" A ONE-YEAR OBSERVATIONAL STUDY COMPARING SIZE OF WOUND AFTER BEING SUBJECTED TO COLLAGEN DRESSINGS AND CONVENTIONAL DRESSINGS AT A TERTIARY CARE HOSPITAL"

BY

REGISTRATION NO: BH0122017

Dissertation

Submitted to the KLE Academy of Higher Education and Research, Belagavi, Karnataka
In Partial Fulfilment of the Requirements for the Degree of

MASTER OF SURGERY (M.S.)
in
GENERAL SURGERY

JAWAHARLAL NEHRU MEDICAL COLLEGE,
KAHER, BELAGAVI, 590010, KARNATAKA.

SEPTEMBER/OCTOBER 2025

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH,

BELAGAVI, KARNATAKA

ENDORSEMENT

This is to certify that the dissertation entitled **"A ONE-YEAR OBSERVATIONAL STUDY COMPARING SIZE OF WOUND AFTER BEING SUBJECTED TO COLLAGEN DRESSINGS AND CONVENTIONAL DRESSINGS AT A TERTIARY CARE HOSPITAL."** is a bonafide research work done by **(REG NO. BH0122017)**, Department of General Surgery, Jawaharlal Nehru Medical College, Nehru Nagar, Belagavi, 590010.

DR. S. C. METGUD, M.S.

Professor and Head

Department of General Surgery,
J. N. Medical College,
Belagavi

Date :

Place: Belagavi

DR. N.S. MAHANSHETTI, M.D.

Principal,
J. N. Medical College,
Belagavi

PRINCIPAL
Jawaharlal Nehru Medical College
BELAGAVI

Date:

Place: Belagavi

UNDERTAKING

I, **Reg no- BH0122017,** hereby declare that the information and the data mentioned in my dissertation **"A ONE-YEAR OBSERVATIONAL STUDY COMPARING SIZE OF WOUND AFTER BEING SUBJECTED TO COLLAGEN DRESSINGS AND CONVENTIONAL DRESSINGS AT A TERTIARY CARE HOSPITAL."** Belongs to me and is original. I am aware of the definition of *Plagiarism* as detailed below:

- An act or instance of using or closely imitating the language and thoughts of another author without authorization and the representation of author's work as one's own, as by not crediting the original author.
- A piece of writing or work reflecting such unauthorized use or imitation.
- The deliberate or reckless representation of author's words, thoughts or ideas as one's own without attribution in connection with submission of academic work, whether graded or otherwise.

I hereby declare that the dissertation prepared by me is original one and does not involve plagiarism anywhere. In case at a later stage, it is found that I have indulged in plagiarism, then I am responsible for the same and the institution is at the liberty to take any disciplinary action against me including cancellation of dissertation or any other penalties imposed by the university.

Shreya Siddharth

Date:

Place: Belagavi

REG NO- BH0122017

PLAGIARISM CERTIFICATE

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH

JAWAHARLAL NEHRU MEDICAL COLLEGE

(A constituent unit of KLE Academy of Higher Education & Research Deemed-to-be-University)

(Recognized by National Medical Commission, New Delhi)

Accredited 'A+' Grade by NAAC (3rd Cycle) **Placed in Category 'A' by MoE (GoI)**

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 - 2471350 0831 - 2470759 www.jnmc.edu principal@jnmc.edu

Ref No: MDC/PG/ Date: 19-03-2025

"ACCEPTANCE LETTER"

The softcopy of thesis entitled: **"A ONE-YEAR OBSERVATIONAL STUDY COMPARING SIZE OF WOUND AFTER BEING SUBJECTED TO COLLAGEN DRESSINGS AND CONVENTIONAL DRESSINGS AT A TERTIARY CARE HOSPITAL"** has been submitted for anti-plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of **04%** which is within the acceptable limits of **10%** as per the guidelines given by UGC.

Guide

KAHER BELAGAVI J.N. MEDICAL COLLEGE

Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BH0122017
Postgraduate Student,
2022-23 Batch,
Department of General Surgery
J. N. Medical College, Belagavi.

ETHICAL CLEARANCE LETTER

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)
JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref No.MDC/JNMCIEC/ 288 **Date: 24/06/2023**

To,
REGISTRATION NO: BH0122017
PG Student in General Surgery
J. N. Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"A ONE-YEAR OBSERVATIONAL STUDY COMPARING SIZE OF WOUND AFTER BEING SUBJECTED TO COLLAGEN DRESSINGS AND CONVENTIONAL DRESSINGS AT TERTIARY CARE HOSPITAL"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi

ABBREVIATIONS

CD – Cluster of Differentiation

CXCR3 – C-X-C Motif Chemokine Receptor 3

DAMPs – Damage-Associated Molecular Patterns

DCs – Dendritic Cells

DETCs – Dendritic Epidermal T Cells

ECM – Extracellular Matrix

ECs – Endothelial Cells

ELR – Glutamic acid-Leucine-Arginine motif

EPCs – Endothelial Progenitor Cells

FGF – Fibroblast Growth Factor

GPCRs – G Protein-Coupled Receptors

HBOT – Hyperbaric Oxygen Therapy

hCAP-18 – Human Cationic Antimicrobial Protein

HSCs – Hematopoietic Stem Cells

ICAM-1 – Intercellular Adhesion Molecule-1

IFE – Interfollicular Epidermis

IL – Interleukin

McSCs – Melanocyte Stem Cells

MMPs – Matrix Metalloproteinases

MSCs – Mesenchymal Stem Cells

NETs – Neutrophil Extracellular Traps

NG2 – Neuron-Glial Antigen 2

NO – Nitric Oxide

PDGF – Platelet-Derived Growth Factor

PDGF-B – Platelet-Derived Growth Factor-B

PDGFR-β – Platelet-Derived Growth Factor Receptor Beta

ROS – Reactive Oxygen Species

TGF-β – Transforming Growth Factor Beta

TNF-α – Tumor Necrosis Factor-alpha

VCAM-1 – Vascular Cell Adhesion Molecule-1

VEGF – Vascular Endothelial Growth Factor

vWF – von Willebrand Factor

ABSTRACT

Background: "Chronic foot ulcers are a major healthcare concern, commonly associated with diabetes, venous disease, and peripheral arterial disease. They significantly impact patients' quality of life, leading to pain, infection, and potential limb loss. Various dressing techniques are employed to accelerate wound healing, with collagen dressings showing promise in enhancing granulation tissue formation and reducing hospital stay.

Aim: This study aims to compare the wound size reduction and rate of wound healing in patients receiving collagen dressings versus those receiving conventional saline dressings over a two-week period.

Materials and Methods: This prospective study was conducted among 82 patients with chronic ulcers at a tertiary care hospital. Patients were randomly assigned to two groups: Group A (collagen dressing) and Group B (conventional saline dressing). Wound size was measured at baseline and after two weeks using the Imitomeasure smartphone application. The rate of wound healing was calculated as the change in wound area over 14 days. Statistical analysis was performed using SPSS v23.0, with p-values <0.05 considered statistically significant."

Results: Both groups were comparable in terms of baseline characteristics, including age, gender, and comorbidities. By day 14, the mean wound area reduction was significantly greater in Group A (6.92 ± 3.3 cm²) than in Group B (5.09 ± 3.43 cm²) ($p<0.05$). The percentage reduction in wound area was also higher in Group A ($25.51\pm9.2\%$) compared to Group B ($19.47\pm10.9\%$) ($p<0.05$). The rate of wound

healing was significantly higher in Group A (0.49±0.25 cm²/day) than in Group B (0.37±0.25 cm²/day) ($p<0.05$).

Conclusion: Collagen dressings were more effective in promoting wound healing than conventional saline dressings, demonstrating greater wound size reduction and a faster healing rate. These findings suggest that collagen dressings may serve as a superior alternative in managing chronic ulcers, improving patient outcomes and reducing healthcare burden.

Keywords: Chronic ulcers, collagen dressing, conventional dressing, wound healing, granulation tissue, diabetic foot ulcer

---

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF PHOTOGRAPHS

INTRODUCTION

A "Chronic foot ulcers are characterized by a persistent or slow-healing disruption of the epidermal and dermal layers on the foot, lasting longer than six weeks. These ulcers are commonly linked to conditions such as venous disease, peripheral arterial disease, mixed arterio-venous disease, and diabetes. In individuals with diabetes, foot ulcers typically result from multiple factors, particularly peripheral vascular disease and sensory loss due to peripheral neuropathy. Moreover, untreated foot ulcers can lead to severe complications, potentially resulting in limb amputation. Effective management of diabetic foot ulcers is crucial in minimizing the risk of amputations and improving patient outcomes.."[1]

Venous leg ulcers "affect up to 3.5% of the general population, while foot ulceration occurs in approximately 15% of individuals with diabetes at some point in their lives. Women are more commonly affected than men, with a prevalence ratio of more than 2:1. Regardless of the underlying cause, foot ulcers impose significant and prolonged distress on patients. They are often associated with persistent pain or aching discomfort, which worsens during dressing changes. Secondary infections are common, leading to the accumulation of foul-smelling slough and excessive exudate, further exacerbating distress and contributing to social isolation. The impact on daily life is considerable, with many patients experiencing reduced mobility, embarrassment from visible dressings, and an inability to maintain employment, ultimately diminishing their overall quality of life."

"Collagen dressings accelerate wound healing more effectively than moistened gauze while also significantly reducing follow-up duration and the need for antibiotics compared to conventional dressings. Their spongy structure likely aids in absorbing exudate and sealing wound extensions, thereby inhibiting bacterial proliferation that

could otherwise hinder the healing process.[1] The study primarily focused on leg ulcers, with an unequal distribution of patients between the groups. The application of collagen granule dressings enhances wound healing in chronic ulcers, leading to a reduction in ulcer size. This, in turn, facilitates an earlier return to work, ultimately easing the financial burden on patients."[2]

Collagen particles "promote faster wound healing by facilitating early granulation tissue formation and wound contraction, thereby reducing the need for frequent debridements and dressings, as demonstrated in the present study. Frequent daily dressings can cause discomfort and pain, negatively impacting a patient's social well-being. However, collagen dressings, which can be changed every 2-3 days depending on wound severity, minimize discomfort. The study also observed a significant reduction in wound size in the experimental group compared to the control group. Overall, our findings confirm that collagen dressings are superior to conventional dressings in promoting early granulation tissue formation and reducing hospital stay."[3]

OBJECTIVES

Objective of the study

Primary objective: To compare the size of the wound after 2 weeks of dressing after being subjected to collagen dressings or conventional dressings at a tertiary care hospital.

Secondary objective: To assess rate of wound healing

REVIEW OF LITERATURE

Wound healing

"One of the most intricate processes in the human body is wound healing. Numerous cell types with different functions in the stages of hemostasis, inflammation, growth, re-epithelialization, and remodeling are synchronized both spatially and temporally. The development of single-cell technology has made it feasible to identify functional and phenotypic variation within a number of these cell types.

Individuals with diabetes, the elderly, and those with genetic conditions such as sickle cell disease are particularly prone to experiencing impaired wound healing, leading to long-lasting complications. Surprisingly, existing interventions have not made a significant impact on this issue. Although various therapies for wound healing are available, their effectiveness remains only moderate." Therefore, there is a pressing need for more efficient treatments to address wound healing.

"The process of skin repair necessitates the coordinated interaction of multiple cell types across different layers in a sequential manner. In uninjured skin, the outer layer, known as the epidermis, serves as a protective barrier against external factors and houses structures like sebaceous glands, sweat glands, and hair follicles. Beneath the epidermis lies the dermis, which is abundant in extracellular matrix (ECM), blood vessels, and mechanoreceptors, providing the skin with structural support, nutrients, and defense mechanisms. Adjacent to the dermis is the subcutaneous adipose tissue, which not only acts as an energy reservoir but also serves as a continual source of growth factors for the dermal layer. Each of these layers also contains resident immune cells that constantly monitor the skin for any signs of damage."

Upon injury, "various cell types within these layers must coordinate their activities at specific stages to initiate the healing process. These stages include hemostasis, inflammation, angiogenesis, proliferation, re-epithelialization, and remodeling. Although these stages occur sequentially, they also overlap, making skin repair one of the most intricate processes in the human body."

- "Injured blood arteries constrict and a fibrin clot forms as the body's first reaction to a wound; this stops blood flow and provides a framework for inflammatory cells."[4,5]

- "Neutrophils are the first immune cells recruited to the wound to combat bacterial infection."[4]

- After that, monocytes are drawn in and develop into tissue-activated macrophages, which help with tissue restoration.

To protect against both external and self-inflicted antigens, "the adaptive immune system—which includes T cells, cutaneous dendritic cells, and Langerhans cells—is triggered.

- Understanding the diversity within immune cell populations is crucial, particularly their roles in debris clearance and infection resolution.[6,7]

- Angiogenesis, which involves the multiplication of endothelial cells and the activation of pericytes to give structural support to newly formed blood vessels, follows the inflammatory phase.

- Progenitor cells that circulate from the bone marrow also aid in the development of new blood vessels.

- To help with wound closure, resident fibroblasts multiply and infiltrate the clot to generate contractile granulation tissue. Some of these fibroblasts go on to differentiate into myofibroblasts.[8–10]

- The extracellular matrix (ECM) that fibroblasts produce causes the wound microenvironment to change from an inflammatory to a growing state.

- The dedifferentiation of terminally differentiated epidermal cells and the proliferation of epidermal stem cells take place concurrently with re-epithelialization.

- Tissue-resident stem cells for skin appendages exhibit great flexibility during wound healing, activating local appendage repair in response to damage.

- Subcutaneous adipose tissue's stromal vascular cells produce cytokines and growth factors that are essential for wound healing and neovascularization.

- Increased inflammation caused by inflammatory cells in subcutaneous tissue, especially in obesity and type 2 diabetes, might affect the course of wound healing.

- Adult wound healing usually leads to fibrotic scarring instead of the natural skin architecture that is restored in the case of prenatal wound healing.

Hypertrophic scarring and keloid development can result from excessive scarring, and these conditions are frequently impacted by differentiating cellular reactions to mechanical stress."[11,12]

- Impairments in wound healing can "result in chronic wounds, which are common in conditions like diabetes, vascular disease, aging, and hemoglobinopathies, potentially leading to limb amputations and mortality.

Cellular responses during wound healing

A. Hemostasis
B. Inflammatory phase
C. Growth phase
D. Re-epithelialization
E. Tissue maturation and remodeling in wound healing

A. Hemostasis:

Hemostasis, the initial phase of wound healing, plays a crucial role in halting bleeding following vascular injury. This process involves three steps: vasoconstriction, primary hemostasis, and secondary hemostasis. Platelets are key players in hemostasis, while fibrinogen is a critical component of the matrix. Under normal conditions, platelets remain inactive due to the protective endothelial cell layer lining the blood vessels. However, upon injury, vasoconstriction occurs to stop bleeding, followed by primary and secondary hemostasis pathways.[13,14] Primary hemostasis involves platelet aggregation and plug formation triggered by collagen exposure, while secondary hemostasis activates the coagulation cascade, converting soluble fibrinogen into insoluble fibrin strands to form a mesh. The combined action of platelet plugs and fibrin meshes forms a thrombus, stopping bleeding and providing a scaffold for cells necessary for wound healing.[14]

- Vasoconstriction
- Formation of platelet plug which is primary hemostasis
- Coagulation and reinforcement of the platelet plug

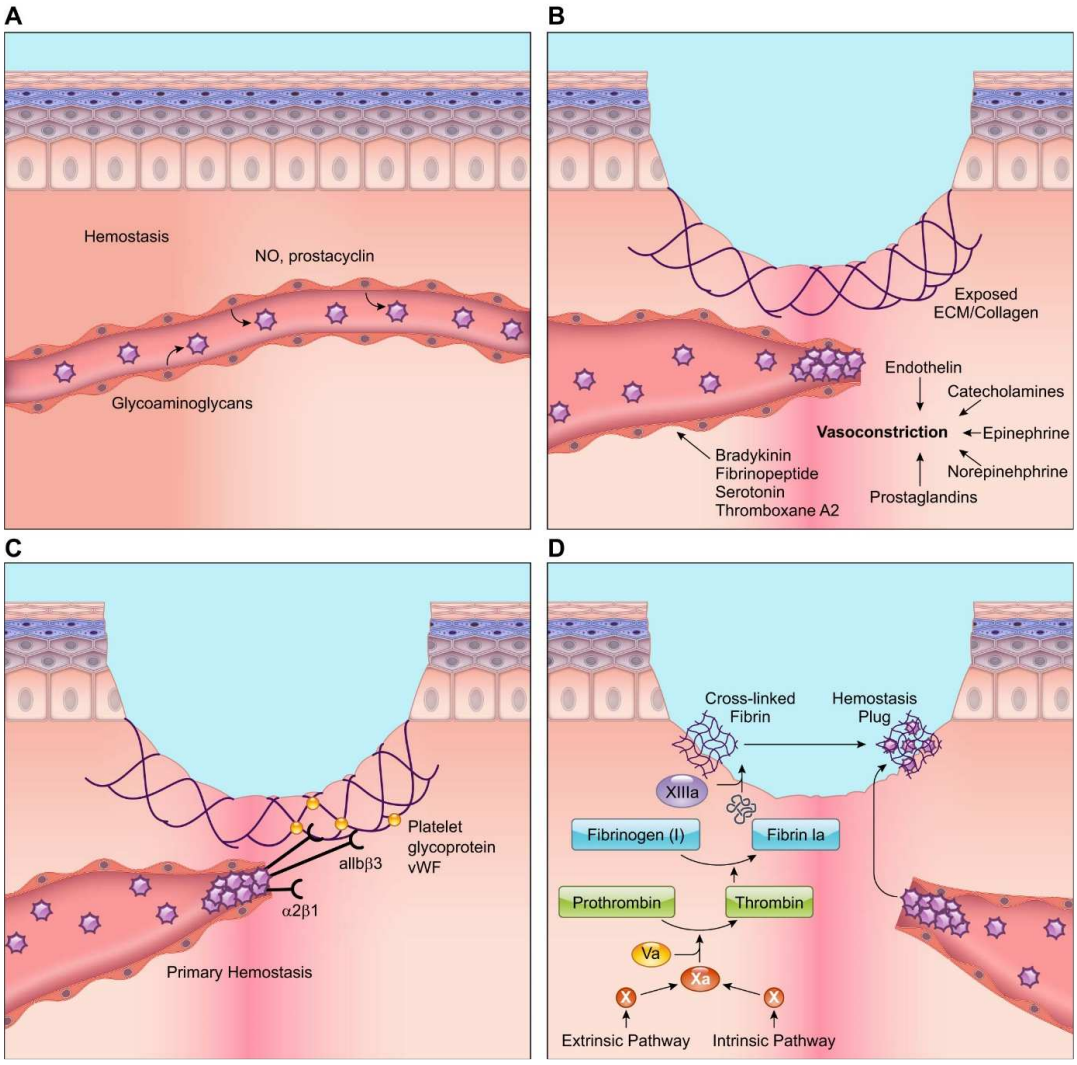


Figure 1: Cellular response during the hemostatis phase of wound healing"[15]

"During hemostasis, platelets are normally prevented from attaching to the vessel wall and aggregating by anti-thrombotic agents like nitric oxide (NO) and prostacyclin released from endothelial cells. When a wound occurs, injured cells release vasoconstrictors, causing temporary cessation of bleeding by contracting smooth muscles. Blood vessel rupture exposes the subendothelial matrix, where platelets bind using surface receptors and glycoproteins, along with von Willebrand factor (vWF) released by platelets. This strengthens the platelet plug. The activation of Factor X through extrinsic and intrinsic pathways leads to the conversion of fibrinogen to

fibrin. Cross-linked fibrin binds the aggregated platelet plug, forming a thrombus that halts blood flow and provides a scaffold for healing. This summary simplifies the process of hemostasis and wound healing based on current understanding.

B. Inflammatory phase of wound healing

a. Mechanisms of inflammatory cell recruitment:

Wound healing initiates with the activation of cellular response through transcription-independent pathways like Ca2+ waves, reactive oxygen species (ROS) gradients, and purigenic molecules.

Damage-associated molecular patterns (DAMPs), hydrogen peroxide (H2O2), lipid mediators, and chemokines released from injured cells recruit inflammatory cells, particularly neutrophils.

Chemokines are small proteins that bind to G protein-coupled receptors (GPCRs), attracting various immune cells. ELR+ chemokines preferentially attract neutrophils, while ELR- chemokines attract lymphocytes."

Mast cells release inflammatory mediators upon injury, enhancing immune cell recruitment. "Mast cell enzymes like mast cell proteases 4 and 5 play a crucial role in neutrophil recruitment during wound healing.

b. Neutrophils in wound healing:

Neutrophils, typically absent in normal skin, are recruited from the bone marrow in response to "find me" signals released from injured areas.

Neutrophils express various surface receptors that aid in detecting injury signals and constitute a significant portion of cells in the wound early in the healing process.

Activated neutrophils eliminate pathogens through toxic granules, oxidative burst, phagocytosis, and production of neutrophil extracellular traps (NETs).

Neutrophils develop different granules containing antimicrobial agents like proteases, human cationic antimicrobial protein (hCAP-18), and matrix metalloprotease (MMPs) during their maturation in the bone marrow.

Proteases in neutrophil granules play a crucial role in antimicrobial activity and tissue remodeling but can also cause tissue damage if produced excessively, as observed in chronic wounds.

NETs, released by neutrophils, capture and eliminate pathogens through chromatin filaments coated with histones, cytosolic proteins, and proteases. NETs are released either through suicidal NETosis or vital NETosis, depending on the activation pathways involved.

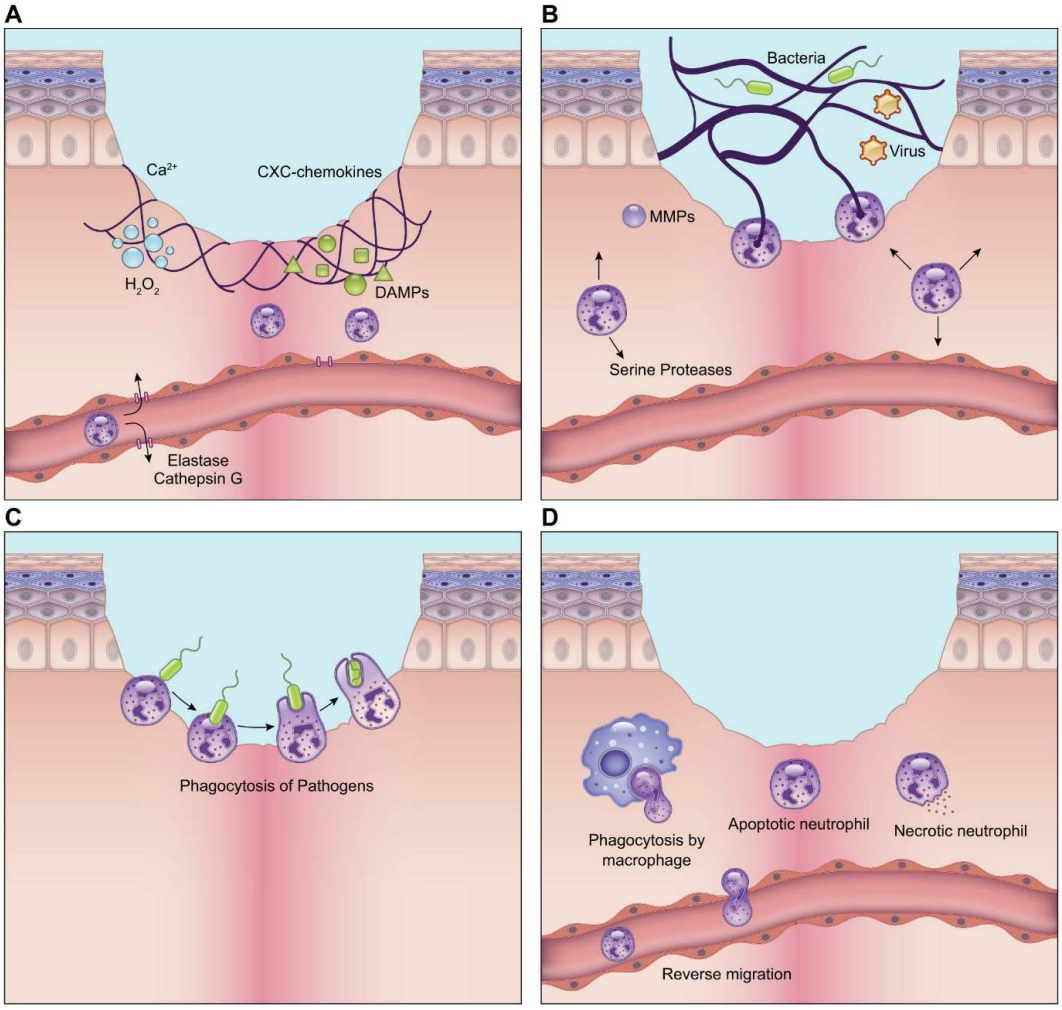


Figure 2: Role of neutrophils in wound healing"[15]

c. Macrophages in wound healing

"Macrophages play a crucial role in wound healing, identified by surface markers like CD45+/ CD11b+/ F480+ in mice and CD45+/ Cd11b+/ CD66B- in humans. Within 24-48 hours post-injury, macrophages accumulate at the wound site, peaking around day 3 and declining by day 10. They originate from both local tissue-resident macrophages and recruited monocytes from the bone marrow. Depletion of macrophages delays wound closure, while increasing their numbers accelerates healing in various organisms, including mice and salamanders."[16,17]

"In the early stages of healing, macrophages exhibit a microbicidal and pro-inflammatory phenotype known as M1, expressing TNF-α, IL-6, and IL-1β. They engulf pathogens, synthesize MMPs to digest the extracellular matrix (ECM), and perform efferocytosis to eliminate spent neutrophils." This pro-inflammatory response aids in clearing pathogens and promoting tissue repair. However, prolonged inflammation due to improper neutrophil clearance can lead to tissue damage.[18,19]

"Macrophages also transition to a reparative phenotype, facilitating tissue regeneration during the later stages of healing. They induce the transition of fibroblasts to myofibroblasts, contributing to collagen deposition and wound contraction. Additionally, macrophages participate in tissue remodeling by phagocytizing excess cells and matrix components. Dysregulated macrophage functions are implicated in fibrotic diseases like keloids and hypertrophic scars, as well as impaired wound healing in conditions like diabetes. Understanding the diverse roles of macrophages in wound healing is crucial for developing effective therapeutic strategies."

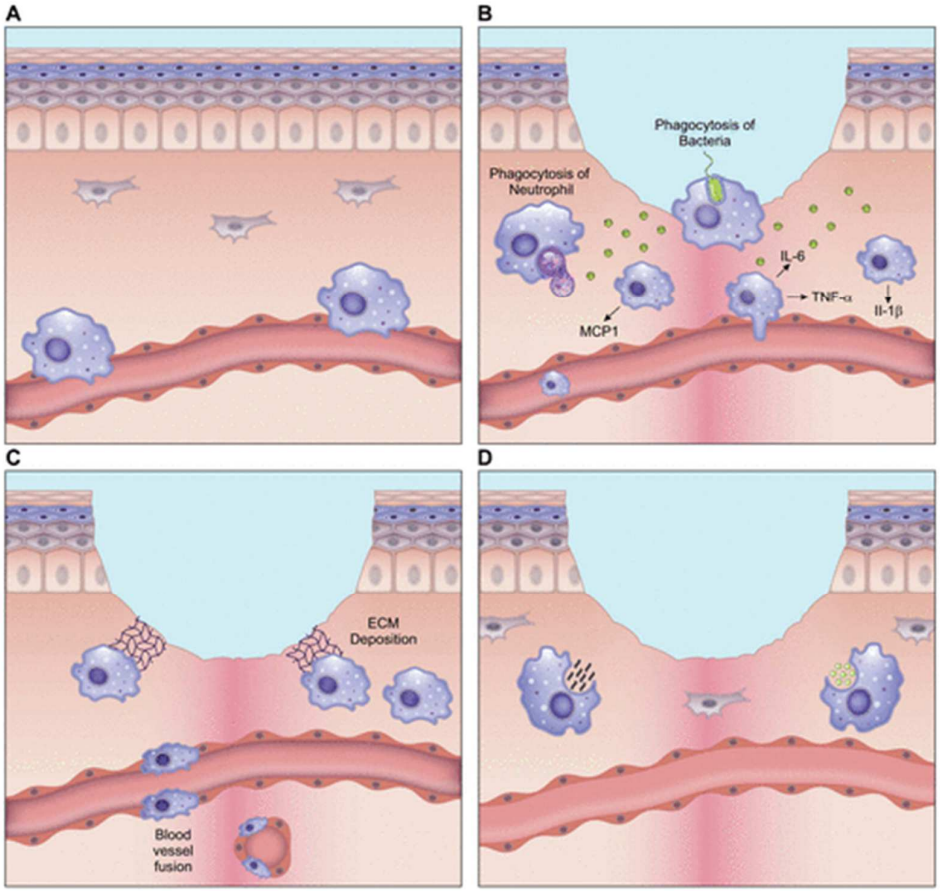


Figure 3: Macrophage phenotypes in wound healing[15]

d. Mast cell in wound healing

"Paul Ehrlich first identified mast cells in 1878. These cells come from progenitors in the bone marrow and move to perivascular areas of the skin and mucosa, where they undergo differentiation. Due to contradictory results in mast cell-deficient animals, their function in wound healing is up for discussion. But during wound healing, they interact with different cell types and are linked to reactions that cause scarring, such as scleroderma and hypertrophic scarring."[20]

Mast cells generate histamines, VEGF, chymase and tryptase, antimicrobial peptides, and other substances that facilitate vascular permeability and keratinocyte proliferation during the early phases of wound healing. Histamine enhances

keratinocyte proliferation, whereas tryptase and histamine boost fibroblast proliferation and collagen production, facilitating wound contraction.[21,22]

Skin fibrosis and scarring are linked to elevated mast cell counts. Research employing a fetal wound healing model indicates that mast cells impact the development of scars; injections of mast cell lysate are shown to change scarless healing into the production of scars. The precise processes, however, remain unknown, and further research is needed to fully understand the function of mast cells in chronic wounds, particularly in diseases like diabetes. The microenvironment of mast cells influences their functional variability. "There may be distinct mast cell subgroups in wounds, each with their own roles, requiring more investigation.[23,24]

e. Dendritic cells in wound healing

Dendritic cells (DCs) are crucial antigen-presenting cells involved in priming T-cell responses. They exist in the epidermis as Langerhans cells, named after Paul Langerhans, and in the dermis. Although some debate exists about their classification as macrophages due to shared characteristics, they are distinct based on their primary functions. DCs have a stronger antigen-presenting ability than macrophages and migrate to draining lymph nodes to activate T-cell responses.

In murine dermis, two resident DC subtypes are typically found: CD11b+ DCs and CD103+ DCs, analogous to CD141+ DCs in humans. CD103+ dermal DCs are responsible for cross-presenting antigens to induce CD8+ T-cell responses and play roles in viral immunity. They recognize DAMPs on dying cells and viruses through specific surface receptors. CD11b+ DCs in mice correspond to CD1c+ and CD14+ DC subsets in humans and preferentially present antigens to CD4+ T cells during infection, regulating the adaptive immune response.[25,26]

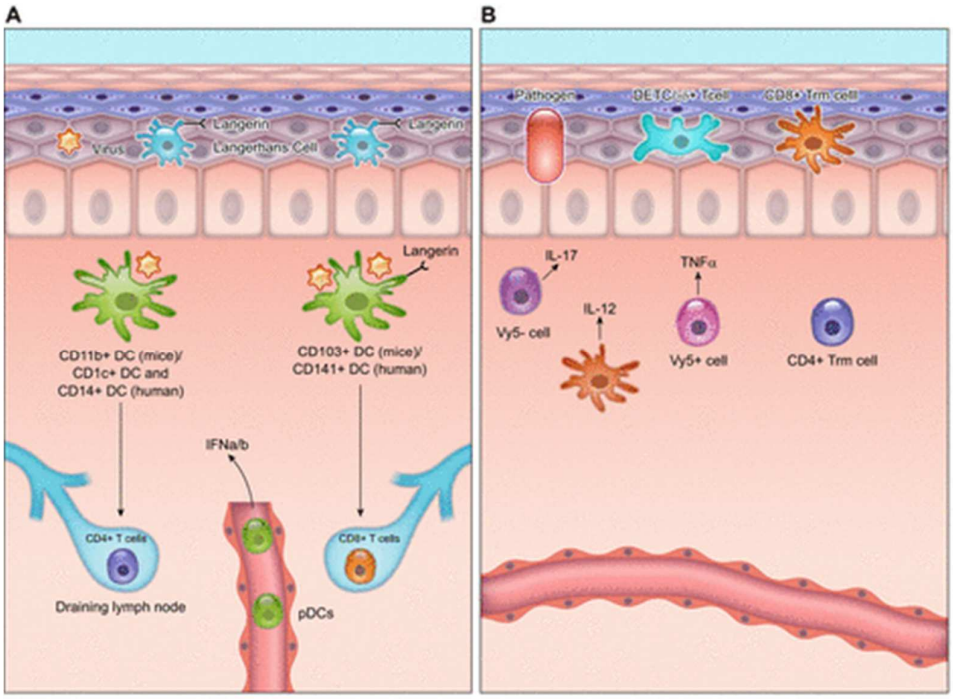


Figure 4: Dendritic cells (DCs) and T cells in the wound healing response[15]

f. Role of T cells in wound healing

There are two types of T cells found in the skin layers of humans: γδ+ T cells and αβ+ T cells. While the dermis of human skin primarily contains αβ+ T cells, the epidermis of mice is predominantly populated by γδ+ T cells, also known as DETCs, due to cellular structure differences. DETCs originate in the fetal thymus and migrate to the epidermis, where they slowly grow in number in response to signals like interleukins, particularly IL-15. Positioned in the basal layers of the epidermis, they extend their dendrites into the suprabasal layers to actively monitor for certain molecules that signal epidermal stress, such as infections or abnormal cell presence. Unlike other T cells, DETCs typically remain stationary in the skin." Research on T cells in wound healing often focuses on DETCs because they are the only T cell subtype known to release cytokines and growth factors that aid in skin cell regeneration. Additionally, studies show that mice lacking DETCs experience significant delays in wound

healing, and DETCs possess a unique T-cell receptor, Vγ3Vδ1, specific to skin T cells.

3. Growth phase of wound healing

a. formation of granulation tissue and neovascularisation

"During the proliferative phase of wound healing, various processes occur simultaneously, including the formation of new connective tissue known as granulation tissue, alongside re-epithelialization, neovascularization, and immunomodulation. Granulation tissue, first described by John Hunter in the late 18th century and further characterized by Alexis Carrel in the 19th century, is primarily composed of activated fibroblasts. These fibroblasts produce new extracellular matrix (ECM) and aid in wound contraction. In addition, granulation tissue serves as a framework for newly created blood vessels and inflammatory cells, among other cellular and structural elements. In the course of the wound remodeling phase, granulation tissue eventually gives way to normal connective tissue."

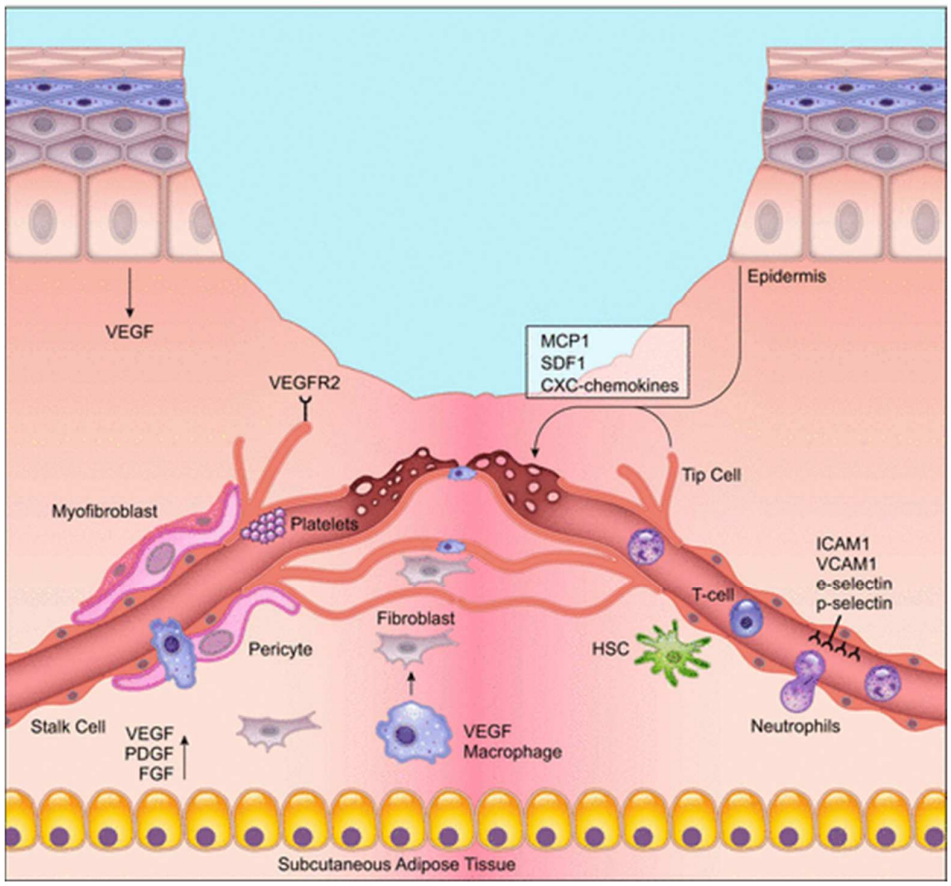


Figure 5: Angiogenesis during wound healing. [15]

Neovascularization, crucial for effective wound healing, facilitates nutrient delivery and oxygen balance necessary for cellular proliferation and tissue regeneration. Vasculogenesis is the process by which angioblasts, endothelial progenitor cells (EPCs), give birth to primitive blood arteries during embryonic development. Despite the fact that it was once believed that adult tissue healing included vasculogenesis through EPCs produced from bone marrow, later research on mice showed that the putative EPCs are mostly macrophages and monocytes that facilitate neovascularization. Adults produce new blood vessels mostly by angiogenesis, a process in which local microvascular endothelial cells (ECs) activate growth hormones such as PDGF and VEGF in response to hypoxia. Activated endothelial cells (ECs) break down extracellular matrix (ECM), multiply, move, and create new

capillaries, which improves tissue regeneration by promoting oxygen and nutrient supply. This process involves endothelial cells and pericytes. "Additionally, to explore circulating progenitor cells' role in wound healing and discuss fibroblast subtypes supporting granulation tissue formation."[27,28]

b. Endothelial cell and new vessel formation

"Angiogenesis, the process of generating new blood vessels, is greatly aided by microvascular endothelial cells (ECs), which line the inside of blood vessels. Growth factors include VEGF, FGF, PDGF-B, TGF-β, and angiopoietins stimulate ECs, causing them to proliferate and migrate into fibrin/fibronectin-rich clots. ECs develop into stalk cells, which follow and preserve the structure, and tip cells, which drive the growth, during angiogenesis. These cells combine with existing vessels to produce new endothelial tubules. Endothelial cell receptors are essential for angiogenesis. Normally, ECs have few surface receptors, preventing interactions with platelets and immune cells, but allowing monocyte surveillance. Upon injury, ECs express glycoprotein receptors like P-selectin and E-selectin, facilitating leukocyte adhesion and infiltration. They also upregulate ICAM-1 and VCAM-1, which help stop leukocyte movement. The absence of these receptors impairs both new blood vessel formation and wound healing, highlighting their role in skin repair."[29–31]

c. Role of pericytes in neovascularization and wound healing

"Mature pericytes are defined as cells embedded in the vascular basement membrane; this description makes it difficult to identify them in the context of ongoing neovascularization. This problem stems from the fact that the perivascular region is also inhabited by various cell types, including fibroblasts, macrophages, circulating progenitor cells, and vascular smooth muscle cells. Furthermore, pericytes cannot be

easily distinguished from these other cells by a specific molecular signature. As a result, it is challenging to recognize pericytes in tissue slices, and it is yet unknown whether systemic recruitment of pericytes from a common reservoir during vessel construction or local proliferation of preexisting pericytes forms new pericytes."[32,33]

"Various surface markers such as nestin, NG2, PDGFR-β, and desmin have been used to define pericytes, but these markers may not be uniformly expressed on all pericytes."[34]

d. circulating progenitor cell in neovascularization and wound healing

Early research suggested that "both hematopoietic stem cells (HSCs) and non-hematopoietic progenitor cells, primarily endothelial progenitor cells (EPCs), contribute to blood vessel regeneration. These cells follow a three-step process to reach ischemic tissue: mobilization from the bone marrow into circulation due to chemokine release at the injured site, migration through circulation towards increasing chemokine gradients, and preferential homing to the ischemic region where they integrate into the sprouting endothelium and differentiate into endothelial cells.[35,36,37].

e. Role of fibroblasts in wound healing

Fibroblasts, present throughout the body's connective tissue, play crucial roles in extracellular matrix (ECM) deposition and remodeling. They exhibit notable diversity based on tissue origin, developmental stage, and activation status, leading to varied functions in wound healing, including ECM organization, growth factor secretion, and immunomodulation. Historically, characterizing fibroblasts has been challenging due to a lack of distinct markers, but recent advancements in marker identification and

functional assays are enhancing our understanding. Fibroblast diversity can be positional, determined by their location relative to the epidermis, and anatomical, based on their location within the body. In murine skin, differences exist between fibroblasts in the upper and lower dermis, with lower lineage fibroblasts initially contributing to dermal repair and scar formation." These scar-forming fibroblasts express myofibroblast markers and can be isolated using specific surface markers, with inhibition of these markers showing potential in reducing scar formation, carrying clinical implications.[38,39]

f. Role of Myofibroblasts in wound healing

A vital component of wound healing, wound contraction increases mechanical strength by aligning collagen fibrils perpendicular to the wound edges, reducing the surface area of the wound that requires re-epithelialization. Because of this changed stiffness, fibroblasts become myofibroblasts that are positive for α-SMA, which causes them to momentarily deposit extracellular matrix (ECM) and exhibit contractile characteristics. "Growth factors, mechanosensory signals in granulation tissue, and interactions between cells and the extracellular matrix drive this process. Although local fibroblasts are the primary source of myofibroblasts, their number may also be augmented during wound healing by fibrocytes, mesenchymal stem cells (MSCs), pericytes, and epithelial cells.

After enough tissue integrity has been restored, myofibroblasts finally die off in the wound region. It is still unclear if myofibroblasts can return to the fibroblast phenotype seen in skin that is not damaged after healing. Myofibroblasts frequently avoid apoptosis in a variety of fibrotic diseases, including hypertrophic scarring, which aids in the formation of scar tissue. This idea is supported by research done on

mice with hypertrophic scarring, which shows that more myofibroblast survival causes scar formation to spread out after mechanical loading. As a result, myofibroblasts are an attractive target for the development of fibrosis and scarring therapies since they are essential to the latter phases of granulation tissue production.

4. Re-epithelialization

The epidermis provides protection against mechanical stress, microorganisms, ultraviolet radiation, water loss, and extreme temperatures. It comprises a layered epithelium consisting primarily of keratinocytes, which are linked to adjacent keratinocytes through desmosomes. The basal layer, the lowest layer, connects to a specialized extracellular matrix (ECM) known as the basement membrane via hemidesmosomes and focal adhesions. Above the basal layer are the spinous layer, granular layer, and the outermost layer, the stratum corneum, composed of impermeable cornified cells that are continuously shed. In addition to keratinocytes, the epidermis contains resident immune cells, hair follicles, sebaceous glands, and sweat glands. Due to its susceptibility to injury, resident stem cells are essential for maintaining skin homeostasis and facilitating repair. Stem cell division and differentiation replenish lost cells, aiding in both regular maintenance and healing processes of the skin."[40,41]

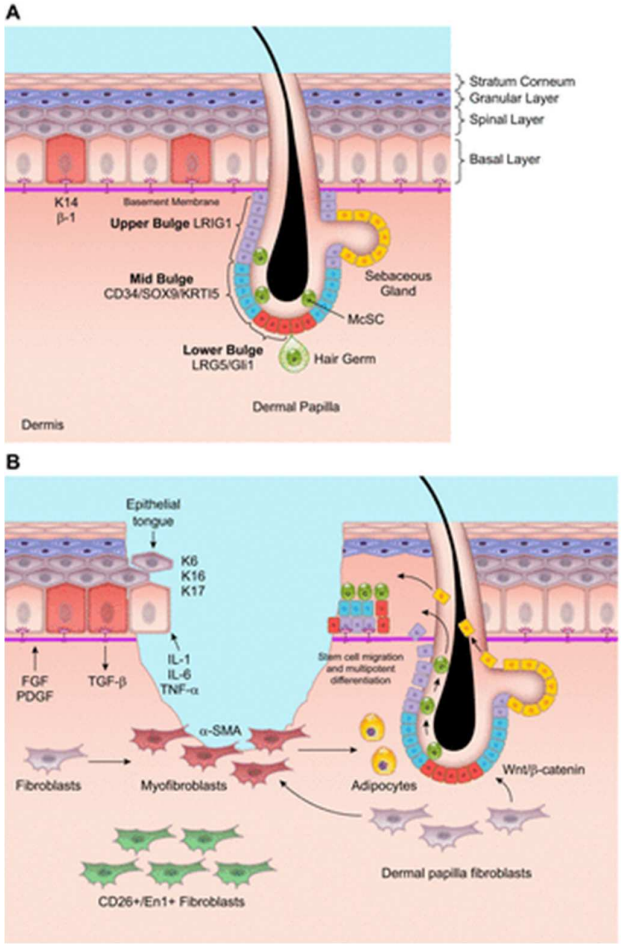


Figure 6: Re-epithelialization and fibroblast epidermal cell interactions during wound healing

The intrafollicular epidermis during wound healing

"Extrinsic signals from the stem cell niche, consisting of cues from the extracellular matrix (ECM), growth factors, and neighboring cells, are crucial in determining the fate of stem cells. In the interfollicular epidermis (IFE), stem cells are grouped rather than dispersed individually and exhibit higher adhesiveness due to elevated integrin expression compared to transit amplifying cells. During homeostasis, integrins are primarily found in basal layer cells. Key integrins present on basal cells include α2β1, which binds collagen, α3β1 and α6β4, binding laminin, and αvβ5, binding vitronectin.

α6β4 is concentrated distally on the basement membrane, while α3β1 is located at the leading apical edge. Other integrins are distributed across the basal cells' basal, lateral, and apical surfaces."

Regeneration of hair follicles

Melanocytes in wound healing

Because of "changes in melanocyte proliferation and activation, partial thickness and deep full thickness injuries—especially those brought on by burns—often result in skin discoloration, either hyperpigmentation or hypopigmentation. Specialized dendritic cells called melanocytes are formed from the neural crest and are in charge of creating melanin, a pigment that protects the skin from oxidative damage and UV light. Melanocytes are found in hair follicles and the interfollicular epidermis (IFE) in humans, whereas they are mostly found in hair follicles in mice, with the exception of few places like the ear and tail skin, where they are also found in the IFE. In the area of the hair follicle bulge, melanocyte stem cells (McSCs) replace melanocytes during normal skin function. Numerous growth factors, including TGF-β and endothelin-2, as well as signaling molecules, such WNT and Notch, generated by nearby hair follicle stem cells, have an impact on these McSCs. Melanocyte repopulation takes place in tandem with the growth phase of the hair cycle.[42,43]

5. Tissue maturation and remodeling in wound healing

In wound healing, closure of acute and chronic wounds is typically considered the endpoint, but the process continues with tissue remodeling or maturation, which may last for months or even years. This phase is crucial as it determines whether scarring will occur or if the wound will recur. During the remodeling phase, neovasculature

regresses, and there is periodic deposition and reconstitution of the extracellular matrix (ECM), transforming granulation tissue into scar tissue. Initially rich in collagen III, granulation tissue gradually transitions to contain more collagen I, which is stronger. This shift results from concurrent collagen I synthesis and collagen III breakdown, followed by ECM reorganization.[27]

During angiogenesis, newly formed blood vessels in the wound area lack tight cell-cell contacts and pericyte coverage, facilitating immune cell infiltration. In the remodeling phase, neovessels undergo pruning to establish stable, well-perfused vessels that can restore homeostasis." This process involves endothelial cell apoptosis, though the exact mechanisms are unclear. Re-epithelialization may also contribute to vessel pruning by reducing hypoxia in the healed wound bed, promoting endothelial cell quiescence.

Vasohibin and sprouty proteins are examples of negative-feedback systems found in endothelial cells that function as "anti-angiogenic switches" by controlling the cell's sensitivity to VEGF. "Furthermore, endothelial cells produce CXCR3, which, when attached to its ligand, CXCL10, suppresses the development of endothelial tubes during the late stages of wound healing. CXCR3 is essential for wound remodeling, as demonstrated by the hypertrophic scarring seen in mice devoid of the protein." "Comprehending alternative cellular signaling pathways that exhibit preferential expression during wound remodeling might potentially clarify the reasons behind dystrophic healing in some wounds, such keloids and hypertrophic scarring.

Risk factors which increase the patients susceptibility of infection

Intrinsic factors	Extrinsic factors
Extremes of age: Children < 1 year and elderly >65 yerars	Drug therapy- steroids, cytotoxic drugs.
Underlying disorders-diabetes, haematological disorders, respiratory disorders	Break in the integrity of the skin in burns.
Smoking and alcohol	Presence of foreign bodies
Nutritional status of the patient.	Bypassing of defense mechanisms through devices eg.intubations.

Techniques to enhance the wound healing in the patients with chronic wound

Local care

- Debridement
- Dressing

Adjunctive local therapies

- Negative pressure wound therapy
- Growth factors
- Skin graft and substitutes
- Topical oxygen therapy
- Shock wave therapy
- Hyperbaric oxygen therapy

The removal of necrotic tissue is critical for ulcer healing. The frequency of examination and correct care may be more important than the type of debridement in wound healing. A analysis **Debridement:** of chronic wound care among veterans found that when debridement was conducted at 80 percent of visits, the risk of diabetic ulcer healing rose 2.5-fold and doubled when ischemia was measured at the initial visit."[44,45]

Dressings: After debridement, ulcers must be kept clean and adequately moist while avoiding excessive fluid buildup. "The choice of dressing should be tailored to the ulcer's characteristics, including exudate levels, dryness, or necrotic tissue presence. While some dressings serve primarily as protective barriers, others aid in maintaining optimal hydration or preventing excessive moisture. Wet-to-dry saline dressings are commonly used but can inadvertently remove both necrotic and healthy tissue, potentially leading to wound desiccation. Alternatively, antimicrobial-impregnated dressings help prevent infection and promote healing. However, there is no strong evidence to suggest that any specific type of dressing significantly outperforms others in the treatment of diabetic foot ulcers.[46,47]

Skin grafts and substitutes: Human skin grafts and bioengineered skin substitutes (eg, Dermagraft, Apligraf, TheraSkin, Graftskin, EpiFix, Zelen, Graftjacket, Hyalograft 3D, Kaloderm, OrCel) have been studied in individuals with noninfected, nonischemic chronic plantar diabetic foot ulcers[48–50]

Hyperbaric oxygen therapy: As a component of diabetic ulcer management, hyperbaric oxygen therapy (HBOT) may be related with enhanced healing; however, the indications for HBOT in the treatment of non-healing diabetic foot ulcers remain

unknown. Most meta-analyses of randomized trials indicate that hyperbaric oxygen therapy may be beneficial in the treatment of diabetic foot ulcers; nevertheless, each meta-analysis acknowledged diversity in the methodologic quality of the included research."[50–56]

Topical oxygen therapy: "Improved healing of diabetic foot ulcers may be connected with topical oxygen therapy/continuous diffusion of oxygen. This therapy involves the delivery of oxygen locally and appears to promote epithelialization by increasing VEGF expression and collagen synthesis, improving overall matrix deposition, and modifying microbial ecology. Several randomized, double-blind, sham-controlled trials support the use of this therapy, including a multinational study with 220 individuals that found a 4.5-fold higher rate of healing in those getting active topical oxygen therapy at home compared to placebo.[57–59]

Shock wave therapy: Shock wave therapy, which involves utilizing a handheld probe to administer high-energy pulses locally to the wound, is said to improve local perfusion and angiogenesis, break biofilm, and maybe upregulate growth factors. Shock wave therapy appears to promote healing of chronic diabetic foot ulcers in observational and small randomized trials. 336 patients were randomly assigned to shock wave therapy (DermaPACE) or normal care, which included wet-to-dry dressings or debridement, in two separate trials. At the 24-week follow-up, considerably more patients in the shock wave group had complete wound closure than in the conventional treatment group (44 versus 30 percent).[60,61]

Negative pressure wound therapy (NPWT): NPWT, also known as vacuum-assisted closure (VAC), involves applying regulated sub-atmospheric pressure to the

ulcer's surface. NPWT promotes healing by enhancing wound perfusion, decreasing edema, decreasing the local bacterial burden, and boosting granulation tissue development."

Various articles;

In a study conducted by Veves A et al., (2002) to "assess the collagen versus standard treatment in management of diabetic foot ulcer. After 12 weeks of treatment, complete wound closure was achieved in 37% of Promogran-treated patients compared to 28.3% in the control group, though the difference was not statistically significant (P = .12). However, in patients with ulcers less than six months old, Promogran showed a marginally significant advantage, with a healing rate of 45% versus 33% in controls (P = .056). No significant difference was observed in patients with ulcers lasting six months or more, and safety profiles were similar across both groups. Patients and investigators showed a strong preference for Promogran over moistened gauze. While overall healing rates were comparable, Promogran may offer additional benefits in managing diabetic foot ulcers, particularly for those with a shorter duration."[3]

In a retrospective study conducted by Singh O et al., (2011) to "assess the collagen granule versus conventional dressing in management of chronic ulcer. After two weeks of treatment, wound sterility was achieved in 60% of patients in the collagen group compared to 42% in the conventional dressing group (P=0.03). Granulation tissue developed earlier in collagen-treated wounds (P=0.03). By the eighth week, 87% of wounds in the collagen group and 80% in the conventional group had healed by more than 75% (P=0.21). Partial split-skin grafting was required in fewer patients in the collagen group (8 vs. 12; P=0.04). While no significant difference was observed

in complete wound healing between the two dressing methods, collagen dressings reduced the need for skin grafting and improved patient comfort and mobility."[62]

In a prospective comparative study conducted by Rao H et al., (2012) to "assess the wound healing in collagen dressing versus conventional dressing. A study involving 100 patients compared the effectiveness of collagen dressings (applied to 75 patients) with conventional dressings (used in 25 patients) for foot ulcer treatment. At enrollment, the median wound size was smaller in the collagen group (33.5 cm^2) than in the conventional dressing group (48 cm^2). Patients treated with collagen dressings experienced significantly faster healing (4.02 ± 0.59 vs. 7.6 ± 1.38 days), required a shorter duration of antibiotic therapy (15.12 ± 4.55 vs. 24.08 ± 6.5 days), and had a reduced follow-up period (2.40 ± 0.61 vs. 2.96 ± 1.2 months) compared to those receiving conventional treatment ($P<0.001$). No adverse events were observed in either group. These findings suggest that collagen dressings are a safe and effective option for foot ulcer management, promoting faster recovery and reducing treatment duration."[1]

In a study conducted by Shankar N et al., (2015) to assess the collagen granule dressing versus conventional dressing in deep wounds. In our study, the mean percentage of granulation tissue at two weeks was significantly higher in the collagen-treated group (93.68±10.09) compared to the control group (65.59±15.80) ($P<0.01$). Additionally, the mean wound bed score was notably better in the collagen group (14.2±1.63) than in the control group (10.09±2.45) ($P<0.01$). These findings indicate that collagen granules promote faster and more effective wound healing.[63]

In a study conducted by Chalimidi KR et al., (2015) to "assess the efficacy of collagen particle in chronic non healing ulcers. The experimental group showed a

significant reduction in wound size, with a mean decrease of 37.29 compared to 14.29 in the control group. Collagen dressings proved more effective than conventional betadine dressings in managing chronic non-healing ulcers by promoting early granulation tissue formation, ultimately leading to faster healing and a shorter hospital stay."[64]

In a study conducted by Shanmugam S et al., (2017) to "assess the effect of collagen dressing in diabetic foot ulcer. In a hospital-based case-control prospective study of 30 patients with chronic diabetic foot ulcers, collagen and conventional dressings were applied, with daily dressing changes for up to 12 weeks. Wound size was assessed at dressing removal, as well as at 4 and 12 weeks. The study found a statistically significant difference in healing outcomes, with collagen dressings demonstrating a superior healing response compared to saline dressings when used alongside standard diabetic foot ulcer treatment."

In a study conducted by Shimikore SS et al., (2018) to "assess the efficacy of collagen granule based dressing versus conventional dressing in diabetic foot ulcer. Collagen granule treatment for diabetic foot ulcers significantly reduced wound area, slough/necrotic tissue, and wound discharge compared to conventional dressings, promoting faster healing. By the end of week 2, Group A showed a notably smaller wound area and fewer patients with necrotic tissue ($P \leq 0.001$). By week 4, no cases of wound discharge were observed in Group A ($P = 0.005$). These findings highlight the effectiveness of collagen granules in accelerating wound healing in diabetic foot ulcers."[65]

In a study conducted by Park KH et al., (2019) to assess the "collagen dressing in treatment of diabetic foot ulcers. A study involving 30 patients (17 in the collagen

group and 13 in the control group) found no significant differences in demographics or baseline DFU characteristics. However, the collagen group demonstrated a significantly higher complete healing rate (82.4% vs. 38.5%, P = .022), a faster healing velocity (P < .05), and a shorter median time to achieve a 50% wound size reduction (21 vs. 42 days; hazard ratio = 1.94, P < .05) compared to the control group. These findings suggest that collagen-based wound management significantly accelerates healing in diabetic foot ulcers."[66]

In a comparative study conducted by Kanchana B et al., (2020) to assess the "collagen dressing versus conventional dressing in chronic non healing ulcers. Collagen dressing accelerates wound healing compared to moistened gauze, while also reducing the need for skin grafting, follow-up visits, and antibiotic use. Its simple application, good tolerance, safety, and non-allergic properties make it a reliable temporary biological dressing material. Given its effectiveness in treating foot ulcers by significantly shortening healing time and reducing antibiotic therapy duration, collagen dressing can be recommended as a safe and efficient option for wound management."[67]

In a study conducted by Jegoda RK et al., (2020) to assess the "collagen granules versus conventional dressing in management of chronic ulcer. The initial ulcer sizes in Group A (16.29 ± 6.07 cm^2) and Group B (14.73 ± 6.37 cm^2) were comparable, with a Z value of 0.93 and a p-value >0.5, indicating no statistically significant difference at baseline. However, the use of collagen granule dressings significantly accelerated wound healing in chronic ulcers, with a noticeable improvement observed after two weeks."[2]

In a study conducted by Chaurasia S et al., (2021) to assess the "collagen based dressing versus conventional dressing in chronic ulcers. Collagen dressing significantly reduced the time required for a 50% wound size reduction, with a mean difference of 18.5 days compared to 37.5 days in the normal saline group and 33.0 days in the povidone-iodine group. Statistical analysis using the chi-square test for proportions and t-test for mean comparisons confirmed the significance of these differences ($P < 0.05$). Collagen particles promoted faster healing by facilitating early granulation tissue formation and wound contraction, leading to fewer dressing changes (every 3–4 days), reduced need for skin grafting, and a shorter hospital stay compared to conventional dressings."[68]

In a study conducted by Colak B et al., (2022) to assess the "collagen granule dressing versus conventional dressing in patients with diabetic foot ulcer. A study of 64 diabetic foot ulcer (DFU) patients compared the effectiveness of platelet-rich plasma spray (PS) and collagen dressings, with 30 patients receiving PS and 34 treated with collagen. After 12 weeks, complete wound closure was achieved in 56.6% of the PS group and 73.5% of the collagen group. The mean treatment duration was 9.2 weeks (range: 6–12 weeks) for PS and 8.08 weeks (range: 5–12 weeks) for collagen. Patients treated with collagen dressings demonstrated faster recovery and higher healing rates than those in the PS group. These findings indicate that collagen dressings are more effective than conventional treatments, promoting early granulation tissue formation and reducing hospital stays."[69]

MATERIALS AND METHODS

Source of Data: A study conducted amongst patient admitted in "KLES Dr. Prabhakar Kore Hospital & MRC, Belagavi and Dr. Prabhakar Kore Charitable Hospital, Belagavi wards with chronic ulcer.

Study Design: A Prospective study

Study Period: from 1st September 2023 to 31st August 2024

Sample Size:

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 (SD_1^2 + SD_2^2)}{(X_1 - X_2)^2} * 20\% \text{ attrition}$$

$$n = \frac{(1.96+0.85)^2 (3.4^2+2.89^2)}{(6.49-8.63)^2} * 20\% \text{ attrition}$$

n= 35 in each group * 20% attrition

n=41 in each group

n= 82

Sample size is calculated with 95% confidence interval and 20% attrition rate."

Group A: 41

Group B: 41

Sampling technique: Simple random sampling

Inclusion Criteria:

- Patient with chronic ulcer (more than 6 weeks duration) (diabetic ulcer, venous ulcer, arterial ulcer, pressure ulcer, non-healing ulcer)
- Chronic ulcers of 6cm ±3cm diameter
- Patient giving informed consent
- Patient between 18–60-year age group

Exclusion Criteria:

1) Patient with infective ulcer
2) Critically ill patient
3) Patient refusing
4) Any evidence of underlying bone osteomyelitis
5) Malignancy
6) immunocompromised state
7) Age more than 60 years.

Study protocol: Consort flow chart for RCTs: Not applicable

Data collection procedure: The patient with chronic wound size 6cm ± 3cm in diameter will be placed in group A or group B. Group A patients dressing was done with collagen granule and Group B patients with conventional normal saline dressing, results were compared after 2 weeks. The maximum diameter of the wound was taken once at the beginning of the study and then once at the end of the study, average reduction of size in both the groups was compared. The maximum diameter of the

wound was measured by an app named Imitomeasure, which is a smartphone application used to precisely measure wound size.

Data processing and analysis/statistical analysis: The study is focused on comparison of average reduction of size of wound after two weeks of dressing between 2 groups. The patient with chronic wound size 6cm ± 3cm in diameter were placed in group A or group B. Group A patients dressing was done with collagen granule and Group B patients with conventional normal saline dressing, results will be compared after 2 weeks. The maximum diameter of the wound was taken once at the beginning of the study and then once at the end of the study, average reduction of size in both the groups was compared. The maximum diameter of the wound was measured by an app named Imitomeasure, which is a smartphone application used to precisely measure wound size. The results from both the groups were compared after observing for 2 weeks, average reduction of size in both the groups were compared.

"Are there any anticipated serious adverse events (SAE) or adverse events which may occur during course of your study. No

Does the study require any investigations or interventions to be conducted on patients If so, please describe briefly. No

If there are any investigations / Interventions necessary which have to be conducted for completion of your study, in such situation who will bear the cost of the investigations. No

Method:

The patient with chronic wound size 6cm ± 3cm in diameter were placed in group A or group B. Group A patients dressing was done with collagen granule and Group B patients with conventional normal saline dressing, results were compared after 2 weeks. The maximum diameter of the wound was taken once at the beginning of the study and then once at the end of the study, average reduction of size in both the groups was compared. The maximum diameter of the wound was measured by an app named Imitomeasure, which is a smartphone application used to precisely measure wound size.

The rate of wound healing is typically calculated as the change in wound area over a given period of time.

Maximum diameter of wound in cm and area of the wound in cm^2."

For rate of wound healing:

- Measure initial wound area (Ai) and final wound area (Af).
- Determine absolute reduction in areas: Ai - Af
- Divide absolute reduction in area by number of days(14)

  Ai – Af / 14
- Daily healing rate: Ai – Af / 14 (cm^2/day)

STATISTICAL ANALYSIS

"All the data were collected in proforma and entered in excel sheet. The continuous data were summarised as mean, standard deviation and categorical data using frequency and percentage. The summarised data were represented using tables, figures, bar diagram and pie chart. The mean difference between the groups were compared using unpaired t-test and follow-up data using paired t-test. The categorical data were compared using chi-square test. For all statistical purpose a p-value of <0.05 was considered statistically significant and all the analysis were performed using SPSS v23.0."

RESULTS

Present study included to total of "82 patients fulfilling inclusion criteria with divided into two groups as group A and group B. Group A patients dressing was done with collagen granule and Group B patients with conventional normal saline dressing,

Table 1: Comparison of mean age between the groups

	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Age	52.1	6.8	47.9	8.6	0.32

The mean age between the groups were comparable with no significant difference noted. The mean age in group A was 52.1yrs and in group B was 47.9yrs.

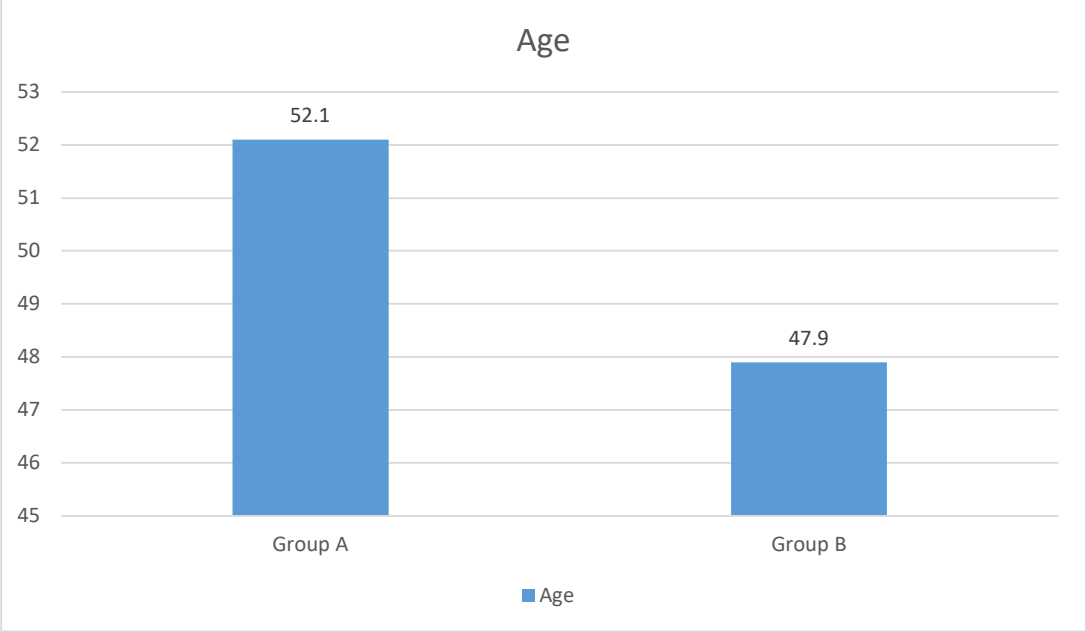


Figure 1: Comparison of mean age between the groups

Table 2: Comparison of gender distribution between the groups

		Group A		Group B		Chi-square (p-value)"
		Count	N %	Count	N %	
Gender	Female	12	30.0%	16	38.1%	1.32 (0.64)
	Male	29	70.0%	25	61.9%	

Gender distribution "between the groups were comparable with no significant difference noted.

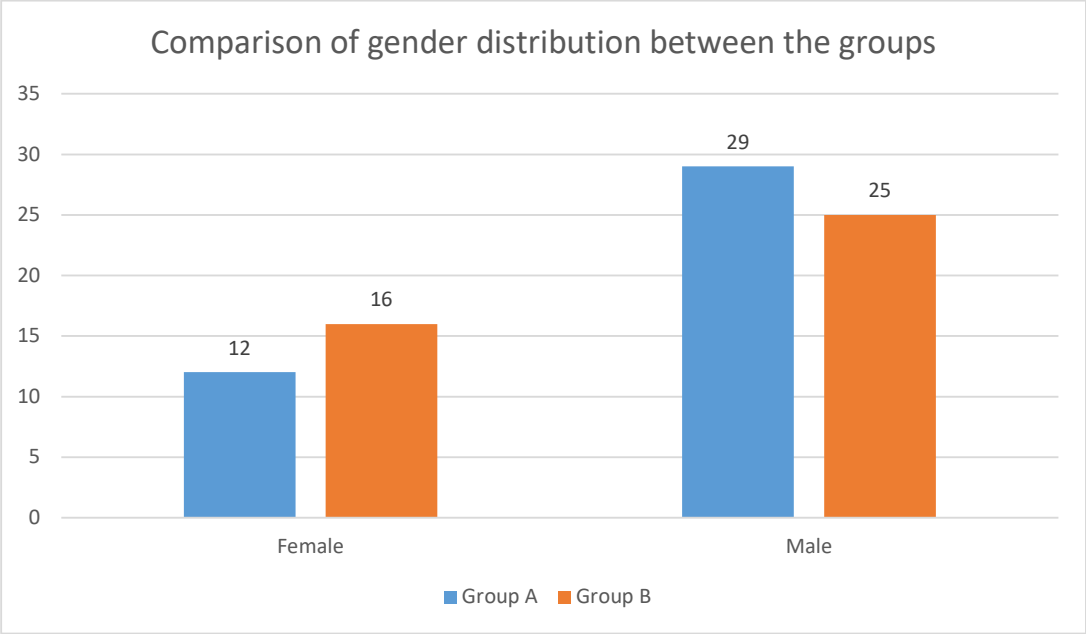


Figure 2: Comparison of gender distribution between the groups

Table 3: Comparison of smoking, hypertension and diabetes mellitus between the groups

		Group A		Group B		Chi-square
		Count	N %	Count	N %	(p-value)
Smoking	No	23	57.5%	25	59.5%	0.035 (0.85)
	Yes	18	42.5%	16	40.5%	
Hypertension	No	24	60.0%	29	69.0%	0.734 (0.39)
	Yes	17	40.0%	12	31.0%	
Diabetes mellitus	No	12	27.5%	15	38.1%	2.17 (0.33)
	Yes	29	72.5%	26	61.9%	

The history of cigarette smoking, hypertension and diabetes mellitus were comparable between the groups.

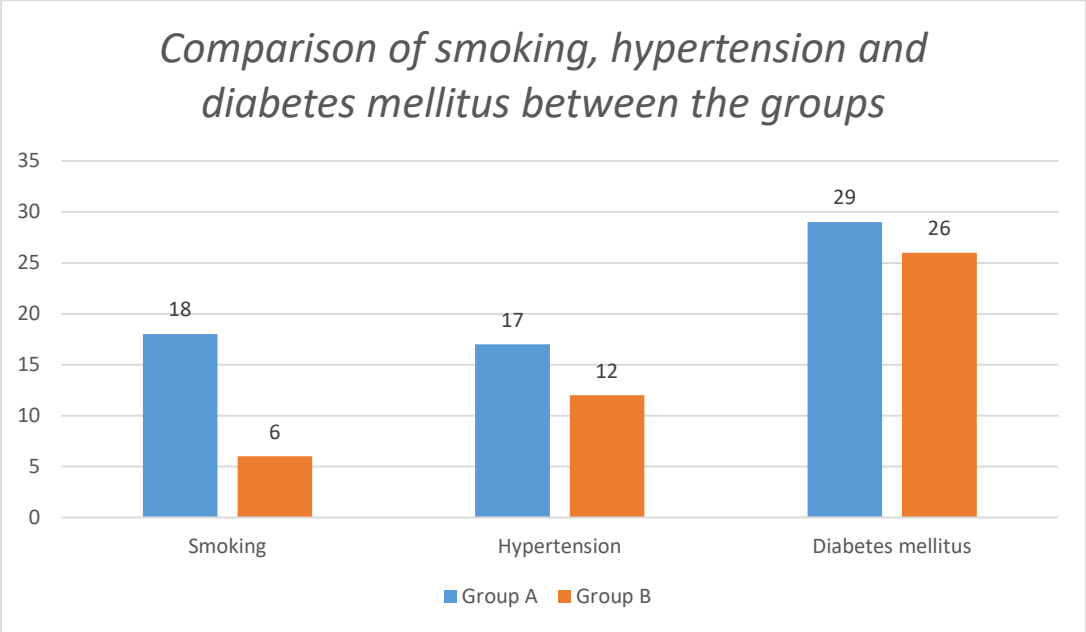


Figure 3: Comparison of smoking, hypertension and diabetes mellitus between the groups

Table 4: Comparison of the diameters between the groups

	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Day 0 max. Diameter (cm)	5.75	.72	5.72	.94	0.865
Day 14 max. Diameter (cm)	4.94	.59	5.14	.94	0.266

The day 0 and day 14 maximum diameter were found to be comparable between the groups with no significant difference noted.

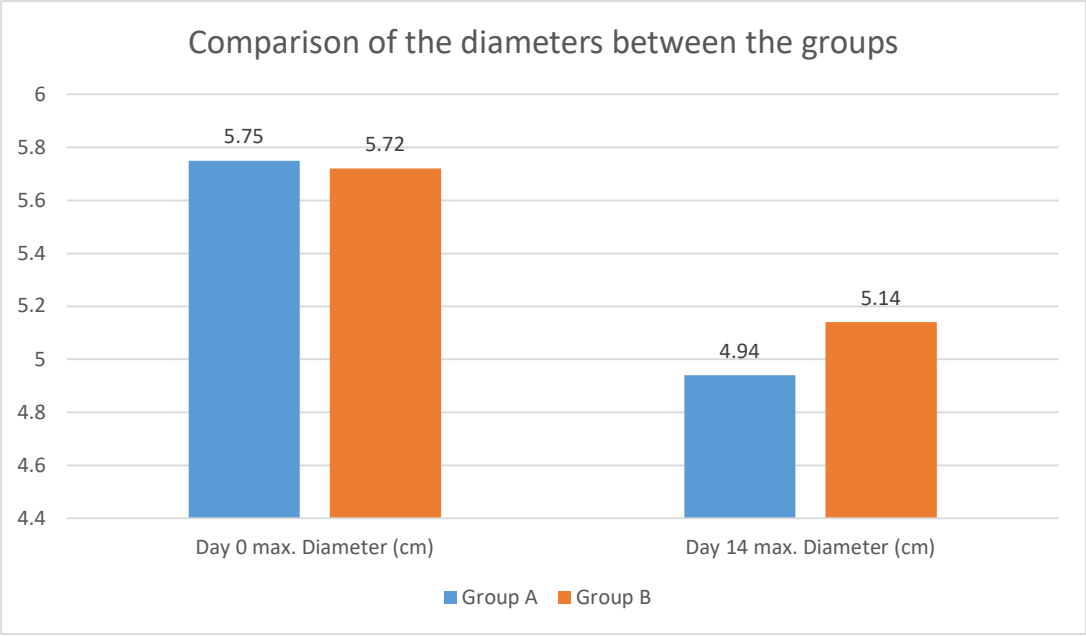


Figure 4: Comparison of the diameters between the groups

Table 5: Comparison of the area measurements between the groups

	Group A		Group B		p-value”
	Mean	SD	Mean	SD	
Area day 0 (cm2)	26.37	6.24	26.36	7.83	0.99
Area day 14 (cm2)	19.44	4.50	21.41	7.20	0.144

The area on day 0 and day 14 were “comparable between two groups with no significant difference. However the mean are on day 14 was lower in group A compared to patients in group B.

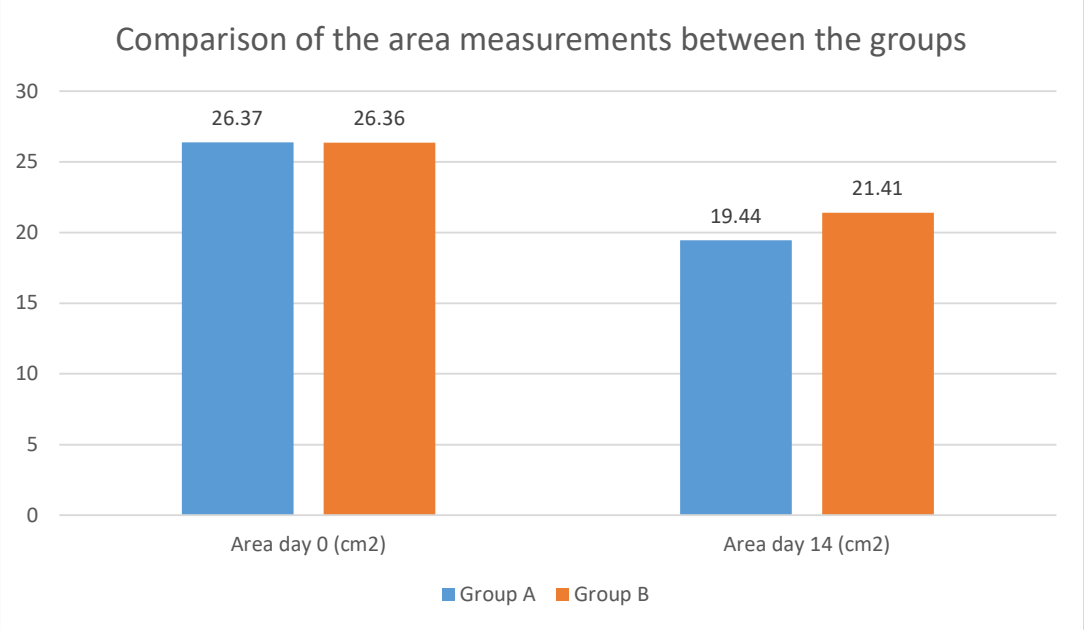


Figure 5: Comparison of the area measurements between the groups

Table 6: Comparison of reduction in area, percent reduction in area and rate of wound healing between the groups

	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Reduction in area (cm2)	6.92	3.38	5.09	3.43	0.01*
%Reduction in area	25.51	9.26	19.47	10.99	0.01*
Rate of wound healing (cm2/day)	.49	.25	.37	.25	0.05*

There is significant reduction in area in group A patients (6.92±3.3) compared to group B (5.09±3.43). similarly, the percentage reduction of area was significantly higher in group A (25.51±9.2) compared to group B (19.47±10.9). The rate of wound healing was significantly higher in group A (0.49±0.25) compared to group B patients (0.37±0.25). ($p<0.05$)

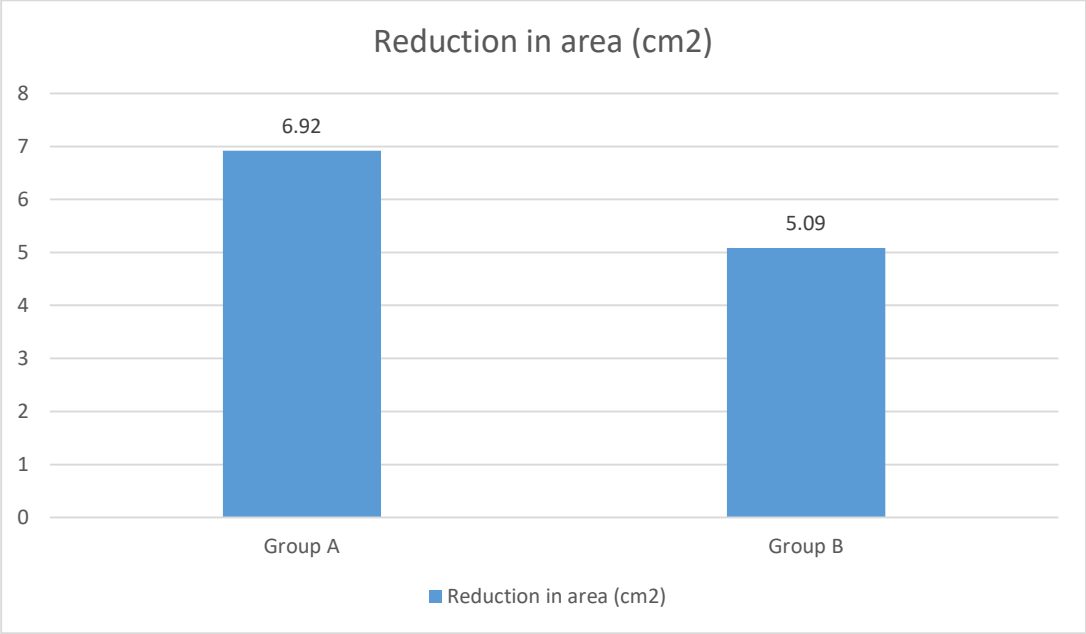


Figure 6: Comparison of reduction in area between the groups

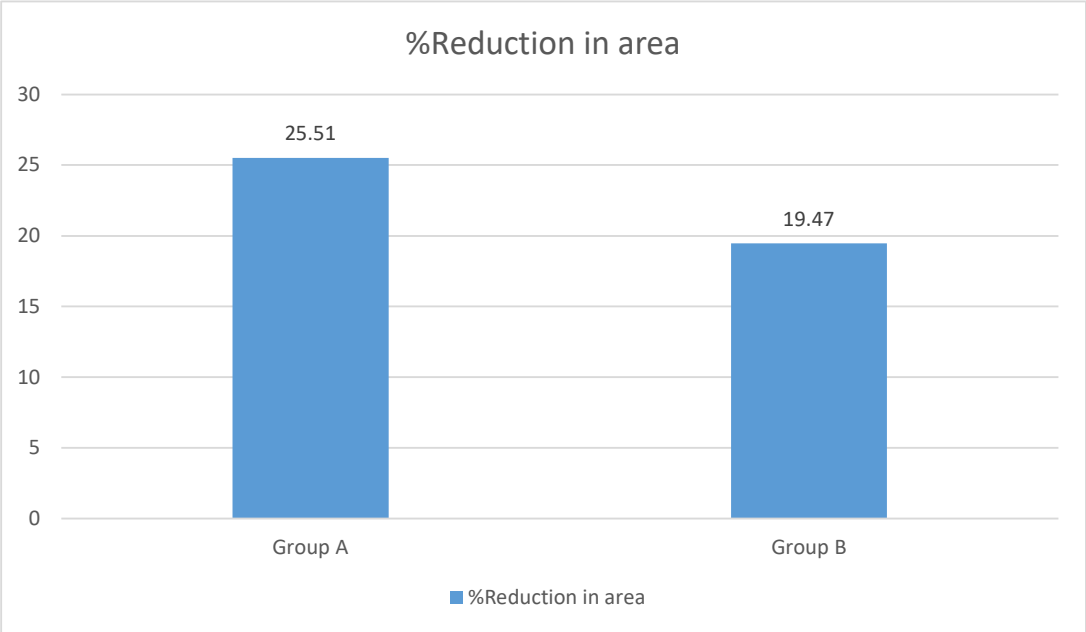


Figure 7: Comparison of percent reduction in area between the groups

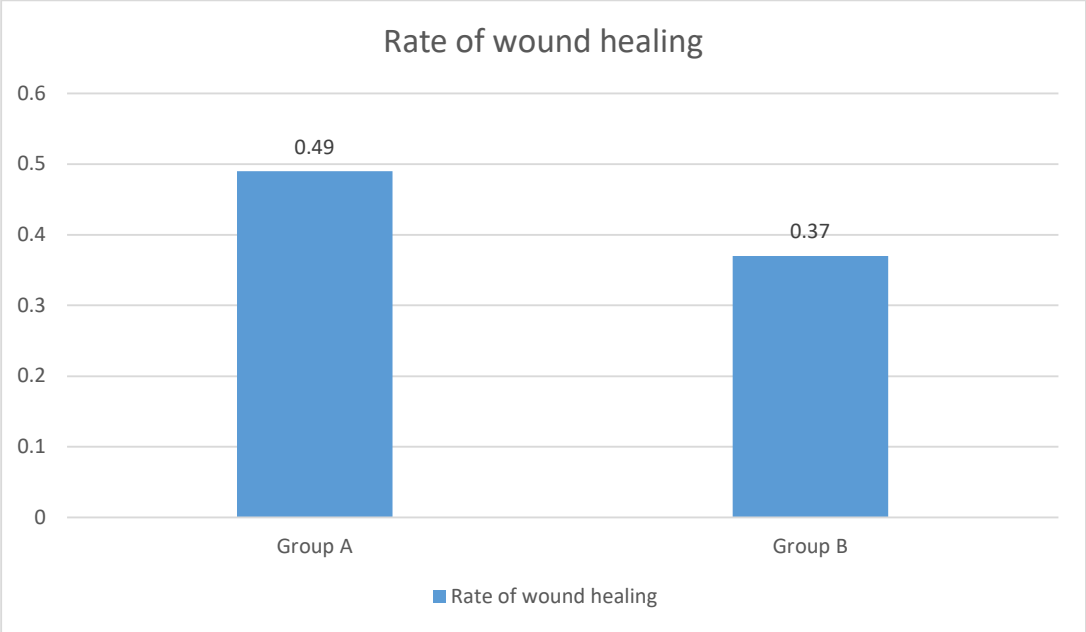


Figure 8: Comparison of rate of wound healing between the groups

Table 7: Comparison of the floor of wound finding between the groups

		Group A		Group B		Chi-square (p-value)"
		Count	N %	Count	N %	
Floor day 0	Granulation tissue	30	72.5%	33	81.0%	0.822 (0.36)
	Slough	11	27.5%	8	19.0%	
Floor day 14	Granulation tissue	34	82.5%	33	81.0%	0.033 (0.85)
	Slough	7	17.5%	8	19.0%	

There was comparable status of granulation tissue between the groups at day 0 and day 14.

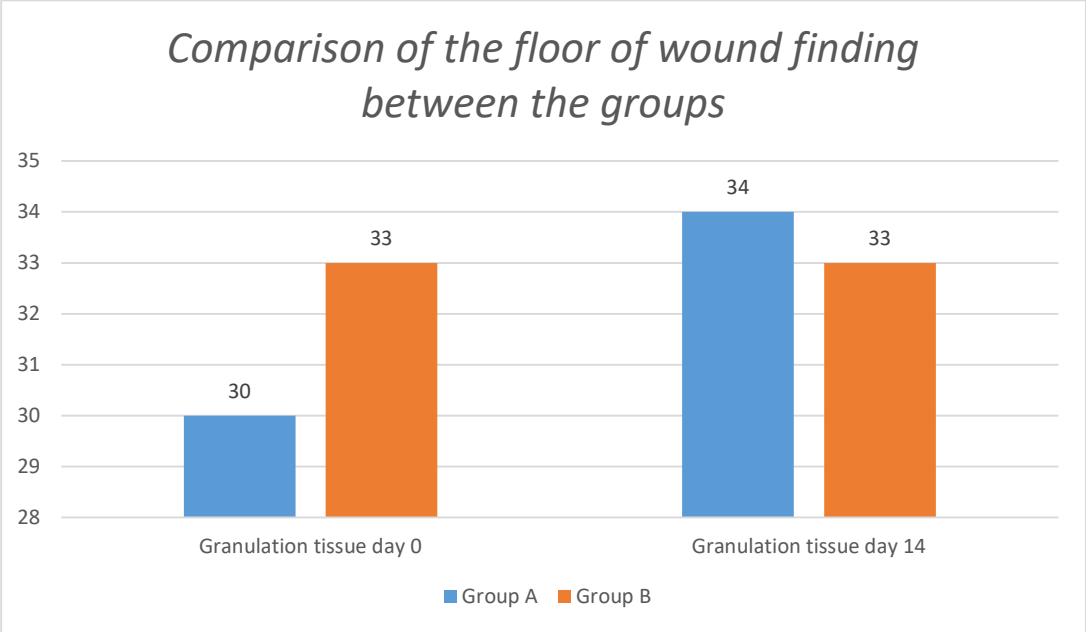


Figure 9: Comparison of the floor of wound finding between the groups

DISCUSSION

Wound healing is a complex biological process influenced by various factors, including the type of dressing used. The primary goal of this study was to compare the effectiveness of collagen dressings and conventional dressings in reducing wound size. Collagen dressings have been increasingly recognized for their ability to promote faster and more efficient wound healing due to their bioactive properties, which support cell proliferation, angiogenesis, and extracellular matrix remodeling. Conversely, conventional dressings primarily serve as protective barriers, preventing infection and maintaining moisture but lacking the bioactive components that enhance cellular activities involved in wound repair.

The comparison between these two dressing types was based on changes in wound size over a defined period. Wound contraction is a critical parameter in assessing healing efficiency, and previous studies have indicated that collagen-based dressings can accelerate wound closure by providing a scaffold for cell migration and promoting the deposition of new tissue. However, conventional dressings remain widely used due to their accessibility, cost-effectiveness, and ability to maintain a controlled healing environment.

The findings from this study contribute to the growing body of evidence regarding the benefits of bioactive dressings in wound care. By analyzing the differences in wound size reduction between the two dressing types, this study aims to provide insights into their clinical efficacy. Factors such as wound type, patient response, and external influences, including infection control and moisture balance, were also considered in evaluating the outcomes.

Present study included to total of "82 patients fulfilling inclusion criteria with divided into two groups as group A and group B. Group A patients dressing was done with collagen granule and Group B patients with conventional normal saline dressing, The mean age between the groups were comparable with no significant difference noted. The mean age in group A was 52.1yrs and in group B was 47.9yrs. Gender distribution between the groups were comparable with no significant difference noted. The history of cigarette smoking, hypertension and diabetes mellitus were comparable between the groups."

In similar study by Shimikore SS et al., "documented male preponderance in both the groups. The mean age of patients in group A was 49yrs and group B in 49.6yrs with no significant difference." [65] In similar study by Rao H et al., documented with 75% male and 25% female patients in their study, with mean age of 50.58yrs in conventional dressing group and 46.13yrs in collagen dressing group.[1]

The day 0 and day 14 maximum diameter were found to be "comparable between the groups with no significant difference noted. The area on day 0 and day 14 were comparable between two groups with no significant difference. However the mean are on day 14 was lower in group A compared to patients in group B. There is significant reduction in area in group A patients (6.92±3.3) compared to group B (5.09±3.43). similarly, the percentage reduction of area was significantly higher in group A (25.51±9.2) compared to group B (19.47±10.9). The rate of wound healing was significantly higher in group A (0.49±0.25) compared to group B patients (0.37±0.25). ($p<0.05$) There was comparable status of granulation tissue between the groups at day 0 and day 14."

In line with present study Park KH et al., "collagen group demonstrated a significantly higher complete healing rate (82.4% vs. 38.5%, P = .022), a faster healing velocity (P < .05), and a shorter median time to achieve a 50% wound size reduction (21 vs. 42 days; hazard ratio = 1.94, P < .05) compared to the control group. These findings suggest that collagen-based wound management significantly accelerates healing in diabetic foot ulcers.[66] Shimikore SS et al., found that at end of week 2, Group A showed a notably smaller wound area and fewer patients with necrotic tissue (P ≤ 0.001). By week 4, no cases of wound discharge were observed in Group A (P = 0.005). These findings highlight the effectiveness of collagen granules in accelerating wound healing in diabetic foot ulcers."[65]

In similar terms Chalimidi KR et al., the "experimental group showed a significant reduction in wound size, with a mean decrease of 37.29 compared to 14.29 in the control group. Collagen dressings proved more effective than conventional betadine dressings in managing chronic non-healing ulcers by promoting early granulation tissue formation, ultimately leading to faster healing and a shorter hospital stay."[64]

In concordance Colak B et al., found that after 12 weeks, "complete wound closure was achieved in 56.6% of the PS group and 73.5% of the collagen group. The mean treatment duration was 9.2 weeks (range: 6–12 weeks) for PS and 8.08 weeks (range: 5–12 weeks) for collagen. Patients treated with collagen dressings demonstrated faster recovery and higher healing rates than those in the PS group. These findings indicate that collagen dressings are more effective than conventional treatments, promoting early granulation tissue formation and reducing hospital stays."[69] Another study by Chaurasia S et al., "Collagen dressing significantly reduced the time required for a 50% wound size reduction, with a mean difference of 18.5 days compared to 37.5

days in the normal saline group and 33.0 days in the povidone-iodine group. Collagen particles promoted faster healing by facilitating early granulation tissue formation and wound contraction, leading to fewer dressing changes (every 3–4 days), reduced need for skin grafting, and a shorter hospital stay compared to conventional dressings."[68]

Another study by Kanchana B et al., the "Collagen dressing accelerates wound healing compared to moistened gauze, while also reducing the need for skin grafting, follow-up visits, and antibiotic use. Its simple application, good tolerance, safety, and non-allergic properties make it a reliable temporary biological dressing material. Given its effectiveness in treating foot ulcers by significantly shortening healing time and reducing antibiotic therapy duration, collagen dressing can be recommended as a safe and efficient option for wound management."[67]

Shankar N et al., found the "mean percentage of granulation tissue at two weeks was significantly higher in the collagen-treated group (93.68±10.09) compared to the control group (65.59±15.80) ($P<0.01$). Additionally, the mean wound bed score was notably better in the collagen group (14.2±1.63) than in the control group (10.09±2.45) ($P<0.01$). These findings indicate that collagen granules promote faster and more effective wound healing."[63] Also in study by Rao H et al., "patients treated with collagen dressings experienced significantly faster healing (4.02 ± 0.59 vs. 7.6 ± 1.38 days), required a shorter duration of antibiotic therapy (15.12 ± 4.55 vs. 24.08 ± 6.5 days), and had a reduced follow-up period (2.40 ± 0.61 vs. 2.96 ± 1.2 months) compared to those receiving conventional treatment ($P<0.001$). No adverse events were observed in either group. These findings suggest that collagen dressings are a safe and effective option for foot ulcer management, promoting faster recovery and reducing treatment duration."[1]

Recommendations

1. **Preferential Use of Collagen Dressings:** Given the significant reduction in wound size and higher percentage of healing observed in the collagen dressing group (Group A), collagen-based dressings should be considered as a first-line option for managing chronic ulcers.
2. **Optimizing Dressing Frequency:** Since collagen dressings contribute to faster wound healing, they may reduce the need for frequent dressing changes. This can improve patient comfort, minimize pain, and lower healthcare costs associated with dressing supplies and nursing care.
3. **Application in High-Risk Patients:** Patients with chronic wounds, particularly those with diabetes, hypertension, or a history of smoking, may benefit from collagen dressings to accelerate healing and prevent complications such as infections or amputations.
4. **Integration into Clinical Guidelines:** Given the significant difference in wound area reduction and healing rates, hospitals and healthcare providers should consider incorporating collagen dressings into standardized wound care protocols, especially for chronic ulcers.
5. **Further Research on Long-Term Outcomes:** While the study demonstrated short-term benefits over two weeks, additional research with a larger sample size and extended follow-up periods is needed to assess the long-term impact of collagen dressings on complete wound closure and recurrence rates.
6. **Cost-Effectiveness Analysis:** Future studies should evaluate the cost-benefit ratio of collagen dressings compared to conventional dressings, considering reduced hospital stays, fewer dressing changes, and lower antibiotic use.

7. **Patient Education and Training:** Healthcare providers should educate patients on the benefits of collagen dressings, proper wound care techniques, and lifestyle modifications to further enhance healing outcomes and prevent recurrence.

These recommendations support the use of collagen dressings as an effective intervention for chronic ulcers, promoting faster healing, reducing patient discomfort, and potentially lowering healthcare burdens.

CONCLUSION

"The present study compared the effectiveness of collagen dressings versus conventional saline dressings in wound healing by analyzing wound size reduction over 14 days. While baseline characteristics, including age, gender distribution, and comorbidities, were comparable between the two groups, significant differences were observed in wound healing outcomes. Although initial wound dimensions were similar in both groups, patients treated with collagen dressings (Group A) exhibited greater wound area reduction and a higher percentage of wound healing compared to those receiving conventional dressings (Group B). The rate of wound healing was also significantly higher in Group A. These findings suggest that collagen dressings may enhance wound healing efficiency, potentially offering a superior alternative to conventional dressings. Further studies with larger sample sizes and extended follow-up periods are recommended to validate these findings and assess long-term benefits."

SUMMARY

- Present study "included to total of 82 patients fulfilling inclusion criteria with divided into two groups as group A and group B. Group A patients dressing was done with collagen granule and Group B patients with conventional normal saline dressing,
- The mean age between the groups were comparable with no significant difference noted. The mean age in group A was 52.1yrs and in group B was 47.9yrs.
- Gender distribution between the groups were comparable with no significant difference noted.
- The history of cigarette smoking, hypertension and diabetes mellitus were comparable between the groups.
- The day 0 and day 14 maximum diameter were found to be comparable between the groups with no significant difference noted.
- The area on day 0 and day 14 were comparable between two groups with no significant difference. However the mean are on day 14 was lower in group A compared to patients in group B.
- There is significant reduction in area in group A patients (6.92±3.3) compared to group B (5.09±3.43). similarly the percentage reduction of area was significantly higher in group A (25.51±9.2) compared to group B (19.47±10.9). The rate of wound healing was significantly higher in group A (0.49±0.25) compared to group B patients (0.37±0.25). ($p<0.05$)
- There was comparable status of granulation tissue between the groups at day 0 and day 14."

BIBLIOGRAPHY

1. Rao H, Pai A, Hussein I, Arun A, Ram HS, Pai A, et al. A comparative study between collagen dressings and conventional dressings in wound healing. Int J Collab Res Intern Med Public Heal. 2012;1:2–12.

2. Jegoda RK. A comparative study of collagen granules vs conventional dressing in the management of chronic ulcer. 2020;

3. Veves A, Sheehan P, Pham HT. A randomized, controlled trial of Promogran (a collagen/oxidized regenerated cellulose dressing) vs standard treatment in the management of diabetic foot ulcers. Arch Surg. 2002;137(7):822–7.

4. Wilgus TA, Roy S, McDaniel JC. Neutrophils and Wound Repair: Positive Actions and Negative Reactions. Vol. 2, Advances in wound care. United States; 2013. p. 379–88.

5. Clark RAF. Fibrin is a many splendored thing. J Invest Dermatol. 2003;121(5):xxi–xxii.

6. Crisan M, Yap S, Casteilla L, Chen CW, Corselli M, Park TS, et al. A perivascular origin for mesenchymal stem cells in multiple human organs. Cell Stem Cell. 2008;3(3):301–13.

7. Tepper OM, Capla JM, Galiano RD, Ceradini DJ, Callaghan MJ, Kleinman ME, et al. Adult vasculogenesis occurs through in situ recruitment, proliferation, and tubulization of circulating bone marrow-derived cells. Blood. 2005;105(3):1068–77.

8. Rennert RC, Januszyk M, Sorkin M, Rodrigues M, Maan ZN, Duscher D, et al. Microfluidic single-cell transcriptional analysis rationally identifies novel surface marker profiles to enhance cell-based therapies. Nat Commun. 2016;7:11945.

9. Jung K, Covington S, Sen CK, Januszyk M, Kirsner RS, Gurtner GC, et al. Rapid identification of slow healing wounds. Wound repair Regen Off Publ Wound Heal Soc [and] Eur Tissue Repair Soc. 2016;24(1):181–8.

10. Wong VW, Rustad KC, Akaishi S, Sorkin M, Glotzbach JP, Januszyk M, et al. Focal adhesion kinase links mechanical force to skin fibrosis via inflammatory signaling. Nat Med. 2011;18(1):148–52.

11. Pastar I, Wong LL, Egger AN, Tomic-Canic M. Descriptive vs mechanistic scientific approach to study wound healing and its inhibition: Is there a value of translational research involving human subjects? Exp Dermatol. 2018;27(5):551–62.

12. Galiano RD, Michaels J 5th, Dobryansky M, Levine JP, Gurtner GC. Quantitative and reproducible murine model of excisional wound healing. Wound repair Regen Off Publ Wound Heal Soc [and] Eur Tissue Repair Soc. 2004;12(4):485–92.

13. Kaplan KL, Broekman MJ, Chernoff A, Lesznik GR, Drillings M. Platelet alpha-granule proteins: studies on release and subcellular localization. Blood. 1979;53(4):604–18.

14. Pool JG. Normal hemostatic mechanisms: a review. Am J Med Technol. 1977;43(8):776–80.

15. Rodrigues M, Kosaric N, Bonham CA, Gurtner GC. Wound Healing: A Cellular Perspective. Physiol Rev. 2019;99(1):665–706.

16. Yates CC, Krishna P, Whaley D, Bodnar R, Turner T, Wells A. Lack of CXC chemokine receptor 3 signaling leads to hypertrophic and hypercellular scarring. Am J Pathol. 2010;176(4):1743–55.

17. Yanez DA, Lacher RK, Vidyarthi A, Colegio OR. The role of macrophages in skin homeostasis. Pflugers Arch. 2017;469(3–4):455–63.

18. Godwin JW, Pinto AR, Rosenthal NA. Macrophages are required for adult salamander limb regeneration. Proc Natl Acad Sci U S A. 2013;110(23):9415–20.

19. Zhu Z, Ding J, Ma Z, Iwashina T, Tredget EE. Systemic depletion of macrophages in the subacute phase of wound healing reduces hypertrophic scar formation. Wound Repair Regen. 2016;24(4):644–56.

20. Sonoda T, Kitamura Y, Haku Y, Hara H, Mori KJ. Mast-cell precursors in various haematopoietic colonies of mice produced in vivo and in vitro. Br J Haematol. 1983;53(4):611–20.

21. Wulff BC, Parent AE, Meleski MA, DiPietro LA, Schrementi ME, Wilgus TA. Mast cells contribute to scar formation during fetal wound healing. J Invest Dermatol. 2012;132(2):458–65.

22. Wilgus TA, Wulff BC. The Importance of Mast Cells in Dermal Scarring. Vol. 3, Advances in wound care. United States; 2014. p. 356–65.

23. Wulff BC, Wilgus TA. Mast cell activity in the healing wound: more than meets the eye? Exp Dermatol. 2013;22(8):507–10.

24. Nakano T, Sonoda T, Hayashi C, Yamatodani A, Kanayama Y, Yamamura T, et al. Fate of bone marrow-derived cultured mast cells after intracutaneous, intraperitoneal, and intravenous transfer into genetically mast cell-deficient W/Wv mice. Evidence that cultured mast cells can give rise to both connective tissue type and mucosal mas. J Exp Med. 1985;162(3):1025–43.

25. Tamoutounour S, Guilliams M, Montanana Sanchis F, Liu H, Terhorst D, Malosse C, et al. Origins and functional specialization of macrophages and of conventional and monocyte-derived dendritic cells in mouse skin. Immunity. 2013;39(5):925–38.

26. Haniffa M, Shin A, Bigley V, McGovern N, Teo P, See P, et al. Human tissues contain CD141hi cross-presenting dendritic cells with functional homology to mouse CD103+ nonlymphoid dendritic cells. Immunity. 2012;37(1):60–73.

27. Gurtner GC, Werner S, Barrandon Y, Longaker MT. Wound repair and regeneration. Nature. 2008;453(7193):314–21.

28. Eilken HM, Adams RH. Dynamics of endothelial cell behavior in sprouting angiogenesis. Curr Opin Cell Biol. 2010;22(5):617–25.

29. Cook-Mills JM, Deem TL. Active participation of endothelial cells in inflammation. J Leukoc Biol. 2005;77(4):487–95.

30. Subramaniam M, Saffaripour S, Van De Water L, Frenette PS, Mayadas TN, Hynes RO, et al. Role of endothelial selectins in wound repair. Am J Pathol. 1997;150(5):1701–9.

31. Nagaoka T, Kaburagi Y, Hamaguchi Y, Hasegawa M, Takehara K, Steeber DA, et al. Delayed wound healing in the absence of intercellular adhesion molecule-1 or L-selectin expression. Am J Pathol. 2000;157(1):237–47.

32. Armulik A, Genové G, Betsholtz C. Pericytes: developmental, physiological, and pathological perspectives, problems, and promises. Dev Cell. 2011;21(2):193–215.

33. Asahara T, Murohara T, Sullivan A, Silver M, van der Zee R, Li T, et al. Isolation of putative progenitor endothelial cells for angiogenesis. Science. 1997;275(5302):964–7.

34. Nehls V, Drenckhahn D. Heterogeneity of microvascular pericytes for smooth muscle type alpha-actin. J Cell Biol. 1991;113(1):147–54.

35. Takahashi T, Kalka C, Masuda H, Chen D, Silver M, Kearney M, et al. Ischemia- and cytokine-induced mobilization of bone marrow-derived endothelial progenitor cells for neovascularization. Nat Med. 1999;5(4):434–8.

36. Rehman J, Li J, Orschell CM, March KL. Peripheral blood "endothelial progenitor cells" are derived from monocyte/macrophages and secrete angiogenic growth factors. Circulation. 2003;107(8):1164–9.

37. Yamaguchi Y, Okazaki Y, Seta N, Satoh T, Takahashi K, Ikezawa Z, et al. Enhanced angiogenic potency of monocytic endothelial progenitor cells in patients with systemic sclerosis. Arthritis Res Ther. 2010;12(6):R205.

38. Sinha R, Stanley G, Gulati GS, Ezran C, Travaglini KJ, Wei E, et al. Index switching causes "spreading-of-signal" among multiplexed samples in Illumina HiSeq 4000 DNA sequencing. BioRxiv. 2017;125724.

39. Driskell RR, Lichtenberger BM, Hoste E, Kretzschmar K, Simons BD, Charalambous M, et al. Distinct fibroblast lineages determine dermal architecture in skin development and repair. Nature. 2013;504(7479):277–81.

40. Tomasek JJ, Gabbiani G, Hinz B, Chaponnier C, Brown RA. Myofibroblasts and mechano-regulation of connective tissue remodelling. Nat Rev Mol Cell Biol. 2002;3(5):349–63.

41. Hinz B. The myofibroblast: paradigm for a mechanically active cell. J Biomech. 2010;43(1):146–55.

42. Perdiguero EG, Geissmann F. The development and maintenance of resident macrophages. Nat Immunol. 2016;17(1):2–8.

43. Nishimura EK, Jordan SA, Oshima H, Yoshida H, Osawa M, Moriyama M, et al. Dominant role of the niche in melanocyte stem-cell fate determination. Nature. 2002;416(6883):854–60.

44. Lebrun E, Tomic-Canic M, Kirsner RS. The role of surgical debridement in healing of diabetic foot ulcers. Wound repair Regen Off Publ Wound Heal Soc [and] Eur Tissue Repair Soc. 2010;18(5):433–8.

45. Karavan M, Olerud J, Bouldin E, Taylor L, Reiber GE. Evidence-based chronic ulcer care and lower limb outcomes among Pacific Northwest veterans. Wound Repair Regen. 2015;23(5):745–52.

46. Wu L, Norman G, Dumville JC, O'Meara S, Bell-Syer SEM. Dressings for treating foot ulcers in people with diabetes: an overview of systematic reviews. Cochrane database Syst Rev. 2015;2015(7):CD010471.

47. Bergin SM, Wraight P. Silver based wound dressings and topical agents for treating diabetic foot ulcers. Cochrane database Syst Rev. 2006;(1):CD005082.

48. Veves A, Falanga V, Armstrong DG, Sabolinski ML. Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers: a prospective randomized multicenter clinical trial. Diabetes Care. 2001;24(2):290–5.

49. Naughton G, Mansbridge J, Gentzkow G. A metabolically active human dermal replacement for the treatment of diabetic foot ulcers. Artif Organs. 1997;21(11):1203–10.

50. Marston WA, Hanft J, Norwood P, Pollak R. The efficacy and safety of Dermagraft in improving the healing of chronic diabetic foot ulcers: results of a prospective randomized trial. Diabetes Care. 2003;26(6):1701–5.

51. Liu R, Li L, Yang M, Boden G, Yang G. Systematic review of the effectiveness of hyperbaric oxygenation therapy in the management of chronic diabetic foot ulcers. Mayo Clin Proc. 2013;88(2):166–75.

52. Wang C, Schwaitzberg S, Berliner E, Zarin DA, Lau J. Hyperbaric oxygen for treating wounds: a systematic review of the literature. Arch Surg. 2003;138(3):272–9; discussion 280.

53. Roeckl-Wiedmann I, Bennett M, Kranke P. Systematic review of hyperbaric oxygen in the management of chronic wounds. Br J Surg. 2005;92(1):24–32.

54. Goldman RJ. Hyperbaric oxygen therapy for wound healing and limb salvage: a systematic review. PM R. 2009;1(5):471–89.

55. Stoekenbroek RM, Santema TB, Legemate DA, Ubbink DT, van den Brink A, Koelemay MJW. Hyperbaric oxygen for the treatment of diabetic foot ulcers: a systematic review. Eur J Vasc Endovasc Surg. 2014;47(6):647–55.

56. Kranke P, Bennett M, Roeckl-Wiedmann I, Debus S. Hyperbaric oxygen therapy for chronic wounds. Cochrane database Syst Rev. 2004;(2):CD004123.

57. Gordillo GM, Sen CK. Revisiting the essential role of oxygen in wound healing. Am J Surg. 2003;186(3):259–63.

58. Frykberg RG, Franks PJ, Edmonds M, Brantley JN, Téot L, Wild T, et al. A Multinational, Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy of Cyclical Topical Wound Oxygen (TWO2) Therapy in the Treatment of Chronic Diabetic Foot Ulcers: The TWO2 Study. Diabetes Care. 2020;43(3):616–24.

59. Hunter P, Greco E, Cross K, Perry J. Topical Oxygen Therapy Shifts Microbiome Dynamics in Chronic Diabetic Foot Ulcers. Wounds a Compend Clin Res Pract. 2020;32(3):81–5.

60. Moretti B, Notarnicola A, Maggio G, Moretti L, Pascone M, Tafuri S, et al. The management of neuropathic ulcers of the foot in diabetes by shock wave therapy. BMC Musculoskelet Disord. 2009;10:54.

61. Saggini R, Figus A, Troccola A, Cocco V, Saggini A, Scuderi N. Extracorporeal shock wave therapy for management of chronic ulcers in the lower extremities. Ultrasound Med Biol. 2008;34(8):1261–71.

62. Singh O, Gupta SS, Soni M, Moses S, Shukla S, Mathur RK. Collagen dressing versus conventional dressings in burn and chronic wounds: a retrospective study. J Cutan Aesthet Surg. 2011;4(1):12–6.

63. Shankar N, Eligar R, Ramesh H, Hebsur NI. A comparative study of collagen granule dressing versus conventional dressing in deep wounds. IOSR J Dent Med Sci. 2015;14:23–8.

64. Chalimidi KR, Kumar Y, Kini UA. Efficacy of collagen particles in chronic non healing ulcers. J Clin Diagnostic Res JCDR. 2015;9(6):PC01.

65. Shimikore SS, Pawar GB. A randomized controlled trial to compare efficacy of collagen granule-based dressing versus conventional dressing in the management of diabetic foot ulcers. Arch Med Heal Sci. 2018;6(1):28–31.

66. Park KH, Kwon JB, Park JH, Shin JC, Han SH, Lee JW. Collagen dressing in the treatment of diabetic foot ulcer: a prospective, randomized, placebo-controlled, single-center study. Diabetes Res Clin Pract. 2019;156:107861.

67. Kanchana B, Karthick PP. A Comparative Study of Collagen Dressing Versus Conventional Dressing in Chronic Non Healing Ulcers. IOSR J Dent Med Sci. 2020;19(6):18–29.

68. Chaurasia S, Diwaker A, Garg N. A comparative study of collagen-based dressing versus conventional dressing in chronic ulcers. Int J Res Med Sci. 2021;9(8):2289.

69. Colak B, Yormaz S, Ece I, Çalişir A, Körez K, Çınar M, et al. Comparison of collagen granule dressing versus conventional dressing in patients with diabetic foot ulcer. Int J Low Extrem Wounds. 2022;21(3):279–89.

ANNEXURE I:
KAHERs JNMC
BELAGAVI
INFORMED CONSENT FORM

A one-year observational study comparing size of wound after being subjected to collagen dressings and conventional dressings at a tertiary care hospital.

Introduction: The use of collagen granules dressing accelerated the rate of wound healing in chronic ulcers. In this study authors found that the rate of wound healing was significantly better in using collagen granules but after two weeks. Thus, reducing the ulcer size can help patient to early return to work. Early return to work does reduce the financial burden on the patient**.**

Explanation of procedure: The patient with chronic wound size 6cm ± 3cm in diameter will be placed in group A or group B. Group A patients dressing will be done with collagen granule and Group B patients will have conventional normal saline dressing, results will be compared after 2 weeks. The maximum diameter of the wound will be taken once at the beginning of the study and then once at the end of the study, average reduction of size in both the groups will be compared. The maximum diameter of the wound will be measured by an app named Imitomeasure, which is a smartphone application used to precisely measure wound size.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will not get any harm by participating in this study. The collagen granule will not cause any harmful effect in the body. The data gathered will help population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person to identify you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Cost of investigations done during the course of study will be paid by the **principal investigator.**

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purpose and or presented to scientific groups. However, your identity will never be revealed.

Questions:

If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights

STATEMENT

I am making a voluntary decision to participate in the study "An observational study comparing rate of wound healing between collagen dressings and conventional dressings" . My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

ANNEXURE II: PROFORMA

Title: A one-year observational study comparing size of wound after being subjected to collagen dressings and conventional dressings at a tertiary care hospital

Participant Information

1. Participant ID: _____

2. Age: _____

3. Gender: ☐ Male ☐ Female ☐ Other

4. Contact Information: _____

5. Inclusion Date: _____

Baseline Data

1. Wound Type (select one):

   ☐ Diabetic Ulcer

   ☐ Pressure Ulcer

   ☐ Venous Ulcer

   ☐ Other: _____

2. Wound Characteristics:

   - Location: _____

   - Initial Diameter (cm): _____ (Measured using 'Imitomeasure')

   - Wound Area (if needed): _____

3. Medical History:

   - Diabetes: ☐ Yes ☐ No

   - Hypertension: ☐ Yes ☐ No

- Smoking Status: ☐ Smoker ☐ Non-smoker

- Other Comorbidities: _____

4. Initial Qualitative Observations:

- Granulation Tissue: ☐ Present ☐ Absent

- Infection: ☐ Present ☐ Absent

Group Details

1. Group Allocation:

☐ Group A (Collagen Granule Dressing)

☐ Group B (Conventional Saline Dressing)

2. Frequency of Dressing Change: _____

Follow-Up (Day 14)

1. Wound Reassessment:

- Final Diameter (cm): _____ (Measured using 'Imitomeasure')

- Wound Area (if needed): _____

2. Reduction in Size:

Change in Diameter (cm) = Initial Diameter - Final Diameter

- Percentage Reduction: _____%

3. Qualitative Observations:

- Granulation Tissue: ☐ Present ☐ Absent

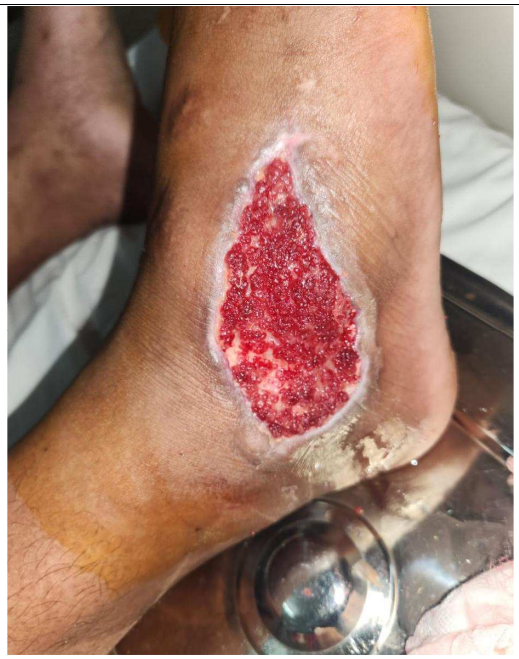
- Discharge: ☐ Present ☐ Absent

Rate of wound healing:

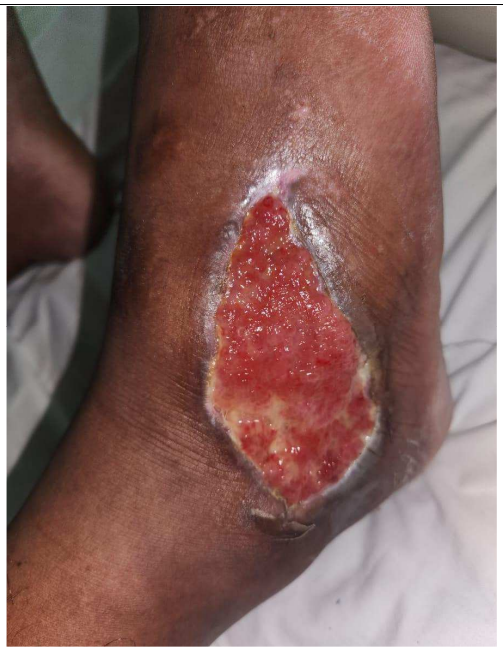
Other Observations

Complications (if any): _____

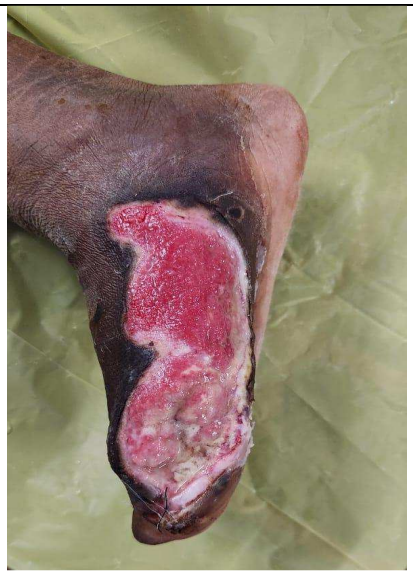
ANNEXURE III PHOTOGRAPHS



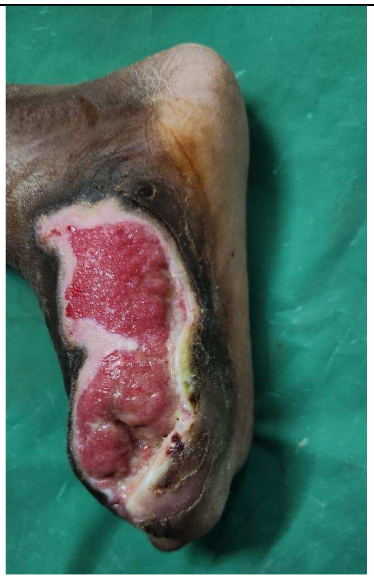
CONVENTIONAL DRESSING DAY 1



CONVENTIONAL DRESSING DAY 14



COLLAGEN DRESSING DAY 1



COLLAGEN DRESSING DAY 14

POST DEBRIDEMENT WOUND

MASTERCHART

S.NO	PATIENT NO	AGE	SEX	SMOKING	HYPERTENSION	DIABETES MELLITUS	COLLAGEN DRESSING	NORMAL SALINE DRESSING	SITE	DAY 0 MAX. DIAMETER (cm)	AREA DAY 0 (cm2)	DAY 14 MAX. DIAMETER (cm)	AREA DAY 14 (cm2)	a	%REDUCTION IN AREA	RATE OF WOUND HEALING (cm2/day)	FLOOR DAY 0	FLOOR DAY 14
1	10038588	56	Male	YES	YES	NO	YES	NO	DLF	5.5	23.5	4.91	18.96	4.54	19.31914894	0.32	GRANULATION TISSUE	GRANULATION TISSUE
2	10027855	60	Male	YES	YES	NO	YES	NO	DRF	5.49	23.7	4.94	19.2	4.5	18.98734177	0.32	GRANULATION TISSUE	GRANULATION TISSUE
3	10043943	54	Male	NO	NO	YES	YES	NO	DLF	6.42	32.4	5.11	20.5	11.9	36.72839506	0.85	GRANULATION TISSUE	GRANULATION TISSUE
4	6555216	53	Male	YES	NO	YES	YES	NO	DRF	4.27	14.3	4.05	12.86	1.44	10.06993007	0.1	GRANULATION TISSUE	SLOUGH
5	10035012	52	Male	NO	NO	YES	YES	NO	PLF	4.43	15.4	3.91	12	3.4	22.07792208	0.24	GRANULATION TISSUE	GRANULATION TISSUE
6	10014152	54	Female	YES	NO	YES	YES	NO	PLF	5.69	25.4	4.46	15.6	9.8	38.58267717	0.7	SLOUGH	GRANULATION TISSUE
7	1157708	43	Male	NO	NO	YES	YES	NO	HRF	5.66	25.25	4.98	19.5	5.75	22.77227723	0.39	GRANULATION TISSUE	GRANULATION TISSUE
8	1915996	60	Male	YES	NO	YES	YES	NO	DRF	6.63	34.5	5.53	24	10.5	30.43478261	0.75	GRANULATION TISSUE	GRANULATION TISSUE
9	6473377	58	Male	YES	NO	YES	YES	NO	PLF	5.73	25.86	5.35	22.5	3.36	12.99303944	1.05	GRANULATION TISSUE	SLOUGH
10	6928984	53	Male	YES	NO	YES	YES	NO	DRF	6.74	35.63	5.17	21	14.63	41.06090373	0.56	GRANULATION TISSUE	GRANULATION TISSUE
11	6990849	48	Male	YES	YES	YES	YES	NO	DLF	6.15	29.66	5.27	21.84	7.82	26.36547539	0.77	SLOUGH	GRANULATION TISSUE
12	6897024	60	Male	YES	NO	YES	YES	NO	PRF	5.9	27.34	4.59	16.56	10.78	39.42940746	0.65	GRANULATION TISSUE	GRANULATION TISSUE
13	1158129	60	Male	NO	YES	NO	YES	NO	DLF	6.29	31.1	5.29	22	9.1	29.26045016	0.45	GRANULATION TISSUE	GRANULATION TISSUE
14	1038888	52	Male	NO	YES	NO	YES	NO	DLF	6.63	34.55	5.99	28.2	6.35	18.37916064	0.13	GRANULATION TISSUE	GRANULATION TISSUE
15	10042913	55	Male	YES	YES	YES	YES	NO	PRF	4.76	17.83	4.51	15.96	1.87	10.48794167	0.13	GRANULATION TISSUE	SLOUGH
16	10044291	40	Female	NO	YES	YES	YES	NO	DLF	5.88	27.2	5.08	20.3	6.9	25.36764706	0.49	SLOUGH	GRANULATION TISSUE
17	10043375	53	Male	NO	NO	YES	YES	NO	PRF	6.48	33	5.2	21.2	11.8	35.75757576	0.84	SLOUGH	GRANULATION TISSUE
18	10043528	58	Male	NO	NO	YES	YES	NO	DLF	5.69	25.4	4.69	17.26	8.14	32.04724409	0.58	SLOUGH	GRANULATION TISSUE
19	10045355	57	Male	NO	NO	NO	YES	NO	DRF	5.29	21.96	5.02	19.8	2.16	9.836065574	0.15	SLOUGH	SLOUGH
20	10039373	57	Male	NO	NO	YES	YES	NO	HLF	5.6	24.6	5.08	20.3	4.3	17.4796748	0.31	SLOUGH	GRANULATION TISSUE
21	10050618	55	Female	NO	YES	YES	YES	NO	DLF	4.27	14.3	3.59	10.1	4.2	29.37062937	0.3	GRANULATION TISSUE	GRANULATION TISSUE
22	1167694	53	Female	NO	YES	YES	YES	NO	PRF	5.59	24.56	5.14	20.78	3.78	15.39087948	0.27	GRANULATION TISSUE	SLOUGH
23	10053063	52	Male	NO	NO	YES	YES	NO	DRF	4.44	15.5	3.86	11.66	3.84	24.77419355	0.27	GRANULATION TISSUE	GRANULATION TISSUE
24	10051933	46	Male	NO	YES	YES	YES	NO	PRF	5.92	27.5	4.68	17.2	10.3	37.45454545	0.74	GRANULATION TISSUE	GRANULATION TISSUE
25	10039373	55	Female	YES	NO	YES	YES	NO	DRF	6.78	36	5.72	25.7	10.3	28.61111111	0.74	GRANULATION TISSUE	GRANULATION TISSUE
26	10042023	48	Female	YES	NO	NO	YES	NO	DLF	5.49	23.68	4.36	14.9	8.78	37.0777027	0.41	GRANULATION TISSUE	GRANULATION TISSUE

27	10050077	36	Female	YES	NO	NO	YES	NO	DLF	6.6	34.2	5.29	22	12.2	35.67251462	0.87	GRANULATION TISSUE	GRANULATION TISSUE
28	10052569	40	Female	YES	YES	NO	YES	NO	DLF	4.46	15.6	3.78	11.2	4.4	28.20512821	0.31	GRANULATION TISSUE	GRANULATION TISSUE
29	10043294	42	Female	YES	NO	NO	YES	NO	PRF	6.46	32.8	5.29	22	10.8	32.92682927	0.77	SLOUGH	GRANULATION TISSUE
30	10059117	60	Male	YES	NO	NO	YES	NO	DLF	5.7	25.48	4.55	16.24	9.24	36.26373626	0.66	SLOUGH	GRANULATION TISSUE
31	66232254	60	Female	NO	YES	YES	YES	NO	DLF	5.71	25.6	5.34	22.4	3.2	12.5	0.23	GRANULATION TISSUE	SLOUGH
32	1201805	50	Female	NO	YES	YES	YES	NO	DRF	5.84	26.8	5	19.6	7.2	26.86567164	0.51	GRANULATION TISSUE	GRANULATION TISSUE
33	1199098	59	Male	NO	YES	YES	YES	NO	DLF	5.92	27.55	5.17	21	6.55	23.77495463	0.47	GRANULATION TISSUE	GRANULATION TISSUE
34	6530851	51	Male	NO	YES	YES	YES	NO	PRF	6.43	32.44	6.16	29.8	2.64	8.13810111	0.19	GRANULATION TISSUE	SLOUGH
35	1054125	40	Male	N0	NO	YES	YES	NO	DRF	4.97	19.4	4.25	14.2	5.2	26.80412371	0.37	GRANULATION TISSUE	GRANULATION TISSUE
36	1051486	54	Male	YES	NO	YES	YES	NO	DLF	5.2	21.2	4.76	17.8	3.4	16.03773585	0.24	GRANULATION TISSUE	GRANULATION TISSUE
37	1156769	43	Male	NO	NO	NO	YES	NO	DRF	6.53	33.5	5.45	23.3	10.2	30.44776119	0.73	GRANULATION TISSUE	GRANULATION TISSUE
38	6475567	59	Male	NO	NO	YES	YES	NO	PLF	6.47	32.9	5.83	26.6	6.3	19.14893617	0.45	GRANULATION TISSUE	GRANULATION TISSUE
39	6188538	41	Male	NO	NO	YES	YES	NO	DLF	5.94	27.7	5.2	21.2	6.5	23.46570397	0.46	SLOUGH	GRANULATION TISSUE
40	6326114	55	Female	NO	YES	YES	NO	YES	DRF	6.11	29.34	5.12	20.56	8.78	29.93	0.63	SLOUGH	GRANULATION TISSUE
41	1200218	58	Female	YES	NO	YN	NO	YES	DRF	6.48	33	5.2	21.2	11.8	35.75757576	0.84	GRANULATION TISSUE	GRANULATION TISSUE
42	1176857	55	Male	NO	YES	NO	NO	YES	HLF	5.69	25.4	4.69	17.26	8.14	32.04724409	0.58	GRANULATION TISSUE	GRANULATION TISSUE
43	1166912	49	Female	YES	NO	NO	NO	YES	DLF	5.6	24.6	5.09	20.3	4.3	17.4796748	0.31	SLOUGH	SLOUGH
44	4417601	52	Male	NO	NO	NO	NO	YES	PRF	4.27	14.3	3.59	10.1	4.2	29.37062937	0.3	SLOUGH	SLOUGH
45	6390081	56	Male	YES	NO	NO	NO	YES	DRF	6.63	34.5	5.53	24	10.5	30.43478261	0.75	SLOUGH	GRANULATION TISSUE
46	1139736	51	Male	NO	YES	NO	NO	YES	PRF	5.9	27.34	4.59	16.56	10.78	39.42940746	0.77	GRANULATION TISSUE	GRANULATION TISSUE
47	1199203	48	Female	YES	YES	YES	NO	YES	DRF	6.74	35.63	5.17	21	14.63	41.06090373	1.04	GRANULATION TISSUE	GRANULATION TISSUE
48	7096596	60	Female	NO	NO	YES	NO	YES	DLF	6.15	29.66	5.27	21.84	7.82	26.36547539	0.56	GRANULATION TISSUE	GRANULATION TISSUE
49	6792266	56	Female	NO	NO	YES	NO	YES	DLF	5.9	27.34	4.59	16.56	10.78	39.42940746	0.77	GRANULATION TISSUE	GRANULATION TISSUE
50	1199675	58	Female	NO	NO	NO	NO	YES	DLF	6.6	34.2	5.29	22	12.2	35.67251	0.73	GRANULATION TISSUE	GRANULATION TISSUE
51	66232254	50	Male	NO	NO	YES	NO	YES	PLF	6.72	35.46	6.37	31.82	3.64	10.26509	0.26	GRANULATION TISSUE	GRANULATION TISSUE
52	1201805	38	Male	YES	NO	NO	NO	YES	PLF	6.32	31.34	6.01	28.35	2.99	9.540523	0.21	GRANULATION TISSUE	SLOUGH
53	1199098	29	Male	YES	YES	YES	NO	YES	DRF	5.84	26.81	5.49	23.66	3.15	11.74935	0.23	GRANULATION TISSUE	GRANULATION TISSUE
54	6530851	55	Male	NO	YES	YES	NO	YES	PRF	6.72	35.47	6.25	30.7	4.77	13.44798	0.34	GRANULATION TISSUE	GRANULATION TISSUE
55	1054125	48	Male	NO	NO	YES	NO	YES	PLF	3.85	11.65	3.53	9.8	1.85	15.87983	0.13	GRANULATION TISSUE	SLOUGH
56	1051486	43	Female	NO	NO	NO	NO	YES	DRF	4.17	13.67	3.88	11.8	1.87	13.67959	0.13	GRANULATION TISSUE	GRANULATION TISSUE
57	1156769	45	Male	NO	NO	NO	NO	YES	DRF	6.72	35.23	6.35	31.67	3.56	10.10502	0.25	GRANULATION TISSUE	GRANULATION TISSUE

58	6475567	60	Male	NO	NO	YES	NO	YES	DLF	4.04	12.8	3.51	9.68	3.12	24.375	0.22	GRANULATION TISSUE	GRANULATION TISSUE
59	6188538	55	Male	NO	NO	NO	NO	YES	DLF	6.08	29	5.69	25.37	3.63	12.51724	0.26	GRANULATION TISSUE	GRANULATION TISSUE
60	6326114	54	Male	YES	YES	NO	NO	YES	PRF	5.84	26.78	5.46	23.45	3.33	12.43465	0.24	GRANULATION TISSUE	GRANULATION TISSUE
61	1200218	50	Male	YES	YES	YES	NO	YES	DLF	5.68	25.34	5.29	21.99	3.35	13.22021	0.24	GRANULATION TISSUE	GRANULATION TISSUE
62	1176857	39	Male	YES	NO	YES	NO	YES	HRF	6.4	32.18	6.07	28.94	3.24	10.06837	0.23	SLOUGH	GRANULATION TISSUE
63	1166912	48	Male	NO	NO	YES	NO	YES	DRF	4.62	16.78	4.25	14.16	2.62	15.61383	0.19	GRANULATION TISSUE	GRANULATION TISSUE
64	4417601	47	Male	NO	NO	YES	NO	YES	HLF	3.53	9.8	3.23	8.2	1.6	16.32653	0.11	GRANULATION TISSUE	SLOUGH
65	6390081	42	Male	YES	YES	NO	NO	YES	DRF	4.94	19.2	3.76	11.1	8.1	42.1875	0.58	GRANULATION TISSUE	SLOUGH
66	1139736	57	Female	NO	NO	YES	NO	YES	DLF	5.48	23.56	5.21	21.34	2.22	9.42275	0.16	GRANULATION TISSUE	GRANULATION TISSUE
67	1199203	29	Male	NO	YES	NO	NO	YES	DRF	4.33	14.72	4	12.56	2.16	14.67391	0.15	GRANULATION TISSUE	GRANULATION TISSUE
68	7096596	30	Male	YES	NO	YES	NO	YES	PRF	6.36	31.8	5.96	27.91	3.89	12.2327	0.28	GRANULATION TISSUE	GRANULATION TISSUE
69	6792266	55	Male	YES	YES	NO	NO	YES	PLF	5.71	25.6	5.4	22.86	2.74	10.70313	0.2	GRANULATION TISSUE	GRANULATION TISSUE
70	1199675	57	Male	YES	NO	YES	NO	YES	DLF	5	19.67	4.76	17.77	1.9	9.65938	0.14	GRANULATION TISSUE	GRANULATION TISSUE
71	1191397	49	Female	NO	NO	YES	NO	YES	DRF	6.5	33.18	6.12	29.42	3.76	11.33213	0.27	SLOUGH	GRANULATION TISSUE
72	6813830	41	Female	NO	NO	YES	NO	YES	HRF	6.64	34.67	6.15	29.72	4.95	14.27747	0.35	SLOUGH	GRANULATION TISSUE
73	1196671	44	Male	NO	YES	YES	NO	YES	PRF	5.33	22.34	4.89	18.79	3.55	15.89078	0.25	GRANULATION TISSUE	GRANULATION TISSUE
74	1187787	37	Male	YES	NO	YES	NO	YES	DLF	6.6	34.26	6.15	29.66	4.6	13.42674	0.33	GRANULATION TISSUE	GRANULATION TISSUE
75	10052289	56	Female	NO	NO	YES	NO	YES	DRF	5.64	25	5.14	20.78	4.22	16.88	0.3	GRANULATION TISSUE	SLOUGH
76	10047365	51	Female	NO	NO	YES	NO	YES	DRF	5.83	26.68	5.55	24.23	2.45	9.182909	0.18	GRANULATION TISSUE	GRANULATION TISSUE
77	1171070	40	Female	NO	YES	YES	NO	YES	DRF	6.25	30.65	5.94	27.67	2.98	9.722675	0.21	SLOUGH	GRANULATION TISSUE
78	1164818	44	Male	YES	NO	YES	NO	YES	DLF	3.85	11.65	3	7.07	4.58	39.3	0.33	SLOUGH	GRANULATION TISSUE
79	1163539	49	Female	NO	NO	NO	NO	YES	PRF	6.72	35.46	6.33	31.47	3.99	11.25212	0.29	GRANULATION TISSUE	GRANULATION TISSUE
80	1209047	38	Male	YES	NO	NO	NO	YES	DLF	5.94	27.7	5.45	23.3	4.4	15.88448	1.03	GRANULATION TISSUE	SLOUGH
81	1208506	33	Female	NO	NO	YES	NO	YES	DRF	6.63	34.5	6.3	31.2	3.3	9.565217	0.24	GRANULATION TISSUE	GRANULATION TISSUE
82	1204815	55	Female	YES	YES	YES	NO	YES	PLF	5.98	28.1	5.29	22	12.2	35.67251462	0.73	GRANULATION TISSUE	GRANULATION TISSUE