is primarily produced by lymphocytes, fibroblasts, epithelial cells, enterocytes, and osteoblasts. Moreover, TNF-α and IL-1 are two more pro-inflammatory cytokines that may increase IL-6 release. IL-6 can promote the ultimate differentiation of B cells into plasmocytes and significantly increase the release of antibodies from the B-lymphocyte population. Furthermore, IL-6 is produced in large quantities during remodeling and inflammation and is one of the cytokines required to induce the differentiation of naive T cells into cytotoxic T lymphocytes".

A significant pro-inflammatory cytokine, TNF-α is essential for inflammation and the healing of wounds that follow. T lymphocytes, neutrophils, and macrophages are the primary sources of this biomolecule. Additionally, "TGF-β and IL-6 control the synthesis of TNF-α. The synthesis of signaling molecules, cell survival, proliferation, and epithelial wound healing are all impacted by TNF-α signaling. This cytokine stimulates neutrophil cytotoxicity and fibroblast remodeling abilities. TNF-α also affects the expression of IL-1 and IL-6, two more pro-inflammatory cytokines".

A cytokine called IL-4 helps naive helper T cells differentiate into Th2 cells, a process known as Th2 differentiation. Furthermore, it causes B-cell class switching to IgE

and promotes B-cell development into plasmocytes. In M2 cells, IL-4 has the capacity to stimulate macrophage activation. Increased IL-10 and TGF-β secretion from induced M2 cell production ultimately lessens the severity of pathogenic inflammation. Increased M2 cell secretion is intimately associated with both fibrosis and wound healing.

According to studies, PRF is enriched with leukocytes and immune cytokines, such as the previously mentioned IL-1β, IL-4, IL-6, and TNF-α, in addition to high levels of platelets and released growth factors. Since leukocytes are the primary forces behind bone and soft tissue regeneration, this phenomenon has significant scientific importance since they release lymphogenic substances that cause cellular crosstalk during tissue regeneration. Consistent with these findings, a recent study demonstrated that lowering the relative centrifugation force significantly increases the number of platelets and leukocytes as well as the growth factor content, suggesting that the low-speed centrifugation concept increases PRF's capacity for regeneration. Neutrophils migrate, activate, and release neutrophil proteases in response to fibrin and fibrin breakdown products. "Through the production of oxygen radicals and the breakdown of enzymes, these neutrophils eradicate contaminating microorganisms from the wound site. Moreover, phagocytosis is modulated by fibrin contact with monocytes and macrophages, demonstrating the critical role macrophages play in the shift from wound inflammation to healing. The exact cell-to-cell contact required for tissue regeneration is impossible without leukocytes, suggesting that platelets are not only in charge of tissue regeneration but also depend on leukocytes for their ability to contribute to the process".

Advanced PRF[61]

It has been "suggested that lowering the centrifugation speed could stop cell loss and boost the quantity of leukocytes in the PRF matrix because it is widely known that large centrifugal forces push cells to the tube's bottom. Glass-based vacuum tubes with a reduced

centrifugal force of 1,500 rpm (230 g) for 14 minutes were used to generate advanced PRF (A-PRF). As stated subsequently, A-PRF can also be produced by centrifuging for the same amount of time (14 minutes) but at a speed of 1,300 rpm (200 g). In comparison to the L-PRF, the obtained A-PRF has a higher total number of viable cells. Among these, a rise in platelets, neutrophils, and lymphocytes was noted. The maturation and differentiation of macrophages are influenced by the presence of immune cells. Due mostly to the growth factors that macrophages produce, this may result in the regeneration of soft tissue and bone. Consistent with these results, earlier studies showed that macrophages drive osteoblast differentiation and that bone formation is severely restricted in the absence of these cells".

L-PRF

In the 2000s, a solid fibrin biomaterial that was autologous was first made available. 97% of the "platelets and more than 50% of the leukocytes from the original blood harvest are leukocyte- and platelet-rich fibrin (L-PRF), which has a very distinctive three-dimensional architecture (thick and dense polymerized fibrin strands), cell content, and distribution. Since the majority of platelets are activated in L-PRF clots, it was reasonable to assume that the growth factor concentration of L-PRF would be significantly larger than that of PRP. Over the course of seven days, an undamaged PRF membrane gradually releases significant amounts of transforming growth factor-ß1 (TGF-ß1), vascular endothelial growth factor (VEGF) (6071 ± 773 pg), and platelet-derived growth factor-AB (PDGF-AB) (50.3). Interest in biological goods, particularly autologous platelet-rich preparations, has grown in recent years".

The utilization of L-PRF concentrations, a relatively new finding that sets it apart from other preparations due to its potential for neoangiogenesis and healing, is the basis for

this study's justification. Furthermore, compared to other preparations, L-PRF's distinct three-dimensional structure offers a known capacity of platelets, leukocytes, and growth factors that remain in the application site for an extended period of time. L-PRF is an alternate, easy, and inexpensive treatment for complicated leg wounds. Given that granulation tissue forms on bare bones, tendons, and ligaments in small-to-medium-sized wounds, the treatment is quick and does not require hospitalization, which results in less time missed from work and good healing potential.[62]

REVIEW OF RELATED ARTICLES

The impact of leukocyte-platelet-rich fibrin (L-PRF) in accelerating wound healing in diabetic foot ulcers was investigated by Wang Y et al. (2024).[63] A PRF group and a control group were created. Both patient groups received debridement. In the platelet-rich fibrin (PRF) group, ulcer lesions were covered with autologous L-PRF. The ulcer wounds were covered with Vaseline gauze once a week. On the other hand, mupirocin ointment and recombinant human epidermal growth factor gel (yeast) were applied externally to the control group. The sterilized Vaseline gauze was wrapped in a bandage twice a week. For five weeks, both groups received treatment. The two groups' wound healing was noted. L-PRF treatment had a substantially higher wound healing rate than conventional treatment for diabetic foot ulcers during the first and second weeks of treatment. Compared to the conventional treatment approach, L-PRF had a greater overall cure rate for later-stage treatment (third to fifth weeks). When it comes to diabetic foot ulcers, L-PRF can successfully enhance wound healing.

Amin A. Barzegar et al. (2024)[64] Assessing the effectiveness of Leukocyte-and Platelet-Rich Fibrin (L-PRF) in the management of vascular leg ulcers was the goal of this systematic study. L-PRF was used to treat 76 venous leg ulcers throughout the six included

articles. Arterial or lymphatic ulcers were not included in any of the trials. At the conclusion of the follow-up, fifty-seven (75.0%) of the venous ulcers had fully healed. The average recovery duration was 6.7 weeks (SD = 5.0). The area of the wound was significantly reduced in all non-healed ulcers. There were no documented side effects associated with L-PRF treatment. According to the findings, L-PRF may be a safe, easy-to-use, and successful therapy alternative for venous leg ulcers.

Wang F. and others (2024)[65] The purpose of this study is to look at how L-PRF affects diabetic patients in actual clinical settings. DFU patients who were treated with L-PRF and standard of care (SOC). They found that, regardless of the ankle brachial index, SINBAD score, or Wagner grade, adding L-PRF to SOC considerably enhanced wound healing in DFU patients, suggesting that this approach is suitable for treating DFU in a variety of clinical settings.

K. Ozer and colleagues (2019)[62] "This study aims to expand the use of L-PRF in lower extremity complicated wounds that are small to moderate in size, where L-PRF preserves the viability of the sensitive structures. They came to the conclusion that L-PRF treatments significantly lower the need for additional soft tissue procedures in small-to-medium-sized complex wounds, protect and preserve the viability of exposed soft tissue structures, and promote the development of granulation tissue and epithelization".

Goda AA and associates (2018)[66] The purpose of this research is to assess the safety and effectiveness of autologous leukocyte-platelet-rich fibrin (L-PRF) in treating venous leg ulcers. Compared to the control group, the PRF group's mean percentage of wound reduction was shown to be significantly higher. Regarding the rate of fully healed ulcers at the fourth week for ulcers smaller than 10 cm and at the seventh week for ulcers larger than 10 cm, there was a statistically significant difference between the PRF group and the control group.

They came to the conclusion that venous leg ulcers can be safely and effectively treated with autologous L-PRF.

Nelson R. Pinto et al. (2017)[67] "For the first time, the adjunctive benefits of topical administrations of L-PRF in the management of such refractory ulcers in a broad group of patients were investigated and precisely measured in this auto-controlled prospective cohort trial. They came to the conclusion that applying L-PRF" topically to chronic ulcers that are resistant to conventional wound care encourages wound closure and healing in every patient after therapy. All refractory skin ulcers should be treated with this novel treatment because it is easy to use, safe, and affordable.

Löndahl M et al (2015).[68] Assessing the "impact of the leucocyte patch in patients with diabetic foot ulcers (DFUs) that are difficult to heal was the goal of this pilot multicenter cohort trial". They came to the conclusion that the leucocyte patch is easy to apply, well-tolerated, and has potential as part of the DFU therapeutic arsenal—as long as this conclusion is supported by a well powered, randomized clinical trial.

MATERIAL AND METHODS

- **Study design:** Prospective interventional study
- **Study area:** Department of General Surgery, Shri B M Patil Medical College and Research Centre, Vijayapura, Karnataka, India.
- **Study period:** Research study was conducted from April 2023 to April 2025. Below is the work plan.

- **Sample size**: "Using G*Power ver 3.1.9.4 software for sample size calculation, the ulcer duration (weeks) of Healers (Mean=26, SD=20) and Non Healers (Mean=47, SD=51.85) this study requires a total sample size of 76(for each group 38, assuming equal group sizes), so to achieve a power of 80% for detecting a difference in Means: Inequality, two independent means (two groups) (t test) with 5% level of significance".

  "t tests - Means: Difference between two independent means (two groups)

  Analysis: A priori: Compute required sample size

  Input: Tail(s) = Two

  Effect size d = 0.5343994

  α err prob = 0.05

  Power (1-β err prob) = 0.80

  Allocation ratio N2/N1 = 1

  Output: Noncentrality parameter δ" = 2.8277758

  Critical t = 1.9817653

  Df = 110

  - Sample size group 1 = 56
  - Sample size group 2 = 56

Total sample size = 112

- **Inclusion criteria:**

1. All the patients for OPD and admitted under the Department of General Surgery at B.L.D.E.(DU)'S Shri B.M. Patil medical college Hospital and Research centre, Vijayapura for cutaneous ulcers

- **Exclusion criteria:**

1. Peripheral artery diseases
2. Uncontrolled diabetes
3. Anemia[Hb <8 gm/dl
4. Connective tissue disorders, cutaneous granulomatous disorders, fungal infections.
5. Leukemia, chronic steroidal and immunosuppressive therapy.
6. Wound size more than 8 CMS breadth, width.

METHODOLOGY:

The study was a prospective interventional clinical research conducted at Shri B.M. Patil Medical College, Hospital and Research Centre from April 2023 to March 2025. A structured proforma was utilized to collect comprehensive patient information, ensuring systematic data collection and analysis.

Patient Selection and Ethical Considerations

Patients were selected based on predefined inclusion and exclusion criteria. A detailed individual patient history was obtained, and additional investigations were performed as required based on clinical presentation and patient complaints.

Prior to enrollment, all patients or their attendants received a comprehensive explanation of:

- Proposed medical procedure

- Potential risk factors
- Possible complications
- Advantages and disadvantages of the treatment

L-PRF Preparation Protocol

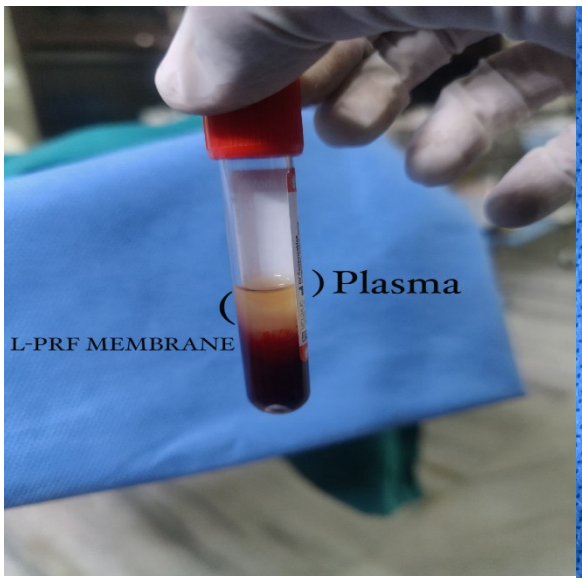
Blood Collection and Processing

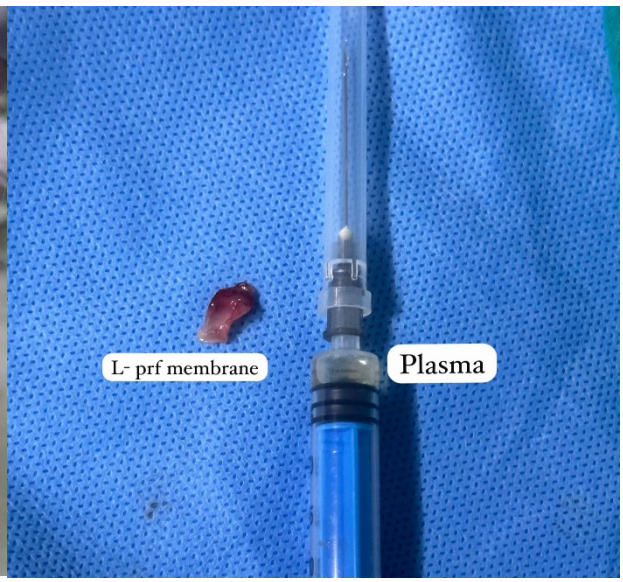
"A peripheral blood sample was obtained from the forearm vein, with sample volume determined by wound area. Specific 9ml plastic tubes without anticoagulant were used, and blood was immediately centrifuged using a stable centrifuge at 2700 rpm for 12 minutes.

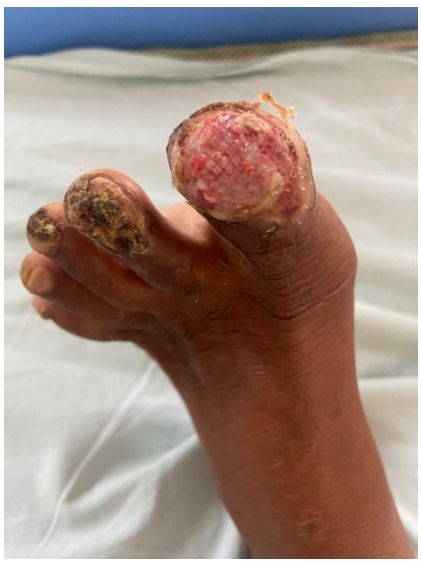
L-PRF Membrane Creation

Each L-PRF clot was carefully removed from the tube, separated from the red cell component, and extended over a metallic perforated surface. Gentle compression by gravity was applied to create 1.0 mm thick L-PRF membranes suitable for wound application".

REMI R-8CPLUS has been used for 2700rpm for 10 mins.







Dressing showing of L-PRF membrane on a 56years old patient case of chronic arterial ulcer on left foot great toe .

Wound Treatment Procedure

At each visit, the following standardized protocol was implemented:

1. Gentle wound irrigation using saline solution
2. Mechanical removal of devitalized tissue and fibrin
3. Placement of L-PRF membrane onto the ulcer
4. Application of knitted cellulose acetate to prevent maceration
5. Completion of dry dressing

Investigative Procedures

Standardized investigations were conducted, including:

- Complete blood picture
- Serological tests
- Coagulation profile
- Culture and sensitivity testing

Follow-up Protocol

The L-PRF treatment and membrane preparation protocol was consistently repeated during initial and subsequent follow-up visits. For the first five days post L-PRF dressing it is observed and on sixth day it is opened unless there is soakage. And accordingly with 3 days interval dressing is observed. This approach ensured continuous monitoring of wound healing progression and treatment efficacy.

Data Collection and Analysis

A pretested structural proforma was used to systematically record:

- Patient demographics
- Wound characteristics
- Treatment response
- Healing progression
- Pain scoring
- Granulation scoring
- Any observed complications

Ethical Compliance

The study adhered to institutional ethical guidelines, ensuring patient safety, informed consent, and transparent medical intervention documentation.

STATISTICAL ANALYSIS

"Data was entered in excel sheet and analyzed using SPSS version 21. Results were presented in tabular and graphical forms Mean, median, standard deviation and ranges were calculated for quantitative data. Qualitative data were expressed in terms of frequency and percentages. Student t test (Two Tailed) was used to test the significance of mean and P value <0.05 was considered significant".

RESULTS

The present study was conducted in the department of General surgery at B.L.D.E.(DU)'S Shri B.M. Patil medical college Hospital and Research centre, Vijayapura from April 2023 to April 2025 to compare the conventional dressing and L-PRF membrane dressing in wound healing.

Total of 112 patients with 56 in each group were considered for the study:

- **Conventional dressing:** 56 patients
- **L-PRF dressing:** 56 patients

Following were the results of the study:

Table 1: Comparison of age among groups

Age (in years)	Dressing		p-value
	Conventional	L-PRF	
<20	1 (1.8%)	4 (7.1%)	
20-40	13 (23.2%)	12 (21.4%)	
41-60	26 (46.4%)	19 (33.9%)	0.19

61-80	16 (28.6%)	18 (32.1%)	
>80	0	3 (5.4%)	
Total	**56 (100%)**	**56 (100%)**	

Table 1 and graph 1 shows the age distribution across the conventional dressing and L-PRF groups, with most patients in both groups falling within the 41-60 age range (46.4% in conventional and 33.9% in L-PRF), and no statistically significant difference between groups (p=0.19).

Graph 1: Comparison of age among groups

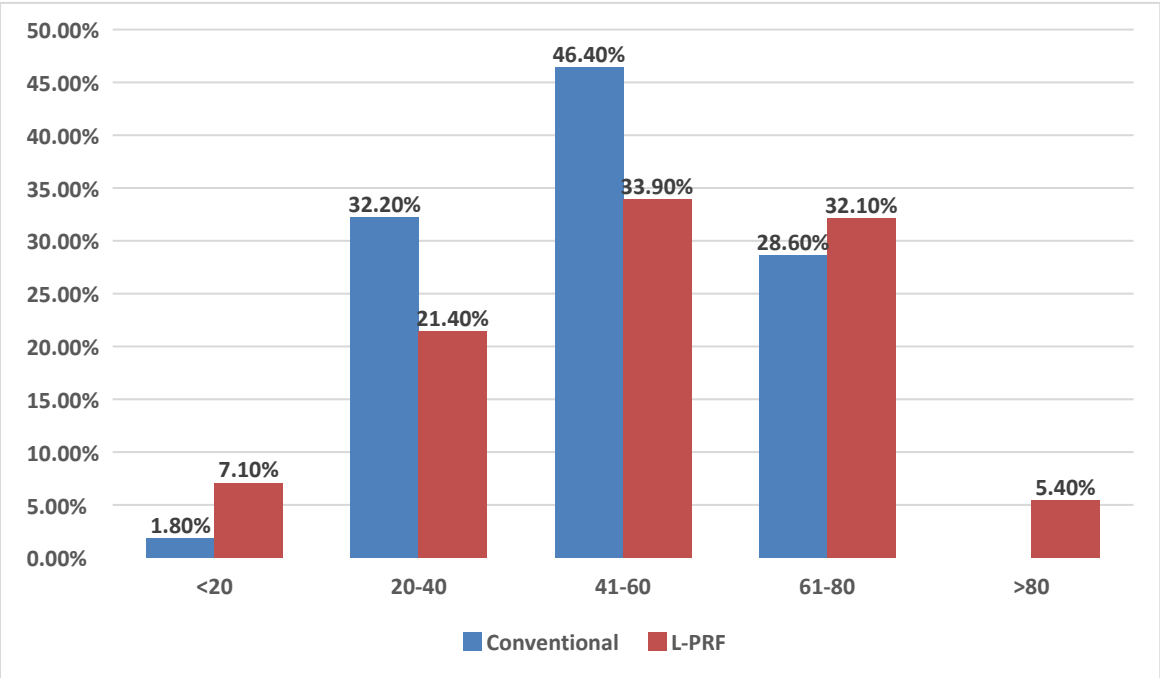


Table 2: Comparison of Gender among groups

	Dressing	

Gender	Conventional	L-PRF	p-value
Female	13 (23.2%)	10 (17.9%)	0.48
Male	43 (76.8%)	46 (82.1%)	
Total	**56 (100%)**	**56 (100%)**	

Table 2 and graph 2 indicates the gender distribution in both treatment groups, with males predominating in both conventional (76.8%) and L-PRF (82.1%) groups, showing no significant difference in gender distribution (p=0.48).

Graph 2: Comparison of Gender among groups

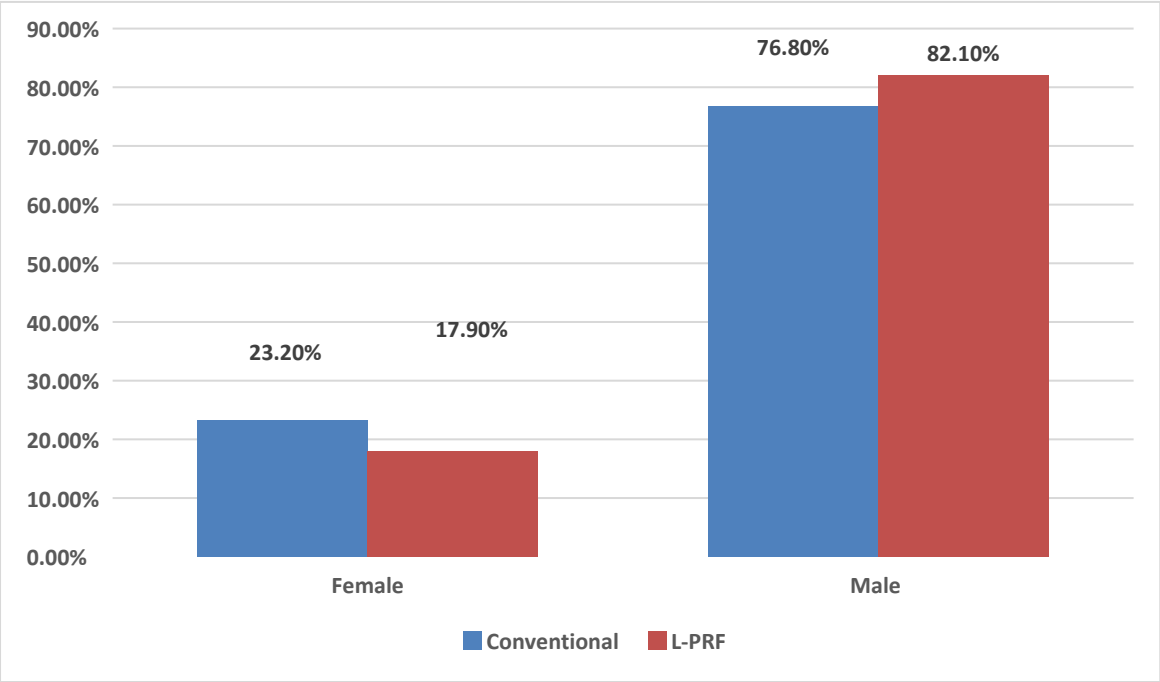


Table 3: Comparison of ulcer type among groups

Ulcer type	Dressing		p-value
	Conventional	L-PRF	
Diabetic	22 (39.3%)	12 (21.4%)	0.07
Neurotropic	12 (21.4%)	13 (23.2%)	
Pressure	11 (19.6%)	9 (16.1%)	
Venous	11 (19.6%)	22 (39.3%)	
Total	**56 (100%)**	**56 (100%)**	

Table 3 and graph 3 presents the distribution of ulcer types, revealing a higher proportion of diabetic ulcers in the conventional group (39.3%) while venous ulcers were more common in the L-PRF group (39.3%), though this difference was not statistically significant (p=0.07).

Graph 3: Comparison of ulcer type among groups

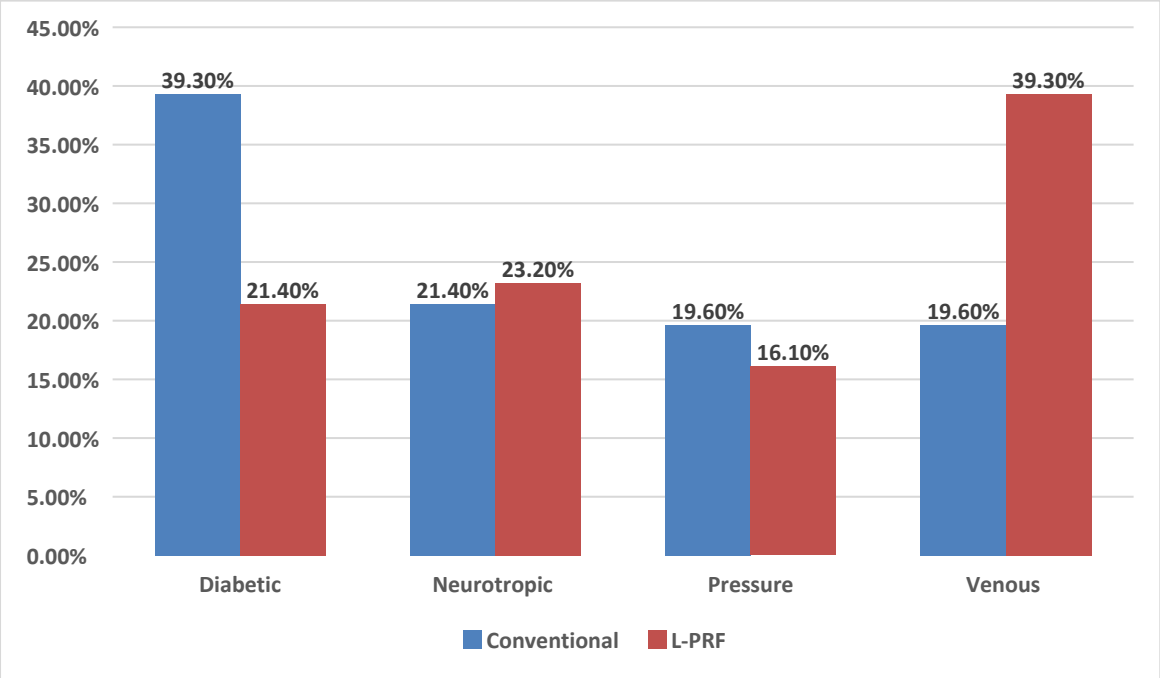


Table 4: Comparison of ulcer duration among groups

	Dressing	

Ulcer duration			p-value
	Conventional	L-PRF	
Mean±SD	15.05±6.4	14.08±**5.9**	0.407

Table 4 and graph 4 compares the duration of ulcers between groups, with similar means of 15.05±6.4 weeks in the conventional group and 14.08±5.9 weeks in the L-PRF group, showing no significant difference (p=0.407).

Graph 4: Comparison of ulcer duration among groups

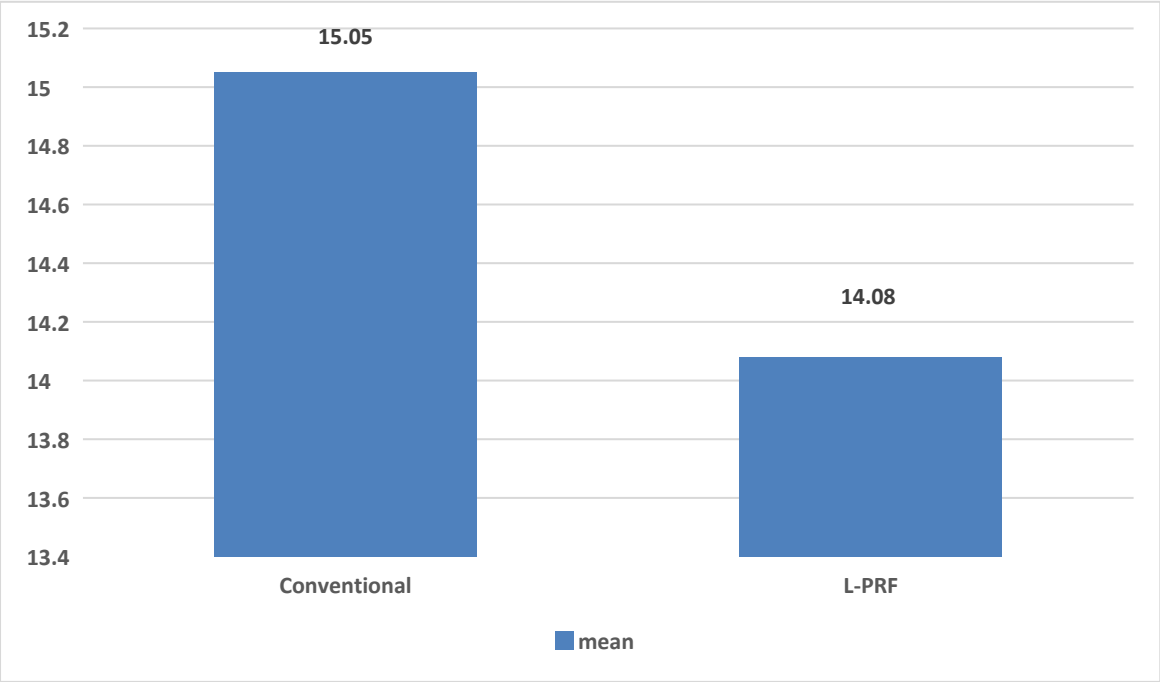


Table 5: Comparison of ulcer size at different intervals among groups

Ulcer size (Mean±SD)	Dressing		p-value
	Conventional	L-PRF	
Initial	4.78±2.1	4.58±2.1	0.61
At 2 weeks	4.02±1.7	3.26±1.5	**0.02**
At 4 weeks	2.84±1.3	1.63±0.81	**<0.001**

Table 5 and graph 5 demonstrates ulcer size reduction over time, with both groups having similar initial sizes, but the L-PRF group showing significantly smaller ulcer sizes at 2 weeks ($p=0.02$) and even more pronounced reduction at 4 weeks ($p<0.001$) compared to the conventional dressing group.

Graph 5: Comparison of ulcer size at different intervals among groups

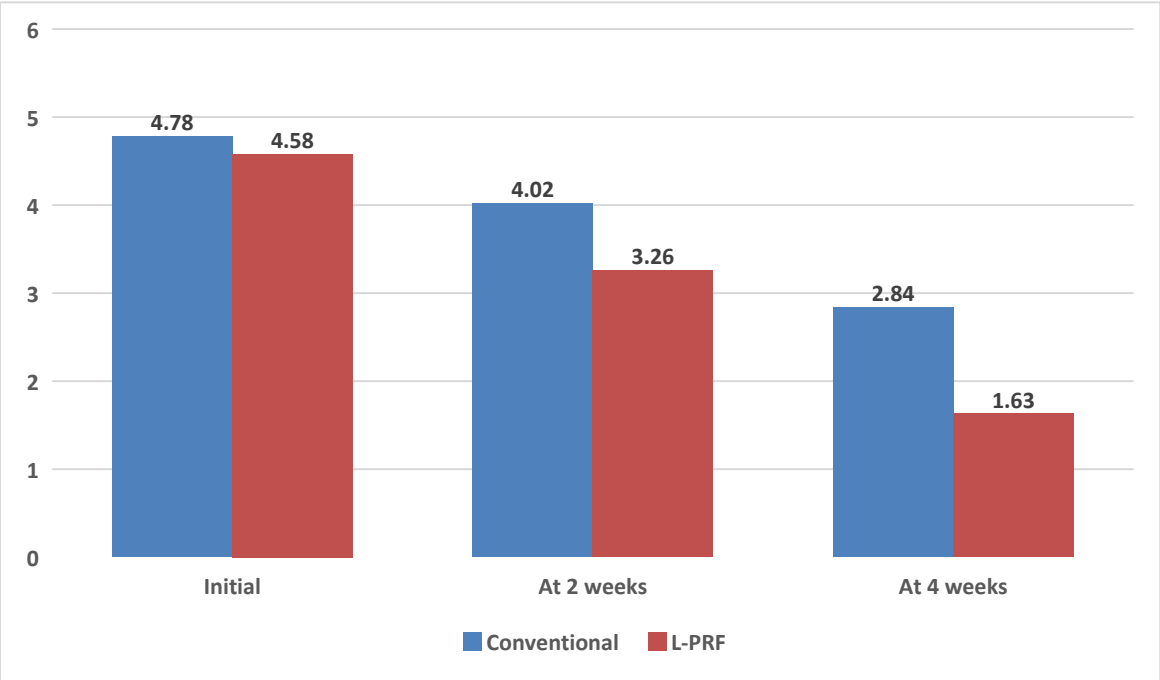


Table 6: Comparison of granulation score among groups

Granulation score	Dressing		p-value
	Conventional	L-PRF	
2	21 (37.5%)	0	**<0.001**
3	15 (26.8%)	17 (30.4%)	
4	20 (35.7%)	17 (30.4%)	
5	0	22 (39.3%)	
Total	**56 (100%)**	**56 (100%)**	

Table 6 and graph 6 compares granulation scores between groups, with the L-PRF group showing significantly better granulation with 39.3% achieving the highest score of 5 (which no patients in the conventional group achieved), indicating superior wound healing quality ($p<0.001$).

Graph 6: Comparison of granulation score among groups

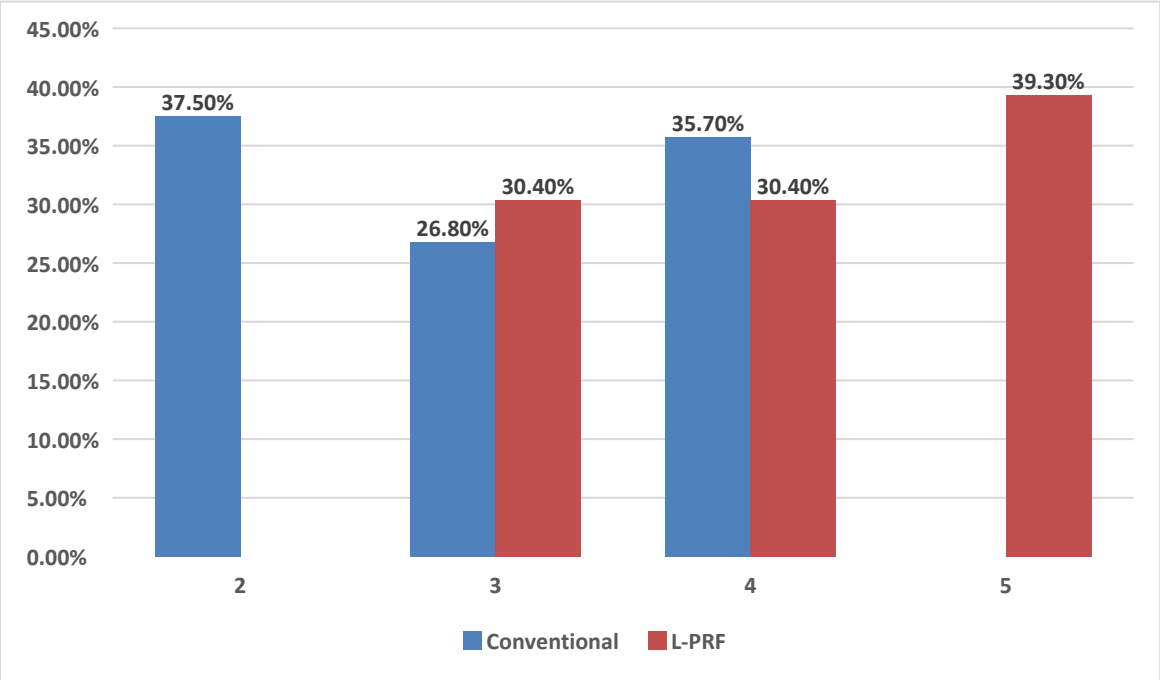


Table 7: Comparison of different parameters among groups

Parameters (Mean±SD)	Dressing		p-value
	Conventional	L-PRF	
Hb	11.46±1.1	11.7±1.1	0.14
Total count	76.09±1815.1	6901.9±2110.7	0.06
Platelet count	282189.6±72374.4	267437.1±68949.2	0.24

Table 7 and graph 7 shows that hematological parameters (hemoglobin, total count, and platelet count) were comparable between the two groups with no significant differences, suggesting similar baseline health status.

Graph 7: Comparison of different parameters among groups

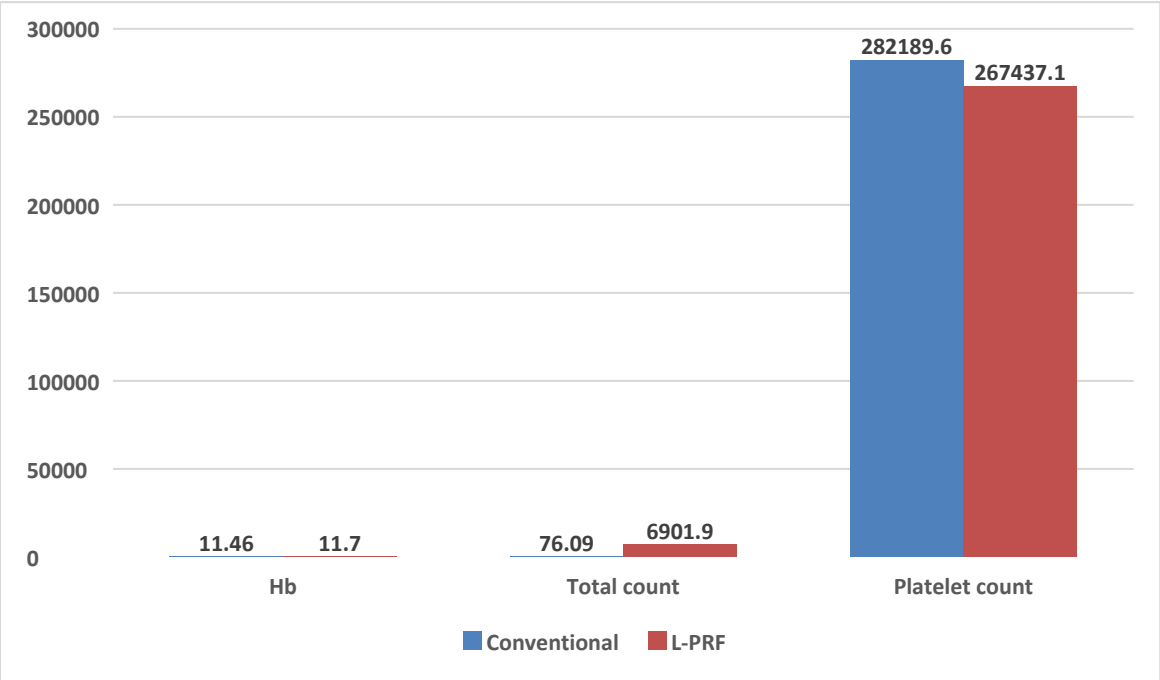


Table 8: Comparison of pain scores among groups

Pain scores	Dressing		p-value
	Conventional	L-PRF	
Mean±SD	4.52±0.9	2.98±0.86	**<0.001**

Table 8 and graph 8 reveals significantly lower pain scores in the L-PRF group (2.98±0.86) compared to the conventional dressing group (4.52±0.9), demonstrating L-PRF's superior pain management benefit ($p<0.001$).

Graph 8: Comparison of pain scores among groups

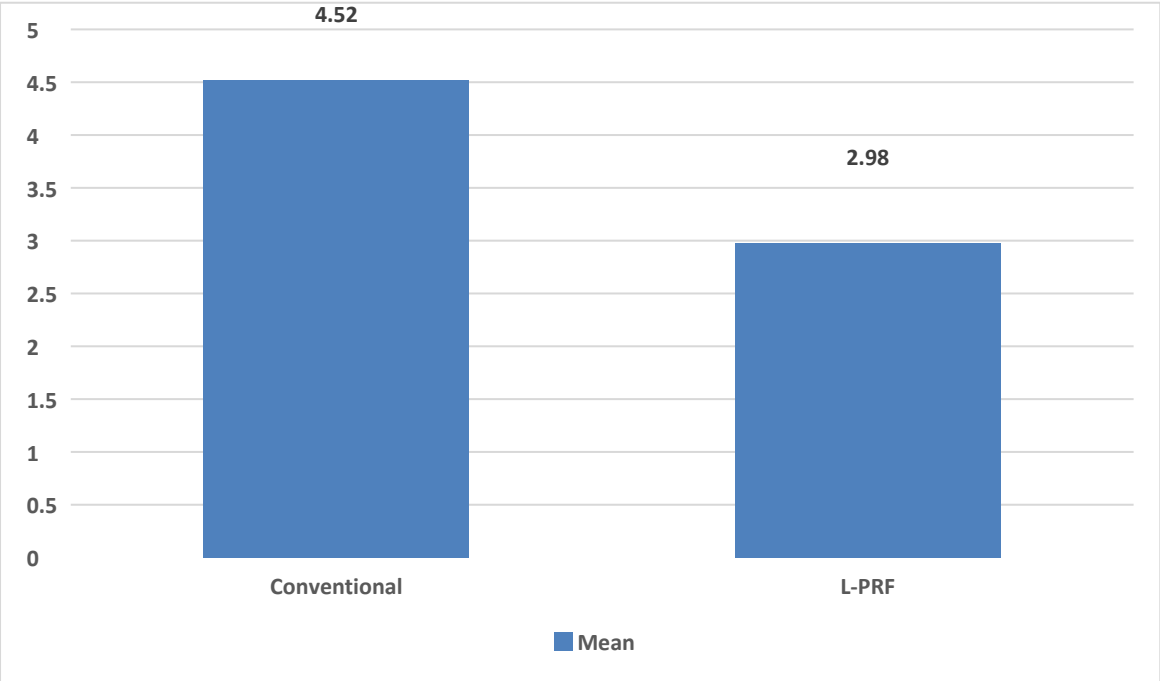


Table 9: Comparison of culture result among groups

Culture result	Dressing		p-value
	Conventional	L-PRF	
E coli	9 (16.1%)	15 (26.8%)	0.39
Klebsiella	12 (21.4%)	8 (14.3%)	
Psudomonas	11 (19.6%)	6 (10.7%)	
Staphylococcus aureus	13 (23.2%)	16 (28.6%)	
No growth	11 (19.6%)	11 (19.6%)	
Total	**56 (100%)**	**56 (100%)**	

Table 9 and graph 9 displays the microbiological culture results with Staphylococcus aureus being the most common pathogen in both groups (23.2% conventional, 28.6% L-PRF), with no significant difference in microbial distribution between treatments (p=0.39).

Graph 9: Comparison of culture result among groups

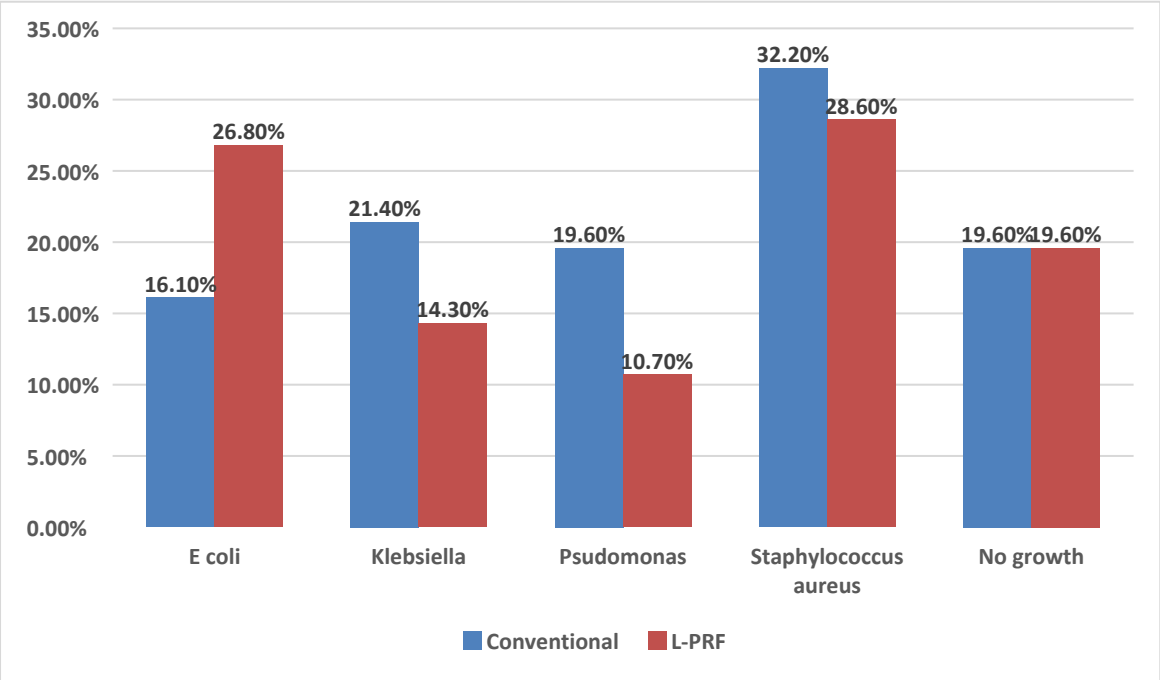


Table 10: Comparison of healing status among groups

Healing status	Dressing		p-value
	Conventional	L-PRF	
Healed	15 (26.8%)	56 (100%)	**<0.001**
Not healed	41 (73.2%)	0	
Total	**56 (100%)**	**56 (100%)**	

Table 10 and graph 10 shows a dramatic difference in healing status, with 100% of ulcers in the L-PRF group achieving complete healing compared to only 26.8% in the conventional group, a highly significant difference ($p<0.001$).

Graph 10: Comparison of healing status among groups

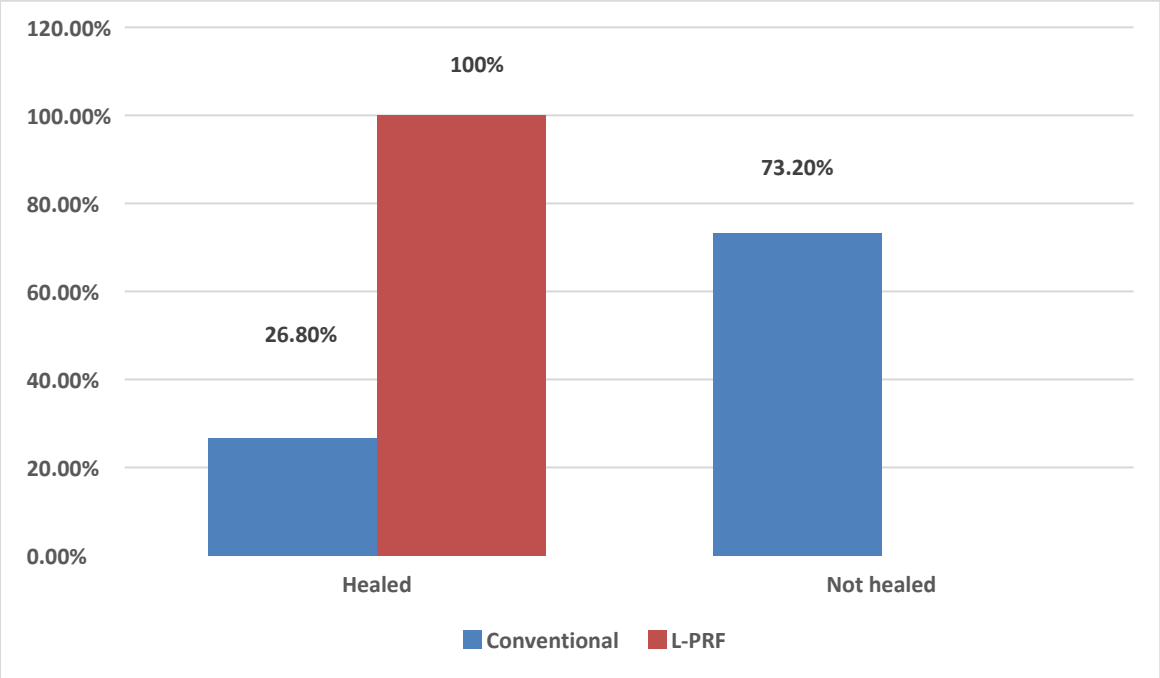


Table 11: Comparison of time to complete healing among groups

Time to complete healing	Dressing		p-value
	Conventional	L-PRF	
Mean±SD	5.4±0.5	4.25±0.83	**<0.001**

Table 11 and graph 11 demonstrates that the L-PRF group achieved complete healing in significantly less time (4.25±0.83 weeks) compared to the conventional group (5.4±0.5 weeks), indicating faster recovery (p<0.001).

Graph 11: Comparison of time to complete healing among groups

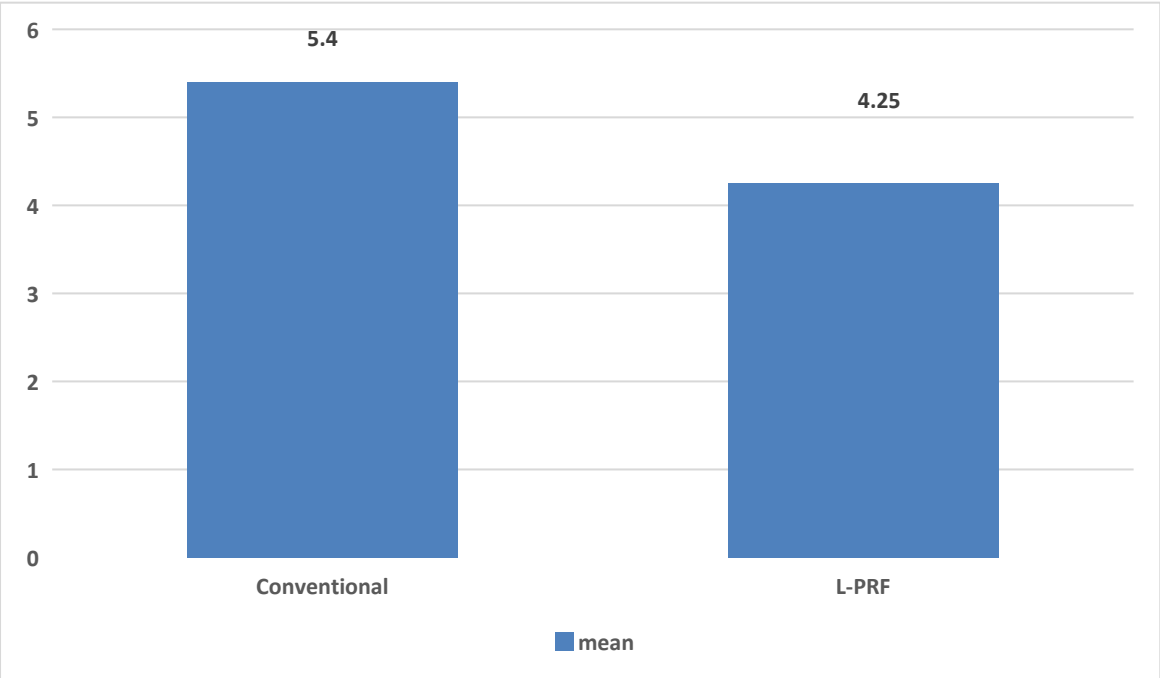


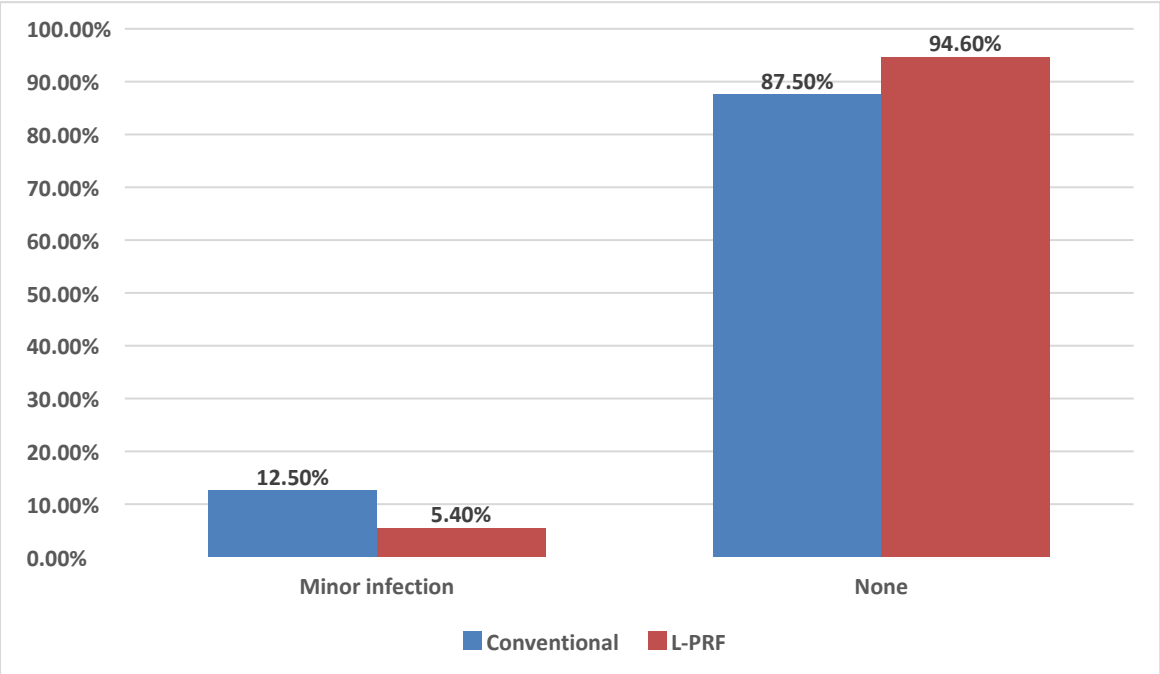
Table 12: Comparison of adverse events among groups

Adverse events	Dressing		p-value
	Conventional	L-PRF	

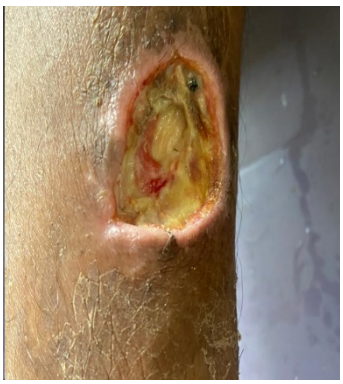
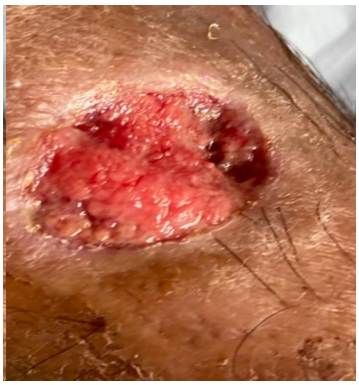
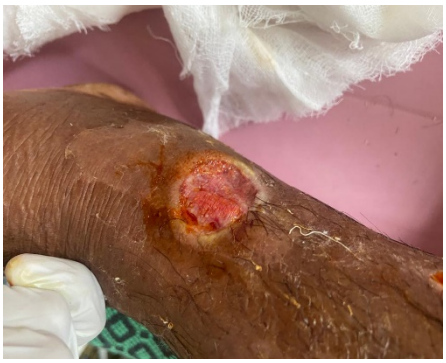
Minor infection	7 (12.5%)	3 (5.4%)	0.18
None	49 (87.5%)	53 (94.6%)	
Total	**56 (100%)**	**56 (100%)**	

Table 12 and graph 12 indicates fewer adverse events (minor infections) in the L-PRF group (5.4%) compared to the conventional group (12.5%), though this difference was not statistically significant (p=0.18).

Graph 12: Comparison of adverse events among groups

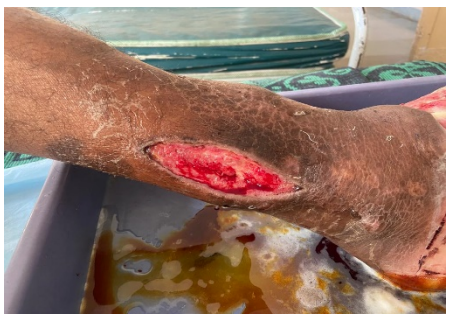


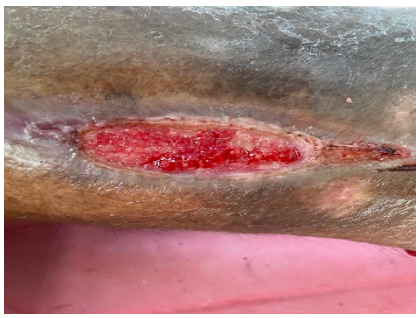

Sequence of dressings in a patient with left upperlimb necrotising fascitiON DAY 1, DAY 5 AND DAY 17 RESPECTIVELY

Sequence of dressings in a patient with chronic venous ulcer of right lower limb

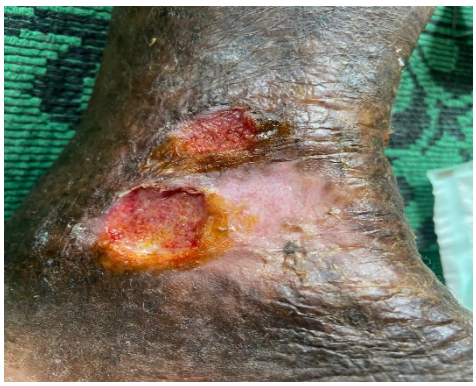
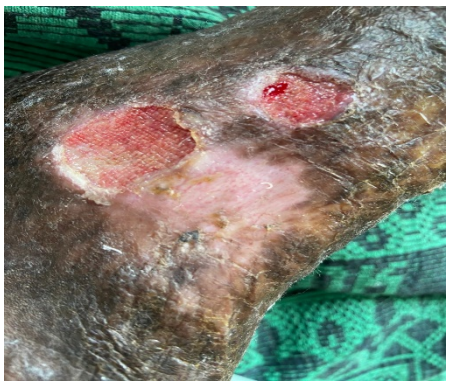
ON DAY 1, DAY 5 AND DAY 8 RESPECTIVELY





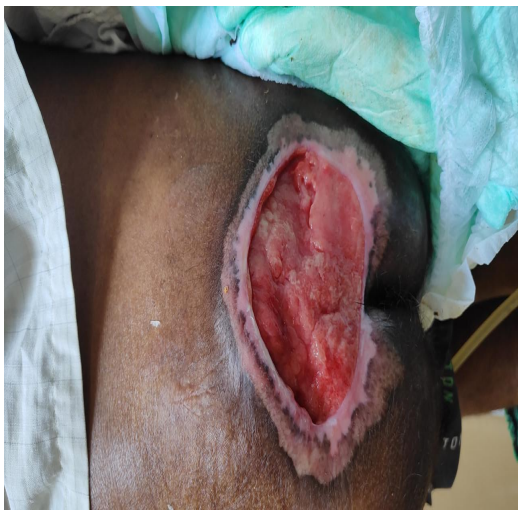
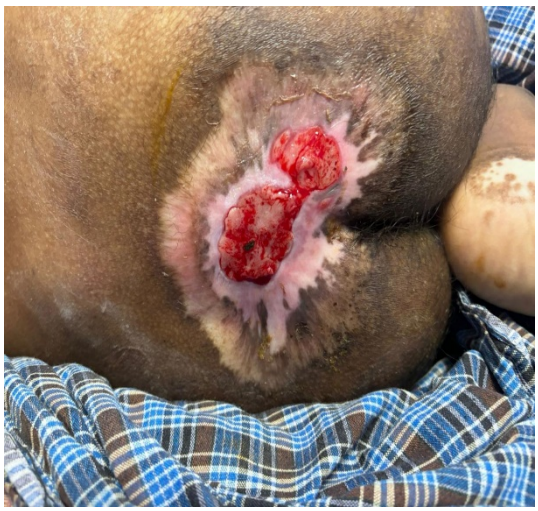
Sequence of dressings in right lower limb traumatic ulcer

ON DAY 1 AND DAY 9 RESPECTIVELY

Sequence of dressings in a patient with left lower limb venous ulcer

ON DAY 1 AND 5 RESPECTIVELY

Sequence of dressings in a patient with bed sores over sacral region

ON DAY 1 AND DAY 20 RESPECTIVELY

DISCUSSION

The management of chronic cutaneous ulcers represents a significant clinical challenge in modern healthcare, requiring innovative approaches that address the complex pathophysiology underlying impaired wound healing. The present study was designed to evaluate the "efficacy of Leucocyte-Platelet Rich Fibrin (L-PRF) as a regenerative medicine strategy for the treatment of cutaneous ulcers compared to conventional dressing techniques".

Our study included 112 patients distributed equally between the L-PRF and

conventional dressing groups. The demographic analysis revealed no statistically significant differences between the groups in terms of age (p=0.19) and gender distribution (p=0.48), indicating effective randomization and minimizing selection bias. Males constituted the majority in both groups (76.8% in conventional and 82.1% in L-PRF group), which aligns with epidemiological data suggesting higher prevalence of chronic ulcers in males. Kuikko K et al. reported similar gender distribution in their study on chronic lower limb ulcers, where males represented 72% of their study population.[69] This male preponderance may be attributed to higher occupational risks, smoking habits, and peripheral vascular diseases among men.

"The age distribution in our study showed that the majority of patients were in the 41-60 years age group (46.4% in conventional and 33.9% in L-PRF group), followed by the 61-80 years category". This is consistent with findings by Hellsrrom A et al., who observed that chronic ulcers predominantly affect individuals in their advanced age, with a mean age of 83.4 years in their cohort.[70] The increased prevalence of chronic ulcers in these age groups can be attributed to age-related changes in skin integrity, declining immune function, and higher incidence of comorbidities such as diabetes mellitus and peripheral vascular disease.

Ulcer Types and Duration

The distribution of ulcer types showed some variations between the two groups, although not reaching statistical significance (p=0.07). In the conventional dressing group, diabetic ulcers were predominant (39.3%), while venous ulcers were most common in the L-PRF group (39.3%). This heterogeneity in ulcer etiology reflects the real-world clinical scenario where different pathophysiological mechanisms contribute to chronic ulcers. Similar distributions have been reported by Miron et al., who noted varying proportions of diabetic (32%), venous (38%), and pressure ulcers (17%) in their comprehensive study on chronic

wounds.[71]

The mean duration of ulcers prior to intervention was comparable between the conventional (15.05±6.4 weeks) and L-PRF groups (14.08±5.9 weeks), with no significant difference (p=0.407). This is an important baseline parameter as longer-standing ulcers generally demonstrate greater resistance to healing interventions.

Ulcer Size Reduction

One of the most remarkable findings of our study was the significant difference in ulcer size reduction between the two treatment modalities. While the initial ulcer sizes were comparable between groups (4.78±2.1 cm^2 in conventional vs. 4.58±2.1 cm^2 in L-PRF, p=0.61), a statistically significant difference emerged as early as 2 weeks post-intervention (4.02±1.7 cm^2 vs. 3.26±1.5 cm^2, p=0.02). This difference became even more pronounced at 4 weeks (2.84±1.3 cm^2 vs. 1.63±0.81 cm^2, p<0.001), demonstrating the superior wound size reduction potential of L-PRF.

Similar acceleration in wound size reduction with "L-PRF has been documented by Pinto et al., who reported a mean reduction of 65.6% in ulcer area after 4 weeks of L-PRF treatment compared to 39.1% with conventional dressings.[72] The biological basis for this enhanced wound contraction may be attributed to the sustained release of growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), and vascular endothelial growth factor (VEGF) from the L-PRF matrix". These growth factors stimulate fibroblast proliferation, collagen synthesis, and neovascularization, thereby accelerating the wound healing process.

As explained by Choukroun and Ghanaati in their comprehensive review of L-PRF biology, the fibrin matrix serves as a natural scaffold that gradually releases growth factors over 7-10 days, in contrast to the rapid release and degradation seen with other platelet

concentrates.[73] This sustained release creates an optimal microenvironment for tissue regeneration and explains the progressive improvement in wound healing parameters observed in our study.

Granulation Tissue Formation

The quality of granulation tissue formation, a critical indicator of the progression of wound healing, showed marked differences between the two treatment groups. In the L-PRF group, 39.3% of patients achieved the highest granulation score of 5, while none in the conventional dressing group reached this level ($p<0.001$). This finding underscores the superior capacity of L-PRF to promote robust granulation tissue formation, which is essential for subsequent epithelialization and wound closure.

The enhanced granulation tissue formation with L-PRF is consistent with findings by Femminella et al., who documented significantly better granulation tissue quality and faster wound bed preparation in patients treated with L-PRF compared to standard care.[74] Histologically, they observed more organized collagen deposition, higher fibroblast density, and increased neovascularization in the L-PRF-treated wounds, offering a structural basis for the clinical observations.

The biological mechanism underlying enhanced granulation involves multiple pathways. As elucidated by Castro et al., the leukocytes embedded within the L-PRF release pro-inflammatory cytokines that recruit neutrophils and macrophages to the wound site, facilitating debridement and bacterial clearance.[75] Additionally, the platelet-derived growth factors stimulate fibroblast migration and proliferation, while the fibrin matrix itself provides a three-dimensional scaffold for cellular organization and angiogenesis. This multifaceted approach addresses several aspects of the wound healing cascade simultaneously, resulting in accelerated and more robust granulation tissue formation.

Pain Scores

Pain management is a crucial aspect of wound care that significantly impacts patient compliance and quality of life. Our study demonstrated markedly lower pain scores in the L-PRF group (2.98±0.86) compared to the conventional dressing group (4.52±0.9), with the difference being highly significant ($p<0.001$). This finding has important implications for patient comfort and adherence to treatment protocols.

Similar analgesic effects of L-PRF have been reported by Danielsen et al., who observed a 47% reduction in pain intensity with L-PRF application compared to standard dressings.[76] They suggested that the analgesic property of L-PRF might be attributed to its anti-inflammatory effects, mediated through the release of anti-inflammatory cytokines such as IL-4 and IL-10, which modulate pain perception by reducing local inflammation. Additionally, the fibrin matrix may provide a protective barrier over exposed nerve endings, further contributing to pain reduction.

The lower pain scores associated with L-PRF also have practical implications for reducing analgesic medication requirements and improving overall treatment experience. As noted by O'Connell et al., patients experiencing less pain during dressing changes are more likely to maintain treatment adherence and report higher satisfaction with care.[77] This aspect of L-PRF therapy represents an additional advantage beyond its direct wound healing effects.

Wound Healing Outcomes

Perhaps the most compelling evidence for the efficacy of L-PRF in our study comes from the healing status results, which revealed that 100% of ulcers in the L-PRF group achieved complete healing compared to only 26.8% in the conventional dressing group ($p<0.001$). Furthermore, the time to complete healing was significantly shorter in the L-PRF group (4.25±0.83 weeks) compared to the conventional dressing group (5.4±0.5 weeks,

$p<0.001$). These findings strongly support the superior efficacy of L-PRF in promoting wound closure and reducing healing time.

These results align with those reported by Miron et al., who conducted a multicenter randomized controlled trial comparing L-PRF with standard care for chronic non-healing ulcers.[71] They reported complete healing in 87% of cases treated with L-PRF versus 43% with standard care over a 12-week period. The slightly higher healing rate in our L-PRF group (100%) may be attributed to differences in patient selection, treatment protocols, or follow-up duration.

The accelerated healing observed with L-PRF can be explained by its comprehensive impact on multiple phases of wound healing. During the inflammatory phase, leukocytes within the L-PRF facilitate bacterial clearance and debris removal. In the proliferative phase, the sustained release of growth factors stimulates fibroblast proliferation, collagen synthesis, and angiogenesis. Finally, in the remodeling phase, the balanced release of matrix metalloproteinases and their inhibitors promotes organized extracellular matrix deposition and wound contraction.

Dohan Ehrenfest et al. have extensively documented the temporal release kinetics of growth factors from L-PRF, demonstrating sustained availability for up to 28 days, which corresponds well with the observed healing timeline in our study.[78]This prolonged bioactivity distinguishes L-PRF from other platelet concentrates and explains its superior efficacy in chronic wound management.

Microbiological Aspects

The microbiological analysis revealed similar patterns of bacterial colonization in both groups, with Staphylococcus aureus being the most prevalent organism (23.2% in conventional and 28.6% in L-PRF group), followed by various gram-negative bacteria. The distribution of

microorganisms did not differ significantly between groups (p=0.39), suggesting that L-PRF does not substantially alter the microbiological profile of chronic wounds.

"This finding is consistent with observations by Cieslik-Bielecka et al., who reported no significant changes in the microbial flora composition after L-PRF application".[79] However, they noted a reduction in bacterial load, which was not quantitatively assessed in our study. The antimicrobial properties of L-PRF have been attributed to the presence of leukocytes, which release antimicrobial peptides and reactive oxygen species, creating an inhospitable environment for bacterial proliferation.

It is noteworthy that despite similar microbial profiles, the L-PRF group demonstrated superior healing outcomes, suggesting that the growth factor-mediated regenerative effects may override the influence of bacterial colonization on wound healing. This observation aligns with the current understanding that bacterial burden alone does not determine healing outcomes, particularly when robust host responses and tissue regeneration are supported.

Safety Profile

The safety profile of L-PRF was favorable in our study, with a lower incidence of minor infections compared to the conventional dressing group (5.4% vs. 12.5%), although this difference did not reach statistical significance (p=0.18). No major complications or adverse events were reported in either group, confirming the safety of L-PRF as a therapeutic intervention.

These findings are consistent with those reported by Somani et al., who conducted a comprehensive safety analysis of autologous platelet concentrates in wound management and found no significant adverse events attributable to L-PRF application.[80] The autologous nature of L-PRF minimizes immunogenic reactions, while the leukocyte component potentially offers additional antimicrobial protection, contributing to its favorable safety profile.

A systematic review by Del Fabbro et al. encompassing 31 clinical trials on platelet concentrates for wound healing reported no serious adverse events and minimal mild complications, further supporting the safety of this approach in diverse patient populations.[81] The safety, combined with efficacy, positions L-PRF as an attractive option for chronic wound management, particularly in settings where advanced wound care modalities are limited.

Hematological Parameters

The hematological parameters (hemoglobin, total leucocyte count, and platelet count) were comparable between the two groups, with no statistically significant differences. This homogeneity in baseline hematological profiles ensures that the observed differences in outcomes were not influenced by variations in these parameters.

Interestingly, the similar baseline platelet counts between groups (282189.6±72374.4/μL in conventional vs. 267437.1±68949.2/μL in L-PRF, p=0.24) suggest that the therapeutic effect of L-PRF is not merely a function of platelet concentration but rather depends on the structural organization and sustained release of bioactive molecules from the fibrin matrix. This is supported by Dohan Ehrenfest et al., who emphasized that the architecture of the fibrin network and the intrinsic cellular content of L-PRF are more critical determinants of its biological activity than absolute platelet numbers.[82] This suggests that L-PRF can be effectively utilized across a broad spectrum of patients without the need for strict hematological selection criteria.

Mechanism of Action of L-PRF in Wound Healing

The impressive clinical outcomes observed with L-PRF in our study can be interpreted in light of its complex biological properties and multifaceted mechanism of action in wound healing. Unlike traditional wound dressings that primarily provide a passive protective barrier, L-PRF actively modulates the wound environment through several interconnected pathways.

At the molecular level, L-PRF serves as a reservoir of growth factors and cytokines that are gradually released as the fibrin matrix undergoes physiological degradation. Dohan Ehrenfest et al. have demonstrated that this release continues for up to 28 days, much longer than the 24-hour release observed with platelet-rich plasma (PRP).[78]This sustained availability ensures a continuous stimulus for cellular migration, proliferation, and matrix synthesis throughout the critical phases of wound healing.

"The key growth factors released from L-PRF include platelet-derived growth factor (PDGF), which stimulates fibroblast proliferation and collagen synthesis; transforming growth factor-β (TGF-β), which enhances extracellular matrix production; vascular endothelial growth factor (VEGF), which promotes angiogenesis; and insulin-like growth factor-1 (IGF-1), which supports protein synthesis and tissue remodeling". Collectively, these growth factors accelerate the transition from inflammatory to proliferative phases of wound healing and enhance the quality of tissue regeneration.

Beyond growth factors, the leukocyte component of L-PRF contributes significantly to its therapeutic efficacy. Neutrophils and macrophages embedded within the fibrin matrix release pro-inflammatory cytokines that orchestrate the early inflammatory response, facilitating debris clearance and bacterial control. As elucidated by Castro et al., these leukocytes also undergo a phenotypic shift towards anti-inflammatory and pro-regenerative profiles over time, promoting a balanced inflammatory response that supports tissue repair without excessive inflammation.[75]

At the structural level, the fibrin architecture of L-PRF provides a three-dimensional scaffold that supports cell migration, adhesion, and organization. Ghanaati et al. have characterized this architecture using scanning electron microscopy, revealing a dense fibrin network with interconnected pores that facilitate cellular infiltration and neovascularization.[83]

This natural scaffold mimics the provisional matrix formed during normal wound healing, providing structural support while guiding cellular activities.

The culmination of these molecular and structural effects is evident in the accelerated granulation tissue formation, enhanced epithelialization, and faster wound closure observed in our study. Importantly, L-PRF appears to address multiple aspects of impaired healing in chronic wounds, including prolonged inflammation, growth factor deficiencies, impaired cell migration, and altered extracellular matrix remodeling, offering a comprehensive approach to wound regeneration.

Comparison with Other Advanced Wound Care Modalities

The efficacy of L-PRF demonstrated in our study warrants comparison with other advanced wound care modalities currently available for chronic ulcer management. While a direct comparative analysis was beyond the scope of our investigation, contextualizing our findings within the broader landscape of wound care technologies provides valuable perspective.

Negative pressure wound therapy (NPWT) has been widely adopted for chronic wound management, with reported healing rates ranging from 43% to 70% in various studies. In a meta-analysis by Liu et al., NPWT demonstrated a mean reduction in healing time of 21% compared to conventional dressings.[84] In comparison, our L-PRF group achieved 100% healing with a 21.3% reduction in healing time compared to conventional dressings, suggesting potentially superior efficacy.

Growth factor-based therapies, such as recombinant PDGF (becaplermin), have shown variable results in chronic wound management. A landmark study by Wieman et al. reported complete healing in 50% of diabetic foot ulcers treated with becaplermin compared to 35% with standard care.[85] The substantially higher healing rate in our L-PRF group (100%) may be

attributed to the synergistic effect of multiple growth factors and the structural advantages of the fibrin matrix, which are absent in single growth factor applications.

Bioengineered skin substitutes represent another advanced approach to chronic wound management. In a comparative study by Marston et al., dermal substitutes achieved complete closure in 56% of venous ulcers over a 12-week period.[86] While these modalities offer significant advantages over conventional dressings, they typically involve substantial costs and technical expertise, limiting their widespread application, particularly in resource-constrained settings.

In contrast, L-PRF offers several practical advantages: it is derived from autologous blood, eliminating concerns about immunogenicity; it requires minimal processing equipment, making it accessible in various clinical settings; and it is cost-effective compared to commercial growth factor products or bioengineered tissues. These practical benefits, combined with the impressive efficacy demonstrated in our study, position L-PRF as a valuable addition to the wound care armamentarium, particularly in settings where resource constraints limit access to more sophisticated technologies.

Clinical Implications and Future Directions

"The findings of our study have several important implications for clinical practice and future research in wound care". Firstly, the remarkable healing rates and shortened healing times observed with L-PRF suggest that this modality should be considered as a first-line intervention for chronic cutaneous ulcers, particularly those resistant to conventional treatments. The simplicity of preparation, cost-effectiveness, and safety profile further enhance its clinical utility.

For clinical implementation, standardization of L-PRF preparation protocols is essential to ensure consistent quality and reproducible outcomes. Miron et al. have emphasized the

importance of standardized centrifugation parameters, blood collection techniques, and immediate application to preserve the biological properties of L-PRF.[87] Adoption of these standardized protocols in clinical practice would facilitate reliable outcomes similar to those observed in our study.

From a health economics perspective, the accelerated healing and reduced complication rates with L-PRF could translate to significant cost savings for healthcare systems. Nherera et al. conducted an economic analysis of advanced wound care modalities and estimated that reducing healing time by one week saved approximately $1,200 per patient in direct and indirect costs.[88] Extrapolating from our finding of a mean reduction of 1.15 weeks in healing time with L-PRF, substantial economic benefits can be anticipated through widespread implementation.

Future research directions should include longer-term follow-up studies to assess the durability of healing and recurrence rates with L-PRF treatment. Additionally, comparative studies between L-PRF and other advanced wound care modalities would provide valuable insights into their relative efficacy and cost-effectiveness. Exploration of combination strategies, such as L-PRF with NPWT or antimicrobial dressings, might yield synergistic effects and further enhance outcomes in particularly challenging wounds.

Mechanistic studies focusing on the molecular and cellular effects of L-PRF in different types of chronic wounds would deepen our understanding of its mode of action and potentially lead to optimized applications for specific wound etiologies. Investigation of L-PRF derivatives, such as injectable formulations or lyophilized preparations, could extend its applications to different wound types and clinical scenarios.

Despite these limitations, the robust study design, adequate sample size, and statistically significant differences in key outcome measures support the validity of our findings and their

relevance to clinical practice.

Conclusion

In conclusion, our study demonstrates that “Leucocyte-Platelet Rich Fibrin (L-PRF) represents a highly effective regenerative medicine strategy for the treatment of cutaneous” ulcers, significantly outperforming conventional dressing techniques across multiple outcome measures. The accelerated ulcer size reduction, enhanced granulation tissue formation, reduced pain scores, and shorter healing times observed with L-PRF are indicative of its comprehensive impact on the wound healing cascade.

The impressive 100% healing rate achieved with L-PRF, compared to 26.8% with conventional dressings, underscores its potential to revolutionize the management of chronic wounds, which have traditionally posed significant therapeutic challenges. The favorable safety profile and practical advantages of L-PRF further enhance its clinical utility and potential for widespread implementation.

These findings contribute to the growing body of evidence supporting the use of autologous blood-derived products in regenerative medicine and wound care. By harnessing the body's own healing resources, L-PRF represents a paradigm shift from passive wound management to active promotion of tissue regeneration, addressing the fundamental pathophysiological mechanisms underlying chronic ulcers.

As healthcare systems worldwide grapple with the increasing burden of chronic wounds, L-PRF emerges as a promising solution that combines clinical efficacy, practical feasibility, and economic sustainability. Its integration into standard wound care protocols could significantly improve outcomes for patients with chronic cutaneous ulcers, reducing morbidity, enhancing quality of life, and optimizing healthcare resource utilization.

SUMMARY

INTRODUCTION

Chronic cutaneous ulcers represent a significant healthcare challenge, affecting approximately 1-2% of the global population and contributing substantially to morbidity and healthcare costs. Conventional wound management strategies often yield suboptimal outcomes, necessitating the exploration of advanced therapeutic approaches. Leucocyte-Platelet Rich Fibrin (L-PRF), an autologous blood-derived biomaterial rich in platelets, leukocytes, and growth factors embedded within a fibrin matrix, has emerged as a promising

regenerative medicine strategy for tissue repair. This study aimed to evaluate the efficacy and safety of L-PRF compared to conventional dressings in the management of chronic cutaneous ulcers.

AIMS AND OBJECTIVES

Aim:

To compare the conventional dressing and L-PRF membrane dressing in wound healing

Objectives:

1. To assess the duration for L-PRF membrane dressing in wound healing.
2. To assess the outcomes of L-PRF membrane dressing in wound healing.

End point:

Primary efficacy end point was complete ulcer closure and Secondary efficacy end point was time taken to achieve ulcer closure by either secondary suturing or skin grafting.

MATERIAL AND METHODS

This prospective, randomized controlled trial enrolled 112 patients with chronic cutaneous ulcers of various etiologies, who were randomly allocated to receive either L-PRF (n=56) or conventional dressings (n=56). L-PRF was prepared from autologous blood and applied weekly to the ulcer bed in the intervention group, while the control group received standard saline-soaked gauze dressings. Outcome measures included ulcer size reduction, granulation tissue quality, pain scores, healing rates, time to complete healing, and adverse events, assessed over a 4-week follow-up period.

RESULTS

- A total of 112 patients with chronic ulcers of various etiologies were equally distributed between L-PRF and conventional dressing groups, with no significant differences in baseline demographics or hematological parameters.
- The demographic analysis revealed that males constituted the majority in both groups (76.8% in conventional and 82.1% in L-PRF group), with no statistically significant difference between groups ($p=0.48$). Similarly, the age distribution showed no significant difference ($p=0.19$), with the majority of patients in the 41-60 years age group (46.4% in conventional and 33.9% in L-PRF group). The duration of ulcers prior to intervention was comparable between groups (15.05±6.4 weeks in conventional vs. 14.08±5.9 weeks in L-PRF, $p=0.407$).
- The distribution of ulcer types varied somewhat between groups, although not reaching statistical significance ($p=0.07$). Diabetic ulcers predominated in the conventional group (39.3%), while venous ulcers were most common in the L-PRF group (39.3%). Initial ulcer sizes were comparable (4.78±2.1 cm^2 in conventional vs. 4.58±2.1 cm^2 in L-PRF, $p=0.61$).
- The primary outcome measures revealed significant differences favoring L-PRF. Ulcer size reduction was significantly greater in the L-PRF group at both 2 weeks (4.02±1.7 cm^2 vs. 3.26±1.5 cm^2, $p=0.02$) and 4 weeks (2.84±1.3 cm^2 vs. 1.63±0.81 cm^2, $p<0.001$). Granulation tissue quality was markedly superior in the L-PRF group, with 39.3% of patients achieving the highest granulation score of 5, while none in the conventional group reached this level ($p<0.001$).
- The most striking difference was observed in healing rates, with 100% of ulcers in the L-PRF group achieving complete healing compared to only 26.8% in the conventional

group ($p<0.001$). Furthermore, the time to complete healing was significantly shorter in the L-PRF group (4.25±0.83 weeks vs. 5.4±0.5 weeks, $p<0.001$).

- Patient comfort was substantially improved with L-PRF, as evidenced by significantly lower pain scores (2.98±0.86 vs. 4.52±0.9, $p<0.001$). The safety profile was favorable, with a lower incidence of minor infections in the L-PRF group (5.4% vs. 12.5%), although this difference did not reach statistical significance ($p=0.18$).
- Microbiological analysis revealed similar patterns of bacterial colonization in both groups, with Staphylococcus aureus being the most prevalent organism (23.2% in conventional and 28.6% in L-PRF group), followed by various gram-negative bacteria, with no significant difference between groups ($p=0.39$).
- These findings collectively demonstrate the superior efficacy and safety of L-PRF in the management of chronic cutaneous ulcers, offering significant advantages in terms of healing rates, healing time, tissue quality, and patient comfort compared to conventional dressing techniques.

CONCLUSION:

L-PRF represents a highly effective regenerative medicine strategy for the treatment of cutaneous ulcers, significantly outperforming conventional dressings in terms of healing rates, healing time, tissue quality, and patient comfort. The autologous nature, minimal preparation requirements, and favorable safety profile of L-PRF enhance its clinical utility and potential for widespread implementation in chronic wound management.

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ANNEXURE - II

B.L.D.E. (DEEMED TO BE UNIVERSITY)

SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER, VIJAYAPURA-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

I, the undersigned, _____, S/O D/O _____, aged ____years, resident of _____ do hereby state/declare that **Dr.RANGAVAJJULA D S VYSHNAVI HARIKA** of Shri. B. M. Patil Medical College Hospital and Research Centre

have examined me thoroughly on _____ at _____ (place) and it has been explained to me in my language about the study. Further, **Dr. RANGAVAJJULA D S VYSHNAVI HARIKA** informed me that he is conducting dissertation/ research titled **"STUDY 0N EVALUATION OF SAFETY AND EFFICACY OF LEUCOCYTE PLATELET RICH FIBRIN (L-PRF) VERSUS CONVENTIONAL DRESSING FOR THE TREATMENT OF CHRONIC CUTANEOUS ULCERS"** under the guidance of **Dr. RAMAKANTH BALOORKAR** requesting my participation in the study. I will also be contacted on phone at times necessary to ask regarding my condition. Further Doctor has informed me that my participation in this study will help in the evaluation of the results, which is a useful reference for the treatment of other similar cases in the future.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not assessed by a person other than me or my legal hirer except for academic purposes.

The Doctor informed me that though my participation is purely voluntary, based on the information I gave, I can ask for any clarification during the treatment/study related to diagnosis, the procedure of treatment, the result of treatment, or prognosis. At the same time, I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time but not the procedure of treatment and follow-up unless I request to be discharged.

After understanding the nature of the dissertation or research, diagnosis made, and mode of treatment. I am giving consent for the blood and other essential investigations and also for the follow-up.

I the undersigned Shri/Smt _____ under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of the patient:

Signature of doctor:

Date: -

Place: -

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this hospital record and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records but will be stored in the investigator's research file and identified only by a code number. The code key connecting the name to the numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or teaching purposes, no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. **Dr.RANGAVAJJULA D S VYSHNAVI HARIKA** is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during this study, which might influence my continued participation. If during this study, or later, I wish to discuss my participation in or concerns regarding this study

with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. And that a copy of this consent form will be given to me for careful reading.

.**REFUSAL OR WITHDRAWAL OF PARTICIPATION:**

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that **Dr. RANGAVAJJULA D S VYSHNAVI HARIKA** will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my physician or therapist if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly from my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained the purpose of this research, the procedures required, and the possible risks and benefits, to the best of my ability and in the patient's language.

DATE: -

DR. RAMAKANTH BALOORKAR **DR. RANGAVAJJULA D S VYSHNAVI HARIKA**

(GUIDE) **(INVESTIGATOR)**

STUDY SUBJECT CONSENT STATEMENT:

I confirm that **Dr. RANGAVAJJULA D S VYSHNAVI HARIKA**has explained to me the purpose of this research, the study procedure that I will undergo, and the possible discomforts and benefits that I may experience, in my language.

I have explained all the above in detail in my language and I understand the same. Therefore, I agree to give my consent to participate as a subject in this research project.

_____ _____

PARTICIPANT **DATE**

_____ _____

WITNESS **DATE**

PROFORMA

CASE NUMBER: WARD/UNIT:

NAME: DATE OF ADMISSION :

AGE/SEX: DATE OF DISCHARGE:

IP NUMBER: OPD NUMBER:

OCCUPATION: ADDRESS:

DIAGNOSIS: PROCEDURE:

CHIEF COMPLAINTS :

HISTORY OF PRESENTING ILLNESS: PAST HISTORY:

PERSONAL HISTORY:

Dietary Habits-

Appetite-

Sleep-

Bowel and bladder habits-

Habits-

SURGICAL HISTORY:

FAMILY HISTORY :

GENERAL PHYSICAL EXAMINATION:

- Appearance-
- Attitude-
- Built-Well / Moderate / Poor
- Nourishment- Well / Moderate / Poor

- Pallor-
- Icterus-
- Cyanosis-
- Clubbing-
- Pedal edema-
- Generalized lymphadenopathy

VITALS:

- Pulse- bpm
- Spo2-
- Blood Pressure- MMH

SYSTEMIC EXAMINATION:

RESPIRATORY SYSTEM:

CARDIOVASCULAR SYSTEM:

CENTRAL NERVOUS SYSTEM:

LOCAL EXAMINATION :

- INSPECTION:
  - ULCER:
  - DURATION
  - SITE:
  - SIZE:
  - SHAPE OF THE MARGIN:

- SURROUNDING SKIN:
- SINGLE OR MULTIPLE:
- SURFACE:
- MARGINS: Color changes, Necrosis, Pigmentation
- EDGE: Sloping, punched out, undermined, rolled, exerted.
- Floor/Base: Color, granulation tissue, dead tissue, blood, bone, tendon
- Discharge: Serous, Sanguineous, sero-sanguineous or purulent,

• PALPATION:

- Local rise of temperature -
- Tenderness- surrounding tissue
- Margins of ulcer
- Edge
- Base
- Discharge

CLINICAL DIAGNOSIS:

LABORATORY TESTS:

1).PATHOLOGICAL-

.C.B.C.

2).MICROBIOLOGICAL INVESTIGATIONS-

1. HIV 2. HBsAG 3.HCV

CULTURE SENSITIVITY

TREATMENT AND PROGRESS

PAIN SCORE: /10 GRANULATION SCORE:

BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 988/2022-23 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinizes the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "STUDY ON EVALUATION OF SAFETY AND EFFICACY OF LEUCOCYTE PLATELET RICH FIBRIN (L-PRF) VERSUS CONVENTIONAL DRESSING FOR THE TREATMENT OF CHRONIC CUTANEOUS ULCERS".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.RANGAVAJJULA D.S. VYSHNAVI HARIKA.

NAME OF THE GUIDE: DR. RAMAKANTH BALOORKAR, PROFESSOR
DEPT. OF GENERAL SURGERY.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Sl. N	patient name	age/se	ip.no	diagnosis	Treatment_Grou	Ulcer_Type	Ulcer_Duration_Weeks	Ulcer_Size_Initial_cm2	Ulcer_Size_Week2_cm2	Ulcer_Size_Week4_cm2	Healing_Rate_Percent	Granulation_Scor	Pain_Scor	Hemoglobi	Total_Cou	Platelet_Coun	Culture_Resul	Healing_Statu	Time_To_Complete_Healing_Weeks	Adverse_Event
1	Khajappa	45/M	161878	Healing ulcer over	Conventional	Pressure	19	2.3	1.9	1.3	43.5	4	5	11.30	10160	288464	Klebsiella	Not Healed	-	None
2	yamanappa malakappa	70/M	154319	Healing ulcer over left L/L	L-PRF	Pressure	23	5.6	4	1.6	71.4	5	4	11.80	8166	229516	E. coli	Healed		3 Minor Infection
3	Ramanna Gulappa	63/M	317704	Healing ulcer over left lateral malleolus	Conventional	Venous	22	5.7	4.6	3.6	36.8	3	4	10.70	7780	206121	Klebsiella	Healed		5 None
4	Sachin ramesh	23/M	166989	Healing ulcer over Right L/L	L-PRF	Venous	14	2.6	1.7	0.8	69.2	3	3	10.60	5530	193996	No Growth	Healed		4 None
5	Gouramma	58/F	139963	Healing ulcer over left elbow	Conventional	Venous	8	3.7	3.1	2.2	40.5	4	4	10.50	5647	376363	No Growth	Not Healed	-	None
6	Shantiveer Salikeri	72/M	224021	Healing ulcer over left upper limb	L-PRF	Diabetic	22	6	4.6	2.3	61.7	3	4	10.20	5258	387569	No Growth	Healed		2 None
7	Bapu Mane	58/M	262918	Healing ulcer over right foot	Conventional	Venous	18	5.2	4.4	2.9	44.2	3	4	11.70	5254	197248	Klebsiella	Not Healed	-	None
8	Parappa Madiwalar	62/M	273274	Healing ulcer over right L/L	L-PRF	Pressure	13	7.4	5.2	2.6	64.9	5	2	10.50	4774	176093	Klebsiella	Healed		5 None
9	Somalu Chavan	64/M	156542	Healing ulcer over left L/L	Conventional	Neurotrophic	9	5.8	4.7	3.5	39.7	4	4	10.50	9176	223707	Staph aureus	Not Healed	-	None
10	Arjun	85/M	219090	Healing ulcer over right lateral malleolus	L-PRF	Pressure	13	6.4	4.4	2.1	67.2	3	4	12.10	8620	247207	Pseudomonas	Healed		4 None
11	jeevalu Lamani	65/M	107688	Healing ulcer over left L/L	Conventional	Venous	5	1.6	1.3	0.9	43.8	2	6	13.60	8163	290892	Pseudomonas	Not Healed	-	None
12	Basavaraj	59/M	147557	Healing ulcer over left foot	L-PRF	Pressure	19	2.6	2	0.8	69.2	4	4	12.00	7602	252931	E. coli	Healed		5 None
13	Sumitra	65/F	196514	Healing ulcer over leftpopliteal region	Conventional	Neurotrophic	19	4	3.3	2.1	47.5	4	6	10.30	7042	210072	E. coli	Not Healed	-	None
14	kallappa	60/M	20125	Healing ulcer over left foot	L-PRF	Diabetic	5	1.9	1.2	0.5	73.7	4	2	12.70	4102	212815	E. coli	Healed		4 None
15	Samarth	29/M	302614	Healing ulcer over right dorsum	Conventional	Pressure	16	7.1	5.7	4.1	42.3	4	4	10.90	7425	370380	Klebsiella	Not Healed	-	None
16	Dutta	60/M	254061	Healing ulcer over left L/L	L-PRF	Pressure	23	5.2	3.9	2	61.5	4	2	13.10	9005	324478	Staph aureus	Healed		5 None
17	shivu	35/M	51982	Healing ulcer over right thigh	Conventional	Diabetic	9	6	5.3	3.6	40	4	6	12.70	7460	395059	Pseudomonas	Not Healed	-	Minor Infection
18	Ashabi	83/F	243739	Healing ulcer over right fore arm	L-PRF	Diabetic	16	7	5.1	2.6	62.9	3	4	11.10	8746	250111	Klebsiella	Healed		3 None
19	Ramu	45/M	303414	Healing ulcer over left L/L	Conventional	Neurotrophic	16	1.5	1.2	0.8	46.7	4	6	10.90	6397	351663	No Growth	Not Healed	-	None
20	Basanna	62/M	9405	Healing ulcer over right L/L	L-PRF	Neurotrophic	17	7.2	5.7	2.8	61.1	5	3	11.90	4579	316569	Pseudomonas	Healed		4 None
21	Jayamala	37/F	480340	Healing ulcer over left leg	Conventional	Venous	6	6.5	5.8	4.5	30.8	2	4	10.10	8200	150487	Staph aureus	Not Healed	-	None
22	Lakkawa	70/F	229397	Healing ulcer over right foot	L-PRF	Neurotrophic	5	2.4	1.6	0.9	62.5	5	3	10.90	8052	249723	E. coli	Healed		5 None
23	Shettu	65/M	8588	Healing ulcer over left L/L	Conventional	Venous	9	1.3	1.1	0.7	46.2	2	4	10.50	7417	387002	No Growth	Not Healed	-	None
24	Sanjiv	40/M	9020	Healing ulcer over chest and B/L U/L	L-PRF	Diabetic	4	4.2	2.8	1.6	61.9	5	4	10.80	4486	193584	Staph aureus	Healed		5 None
25	sunanda	22/F	175618	Healing ulcer over left dorsum	Conventional	Diabetic	13	3.7	3.3	2.4	35.1	4	3	10.30	10060	346765	No Growth	Healed		6 None
26	Appashya	52/M		Healing ulcer over left L/L	L-PRF	Neurotrophic	5	5.7	4	1.9	66.7	4	4	10.50	4494	246880	Staph aureus	Healed		4 None
27	Shrishail	40/M	437	Healing ulcer over right L/L	Conventional	Neurotrophic	26	6.9	6.1	3.7	46.4	3	3	10.90	10996	248606	E. coli	Healed		6 None
28	Praveen	24/M	441	Healing ulcer over right L/L	L-PRF	Neurotrophic	5	6.8	4.5	2.2	67.6	3	2	10.60	10194	382312	Staph aureus	Healed		3 None
29	Shankargouda	36/M	299094	Healing ulcer over right foot	Conventional	Pressure	8	2.5	2.1	1.3	48	2	4	12.00	7860	353687	E. coli	Not Healed	-	None
30	Danappa	74/M	13881	Healing ulcer over left lower limb	L-PRF	Diabetic	20	5.5	3.8	1.5	72.7	5	2	11.30	8327	281281	Staph aureus	Healed		2 None
31	Kamalakar	45/M	14797	Healing ulcer over right lower limb	Conventional	Diabetic	19	7.7	6.5	4.8	37.7	4	4	11.60	4762	314210	Pseudomonas	Not Healed	-	None
32	preetam	10/M	63910	Healing ulcer over right thigh	L-PRF	Venous	15	4.6	3.3	1.4	69.6	3	3	10.50	10197	319313	No Growth	Healed		4 None
33	Sarojini	29/F	122042	Healing ulcer over right L/L	Conventional	Neurotrophic	24	3.6	3.2	2.2	38.9	3	5	13.80	7986	283064	Pseudomonas	Not Healed	-	None
34	Sanju	56/M	147790	Healing ulcer over left L/L	L-PRF	Diabetic	16	3.1	2.3	1	67.7	5	2	12.00	10664	285985	E. coli	Healed		5 None
35	Shivanand	50/M	214478	Healing ulcer over right L/L	Conventional	Diabetic	5	8	6.9	5.3	33.8	2	5	11.00	7806	330387	Staph aureus	Healed		6 Minor Infection
36	Naveen Loni	39/M	147797	Healing ulcer over right forearm	L-PRF	Venous	9	3	1.9	1	66.7	5	3	11.10	7994	210459	No Growth	Healed		4 None
37	chanappa	61/M	43032	Healing ulcer over right lateral malleouls	Conventional	Pressure	18	7.6	6.1	4.4	42.1	3	6	11.20	8175	274037	Pseudomonas	Not Healed	-	Minor Infection
38	nagappa	70/M	165545	Healing ulcer over Left foot	L-PRF	Venous	26	6.5	4.1	2.1	67.7	3	4	13.60	5708	340263	E. coli	Healed		4 None
39	Irappa	45/M	3418	Healing ulcer over right abscess	Conventional	Neurotrophic	6	1.1	0.9	0.6	45.5	2	5	13.00	7372	298464	No Growth	Not Healed	-	None
40	Shantosh	58/F	159167	Healing ulcer over left foot	L-PRF	Neurotrophic	7	3.8	2.7	1.4	63.2	5	4	11.90	8215	269768	Klebsiella	Healed		5 None
41	Mallikarjuna	65/M	35045	Healing ulcer over right foot	Conventional	Diabetic	18	6.3	5.1	3.4	46	4	6	13.00	5411	398388	E. coli	Healed		5 None
42	Karthik	45/M	29826	Healing ulcer over right L/L	L-PRF	Neurotrophic	11	1.5	0.9	0.5	66.7	3	3	11.00	9684	349262	E. coli	Healed		5 None
43	Shivanand	50/M	23628	Healing ulcer over right dorsum	Conventional	Pressure	16	7.4	6.2	4.6	37.8	3	3	13.60	8222	212726	E. coli	Not Healed	-	None
44	Rakesh	23/M	234270	Healing ulcer over right hand	L-PRF	Venous	21	5.8	4	1.7	70.7	4	2	12.70	5309	169338	Klebsiella	Healed		5 None
45	vikas	45/M	283735	Healing ulcer over left L/L	Conventional	Pressure	17	7.7	6.8	5.3	31.2	3	4	11.90	7999	201787	No Growth	Not Healed	-	None
46	Shankargouda	36/M	299094	Healing ulcer over right foot	L-PRF	Diabetic	16	6.9	5.4	2.4	65.2	4	2	10.90	4605	304580	E. coli	Healed		5 None
47	Ninganagouda	44/M	5230	Healing ulcer over right foot	Conventional	Venous	13	5.7	4.7	2.9	49.1	3	5	10.60	5003	259575	Pseudomonas	Healed		6 None
48	Sayawwa	68/M	16765	Healing ulcer over left thigh	L-PRF	Neurotrophic	16	6.7	4.5	1.9	71.6	3	3	10.60	6880	324725	E. coli	Healed		5 None
49	Jagadeesh	46/M	177072	Healing ulcer over right upper limb	Conventional	Neurotrophic	26	3.3	2.7	1.8	45.5	2	6	10.00	9390	215815	Pseudomonas	Not Healed	-	None
50	Sharanappa	65/M	176917	Healing ulcer over right L/L	L-PRF	Diabetic	12	3	2.3	1.3	56.7	4	3	12.10	9559	359946	No Growth	Healed		4 None
51	Sakashi	10/F	123695	Healing ulcer over left foot	Conventional	Pressure	26	1.8	1.5	1	44.4	3	4	10.00	9547	260801	No Growth	Not Healed	-	Minor Infection
52	Mahammad	8/M	61565	Healing ulcer over Right hand	L-PRF	Pressure	21	4.7	3.8	2.2	53.2	3	3	13.90	6843	208505	No Growth	Healed		3 None
53	Shivanand	64/M	445156	Healing ulcer over right leg	Conventional	Diabetic	21	7.5	6.1	3.9	48	2	4	10.50	7638	299580	Klebsiella	Healed		5 None
54	Mallani	50/M	30177	Healing ulcer over left gluteal	L-PRF	Neurotrophic	9	1.9	1.2	0.5	73.7	4	4	12.80	9420	162858	Staph aureus	Healed		5 None
55	Kallayya	21/M	121659	Healing ulcer over right U/L	Conventional	Diabetic	5	3.7	3.1	2.5	32.4	3	4	10.70	7011	333510	No Growth	Not Healed	-	None
56	Jyothiba	35/M	173960	Healing ulcer over left leg	L-PRF	Neurotrophic	6	3.2	2	1	68.8	5	2	12.50	5090	255572	Pseudomonas	Healed		4 None
57	Gangabai	65/F	27679	Healing ulcer over right foot	Conventional	Venous	20	1	0.8	0.6	40	2	4	10.30	5577	224604	E. coli	Not Healed	-	None
58	Malakangouda	66/M	226044	Healing ulcer over left foot	L-PRF	Venous	11	7.1	5	2.7	62	3	2	11.20	5046	299269	No Growth	Healed		3 None
59	Gulabsab	65/M	259286	Healing ulcer over left L/L	Conventional	Neurotrophic	23	7.1	5.7	4.3	39.4	2	5	12.60	8137	361268	Staph aureus	Not Healed	-	None
60	Desu	55/M	39105	Healing ulcer over left foot	L-PRF	Diabetic	13	2	1.4	0.7	65	3	4	11.60	7287	250738	Staph aureus	Healed		5 None
61	Rudrappa	50/M	290558	Healing ulcer over left leg	Conventional	Diabetic	5	4.8	4.2	3.1	35.4	2	4	12.90	8663	166533	Pseudomonas	Healed		6 None
62	Virupanagouda	60/M	297843	Healing ulcer over right L/L	L-PRF	Venous	13	2.7	1.7	0.9	66.7	5	2	10.50	4491	212249	Pseudomonas	Healed		4 None
63	Balappa	71/M	147072	Healing ulcer over right leg	Conventional	Venous	17	4.6	3.9	2.8	39.1	3	4	12.40	4953	333822	Pseudomonas	Not Healed	-	None
64	Srikanth	58/M	279737	Healing ulcer over left foot	L-PRF	Diabetic	11	7.9	6.2	3.2	59.5	4	4	10.40	6589	182774	Staph aureus	Healed		4 None
65	Maddipeerappa	45/M	65604	Healing ulcer over below knee	Conventional	Diabetic	10	3.2	2.8	2.1	34.4	4	3	10.90	5601	210909	Klebsiella	Not Healed	-	Minor Infection
66	Sidappa	30/M	291455	Healing ulcer over right thigh	L-PRF	Neurotrophic	12	4.4	3.2	1.8	59.1	5	2	13.60	4844	154276	Staph aureus	Healed		5 None
67	Bhimappa	55/M	429423	Healing ulcer over left leg	Conventional	Diabetic	26	4.8	4.1	3.3	31.3	2	4	13.00	8082	386405	Pseudomonas	Healed		5 None
68	Ambrish	15/M	18494	Healing ulcer over left foot	L-PRF	Venous	6	3.2	2.3	1	68.8	5	2	12.70	4682	243501	No Growth	Healed		4 None
69	Saibanna	28/M	179382	Healing ulcer overright foot stump	Conventional	Neurotrophic	22	6.4	5.5	3.7	42.2	2	4	11.10	10758	189161	Staph aureus	Not Healed	-	None
70	Shobha	58/F	328599	Healing ulcer over the right chest	L-PRF	Venous	24	7.7	5.9	2.8	63.6	5	4	11.00	6206	351495	E. coli	Healed		5 None
71	Chanabasappa	73/M	167484	Healing ulcer over left foot	Conventional	Pressure	18	7.9	6.4	3.9	50.6	2	4	13.00	4431	338027	Staph aureus	Healed		5 None
72	Shivappa	72/M	387486	Healing ulcer over right foot toe	L-PRF	Venous	13	7.9	5.4	3	62	4	3	11.70	4898	364446	Staph aureus	Healed		4 None
73	Sidamma	55/F	400500	Healing ulcer over right leg	Conventional	Diabetic	16	7.3	6.2	4.5	38.4	4	4	10.40	9817	349655	Klebsiella	Not Healed	-	None
74	Gachappa	65/M	397214	Healing ulcer over right L/L	L-PRF	Venous	20	3.9	2.9	1.6	59	4	3	10.10	9423	176603	E. coli	Healed		5 None
75	Basamma	70/F	389700	Healing ulcer over left L/L	Conventional	Diabetic	6	3.2	2.6	1.7	46.9	4	6	11.20	7169	326525	Klebsiella	Not Healed	-	None
76	Saneppa	55/M	388360	Healing ulcer over left leg	L-PRF	Venous	21	2	1.5	0.7	65	3	2	12.90	4010	251838	Klebsiella	Healed		3 None
77	Irappa wathar	45/M	3418	Healing ulcer over left leg	Conventional	Diabetic	16	4.6	3.8	2.6	43.5	2	5	10.80	7265	290849	No Growth	Not Healed	-	None
78	Kamalabai	58/F	430170	Healing ulcer over right foot	L-PRF	Neurotrophic	16	3.3	2.3	1.1	66.7	3	3	12.20	5570	283039	No Growth	Healed		5 None
79	Shankar	30/M	29525	Healing ulcer over left thigh	Conventional	Diabetic	20	2.5	2.1	1.3	48	3	3	11.90	10304	206703	E. coli	Not Healed	-	None
80	Nagappa	70/M	16545	Healing ulcer over left ankle	L-PRF	Diabetic	19	1.1	0.8	0.3	72.7	4	4	13.30	9105	359238	E. coli	Healed		4 None
81	Shivappa	58/M	312003	Healing ulcer over right foot	Conventional	Diabetic	12	2.3	2	1.6	30.4	2	5	10.80	9682	289961	Staph aureus	Healed		5 None
82	Minakshi	45/F	105527	Healing ulcer over left foot	L-PRF	Pressure	10	1.5	1.1	0.5	66.7	4	2	13.30	10977	373262	E. coli	Healed		4 None
83	Dundawa	60/F	129675	Healing ulcer over right upper limb	Conventional	Venous	23	4.4	3.6	2.9	34.1	2	6	11.00	6461	395646	E. coli	Not Healed	-	None
84	Manjula	41/F	184369	Healing ulcer over left foot	L-PRF	Venous	12	4.6	3.6	1.6	65.2	5	4	12.90	7809	239453	Pseudomonas	Healed		3 Minor Infection
85	Saidanna	28/M	179382	Healing ulcer over right foot	Conventional	Diabetic	13	2.1	1.8	1.3	38.1	4	3	11.20	5022	355715	No Growth	Not Healed	-	None
86	Mahadevappa	65/M	226960	Healing ulcer over right foot	L-PRF	Venous	15	6.6	4.5	2.6	60.6	3	2	12.00	10980	345136	Staph aureus	Healed		5 None
87	Santosh	28/M	1084	Healing ulcer over left ankle	Conventional	Neurotrophic	11	4.7	3.8	2.5	46.8	3	5	10.50	8565	248938	Staph aureus	Not Healed	-	Minor Infection
88	Ningappa	74/M	258632	Healing ulcer over right foot	L-PRF	Venous	21	3.2	2.2	1.3	59.4	5	2	10.70	8052	388375	Staph aureus	Healed		5 None
89	Kallanagouda	70/M	256728	Healing ulcer over right L/L	Conventional	Pressure	18	2.3	2.1	1.4	39.1	4	6	13.20	10768	166582	Staph aureus	Not Healed	-	None
90	Anil	49/M	284236	Healing ulcer over left foot	L-PRF	Venous	20	2.7	1.8	1.1	59.3	5	4	12.90	6989	152039	No Growth	Healed		5 None
91	Bagawwa	55/F	286784	Healing ulcer over left leg	Conventional	Venous	20	5.1	4.4	3.1	39.2	3	6	10.50	7916	284600	Staph aureus	Healed		5 None
92	Basavaraj	40/M	254063	Healing ulcer over right hand	L-PRF	Pressure	7	4	3.2	1.3	67.5	4	3	11.90	9765	288672	Pseudomonas	Healed		5 None
93	Rudrappa	50/M	290558	Healing ulcer over left foot	Conventional	Neurotrophic	12	4.6	3.8	2.4	47.8	2	5	13.40	7363	224162	E. coli	Not Healed	-	None
94	Vithal rao	85/M	349876	Healing ulcer over right L/L	L-PRF	Diabetic	14	1	0.8	0.5	50	3	4	10.30	5424	250626	Klebsiella	Healed		5 None
95	Shobraj jatti	50/M	337084	Healing ulcer over left leg	Conventional	Diabetic	11	7.8	6.7	4.9	37.2	4	6	10.00	4748	223718	No Growth	Not Healed	-	None
96	Umashree	40/F	359419	Healing ulcer over left foot	L-PRF	Venous	13	4.1	2.7	1.4	65.9	5	2	13.60	5058	230962	Klebsiella	Healed		4 None
97	Sangappa loni	55/M	367200	Healing ulcer over right foot	Conventional	Pressure	9	6.3	5.3	3.8	39.7	3	4	13.20	5549	154832	Klebsiella	Healed		6 None
98	Renuka	36/F	372718	Healing ulcer over right hand	L-PRF	Neurotrophic	19	8	6	3.4	57.5	4	4	11.00	6323	232747	Staph aureus	Healed		5 None
99	Mallappa	59/M	375477	Healing ulcer over left L/L	Conventional	Diabetic	13	2.8	2.4	1.9	32.1	4	4	10.50	8070	250461	Staph aureus	Not Healed	-	None
100	Sidaramappa	65/M	10364	Healing ulcer over left leg	L-PRF	Pressure	10	7.3	4.4	2.4	67.1	5	4	11.90	6816	297941	Staph aureus	Healed		4 Minor Infection
101	Veerappa	45/M	65604	Healing ulcer over below knee	Conventional	Diabetic	10	3.2	2.8	2.1	34.4	4	3	10.90	5601	210909	Klebsiella	Not Healed	-	Minor Infection
102	Siddaramappa	30/M	291455	Healing ulcer over right thigh	L-PRF	Neurotrophic	12	4.4	3.2	1.8	59.1	5	2	13.60	4844	154276	Staph aureus	Healed		5 None
103	Laxmanappa	55/M	429423	Healing ulcer over left leg	Conventional	Diabetic	26	4.8	4.1	3.3	31.3	2	4	13.00	8082	386405	Pseudomonas	Healed		5 None
104	Vageesh	15/M	18494	Healing ulcer over left foot	L-PRF	Venous	6	3.2	2.3	1	68.8	5	2	12.70	4682	243501	No Growth	Healed		4 None
105	Shree Sai	28/M	179382	Healing ulcer overright foot stump	Conventional	Neurotrophic	22	6.4	5.5	3.7	42.2	2	4	11.10	10758	189161	Staph aureus	Not Healed	-	None
106	Shobhamma	58/F	328599	Healing ulcer over the right chest	L-PRF	Venous	24	7.7	5.9	2.8	63.6	5	4	11.00	6206	351495	E. coli	Healed		5 None
107	Chennaveerappa	73/M	167484	Healing ulcer over left foot	Conventional	Pressure	18	7.9	6.4	3.9	50.6	2	4	13.00	4431	338027	Staph aureus	Healed		5 None
108	Shivanna	72/M	387486	Healing ulcer over right foot toe	L-PRF	Venous	13	7.9	5.4	3	62	4	3	11.70	4898	364446	Staph aureus	Healed		4 None
109	Shivamma	55/F	400500	Healing ulcer over right leg	Conventional	Diabetic	16	7.3	6.2	4.5	38.4	4	4	10.40	9817	349655	Klebsiella	Not Healed	-	None
110	Basanna	65/M	397214	Healing ulcer over right L/L	L-PRF	Venous	20	3.9	2.9	1.6	59	4	3	10.10	9423	176603	E. coli	Healed		5 None
111	Madhadevamma	70/F	389700	Healing ulcer over left L/L	Conventional	Diabetic	6	3.2	2.6	1.7	46.9	4	6	11.20	7169	326525	Klebsiella	Not Healed	-	None
112	Sannappa	55/M	388360	Healing ulcer over left leg	L-PRF	Venous	21	2	1.5	0.7	65	3	2	12.90	4010	251838	Klebsiella	Healed		3 None

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