

**FUNCTIONAL OUTCOME FOLLOWING ARTHROSCOPIC
DEBRIDEMENT WITH MICROFRACTURE AND PLATELET RICH
PLASMA INJECTION IN OSTEOARTHRITIS OF KNEE-A
PROSPECTIVE STUDY**

By

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**DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF
HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA**

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IN
ORTHOPAEDICS**

Under the Guidance of

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ABSTRACT

Background: Surgical treatment for OA of the knee involves debridement, lavage, with microfracture to enhance chondral resurfacing by providing a suitable environment for tissue regeneration. Platelet-rich plasma (PRP) is known to stimulate the proliferation of chondrocytes. Combining microfracture with PRP injections helps in promoting early clinical improvement, and this study aims to assess the functional outcomes when all three techniques are used simultaneously.

Material and Methods: A prospective, observational and hospital-based conducted at R. L. Jalappa Hospital and Research Centre, SDUMC, Tamaka on patients with OA of the knee from November 2018 to November 2020. Clinical data is collected and evaluated with pre-procedure and post-procedure WOMAC and VAS scoring.

Results: 74.29% had Kellegren-Lawrence grade III knee OA, and 25.71% had grade II knee OA. Patients are evaluated using WOMAC, VAS SCORE for levels of pain and knee function prior to the procedure, and after 1 month, 3 months and 6-month post-procedure. It is observed that 68.57% of the study population had good VAS outcome while 31.43% had a poor VAS outcome. WOMAC score, there is a statistically significant improvement ($p < 0.001$) with a decrease in the WOMAC score from pre-op 67.11 ± 8.73 to 50.14 ± 9.99 at 1 month, and 40.83 ± 7.8 at 3 months and further reduced to 31.66 ± 5.28 at 6 months.

Conclusion: The study concludes that intra-articular PRP injection after debridement and microfracture has more benefit in pain relief and functional improvement, and it also prolongs the treatment efficacy of microfracture in patients with symptomatic knee OA.



Keywords: Osteoarthritis, Knee, debridement, lavage, microfracture, Steadman's, protein-rich plasma rich, WOMAC, VAS

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LIST OF ABBREVIATIONS

GLOSSARY	ABBREVIATIONS
AAOS	American academy of Orthopedics surgeons
ACL	Anterior cruciate Ligament
ACP	Autologous conditioned plasma
ACR	American college of rheumatology
ADL	Activities of daily living
CCT	Controlled clinical trials
ECM	Extracellular matrix
HA	Hyaluronic acid
LCL	Lateral collateral Ligament
LP-PRP	Leukocyte-poor platelet-rich plasma
MCL	Medial collateral Ligament
MSCs	Mesenchymal stem cells
NSAIDs	Non-steroidal anti-inflammatory drugs
OA	Osteoarthritis
OAI	Osteoarthritis initiative
OARSI	Osteoarthritis research society international
PCL	Posterior cruciate Ligament
PFJ	Patellofemoral joint
PMN	Polymorphonuclear
PRP	Platelet-rich plasma
QoL	Quality of life
RTS	Return to sport
TFJ	Tibiofemoral joint
VAS	Visual analogue scale
WBC	White blood cell
WOMAC	Western Ontario and McMaster osteoarthritis index

INTRODUCTION



INTRODUCTION:

Osteoarthritis (OA) is a leading cause of musculoskeletal pain worldwide, and the knee is one of the most commonly affected joints.¹ In 1886, English physician, John Kent Spender, coined the term Osteoarthritis. OA is caused when the hyaline cartilage that is responsible for the frictionless joint movement is injured and degenerated. Hyaline cartilage protects the bone from excessive load and trauma by dissipating the forces produced during movement.² Cartilage defects of the knee cause significant pain and disability. These cartilage defects have limited healing capacity on their own as the cartilage is avascular and has a hypocellular composition.³ Lack of cure for OA has shifted the treatment focus on providing symptomatic relief to the patients by way of reducing the pain and disability. The conservative treatment options mainly focus on maintaining and improving joint mobility.⁴ Surgical intervention is considered depending on the degree of symptoms, stiffness of the knee, pain, patient's age, level of physical activity, and comorbidities.⁵ Arthroscopic procedures for osteoarthritis of the knee include lavage, partial meniscectomy, chondroplasty, synovectomy, removal of loose body, removal of offending osteophytes, and adhesiolysis. These procedures are performed in a proper combination depending on the type of the articular lesion.⁶

Joint space narrowing, osteophytes, etc. noted on radiological films alone do not justify surgical intervention, which is indicated only in combination with relevant symptoms. The prevalence of knee OA from the epidemiological studies vary widely depending on the case definition; the population sampled and the joint(s) involved.⁷ Notably, more than half those with knee OA are <65 years of age.⁸ Overall prevalence of knee OA in India was found to be 28.7%.⁹ A community based cross-sectional study using Kellgren and Lawrence scale, showed the prevalence of 28.7% of OA in the overall sample. City wise estimates vary

slightly with Agra having 35.5%, Bangalore 26.6%, Kolkata 33.7%, Dehradun 27.2% and Pune 21.7%.¹⁰ OA may also negatively impact people's mental health and people with lower limb OA are more prone to developing depressive symptoms than those without the disease.¹¹

Arthroscopic debridement involves lavage to wash out all debris, removal of loose bodies, chondroplasty of unstable chondral flaps, partial meniscectomy and synovectomy of degenerated menisci and ligaments, removal of offending osteophytes, adhesiolysis, and joint insufflation. These procedures are helpful for short-term symptom relief in early arthritis, but ineffective for halting the progression of the disorder. In patients with less than one year's duration OA of the knee, debridement provided better result compared to those with longer duration of symptoms.¹² A prospective study of arthroscopic debridement procedures reported 75% of patients had good or excellent results.¹³ The evidence supporting arthroscopic debridement was somewhat better, but the improvement was frequently of short duration and studies showed that orthopedic surgeons were actually poor at predicting which patients would improve.¹⁴

With the advent of surgical techniques using tissue engineering and biomaterials in the past two decades, more surgical treatment options such as marrow stimulation techniques have come into effect. Steadman in 1997 developed the "microfracture" technique to enhance chondral resurfacing by providing a suitable environment for tissue regeneration. This procedure involves penetration of the subchondral bone plate with an arthroscopic awl to allow bone marrow cells to repopulate defects, filling them with repair tissue.¹⁵ At an average 11.3-year follow-up, 80% of the patients aged 45 years and younger reported significant improvement after microfracture, with patients younger than 35 years showing the most improvement.¹⁶ Results of microfracture for the treatment of full-thickness chondral lesions

with a mean size of 2.8 cm² among National Football League players showed excellent results with three-fourths of them being able to return to active play following season for an average of almost 5 additional seasons.¹⁷ Biopsies at two years after microfracture in patients with single symptomatic cartilage defect on the femoral condyle showed approximately 10% had hyaline cartilage, with the majority having predominantly fibrocartilage.¹⁸ Lesions less than 4 cm² were likely to respond better to microfracture in the first 2 years. Systematic reviews have similarly demonstrated a clear improvement in knee function at 24 months after MF but inconclusive durability and treatment failure beyond 5 years.^{19,20} Another study demonstrated that microfracture in patients with early osteoarthritis with focal full-thickness cartilage defects did not provide any additional benefit to meniscectomy.²¹

More recently, another blood-derived product, platelet-rich plasma (PRP), has gained increasing attention. Due to the growth factors stored in platelet α -granules, found to regulate articular cartilage metabolism²², platelet concentrates have been proposed as a simple and minimally invasive method for injection of a high concentrate of autologous growth factors and other bioactive molecules in physiological proportions.²³ PRP is thought to stimulate the proliferation of chondrocytes and the differentiation of mesenchymal cells of the subchondral bone into the chondrogenic line. Combining microfracture with PRP injections helps in promoting early clinical improvement as PRP is also thought to have an anti-inflammatory action on the synovial membrane.²⁴ Many of aberrant processes associated with knee OA can be altered by using PRP, such as inflammation, the balance between cartilage anabolism and catabolism, and angiogenesis.²⁵

Patients with OA in the joints have different microenvironment based on their disease stage, and hence patients exhibit different therapeutic effects of PRP from the specific milieu

present in the joint.²⁵ Beside an extensive literature with positive reports on PRP use, only a few high-level studies have been currently published. Existing RCTs present overall support to PRP injections for knee OA treatment showing an early beneficial effect slightly superior to what was obtained with viscosupplementation.

NEED OF THE STUDY:

Arthritis of the knee is a degenerative, wear and tear type of articular cartilage and is seen most often in people above 50 years of age, and generally more common in women than men. The prevalence increases dramatically with age. It is the leading cause of significant morbidity, loss of a job, early retirement. Surgical treatment for symptomatic OA of the knee involves arthroscopic debridement, lavage, chondroplasty, synovectomy, removal of loose body, removal of offending osteophytes, and adhesiolysis. Arthroscopic debridement consists of tidal irrigation to wash out all debris, i.e. unstable chondral flaps, redundant synovial, degenerated menisci and ligaments, loose bodies and osteophytes. Microfracture is the penetration of the subchondral bone plate to allow bone marrow cells to repopulate defects, filling them with repair tissue which contains both type 1 and types 2 collagen in the fibrocartilage tissue. Platelet-rich plasma is an autologous blood product; there is no risk of immunological reactions and disease transfer. The above-mentioned techniques have both merits and demerits. There are studies comparing the efficacy of PRP against hyaluronic injections or placebo. Limited data is available where all the three techniques are used simultaneously. Thus, in this study, we intend to assess the functional outcomes of arthroscopic debridement with mild to moderate OA of the knee using Western Ontario And McMaster Osteoarthritis Index (WOMAC) score and visual analogue scale (VAS). We also intend to assess whether the said technique might help in avoiding the need for arthroplasty.

OBJECTIVES



AIM AND OBJECTIVES:

AIM:

- ❖ To assess the functional outcomes of arthroscopic debridement with micro-fracture with PRP injection in mild to moderate OA of the knee using Western Ontario and McMaster Universities Score (WOMAC) and visual analogue scale (VAS).

OBJECTIVES:

- ❖ To assess the pain using the Visual Analogue Scale prior to surgery.
- ❖ To evaluate the functional outcomes of arthroscopic debridement with microfracture and platelet-rich plasma injection on a patient with mild to moderate osteoarthritis of the knee using the WOMAC score and Visual Analog Scale.

RELEVANT ANATOMY

STRUCTURAL ANATOMY OF KNEE:

The knee is a complex modified hinge joint and has a maximum range of movement about the sagittal plane both in flexion and extension. In the frontal plane, it has varus and valgus rotation. In the transverse plane, at the end of the flexion, it facilitates the medial rotation, and at the terminal extension of the knee, it allows lateral rotation in the transverse plane. Knee joint maintains stability and control during a variety of loading situations.

There are two bony articulations in the joint, one between the femur and tibia which bears most of the body weight, and the second articulation is between the patella and femur which is responsible for a frictionless transfer over the knee of the forces generated by contraction of the quadriceps femoris muscle.²⁶ There are two main joints of the knee, namely the femorotibial joint and the patellofemoral joint. These two joints allow the knee to move in the sagittal, transverse, and frontal planes. They also facilitate a range of motion of six degrees with flexion and extension in the sagittal planes; internal and external rotation in the transverse plane; varus and valgus stress in the frontal plane. As the knee is positioned between the femur and tibia, the two longest lever arms of the body, and is responsible for most of the weight-bearing, it is susceptible to injuries.^{27,28}

The muscles, bones, ligaments, cartilage, synovial tissue, synovial fluid and other connective tissues maintain the anatomical function and stability of the knee. The knee functions with the use of the four main stabilizing ligaments, the anterior cruciate (ACL), posterior cruciate (PCL), medial collateral (MCL), and lateral collateral (LCL). The ACL is the ligament that connects from the lateral condyle of the femur to the inter condyloid eminence of the tibia.

ACL helps in preventing the anterior translation of the tibia on the femur. The PCL connects from the medial condyle of the femur to the posterior intercondylar area of the tibia. The function of PCL is to prevent forward displacement of the femur on the tibia.²⁹

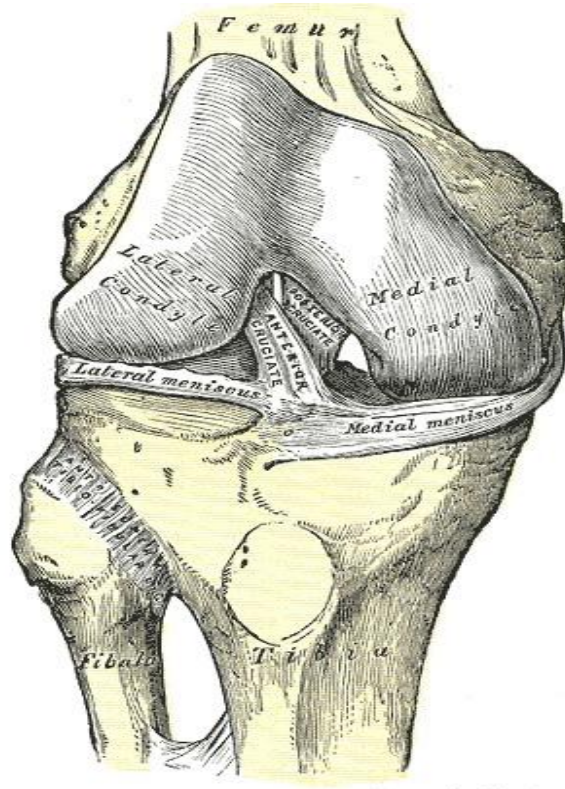


Figure 1: Interior Ligaments of the Right Knee, Anterior superior Tibiofibular Ligament, Anterior Cruciate, Posterior Cruciate, Medial Meniscus, Lateral Meniscus, Tibia, Fibula, Femur. Contributed by Gray's Anatomy Plates.²⁹

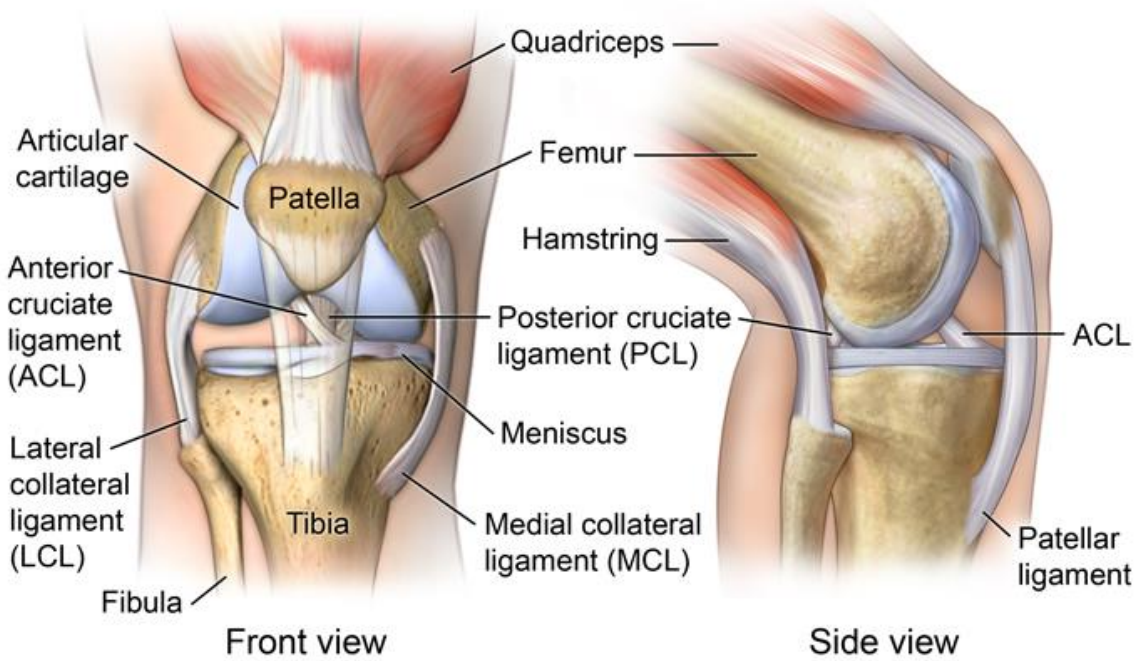


Figure 2: Comprehensive Orthopedics Anatomy of Knee³⁰

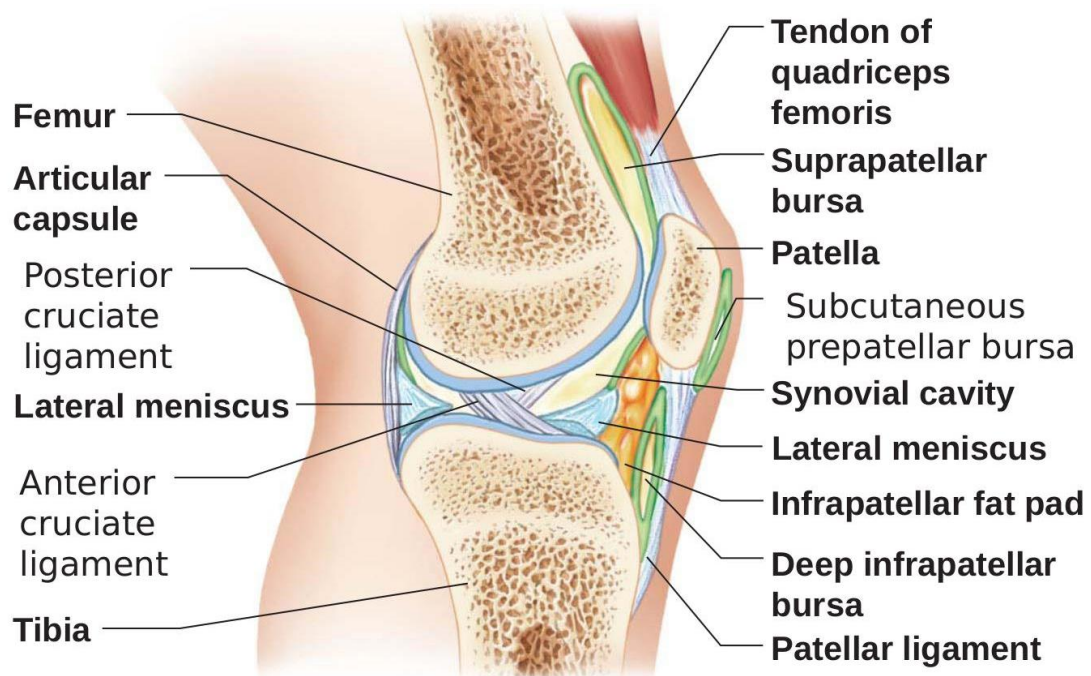


Figure 3: The knee joint.³¹

Femur Articular capsule Posterior cruciate ligament Lateral meniscus Anterior cruciate ligament Tibia Tendon of quadriceps femoris Suprapatellar bursa Patella Subcutaneous prepatellar bursa Synovial cavity Lateral meniscus Infrapatellar fat pad Deep infrapatellar bursa Patellar ligament Sagittal section through the right knee joint.

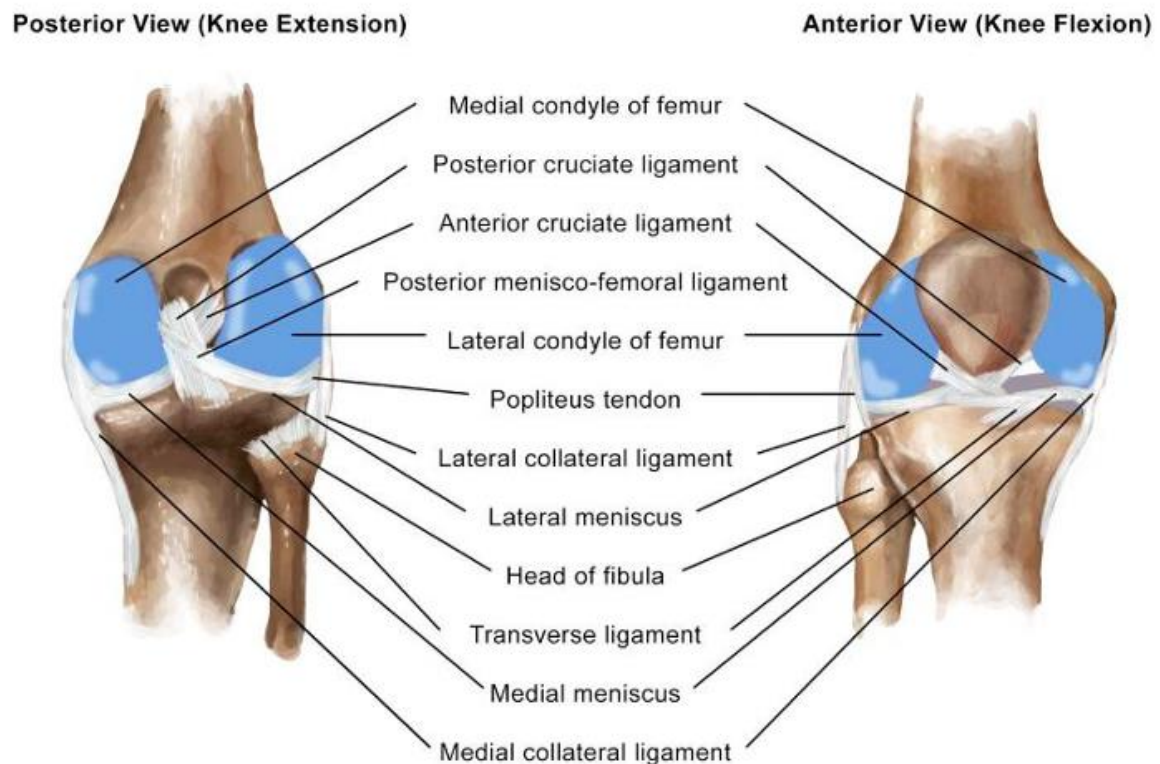


Figure 4: Knee Anatomy Anterior View and Posterior View.³²

In this image, medial condyle of the femur, posterior cruciate ligament, anterior cruciate ligament, posterior menisco-femoral ligament, lateral condyle of the femur, popliteus tendon, lateral collateral ligament, lateral meniscus, head of the fibula, transverse ligament, medial meniscus, medial collateral ligament is marked.

The medial epicondyle of the femur is attached to the medial condyle of the tibia by MCL, which helps in preventing the valgus stress on the knee. Lateral epicondyle of the femur is attached to the head of the fibula by LCL, which prevents the varus stress on the knee. There are two separate fibrocartilage structures located between the articular surfaces of the tibia and femur called medial and lateral menisci. These menisci function as shock absorbers, static stabilizers, and friction reducers during articulation. The distal end of the femur, proximal end of the tibia, and patella constitute the bony structure of the knee. The patella is the largest sesamoid bone in the body. The patella attaches the quadriceps tendon to the patellar ligament and protects the anterior articular surface of the femoral portion of the knee. There are multiple bursas in the knee, which help in reducing the friction between structures of the knee.²⁹

SYNOVIAL MEMBRANE:

The synovial membrane lines the capsule and is attached to the margins of the articular surfaces. On the front and above the joint, it forms a pouch, which extends up beneath the quadriceps femoris muscle for three fingerbreadths above the patella, forming the suprapatellar bursa. At the back of the joint, the synovial membrane is prolonged downward on the deep surface of the tendon of the popliteus, forming the popliteal bursa. The synovial membrane is reflected forward from the posterior part of the capsule around the front of the cruciate ligaments. As a result, the cruciate ligaments lie behind the synovial cavity and are not bathed in synovial fluid.³²

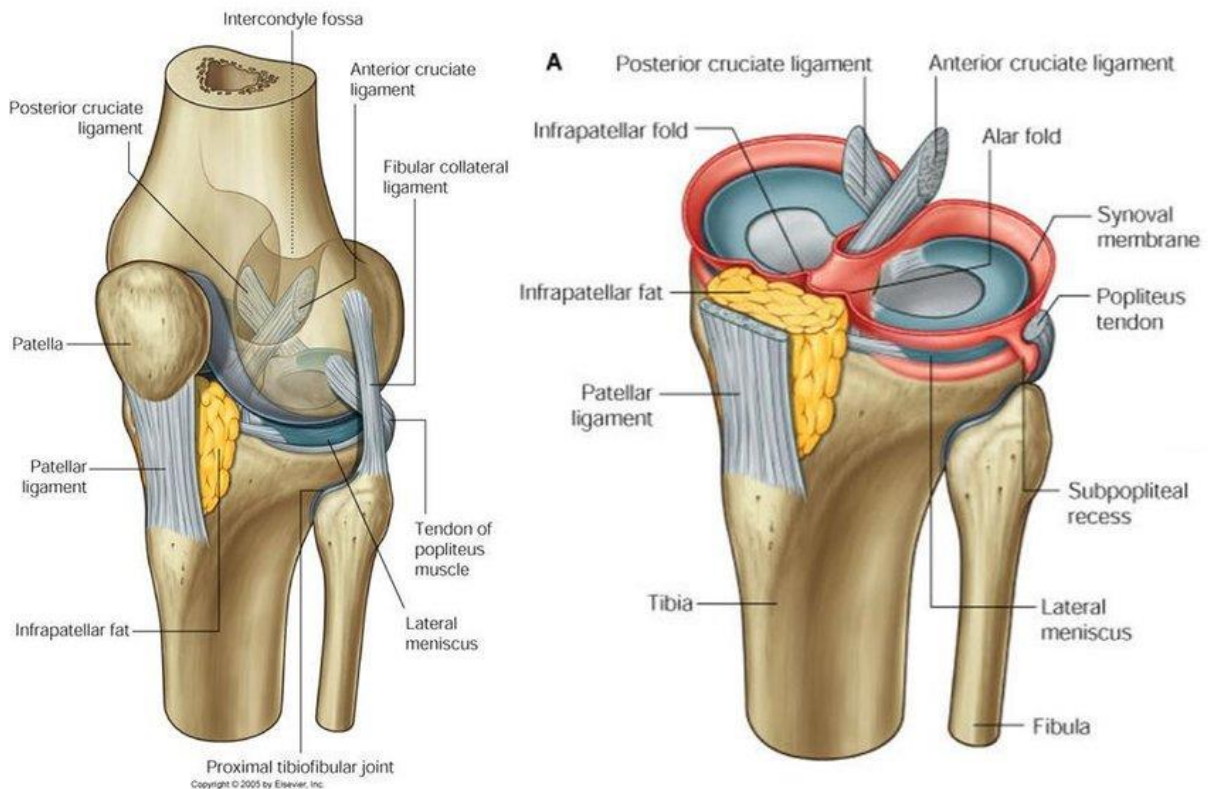


Figure 5: Synovial membrane.³⁴

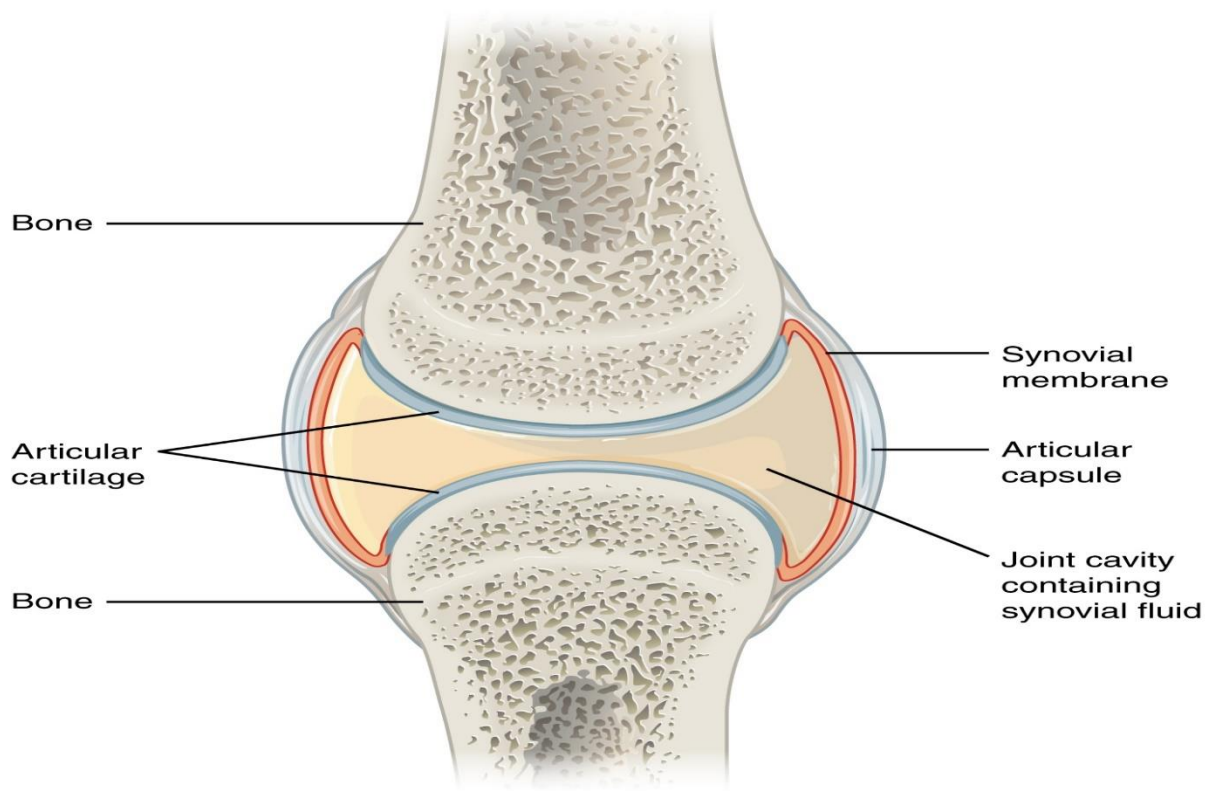


Figure 6: Synovial Joints.³⁵

Synovial joints allow for smooth movements between the adjacent bones. The joint is surrounded by an articular capsule that defines a joint cavity filled with synovial fluid. The articulating surfaces of the bones are covered by a thin layer of articular cartilage. Ligaments support the joint by holding the bones together and resisting excess or abnormal joint motions.

BURSAE RELATED TO THE KNEE JOINT:

The anterior bursae comprise of the suprapatellar bursa, the prepatellar bursa, the superficial infrapatellar bursa, the deep infrapatellar bursa. Posterior Bursae are the popliteal bursa and the semimembranosus bursa. The remaining four bursae are found related to the tendon of insertion of the biceps femoris, tendons of the sartorius, gracilis, and semitendinosus muscles,

beneath the lateral head of origin of the gastrocnemius muscle, and beneath the medial head of origin of the gastrocnemius muscle.³²

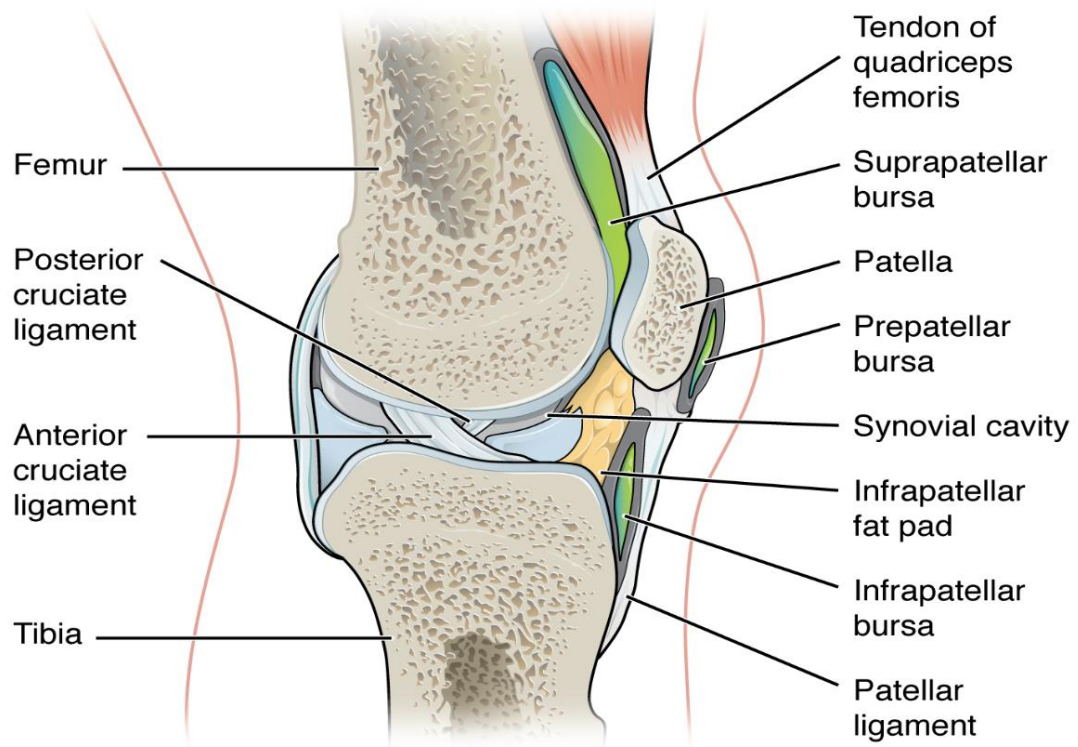


Figure 7: Bursae.³⁶

Bursae are fluid-filled sacs that serve to prevent friction between skin, muscle, or tendon and an underlying bone. Three major bursae and a fat pad are part of the complex joint that unites the femur and tibia of the leg.

ARTICULAR CARTILAGE:

Articular cartilage is the highly specialized connective tissue of diarthrodial joints. Its principal function is to provide a smooth, lubricated surface for articulation and to facilitate the transmission of loads with a low frictional coefficient. Articular cartilage is devoid of blood vessels, lymphatics, and nerves and is subject to a harsh biomechanical environment. Most important, articular cartilage has a limited capacity for intrinsic healing and repair. In this regard, the preservation and health of articular cartilage are paramount to joint health.³⁶

It is composed of a dense extracellular matrix (ECM) with a sparse distribution of highly specialized cells called chondrocytes. The ECM is principally composed of water, collagen, and proteoglycans, with other non-collagenous proteins and glycoproteins present in lesser amounts.³⁶ Along with collagen fiber ultrastructure and ECM, chondrocytes contribute to the various zones of articular cartilage—the superficial zone, the middle zone, the deep zone, and the calcified zone. Within each zone, 3 regions can be identified—the pericellular region, the territorial region, and the interterritorial region.

The main function of articular cartilage is to provide low friction articulation and transmission of the load to the underlying subchondral bone. It also provides creep and stress relaxation response. When there is constant load or deformation articular cartilage shows time-dependent behavior due to its viscoelastic nature.³⁶

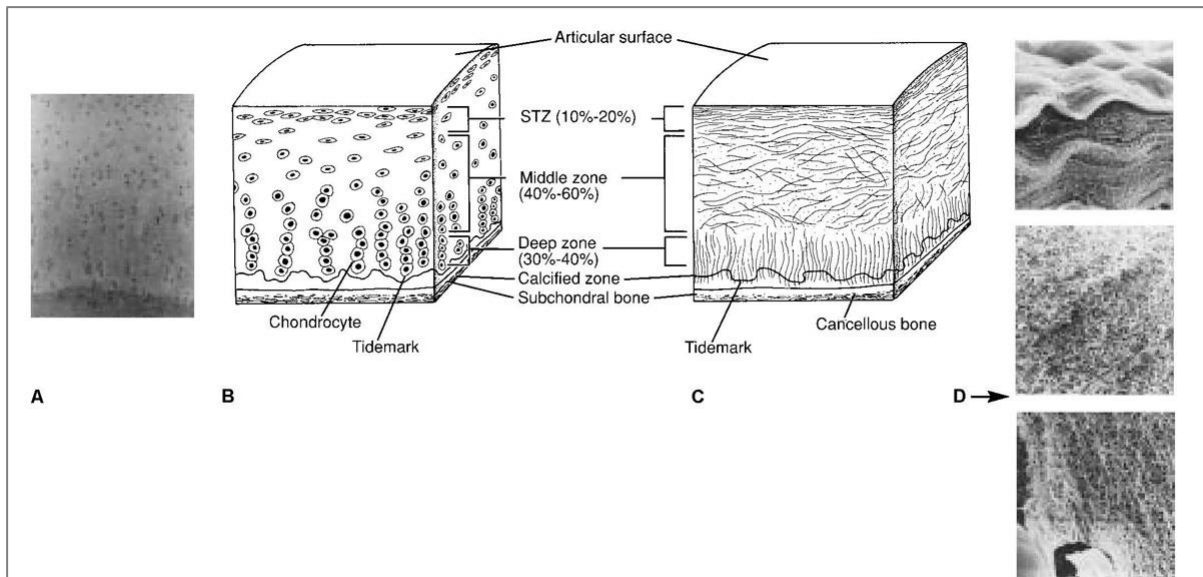


Figure 8: Structure of articular cartilage.³²

- A. Histologic section of cartilage from a young, healthy adult shows even safranin O staining and distribution of chondrocytes.
- B. Schematic diagram of chondrocyte organization in the three main zones of the uncalcified cartilage (STZ = superficial tangential zone), the tidemark, and the subchondral bone.
- C. Sagittal cross-sectional diagram of collagen fiber architecture shows the three salient zones of articular cartilage.
- D. Scanning electron micrographs depict arrangement of collagen in the three zones (top = STZ; center = middle zone; bottom = deep zone).

DEFINITION OF OSTEOARTHRITIS

Osteoarthritis (OA) is cartilage failure resulting in joint pain and loss of joint functions.³⁷ Symptomatic knee OA is due to the certain triggers which result in a molecular cascade, and this ultimately leads to irreversible damage to the articular cartilage. It is difficult to predict the clinical phenotype of the knee OA due to its variability. There is poor coordination between radiographic OA and knee pain, making it more difficult to diagnose knee OA.³⁸ As the knee joint is tri-compartmental, consisting of the patellofemoral joint (PFJ), medial and lateral tibiofemoral joint (TFJ), knee OA manifests in various possible patterns. Generally, knee OA is considered principally as a disorder of the TFJ, and radiographic investigations focused only on the anteroposterior X-ray, neglecting to explore the PFJ.³⁹ With the use of lateral and skyline X-rays, it became apparent that PFJ is also involved in the OA process and is one of the most commonly affected compartments. While just the presence of osteophytes cannot diagnose OA, it is observed that PFJ has a higher frequency of radiographic osteophytes compared with the TFJ compartment.³⁹

OA classification in the knee is most commonly done with radiographs using the 0–4 Kellgren Lawrence (KL) grading system:

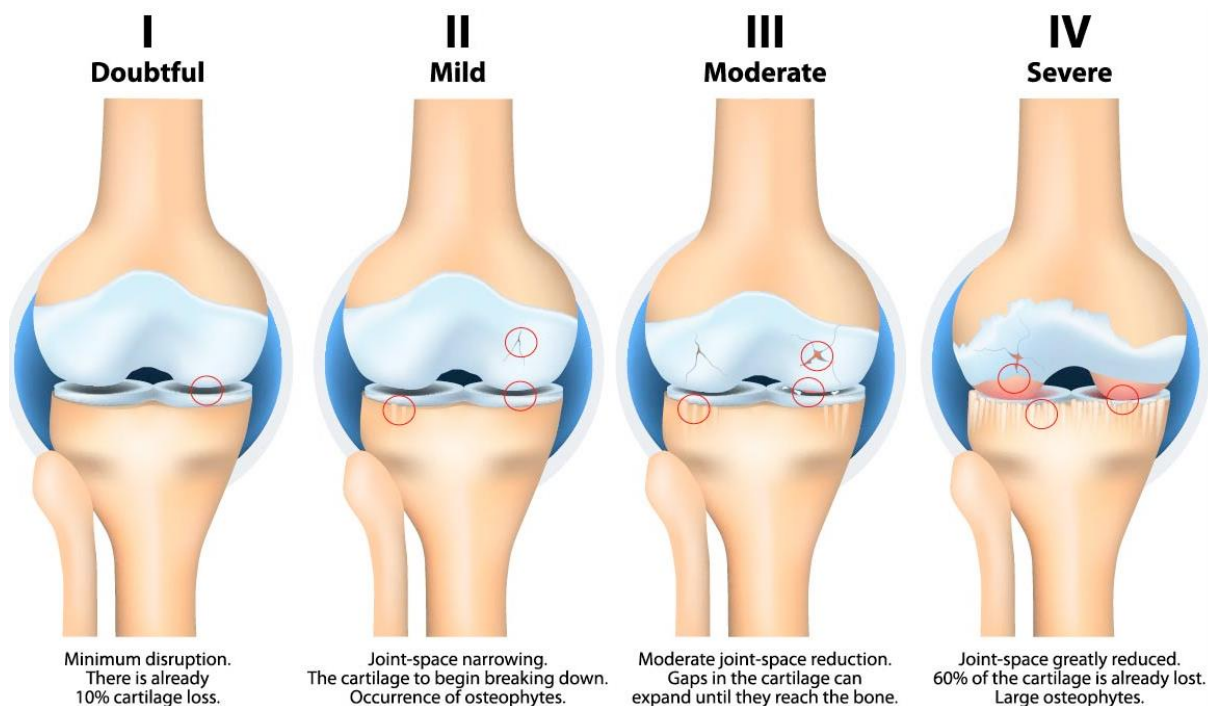


Figure 9: Stages of knee Osteoarthritis (OA).⁴¹

Kellgren and Lawrence criteria for assessment stage of osteoarthritis. The classifications are based on osteophyte formation and joint space narrowing.

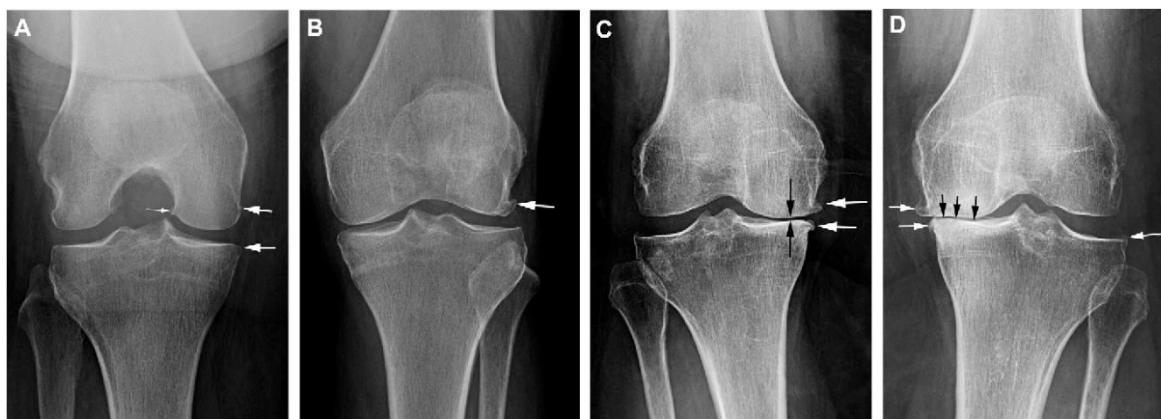


Figure 10: The Kellgren-Lawrence classification is a composite scale of OA severity, taking into account primarily the radiographic OA features of marginal osteophytes and joint space narrowing in the AP radiograph.⁴²

- A. Kellgren-Lawrence, grade 1. Minimal, equivocal osteophytes are observed at the medial joint margins (large arrows). Note that, so-called notch osteophytes at the center of the joint (small arrow) are not considered in the Kellgren-Lawrence scale.
- B. Kellgren-Lawrence grade 2 is characterized by the presence of at least one definite marginal osteophyte (arrow) without evidence of joint space narrowing.
- C. Kellgren-Lawrence grade 3 knees exhibit signs of definite joint space narrowing (black arrows) and marginal osteophytes (white arrows). The amount of joint space narrowing is not taken into account.
- D. Kellgren-Lawrence grade 4 is defined by bone-to-bone contact and complete obliteration of the joint space (black arrows). Note definite marginal osteophytes in addition (white arrows).

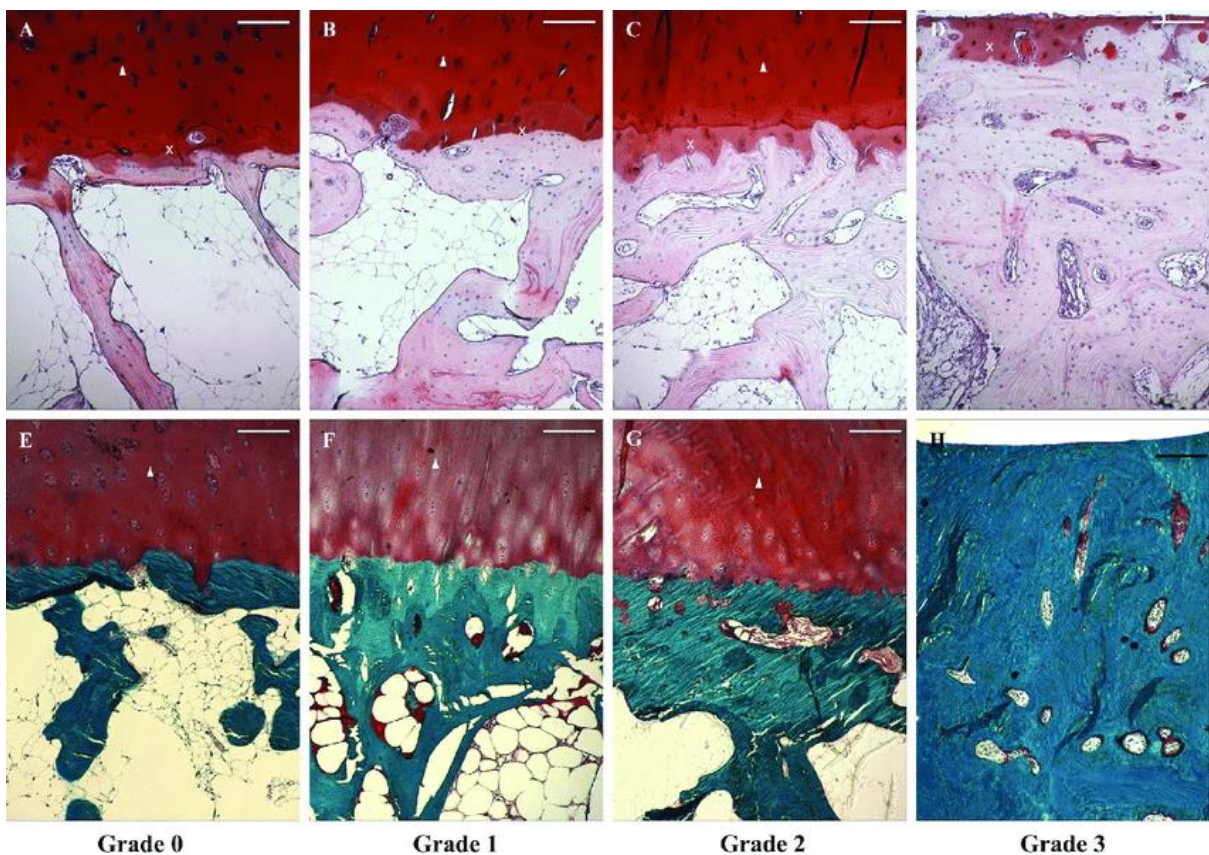


Figure 11: Safranin O (A-D) and Masson's trichrome stained histological samples of subchondral bone grades.⁴³

Images taken with a light microscope using a digital camera. The white triangle marks articular cartilage; the white cross shows calcified cartilage. (A and E) Black asterisks marks fenestrae in subchondral bone plate connecting the articular cartilage to bone marrow in grade 0 and (B and F) grade 1. (C and G) Fibrillation on the subchondral bone plate can be seen in grade 2. (D and H) Distinctive sclerosis and loss of articular cartilage mark late-stage OA in grade 3. Scale bar 200 μm .⁴²

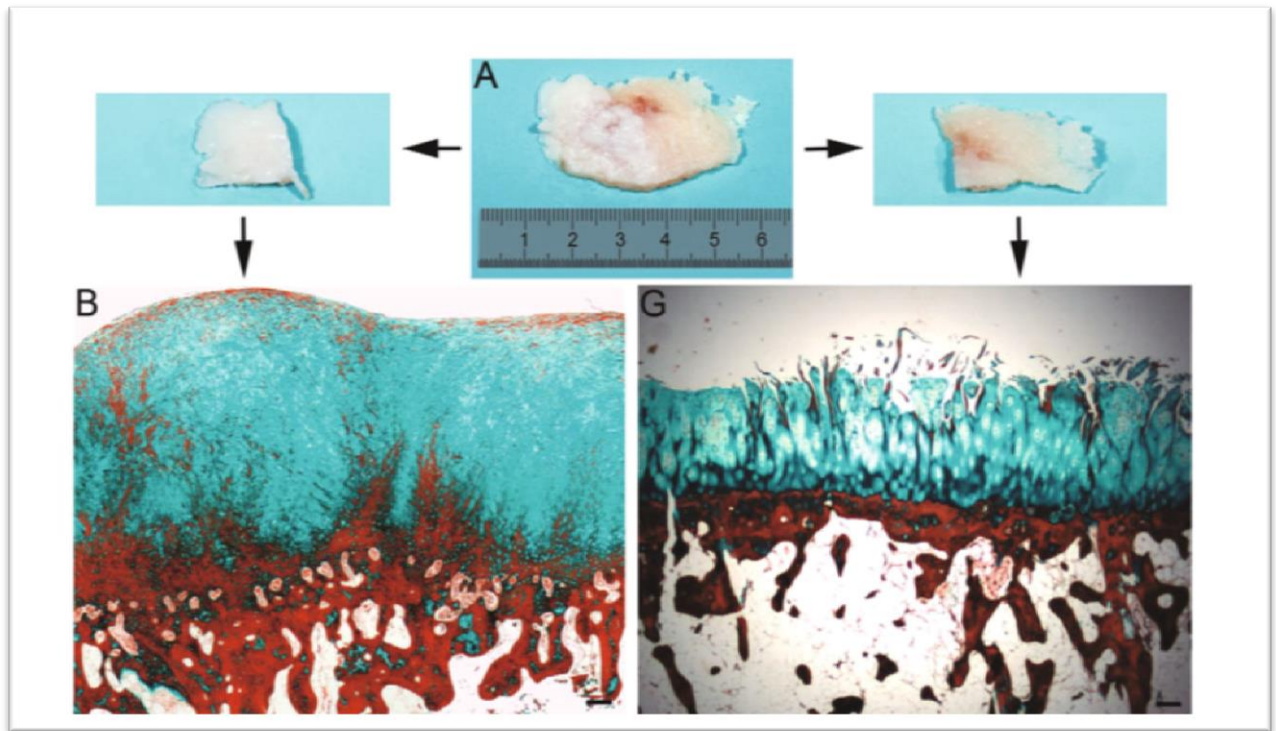


Figure 12: (A) Macroscopic morphology of the sample B and G show panoramic images of the sample (Masson's trichrome staining). comparison of a healthy (left) and OA knee joint (right).⁴⁴

EPIDEMIOLOGY

The prevalence of knee OA from the epidemiological studies vary widely because the estimates depend on the definition of cases (pathological, radiographic or clinical OA), the population sampled (primary versus tertiary care, developed versus developing countries), and the joint(s) involved.⁷ National Health Interview Survey estimated that 14 million people in the US have symptomatic knee OA, including >3 million racial/ethnic minorities.⁸ Notably, more than half those with knee OA are <65 years of age. Recent cohort and community-based studies have also measured the prevalence of OA of different joints in various communities in South America, Asia, and the Middle East.⁸ In a population-based study in Sweden, the greater risk for sick leave or disability among those working in female- or male-dominated job sectors was attributed to knee OA.⁴⁴ Overall prevalence of knee OA in India was found to be 28.7%.⁹

A community based cross-sectional study using Kellgren and Lawrence scale showed the prevalence of 28.7% of OA in the overall sample. City wise estimates vary slightly with Agra having 35.5%, Bangalore 26.6%, Kolkata 33.7%, Dehradun 27.2%, and Pune 21.7%. OA of the knee was seen to more prevalent among those using the western toilet at 42.1%, in sedentary people at 82.9%, in females and in obese.¹⁰ Besides affecting people's physical health, OA may also negatively impact people's mental health. Data from the Osteoarthritis Initiative (OAI) study demonstrated that those with lower limb OA are more prone to developing depressive symptoms than those without the disease.¹¹

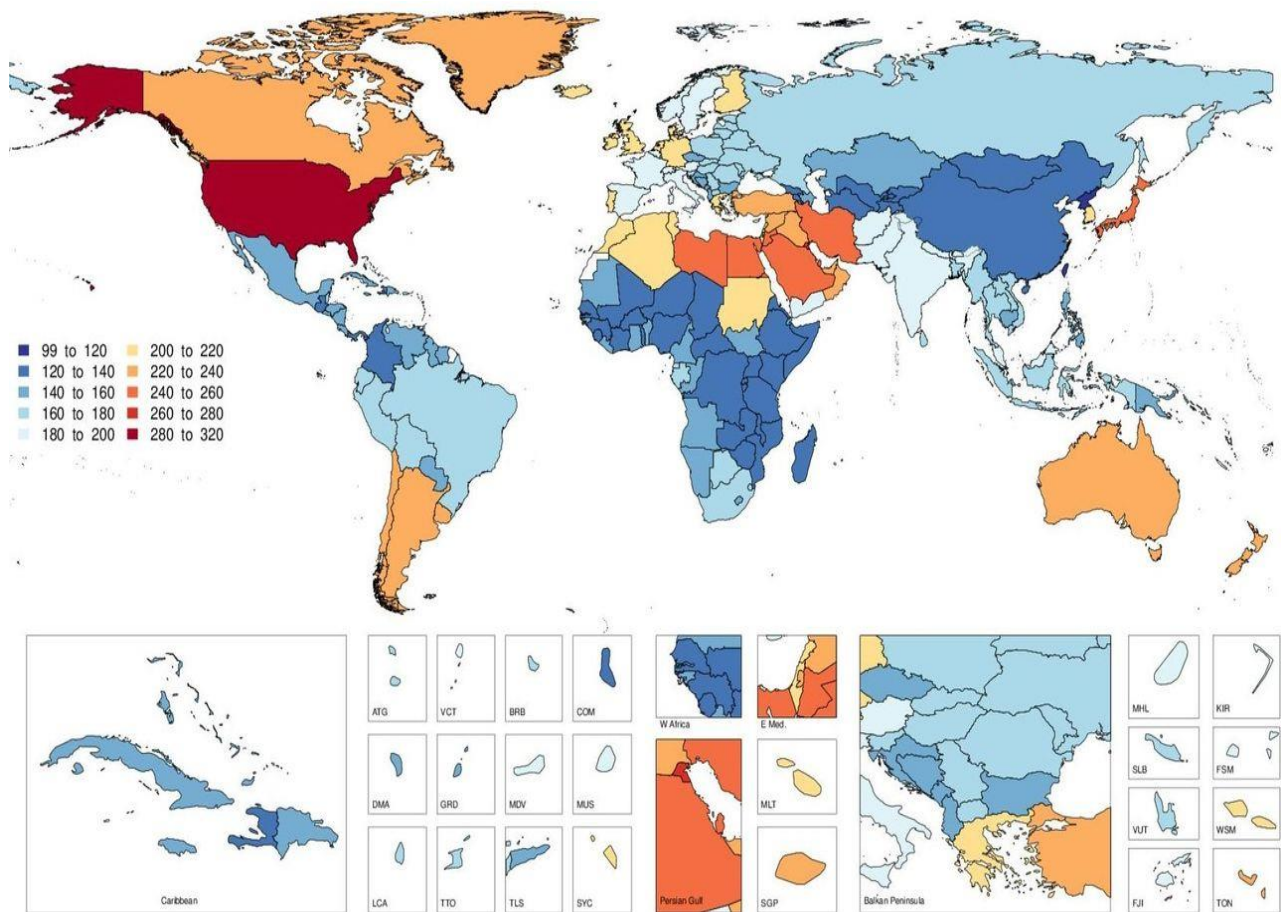


Figure 13: Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017.⁴⁵

ETIOLOGY

Sports participation, injury to the joints, obesity, and genetic susceptibility predispose adolescent athletes to the development of premature osteoarthritis. Previous knee trauma increases the risk of knee OA 3.86 times.⁴⁶ Mechanical forces exerted on the knee joint can lead to OA and one of the most modifiable risk factors as determined by body BMI. Female sex, lower educational levels, obesity, and poor muscular strength are associated with symptomatic disease and subsequent disability.⁴⁷ People who are occupied in work involving longer periods of squatting or kneeling have a two-fold risk of moderate to severe radiographic knee OA. Obesity alone or in patients with metabolic syndrome increases the risk of radiographic knee OA but has a lesser effect progression of knee OA.⁴⁸

Earlier OA was believed to be exclusively a degenerative disease of the cartilage, but recent evidence proves OA is a multifactorial entity with multiple causative factors like trauma, mechanical forces, inflammation, biochemical reactions, and metabolic derangements.⁴⁹ A key role in the pathophysiology of articular cartilage is played by cell/extracellular matrix (ECM) interactions, which are mediated by cell surface integrins. In a physiologic setting, integrins modulate cell/ECM signaling, essential for regulating growth and differentiation and maintaining cartilage homeostasis. During OA, abnormal integrin expression alters cell/ECM signaling and modifies chondrocyte synthesis, with the following imbalance of destructive cytokines over regulatory factors. IL-1, TNF- α and other pro-catabolic cytokines activate the enzymatic degradation of cartilage matrix and are not counterbalanced by the adequate synthesis of inhibitors. The main enzymes involved in ECM breakdown are metalloproteinases (MMPs), which are sequentially activated by an amplifying cascade. MMP activity is partially inhibited by the tissue inhibitors of MMPs (TIMPs), whose synthesis is

low compared with MMP production in OA cartilage. Intriguing is the role of growth factors such as TGF- β , IFG, BMP, NGF, and others, which do not simply repair the tissue damage induced by catabolic factors but play an important role in OA pathogenesis.⁵⁰

It became evident that the cartilaginous tissue is not the only one involved in the OA process. Cartilage tissue is avascular and is devoid of nerves and thus not capable of producing inflammation or pain by itself, at least on early stages of the disease. This points to other sources of pain which are considered to be mainly derived from the changes occurring in the non-cartilaginous components of the joint, like the joint capsule, synovium, subchondral bone, ligaments, and peri-articular muscles.⁴⁹ With the advancement of OA, the joint capsule, synovium subchondral bone, ligaments and peri-articular muscles get affected, and changes including bone remodeling, osteophyte formation, weakening of periarticular muscles, laxity of ligaments, and synovial effusion can become evident.

There is an ongoing debate as to the role of inflammation in OA as to whether the inflammatory reaction is triggering the OA changes or the inflammation is secondary to the OA changes.⁴⁹ The inflammation in OA is different from inflammatory arthritis, where it is chronic and low-grade inflammation with the involvement of innate immune mechanisms. Infiltration of inflammatory cells into the synovium called synovitis is noticed commonly in OA and noticed from the early stages of the disease but is more prevalent towards the more advanced stages and can be related with severity.⁵² Multiple inflammatory mediators are found in synovial fluid in OA such as plasma proteins, prostaglandins, leukotrienes, cytokines, growth factors, nitric oxide, and complement components.⁵²

Prolonged and dysregulated degree of inflammation due to white blood cells as immune response also can lead to tissue destruction.⁵² The body also has protective molecular mechanisms including various growth factors (insulin-like, platelet-derived, fibroblast 18, and transforming growth factor B), which, unfortunately, are altered in patients with knee OA and may become harmful to the joint.^{52,53}

The structural, molecular, cellular and mechanical aging changes in articular cartilage increase the vulnerability of the tissue to degeneration. Articular cartilage aging does not cause osteoarthritis, but aging changes in articular cartilage increase the risk of articular cartilage degeneration and decrease the ability of joint tissues to prevent progression once degeneration begins.

Table 1: Shows differences between articular cartilage aging and articular cartilage degeneration responsible for osteoarthritis.⁵⁴

Parameter	AGING	DEGENERATION
Structural	• Localized fibrillation	• Fibrillation and fragmentation are extending to subchondral bone. • Loss of tissue (decreased cartilage thickness and complete loss of cartilage in some regions). • Formation of fibrocartilaginous repair tissue.
Mechanical	• Decreased tensile strength and stiffness in superficial layers.	• Increased permeability and loss of tensile and compressive stiffness and strength.
Cells	• Decreased chondrocyte density with skeletal growth. • Alteration in synthetic activity (smaller more variable aggrecans). • Decreased anabolic response to growth factors (IGF-I). • Decreased synthetic activity. • Decreased mitotic activity.	• The initial increase in synthetic and proliferative activity • Loss of chondrocytes. • Eventual decreased synthetic activity. • It increased degradative enzyme activity. • The appearance of fibroblast-like cells in regions of fibrocartilaginous repair tissue.

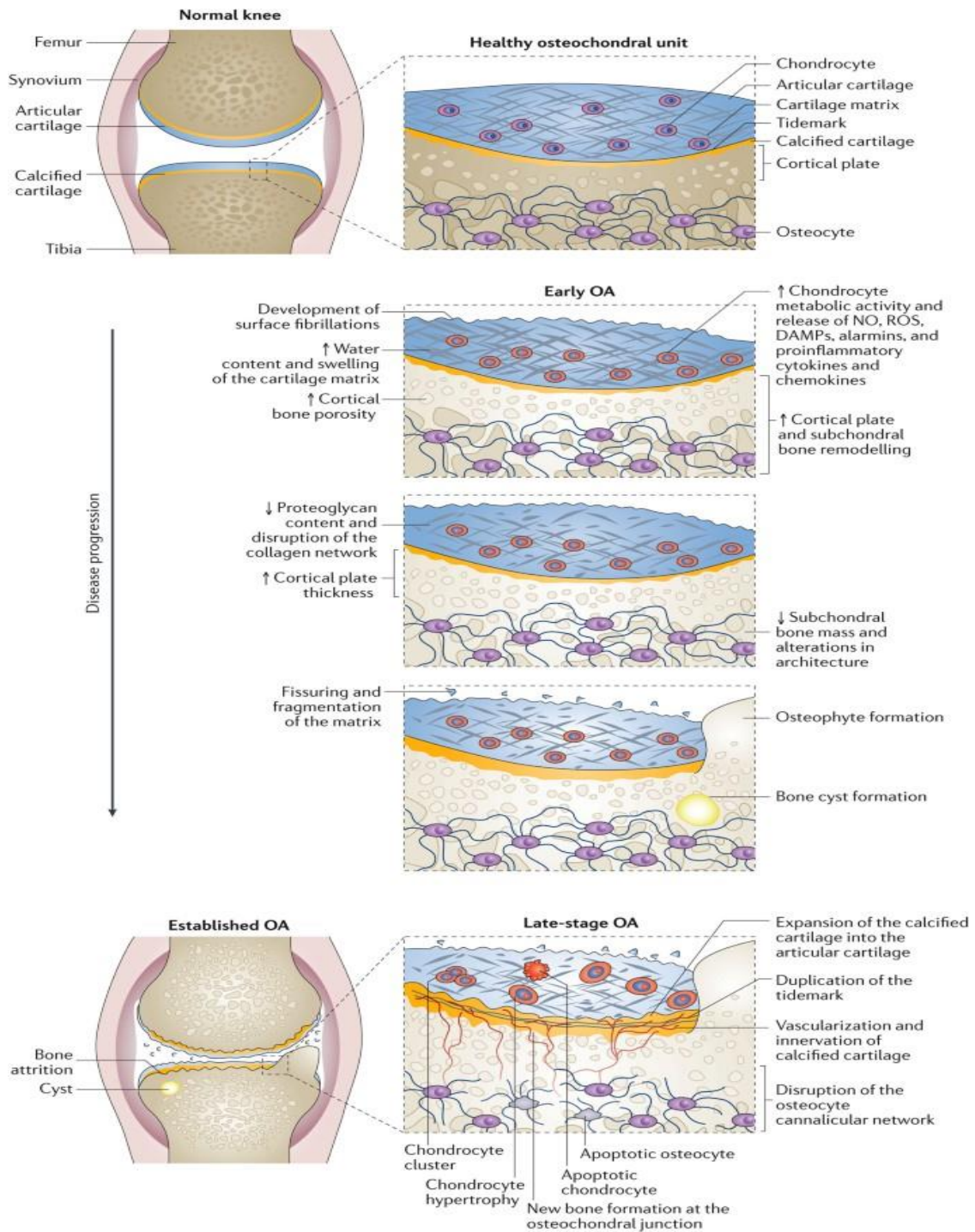


Figure 14: Changes in the osteochondral unit during osteoarthritis.⁵⁵

CLINICAL PRESENTATION

The most common symptom in patients with knee OA is mechanical knee pain. Overall, mechanical knee pain is a pain that is initiated or increased with knee activity/exercise and finished or decreased with the knee resting without morning stiffness or usually along with morning stiffness of less than 30 minutes. In the early phase of knee OA, pain can occur at the beginning of the movement. In a later phase, it can be presented during knee movement and eventually there will be persistent pain. After prolonged resting with flexed knee, pain and/or stiffness at the beginning of the movement of the knee is called “gelling pain” or “gelling phenomena”. The patients with knee OA can complain about thigh, hip, buttock or calf pain instead of knee pain.³⁸

Sometimes exacerbation or initiation of knee pain within cold weather or damp may be the only complaint of the patient. In physical examination, crepitus on knee motion is the most common finding. Bony tenderness and bony enlargement in joint line are the other findings. During a flare-up of osteoarthritis, the knee can show swelling due to joint effusion. This synovial fluid called “Hydrarthrosis” is clear with normal viscosity accompanied by White Blood Cell (WBC) count less than 2000/mm³ with less than 25% of Polymorphonuclear (PMN). It is usually a cold effusion, and sometimes it is accompanied by warmth and mild synovitis or synovial thickening; But moderate to significant knee synovitis and hot or red knee cannot be seen during its OA flare-up.³³

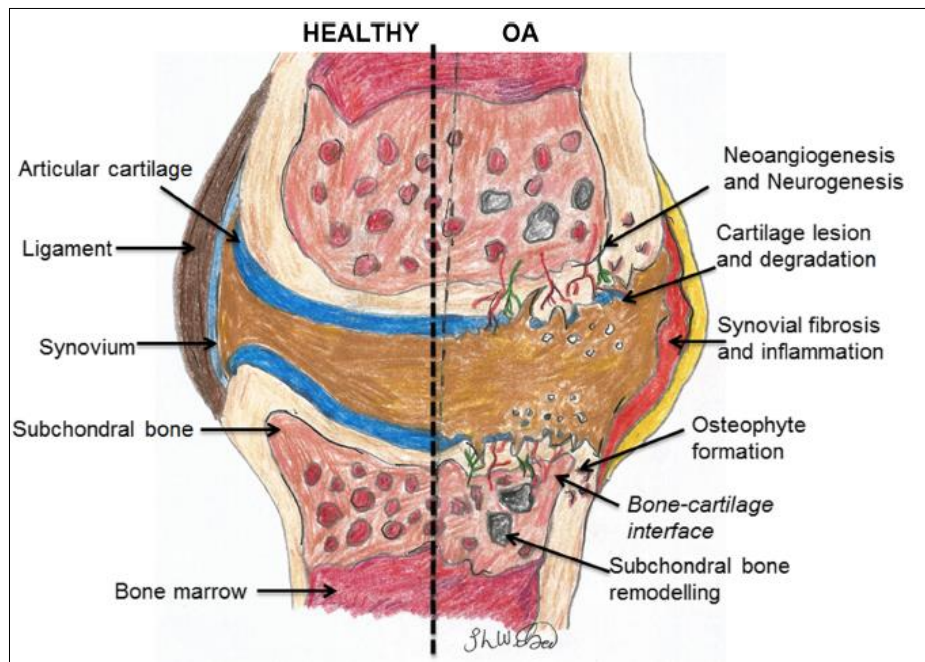


Figure 15: Comparison of a healthy (left) and OA knee joint (right).⁵⁶

DIAGNOSIS:

To diagnose knee OA, the main criteria are patient history, physical examination, and radiologic and laboratory findings.³⁹ The most common physical examination findings are a reduced range of motion, crepitus, and intra-articular joint swelling, also called an effusion.⁵⁷

Plain radiography has low sensitivity regarding knee OA during the early phase of the disease. The major X-Ray findings of OA are including:

- ❖ Narrowing of the joint space
- ❖ Eburnation or subchondral bone sclerosis
- ❖ Osteophytes and
- ❖ Subchondral bone cyst.

Among the above findings; osteophyte has the most specificity for OA.⁴⁹

Table 2: 1986 Criteria for classification of osteoarthritis (OA) of the knee.

CLINICAL AND LABORATORY	CLINICAL AND RADIOGRAPHIC	CLINICAL
Knee pain	Knee pain	Knee pain
+ at least 5 of 9	+ at least 1 of 4	+ at least 3 of 6
- Age > 50 years	- Age > 50 years	- Age > 50 years
- Stiffness < 30 minutes	- Stiffness < 30 minutes	- Stiffness < 30 minutes
- Crepitus	- Crepitus	- Crepitus
- Bony Tenderness	+ Osteophyte	- Bony Tenderness
- Bony enlargement		- Bony enlargement
- No palpable warmth		- No palpable warmth
- ESR < 40 mm / hour		
- RF < 1:40		
- SF OA		
92% sensitive	91% sensitive	95% sensitive
75% specific	86% specific	69% specific

*ESR = erythrocyte sedimentation rate (Westergren); RF = Rheumatoid factor; SF OA = synovial fluid signs of OA (clear, viscous, or white blood cell count < 2000/mm³).

Diagnostic criteria have been developed for osteoarthritis by Altman et al (1986).³⁹

The American College of Rheumatology (ACR) defined three classification criteria for knee OA, mostly used research purposes.³⁷ They are:

1. The ACR Clinical classification criteria of knee OA.
2. The ACR Clinical/Radiographic classification criteria of knee OA.
3. The ACR Clinical/Laboratory classification criteria of knee OA.

The ACR Clinical classification criteria of knee OA, which classifies knee OA based on knee pain in combination with at least three of the following six criteria:

- ❖ Age > 50 years old
- ❖ Morning stiffness < 30 minutes
- ❖ Crepitus on knee motion
- ❖ Bony tenderness
- ❖ Bony enlargement
- ❖ No palpable warmth

The ACR Clinical/Radiographic classification criteria of knee OA, according to which the presence of knee pain with at least one of the following three items along with osteophyte in knee X-Ray can classify the knee OA in the patients:

- ❖ Age > 50 years old
- ❖ Morning stiffness < 30 minutes
- ❖ Crepitus on knee motion

The ACR Clinical/Laboratory classification criteria of knee OA, per which the presence of knee pain along with at least 5 of the following 9 items can classify the knee OA in the patients:

- ❖ Age > 50 years old
- ❖ Morning stiffness < 30 minutes
- ❖ Crepitus on knee motion

- ❖ Bony tenderness
- ❖ Bony enlargement
- ❖ No palpable warmth
- ❖ ESR <40 mm/hr.
- ❖ RF < 140
- ❖ Synovial fluid is compatible with OA.

Entry Criteria:		
	• Knee pain and/or knee bony tenderness	
	• Absence of exclusion criteria ^b	
Domain I:		
	• Mechanical knee pain ^c	1.p
	• Knee bony tenderness	1.p
	• Crepitus on knee motion	1.p
	• Compatible synovial fluid ^d	1.p
Domain II:		
	• 40 < Age at onset ≤ 50 years old	1.p
	• Age at onset > 50 years old	2.p
	• Knee bony enlargement ^e	1.p
	• Osteophyte in knee X-Ray or compatible knee MRI	2.p

Figure 16: 2016 ACR revised criteria for early diagnosis of knee OA.³⁷

- a. In the presence of 3 points out of 10 with at least 1 point from Domain II along with all entry criteria, the diagnosis of knee OA can be established
- b. Exclusion criteria are including 1) moderate to significant knee synovitis 2) Hot or red knee 3) history and/or physical examination findings compatible with the internal derangement of the knee
- c. Knee pain that is initiated or increased with knee activity/exercise and finished or decreased with the knee resting
- d. Clear fluid with normal viscosity accompanied by WBC count less than 2000/mm³ with less than 25% PMN

- e. It must be ignored in the presence of osteophyte in knee X-Ray.

In some patients with suspected clinical features, radiography or MRI is required to confirm OA and determine the extent of joint involvement. Clinical features and risk factors such as age, sex, body mass index, absence of whole leg pain, traumatic onset, difficulties in descending the stairs, palpable effusion, fixed-flexion deformity, restricted-flexion range of motion, and crepitus are helpful and predict the development of radiographic findings in favour of knee OA with a sensitivity and a specificity of 94% and 93%, respectively.⁵⁸ In the early phase of knee OA when the findings in the history and physical examination of the knee are not typical features for knee OA, and we have normal (negative) X-Ray findings; the MRI of the knee must be ordered to rule in/out the diagnosis of knee OA. The presence of partial or full-thickness cartilage defects and Bone Marrow Edema concomitantly are compatible MRI findings for OA.⁵⁹

COMPLICATIONS

Knee OA predisposes the patients to a variety of ailments, and they are at a higher risk of death compared to the general population. As knee OA causes walking disability, they are more prone to diabetes and cardiovascular diseases. Knee OA is the most common form of OA, and it affects younger age groups too; hence it is more important to diagnose and treat it at the earliest. The incidence of knee OA increases by age and further increase with a longer lifetime and a higher average weight of the population.⁶⁰ Pain and other symptoms associated with the knee OA effect the quality of life being detrimental to both physical function and psychological parameters. Knee OA is just not localized to the knee cartilage but is a chronic disease of the whole joint effecting the articular cartilage, meniscus, ligament, and peri-

articular muscle. It is a painful and disabling disease affecting millions of patients in their prime.⁶¹

MANAGEMENT OF OA KNEE

As OA is a progressive and degenerative condition with no scope for regression and restoration of damaged structures, most of the management modalities are focused on controlling the symptoms unless the severity of the disease dictates the necessity of surgical intervention with joint replacement. Different guidelines have been developed by different academic and professional societies to standardize and recommend the available treatment options. Societies recommending the guidelines are Osteoarthritis Research Society International American (OARSI)⁶², College of Rheumatology (ACR)⁶³, and American Academy of Orthopedic Surgeons (AAOS)⁶⁴, publications.

Table 3: Knee osteoarthritis management recommendations from societies.

TREATMENT	OARSI.	ACR.	AAOS.
Exercise (land and water based)	Appropriate	Strong recommendation	Strong recommendation
Transcutaneous electrical nerve stimulation (tens)	Uncertain	Conditional recommendation	Inconclusive
Weight control	Appropriate	Strong recommendation	Moderate recommendation
Chondroitin or glucosamine	Not appropriate for disease modification, Uncertain	Recommended against use	Recommended against use
Acetaminophen	Without comorbidities: appropriate	Conditional recommendation	Inconclusive
Duloxetine	Appropriate	No recommendation	No recommendation
Oral NSAIDS	Without comorbidities:	Conditional recommendation	Strong recommendation

	appropriate with comorbidities: not appropriate		
Topical NSAIDS	Appropriate	Conditional recommendation	Strong recommendation
Opioids	Uncertain	No recommendation	Recommended the only tramadol
Intra-articular corticosteroids	Appropriate	Conditional recommendation	Inconclusive
Intra-articular Visco supplementation	Uncertain	No recommendation	Recommended against use

Surgery is considered when all the above conservative therapies fail and surgical treatments for knee OA consist of arthroscopy, cartilage repair, osteotomy, and knee arthroplasty. Arthroscopic techniques include lavage and debridement, where rough cartilage is shaved to a smooth surface, or degenerated meniscus is smoothened. Theoretically, arthroscopy for OA is supposed to relieve the symptoms by removing the debris and inflammatory cytokines that cause synovitis. Penetration of the subchondral lamina promotes cartilage repair tissue as the pluripotent stem cells arising from the subchondral bone marrow tend to promote chondrogenesis in the defect area.⁶⁵ Steadman et al.¹⁶ described the microfracture technique in which holes are made with an awl to penetrate 2–4 mm into the subchondral lamina placed at 3-4 mm distance from each other. This is a low-cost, simple procedure done arthroscopically. The disadvantages of microfracture are it facilitates only limited hyaline repair tissue, variable repair cartilage volume, and possible functional deterioration. Osteochondral grafts are transplanted to reconstruct the cartilaginous surface or osseocartilaginous defects when indicated. This is mainly done in case of limited size cartilage lesions in younger patients. Cartilage repair is not indicated in case of cartilage damages tending towards an osteoarthritic lesion. Uni-compartmental knee OA with associated varus or valgus deformity is treated with osteotomy. When more than one compartment is involved with advanced knee OA, and

failure of conservative treatments, total knee arthroplasty is a highly effective treatment resulting in substantial improvement in patient functioning and health-related quality of life.⁶⁶

The concept of visco-supplementation has been widely applied in the treatment of knee OA. It is a therapeutic modality based on the replacement of SF with hyaluronic acid.⁶⁷ But in recent years, a more regenerative treatment concept has been used in the treatment of knee OA. The concept uses the application of blood derivatives, especially platelet-rich plasma (PRP), in treating knee OA. Studies have stated that the effect of autologous PRP in treating knee OA is superior to that of HA.⁶⁸

ROLE OF ARTHROSCOPIC DEBRIDE-MENT IN OA KNEE

Arthroscopic debridement is defined as

- ❖ “Cleaning of the joint called “lavage” that includes dilution of the concentration of “degradative enzymes” and also removes all small, loose, mechanically-irritating products of chondral, meniscal, or synovial degeneration; Removal of loose bodies; Partial meniscectomy; and/or Judicious chondroplasty, wherein only unstable cartilage is removed taking care not to touch any of the healthy cartilage and also to not expose the bare bone.”

“Indication for arthroscopic debridement of the osteoarthritic knee include patients with an acute onset or exacerbation of either joint effusion, well-localized joint-line tenderness, or mechanical symptoms such as catching or locking;”

- ❖ “An acute onset of joint effusion or exacerbation of existing joint effusion, well-localized joint-line tenderness, or mechanical symptoms such as catching or locking;”
- ❖ “Patients who associate their symptoms with a specific mechanism of injury or trauma”
- ❖ “Patients having radiologic studies demonstrating intra-articular loose bodies;
- ❖ “Those with earlier stages of degenerative joint disease and without gross mechanical malalignment, without severe joint space, narrowing, and without large or multiple osteophytes; and”
- ❖ “Patients having realistic expectations from the surgery being performed and who specifically realize surgery can only result in diminishing their pain and improve their functional capacity and does not cure their arthritis.”⁶⁹

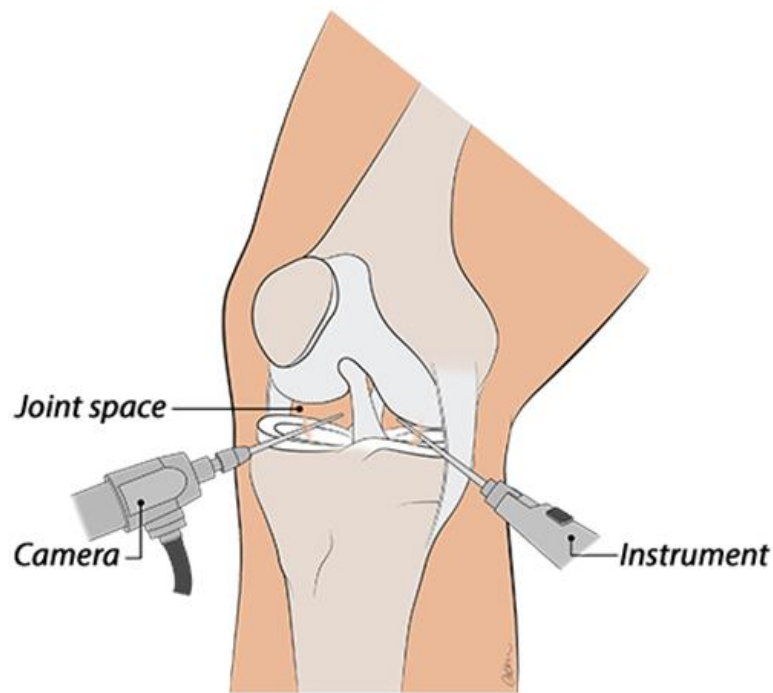


Figure 17: Key-hole surgical procedure.

During this operation, the surgeon shaves away the damaged parts of the cartilage inside the knee and stimulates healing by creating small holes in the bone.

Arthroscopic lavage and debridement give short-term symptomatic relief to most of the patients. Better symptom relief and relief from more persistent pain are seen in patients suffering from the acute onset of pain, mechanical disturbances from cartilage or meniscal fragments, normal lower extremity alignment, and minimal radiographic evidence of degenerative disease. One cannot predict the result from arthroscopic chondroplasty techniques wherein there is no guarantee concerning the durability of the fibrocartilage repair tissue in subchondral penetration procedures and thermal damage to the subchondral bone and adjacent normal articular cartilage in laser/thermal chondroplasty. While some of the recent prospective, randomized, double-blinded studies have demonstrated that outcomes after arthroscopic lavage or debridement were no better than placebo procedure for knee osteoarthritis, controversy still exists. With proper selection, patients with early degenerative

arthritis and mechanical symptoms of locking or catching can benefit from arthroscopic surgery.⁷⁰

ROLE OF ARTHROSCOPIC MICRO-FRACTURE IN OA KNEE

Microfracture technique is a widely used procedure developed by Steadman in the 1980s to treat articular cartilage lesions and is generally regarded as safe and effective.⁷¹ This technique helps in enhancing the chondral resurfacing as it provides an enriched environment for tissue regeneration. Microfracture enhances the body's own healing abilities by providing a favorable environment.⁷² This is a marrow stimulation technique where a healing response is stimulated with exposure of the subchondral bone marrow and the creation of a blood clot. This fills the defect and recruits connective tissue progenitors to repair cartilage lesions.⁷³ Because of the safety and efficacy of the procedure, microfracture is considered to be the first-line treatment used most frequently in clinics for articular cartilage repair.⁷⁴

Microfracture technique is performed through three portals, one for the inflow cannula, one for the arthroscope, and one for the working instruments. After a thorough diagnostic examination, any necessary intraarticular procedures are done, and then microfracture holes are made.⁷⁵ All unstable cartilage is debrided off the exposed bone, and a lesion is made that provides a pool that helps hold the marrow clot as it forms. A curette is used to remove the cap of the calcified cartilage layer on the lesions.⁷⁶ Using an arthroscopic awl, multiple holes or microfractures are made in the exposed subchondral bone plane. Once the arthroscopic irrigation fluid pump pressure is reduced, marrow fat droplets and blood from the microfracture holes are seen to be released into the knee. In microfracture procedure, no intra-

articular drains are placed so as to surgically induce the marrow clot, which is rich in marrow elements that forms and stabilizes while covering the lesion.⁷⁷

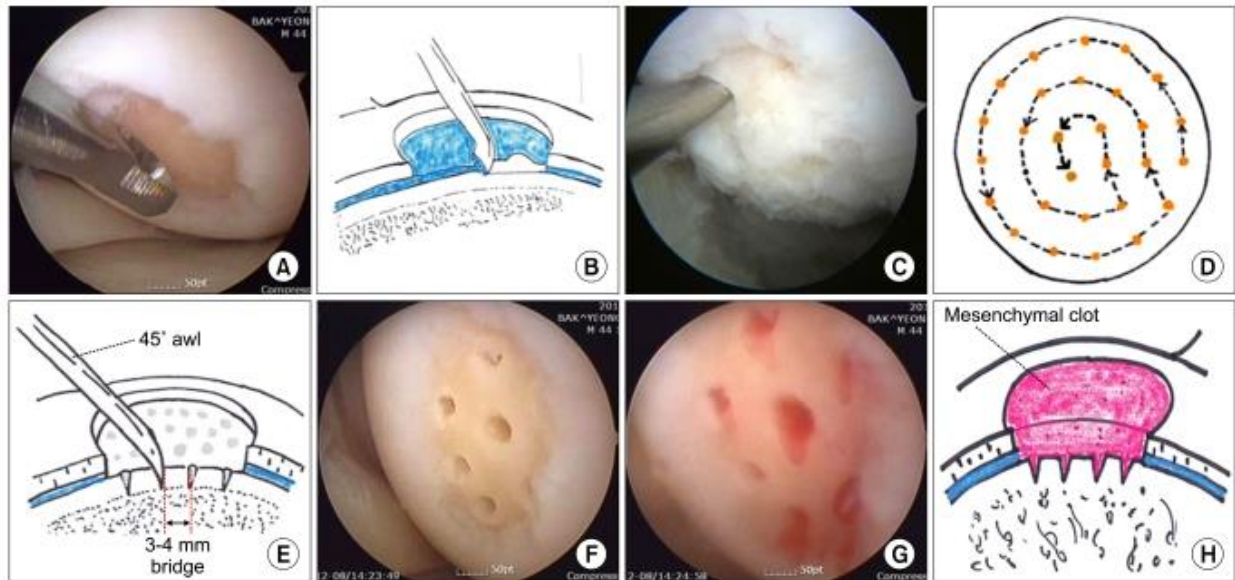


Figure 18: Surgical procedure of microfracture.⁷⁸

- (A) Unstable cartilage flap and calcified cartilage bed are debrided with an open curette.
- (B) It is important to debride the calcified cartilage layer and make a well-contained pocket surrounded healthy cartilage (well-shouldered).
- (C) Subchondral bone is punctured with an awl.
- (D) Microfracture is circumferentially performed from periphery to center.
- (E) The penetration of subchondral bone is 3 to 4 mm deep and apart.
- (F) Arthroscopic photograph showing the final step of microfracture.
- (G) Mesenchymal blood egress from bone marrow through subchondral holes.
- (H) It is important for tissue regeneration to keep the mesenchymal clot in the defect.

The microfracture technique is considered as the golden standard therapy in treating cartilage defects.⁷⁹ It is a simple procedure and cost-effective, which can be done in the clinic. These

inherent advantages allow it to be the predominant treatment method for grade III or IV cartilage damage in symptomatic patients. The microfracture technique is done through standard arthroscopic portals and is minimally invasive. The subchondral bone plate is not completely destroyed as is done in abrasion chondroplasty. In microfracture technique, the subchondral bone is partially preserved between the microfracture holes, improving load-bearing characteristics following healing.⁸⁰

Although microfracture results in a positive outcome at a faster rate in younger populations sufferings from minor articular cartilage damage, there are some limitations. As the defect is filled with fibrocartilage derived from differentiation of pluripotent stem cells instead of hyaline cartilage, it results in an inconsistent composition and inferior biomechanical properties compared to native hyaline cartilage.⁸¹ The regenerated fibrocartilaginous tissue promoted through microfracture technique has some inferior biomechanical properties compared to the normal cartilage.

In a follow-up study at 11.3 years after the microfracture, Steadman et al. reported improved function in 95% of their study population. Indications for microfracture are full-thickness loss of articular cartilage in either a weight-bearing area between the femur and tibia or in an area of contact between the patella and trochlear groove.⁷¹ Indications for microfracture are unstable cartilage that overlies the subchondral bone and degenerative changes in a knee that has a proper axial alignment. While these are not true osteochondral defects, they are due to loss of articular cartilage at the bone-cartilage interface. Microfracture is recommended based on patient age, acceptable biomechanical alignment of the knee, and intended activity level. When these criteria are met implying the patient may benefit from chondral resurfacing, then such a patient should be considered for microfracture.⁸²

At postoperative 2 year follow-up after PRP with microfracture procedure in patients older than 40 years of age for knee cartilage defects up to 4 cm², Lee et al noted that those patients had demonstrated better hardness and elasticity degree compared to those who had only arthroscopic microfracture.⁸³ In patients treated with microfracture plus intraoperative autologous PRP injection affected by chondral lesions of the knee, Manco et al reported better clinical and functional results in short-term follow-up, but at two-year follow-up, both the groups, only microfracture and microfracture plus PRP, had similar clinical results.⁸⁴ In a 2016 systematic review on studies involving PRP and knee osteoarthritis Meheux et al.²⁴ reported out of the six studies examined; five showed positive significant changes in patients treated with PRP.

Microfracture is contraindicated in cases of axial malalignment and partial-thickness defects. When a patient unwilling to follow a strict and rigorous rehabilitation protocol, it is not recommended to go for microfracture. It is contraindicated in those cannot use the opposite leg for weight-bearing during the minimal weight-bearing time. Microfracture is also not recommended in patients older than 60 years.⁷⁸ In the majority of the studies where microfracture is performed, the mean defect size was less than 4 cm², and they included only isolated chondral defects. This is the general recommended lesion size for microfracture.⁸⁵ In cases of any systemic immune-mediated disease, disease-induced arthritis, or cartilage disease, microfracture is contraindicated.⁸²

ROLE OF PRP IN OSTEOARTHRITIS OF KNEE

The use of biological agents, including PRP and mesenchymal stem cells (MSCs) in orthopedics, has increased exponentially over the last few years due to its autologous nature, supposed effectiveness and lack of side-effects. PRP is an autologous blood product with platelet concentrations above baseline values. It has been used in maxillofacial and plastic surgery since the 1990s and given its potential to enhance muscle and tendon healing, its use in sports medicine is growing. In vitro studies suggest that growth factors released by platelets recruit reparative cells and may augment the soft-tissue repair.⁸⁶

PRP is prepared by extracting blood from the patient and subjecting it to centrifuge such that a concentrated suspension of platelets is obtained through plasmapheresis. Then a two-stage centrifugation process is performed to separate the solid and liquid components of the anticoagulated blood.⁸⁷ The initial phase separates the plasma and platelets from the erythrocytes and leucocytes. The second stage uses a hard spin to concentrate the platelets further into platelet-rich and platelet-poor plasma components. The final PRP product is then injected into the knee joint space. There is also debate on the potential benefits of platelet-poor plasma on healing, and some formulations do not incorporate this step.⁸⁸

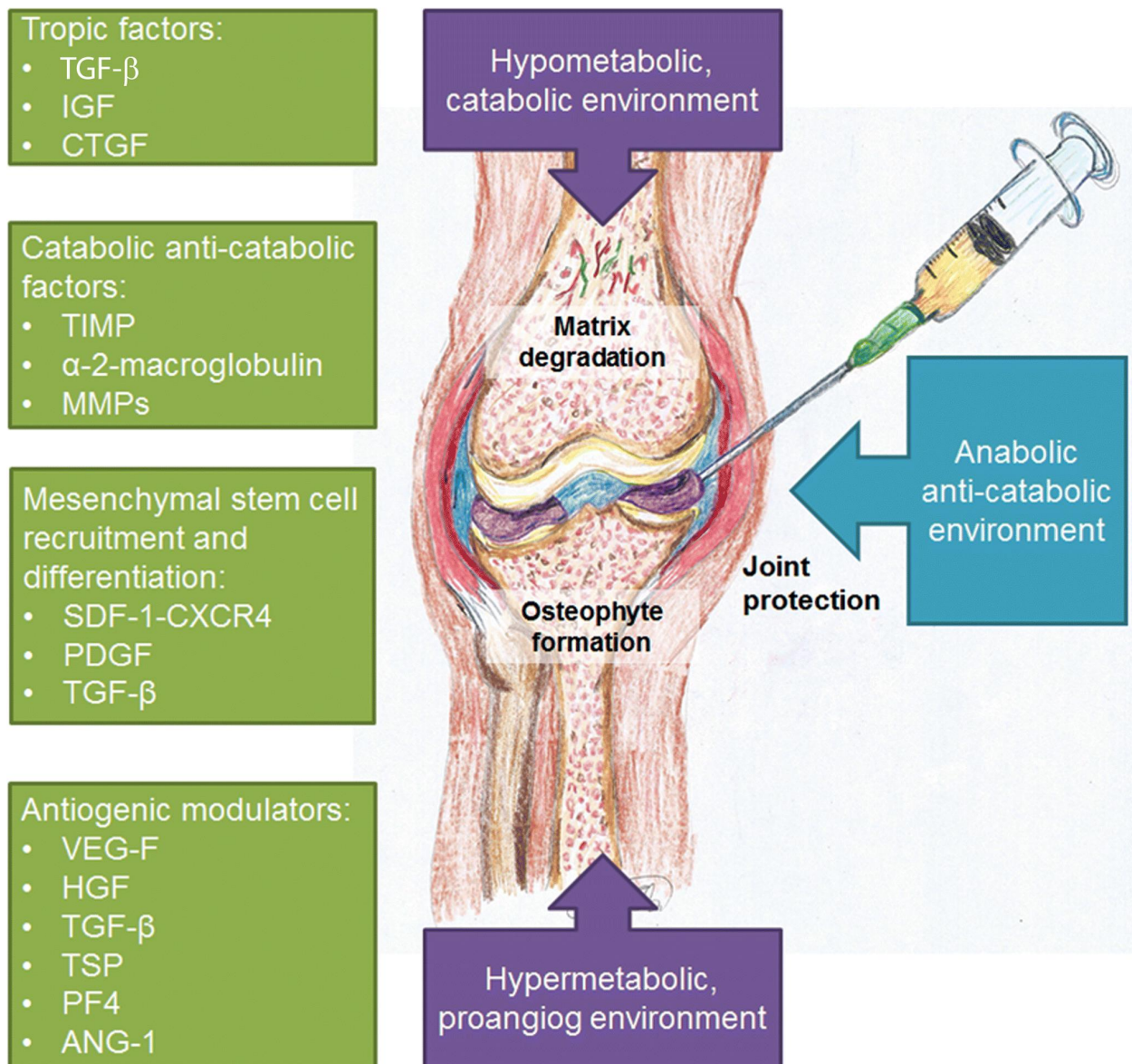


Figure 19: Clinical applications of Platelet Rich Plasma (PRP).⁸⁹

There are essentially three different methods for PRP production.⁸⁸

- ❖ **Blood filtration and plateletpheresis** which result in high concentrations of human platelets and PDGFs and low numbers of contaminating leucocytes;
- ❖ **Single-spinning centrifugation** which results in platelets up to three times that of baseline level;

- ❖ **Double-spinning centrifugation** which results in platelets up to eight times the baseline level with a high leucocyte content.

These result in four categories of products.⁹⁰

- ❖ **Pure PRP (P-PRP)** with a low content of leucocytes. This can be injected as a liquid or a gel.
- ❖ **Leucocyte-rich PRP (L-PRP)** has a greater concentration of platelets than P-PRP. Similarly, to P-PRP, it can be used as an activated gel or in a liquid form to be injected intra-articularly.
- ❖ **Pure platelet-rich fibrin (P-PRF)** is obtained by double-spinning centrifugation. The end product is a platelet-rich fibrin scaffold, which is stiffer than the conventional PRP and takes the form of a gel.
- ❖ **Leucocyte- and platelet-rich fibrin (L-PRF)** which is a leucocyte-rich gel which is non-injectable and is applied locally.

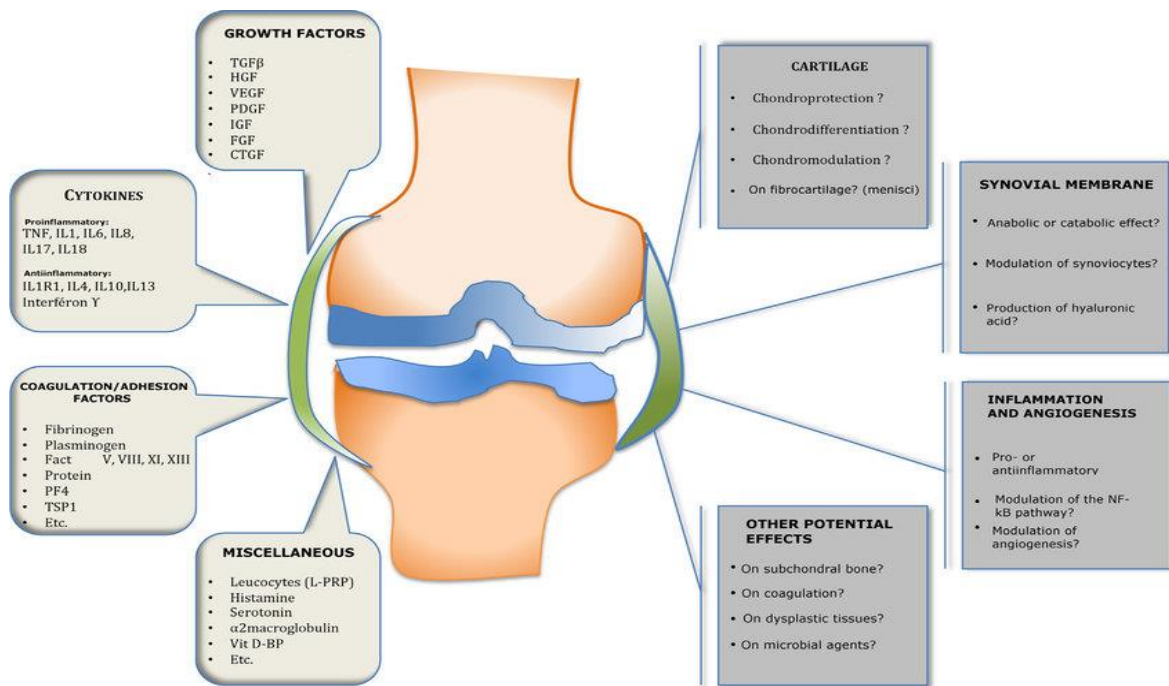


Figure 20: Main components of platelet-rich plasma (PRP), with their potential effects on the osteoarthritis process.⁹¹

Component of PRP and their beneficial effect on the osteoarthritis process.⁸³

The platelet concentrates have clear anti-inflammatory properties which help in promoting the tissue healing, and this aspect could be a mainstay when dealing with articular cartilage lesions. Inflammatory response of appropriate magnitude and timing is necessary for the tissue to heal as controlled inflammation is responsible for the majority of mesenchymal repair. Thus lowering the inflammation in the synovial tissue would lead to a reduction of matrix-metalloproteinases, which are cartilage-matrix degrading enzymes.⁹² In vitro studies have shown that chondrocytes stimulated with PRP increase proteoglycan and collagen synthesis, which have similar histological and biochemical qualities to normal hyaline cartilage. PRP also contains factors such as TGF-β1, thrombospondin-1 and insulin-like growth factor, which are proposed to be useful in treating symptomatic cartilage lesions or osteochondral defects.⁹³

A retrospective cohort study examining the use of PRP in the knee looked at 60 patients with unilateral Ahlback grades 1 to 4 osteoarthritis. The first 30 patients were treated with three injections of PRP, and the remainder had hyaluronic acid injections. At five-week follow-up, those injected with PRP had significantly higher WOMAC (Western Ontario and McMaster Universities Arthritis Index) scores. These results were invalidated by the short follow-up.⁹⁴

In terms of contra-indications, one study suggested that patients undergo a minor hematological evaluation to exclude blood disorders or platelet dysfunction. They suggest the relative contra-indications for PRP are: a platelet count less than $10^5/\mu\text{L}$; a hemoglobin level less than 10 g/dL; the presence of a tumor in the wound bed or metastatic disease; and other active infections.⁹⁵

SCORING SYSTEM

1.WOMAC SCORING

The Western Ontario and McMaster University (WOMAC) OA index was developed by Bellamy et al⁹⁶, in 1982 for assessing the activities of daily living (ADL), functional mobility, gait, general health and quality of life (QoL) in patients with knee OA and validated in 1988. It has total 24 items and three subscales, namely pain (5 items), stiffness (2 items), and function (17 items), scored on a five-point ordinal scale, 0 - none, 1 - mild, 2 - moderate, 3 - severe, and 4 - extremely severe. Higher WOMAC scores indicate worse pain, stiffness, and functional limitations. The test-retest reliability for pain, stiffness, and function is ICC = 0.74, 0.58, and 0.92, respectively.⁹⁷ The pain, stiffness and physical function subscales fulfil conventional criteria for face, content and construct validity, reliability, responsiveness and relative efficiency. WOMAC is a disease-specific purpose-built high-performance instrument for evaluative research in osteoarthritis clinical trials.⁹⁶ It would take approximately 12 min to complete the whole WOMAC directly or indirectly over telephone or online.

WOMAC is a self-administered health status measure that assesses the dimensions of pain, stiffness and function (either separately or as an overall index) in patients with OA of the hip or knee; it is available in 5-point Likert, 11-point numerical rating and 100-mm visual analogue scale (VAS) formats.⁹⁶ The five pain questions reflect pain experienced on five different activities: the five situations are walking on a flat surface, going up or down stairs, at night while in bed, sitting or lying, and standing upright. The patient's response to each question produces a score that is then summed to derive an aggregated score for each dimension. It produces three subscale scores (pain, stiffness and physical function) and a total score (WOMAC index) that reflects disability overall.

The WOMAC pain score range is variously reported and includes VAS 0–10 scale (commonly reported as a 0–50 range), VAS 0–100 scale (commonly reported as a 0–500

range), an 11-box numerical rating scale (NRS) (commonly reported as 0–50 range) or a Likert scale (commonly reported as a 0–20 range). The overall WOMAC score (index) is determined by summing the scores across the three dimensions, and the score ranges include 0–240 (derived from the VAS 0–10 or NRS scale), or 0–2400 (derived from the VAS 0–100) or 0–96 (derived from a 0–4 Likert scale). A number of various transformations and modifications are reported in the literature.⁸⁹

	PATIENT NAME	DOB			
WESTERN ONTARIO AND MCMASTER OSTEOARTHRITIS INDEX (WOMAC) Please circle the appropriate rating for each item.					
RATE YOUR PAIN WHEN...	NONE	SLIGHT	MODERATE	SEVERE	EXTREME
Walking	0	1	2	3	4
Climbing stairs	0	1	2	3	4
Sleeping at night	0	1	2	3	4
Resting	0	1	2	3	4
Standing	0	1	2	3	4
RATE YOUR STIFFNESS IN THE...	NONE	SLIGHT	MODERATE	SEVERE	EXTREME
Morning	0	1	2	3	4
Evening	0	1	2	3	4
RATE YOUR DIFFICULTY WHEN...	NONE	SLIGHT	MODERATE	SEVERE	EXTREME
Descending stairs	0	1	2	3	4
Ascending stairs	0	1	2	3	4
Rising from sitting	0	1	2	3	4
Standing	0	1	2	3	4
Bending to floor	0	1	2	3	4
Walking on even floor	0	1	2	3	4
Getting in/out of car	0	1	2	3	4
Going shopping	0	1	2	3	4
Putting on socks	0	1	2	3	4
Rising from bed	0	1	2	3	4
Taking off socks	0	1	2	3	4
Lying in bed	0	1	2	3	4
Getting in/out of bath	0	1	2	3	4
Sitting	0	1	2	3	4
Getting on/off toilet	0	1	2	3	4
Doing light domestic duties (cooking, dusting)	0	1	2	3	4
Doing heavy domestic duties (moving furniture)	0	1	2	3	4
PATIENT SIGNATURE				DATE	
REVIEWED BY PHYSICAL THERAPIST				DATE	

Figure 21: Western Ontario and McMaster University Score (WOMAC).⁹⁸

In the Likert version, each item offers 5 responses: “none” scored as 0, “mild” as 1, “moderate” as 2, “severe” as 3, and “extreme” as 4. The total score for each subscale is the sum of scores for each response to each item, and can be calculated manually or using a computer. The range for possible subscale scores in the Likert format is pain (0–20; 5 items each scored 0–4), stiffness (2 items, 0–8), and physical function (17 items, 0–68). Higher scores indicate worse pain, stiffness, or physical function. The maximum score obtained by the subjects would be 96. Based on the WOMAC score obtained, patients were categorized as low risk (score ≤ 60), moderate risk (score 60–80) and high risk (score ≥ 81). WOMAC scores are also expressed as percentages and categorized into low risk ($\leq 70\%$) and high risk ($> 70\%$). If 2 or more pain items, both stiffness items, and 4 or more physical function items are missing, the response is regarded as invalid, and the deficient subscale(s) is not included in analysis.⁹⁹

2.VAS SCORING

The Visual Analogue Scale (VAS) is a common form of pain scale used in health outcome studies, which is presented as a single line of 100 mm with anchor statements at the left (no pain) and on the right (extreme pain). VAS was first published in the early 1920s¹⁰⁰, though not widely used at that time.¹⁰¹ This tool was first used in psychology by Freyd in 1923. The Visual Analogue Scale (VAS) consists of a straight line with the endpoints defining extreme limits such as ‘no pain at all’ and ‘worst pain’. The patient is asked to mark his pain level on the line between the two endpoints. The distance between ‘no pain at all’ and the mark then defines the subject’s pain.

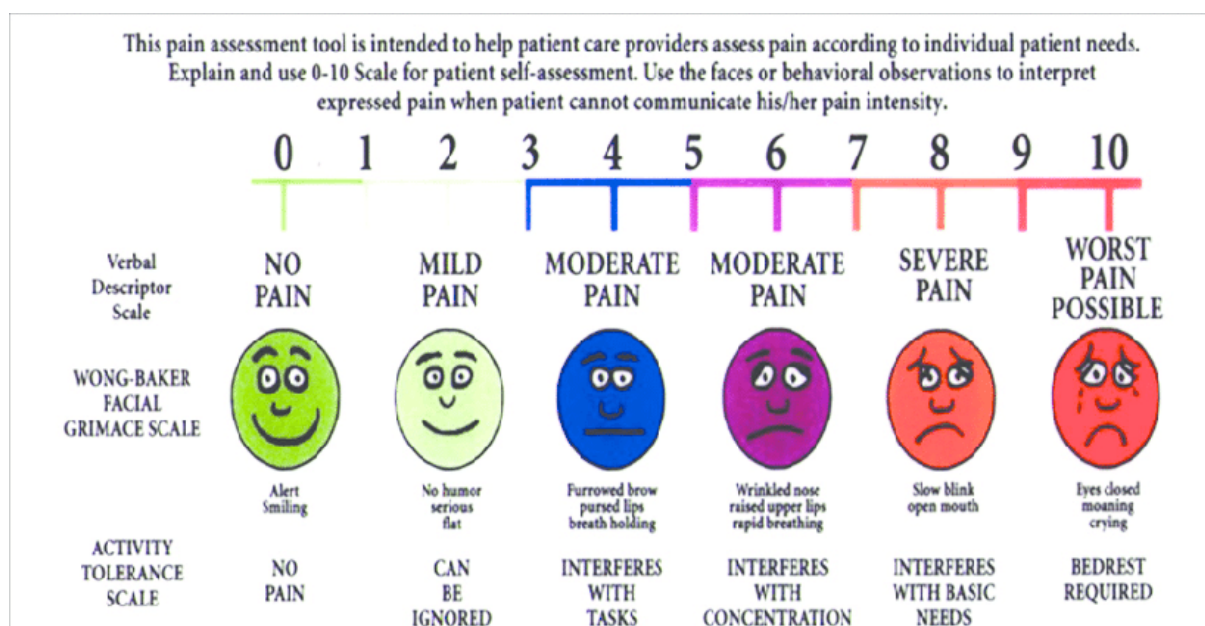


Figure 22: Visual analogue scale pain assessment tool.¹⁰²

Until the 1940s, only a handful of sociomedical and psychological publications addressed the topic of VAS. It was not until the 1960s that the literature showed rekindled interest in the use and study of VAS.¹⁰³ A VAS is considered to bridge the gap raising from variation between individual interpretations of the graduations used for rating scales; is preferred by participants who perceive their desired response as not corresponding with rating scale graduations and enables a finer distinction between subjective states to be made.¹⁰¹ One of the major advantages of VAS is that they are perceived as a continuum, meaning that their data are considered interval-scaled. Two equally sized intervals on a VAS are always interpreted as two equally sized differences by respondents. This makes it possible to calculate the arithmetic mean.¹⁰³

REVIEW OF LITERATURE

A decorative graphic element consisting of a thick horizontal black line and a thick vertical black line intersecting at the right end. Both lines have a subtle gray shadow offset slightly to the right and bottom, creating a 3D effect.

REVIEW OF LITERATURE

Elik et al¹⁰⁴ (2020), conducted a study to determine the effects of PRP in patients with knee OA in terms of pain, functionality, quality of life, and cartilage thickness. In a randomized trial of two groups, the first group was treated with PRP and the second group had a saline solution. At the first and sixth months follow up, the VAS scores of the PRP group were significantly low ($p < 0.001$). PRP group also had the pain sub-score low in the WOMAC assessment in the first month after treatment. At the sixth month follow-up, all parameters of the WOMAC score were lower in the PRP group ($p < 0.05$). It was concluded that PRP treatment had positive effects on patients with knee OA with less pain, increased physical function, and a better quality of life.

Srivastava et al¹⁰⁵ (2020), conducted a prospective study on patients with primary osteoarthritis knee to assess for the effectiveness of arthroscopic lavage and debridement in relieving symptoms of osteoarthritis of the knee and to determine the indications of arthroscopy in osteoarthritis of the knee. A declining trend was seen on follow up over time; 91.4% excellent to good results seen at one month follow up, 76.1% at six months, 49.93% at twelve months, 37.5%, at eighteen months, 23.07% at twenty-four months and 28.5% at thirty months. Results at six months follow up when compared, were better for age less than 50 years (88.8% Vs 73.1% in >50 years age), normal weight patients with BMI 18.5 to 25 (94.5% Vs 58.5% in overweight), varus angulation 100), radiological grade I and II (95-100% Vs 45-50% in grade III and IV) and arthroscopic grade I and II (94-100% Vs 0-77% in grade III and IV). The study concluded that arthroscopic lavage and debridement is an effective method of treatment for osteoarthritis knee in patients with grade I and grade II osteoarthritis having symptoms of pain and locking due to loose bodies or degenerative meniscal tears.

Altamura et al¹⁰⁶ (2020), conducted a study to evaluate a cohort of sport-active patients suffering from cartilage degeneration and OA, in terms of clinical outcome and return to sport (RTS) after platelet-rich plasma (PRP) injective treatment. Design. Patients received 3 PRP injections and were prospectively evaluated at baseline and then at 2, 6, 12, and 24 months follow-up by IKDC subjective EQ-VAS, and Tegner scores. IKDC subjective score improved significantly at all follow-ups, changing from 59.2 ± 13.6 to 70.6 ± 13 at 12 months and to 76.7 ± 12.5 at 24 months. A similar outcome was observed with the EQ-VAS score. The study concluded that sport-active patients affected by knee OA can benefit from PRP injections, with pain and function improvement over time.

Law et al¹⁰⁷ (2019), performed a retrospective, single-surgeon study of 180 consecutive knee arthroscopies performed in 169 patients, aged 40 years and above, who had mechanical symptoms affecting their daily lives and underwent arthroscopic debridement after the failure of a minimum 2 months of optimized medical and physical therapy. Excellent functional outcomes and patient satisfaction were reported in the majority of patients over the follow-up timeframe of 2e8 years. The mean pre-operative Kellgren-Lawrence score was 2.02 (SD 0.580). Significant improvements compared to pre-operative scores were seen across all scoring systems tested. 90% of patients reported good to excellent results. The study concluded that arthroscopic knee debridement can provide good symptomatic relief and sustained benefits in significantly symptomatic patients with early degenerative knees who have failed conservative management. This is most useful in patients with mechanical symptoms secondary to degenerative meniscal tears or chondral flaps, and those with symptomatic patellofemoral osteoarthritis.

Burchard et al¹⁰⁸ (2019), conducted a study to analyze whether the positive effects of PRP injections are associated with the level of cartilage damage, patient satisfaction with the treatment was correlated with the level of knee joint osteoarthritis quantified by MRI. PRP was performed with a low-leukocyte autologous conditioned plasma (ACP) system in 59 patients. Although pain symptoms and severity of clinical osteoarthritis symptoms decreased, regression analysis could not detect a correlation between the degree of cartilage damage measured by the WOMS score and a positive response to PRP therapy. This study suggests that intraarticular injection of PRP might improve osteoarthritis symptoms and reduces the pain in patients suffering from osteoarthritis of the knee joint independent from the level of cartilage damages quantified by the whole-organ MRI scoring method WOMS.

Chu et al¹⁰⁹ (2019), analyzed the curative effect of arthroscopic debridement combined with rehabilitation training in the treatment of knee osteoarthritis. This study shows that the clinical efficacy of combined therapy is significantly better than that of knee arthroscopic debridement alone, and the recurrence rate of knee arthritis treated by knee arthroscopic debridement combined with rehabilitation training is only 1.5%. The long-term effect is better; the difference is statistically significant ($P < 0.05$). Microscopic debridement, combined with rehabilitation training, can significantly improve the clinical efficacy of knee osteoarthritis, reduce postoperative pain, promote the recovery of knee function and reduce the recurrence rate.

Kumar et al¹¹⁰ (2018), conducted a prospective study to determine the effectiveness of intra-articular PRP injections in early-stage OA patients and to evaluate the clinical outcome. The effective sample size was 40 patients with bilateral OA knee in which intra-articular injection was given. And the clinical outcomes and effectiveness were measured in terms of visual

analog scale and Western Ontario and McMaster Universities Osteoarthritis Index scores at the end of 6, 12, and 24 weeks. A p-value <0.05 was considered statistically significant. There was a significant improvement in all scores at the end of 6, 12, and 24 weeks. The study concluded that the PRP treatment showed positive effects in patients with knee OA.

Su et al¹¹¹ (2018), conducted a study to evaluate the benefit provided by intraosseous infiltration combined with intra-articular injection of platelet-rich plasma to treat mild and moderate stages of knee joint degeneration (Kellgren-Lawrence score II–III) compared with other treatments, specifically intra-articular injection of PRP and of HA. All patients were evaluated using the Visual Analogue Scale (VAS), and Western Ontario and McMaster Universities (WOMAC) score before the treatment and at 1, 3, 6, 12, and 18 months after treatment. There were significant improvements at the end of the 1st month. Notably, the patients who received intra-articular combined with intraosseous injection of PRP had significantly superior VAS and WOMAC scores than were observed in others. The study concluded that the combination of intraosseous with intra-articular injections of PRP resulted in a significantly superior clinical outcome, with sustained lower VAS and WOMAC scores and improvement in the quality of life within 18 months.

Nguyen et al¹¹² (2017), conducted a study to evaluate the clinical effects of arthroscopic microfracture (AM) with and without stromal vascular fraction (SVF) injection for patients with OA. Placebo group patients received AM alone; treatment group patients received AM and an adipose tissue- derived SVF injection suspended in PRP. Patient groups were monitored and scored with WOMAC, Lysholm, VAS, and modified Outer bridge classifications before treatment and periodically at 6, 12, and 18 months post- treatment. They noted that the treatment efficacy was significantly different between both the groups.

Patients receiving AM plus SVF had significantly reduced pain and WOMAC scores and increased Lysholm and VAS scores compared to the AM group.

Vasavilbaso et al¹¹³ (2017), conducted a study to assess the effectiveness of PRP compared to standard care after knee arthroscopic debridement in patients with OA. After arthroscopy; patients were randomized to receive 5 injections of HA1, 4 injections of HA2 3 injections of HA3, a single injection of PRP and standard care. Patients are evaluated using the WOMAC periodically at 3, 6, 12, and 18 months. At 3-month follow-up, total WOMAC scores improved in all groups compared to baseline. At 18 months, the higher improvement in total WOMAC was in HA1 with a 65.20% reduction, followed by PRP (55.01%), HA3 (49.57%), and HA2 (29.82%), whereas the control group had a 14.55% increase over baseline ($p=0.001$ control compared to HA1 and HA3). The study concluded that viscosupplementation following arthroscopy is more effective than PRP in patients with OA.

King et al¹¹⁴ (2017), retrospectively analyzed the outcomes in patients who underwent arthroscopic knee debridement with autologous conditioned plasma in 2011. At the mean follow-up period of 6.5 months, they reported Kellgren-Lawrence score Grade 1 in 21.2% of the patients, Grade 2 in 13.5%, Grade 3 in 51.9% and Grade 4 in 13.5%. They noticed an improvement in the range of movement among 32.7% of the patients. They concluded that arthroscopic debridement, in combination with ACP, is beneficial in the treatment of osteoarthritis.

Huang et al¹¹⁵ (2017), conducted a retrospective study to assess the short-term results of repeated intra-articular PRP injections in patients with early OA. All scores showed significant improvements after treatment as compared to the pre-treatment values ($p < 0.05$).

WOMAC score showed a significant difference among the three groups in favor of the three injections group ($p < 0.05$). The group that had 3 injections had higher scores and more improvement even at 12-month follow-up compared to the other two groups. The study concluded that PRP injection is effective in early symptomatic OA knees and three injections per month yielded significantly better results in short-term follow-up.

Simental-Mendia et al¹¹⁶ (2016), compared the efficacy of acetaminophen and intra-articular LP-PRP in patients with early grade 1-2 knee OA. They randomized the patient into two groups, treated one group with acetaminophen and the other with LP-PRP (once every 2 weeks). All patients were evaluated by the VAS, WOMAC score, and the SF-12 health survey at baseline and 6, 12, and 24 weeks of follow-up. LP-PRP group had a decrease in the VAS pain level more than the acetaminophen group ($p < 0.05$). LP-PRP group also had sustained improvement in knee function at week 24 ($p < 0.01$). The study concluded that treatment with LP-PRP injections resulted in a significantly better clinical outcome as compared to treatment with acetaminophen.

Dai et al¹¹⁷ (2016), in a meta-analysis performed a systematic literature search in PubMed, Embase, Scopus, and the Cochrane database through April 2016 to identify Level I randomized controlled trials that evaluated the clinical efficacy of PRP versus control treatments for knee OA. They included 10 randomized controlled trials with a total of 1069 patients. The analysis showed that at 6 months post-injection, PRP and hyaluronic acid (HA) had similar effects with respect to pain relief (WOMAC pain score) and functional improvement (WOMAC function score, WOMAC total score, International Knee Documentation Committee score, Lequesne score). At 12 months post-injection, however, PRP was associated with significantly better pain relief and functional improvement than HA.

Compared with saline, PRP was more effective for pain relief (WOMAC pain score) and functional improvement (WOMAC function score) at 6 months and 12 months post-injection, and the effect sizes of WOMAC pain and function scores at 6 months and 12 months exceeded the MCID. It was concluded that the current evidence indicates that, compared with HA and saline, intra-articular PRP injection may have more benefit in pain relief and functional improvement in patients with symptomatic knee OA at 1-year post-injection.

Manco et al⁸⁴ (2016), performed a prospective observational study in patients with grade III-IV Outer-bridge's classification chondral lesions of the knee and early osteoarthritis with a mean age was 52.4 years. Microfracture technique was for Group A and microfracture + PRP injection for Group B. On follow up, the pre-operative VAS score of 6.62 ± 1.26 in Group A decreased to 3.54 ± 2.26 at 24 months ($p < 0.001$). In Group B, it decreased from 6.43 ± 1.91 to 3.36 ± 2.84 ($p < 0.001$). In Group A, the pre-operative IKDC subjective score of 37.02 ± 12.00 increased to 62.13 ± 19.00 at two years ($p < 0.001$). In Group B, the pre-operative IKDC subjective score of 34.63 ± 15.00 increased to 67.11 ± 26.74 ($p < 0.001$); the SF-36 scores showed a similar trend. The study concluded that the use of autologous PRP in association with the microfracture technique seems to give better clinical and functional results in short-term follow-up, above all as regards pain. At the two-year follow-up, however, the clinical results of the two groups were similar.

Raeissadat et al¹¹⁸ (2015), conducted a study to evaluate the long-term effect of intraarticular injection of PRP and HA on clinical outcome and quality of life of patients with knee OA, grade 1-4 of Kellgren-Lawrence scale. In the PRP group ($n = 87$), two intra-articular injections at the 4-week interval were applied, and in the HA group ($n = 73$), three doses of intra-articular injection at the 1-week interval were applied. At the 12-month follow-up,

WOMAC pain score and bodily pain significantly improved in both groups; however, better results were determined in the PRP group compared to the HA group ($P < 0.001$). Other WOMAC and SF-36 parameters improved only in the PRP group. More improvement (but not statistically significant) was achieved in patients with grade 2 OA in both groups. This study suggests that PRP injection is more efficacious than HA injection in reducing symptoms and improving quality of life and is a therapeutic option in select patients with knee OA who have not responded to conventional treatment.

Duif et al¹¹⁹ (2015), studied the effects of intraoperative applied leukocyte-poor platelet-rich plasma (LP-PRP) during knee arthroscopy in a randomized controlled, double-blind trial (RCT) During arthroscopy, LP-PRP was injected intra-articular in the intervention group. VAS score was significantly lower in the LP-PRP group (VAS 0.9. vs. 2.3) at 6 ($p = 0.008$) but not at 12 months (VAS 1.0 vs. 1.6, $p = 0.063$). The study concluded that intraoperative application of LP-PRP may enhance pain reduction and gain of knee function within 6-12 months compared to arthroscopy alone.

Papalia et al¹²⁰ (2014), conducted a study to compare clinical outcomes of the treatment of knee osteochondral lesion using arthroscopic microfracture technique alone or in association with PRF Intraoperative application using “Vivostat” system or with PRP “ReGen Lab” postoperative injection. 90 patients with clinical and radiographic evidence of osteochondral lesion of the medial or lateral compartment of the knee were enrolled. All patients received arthroscopic debridement and Microfractures and were randomized into 3 groups: 30 patients received microfractures and intraoperative PRF “Vivostat” injection (Group A), 30 patients received microfracture and 3 intra-articular injections of 5.5 mL PRP “Regen” (Group B), 30 patients received microfracture only. IKDC, KOOS and VAS score were administered to all

patients before starting the treatment, at 1, 6 and 12 months from the end of the management. Patients who received microfracture and PRF intraoperative application provided the best outcomes, showing a significant higher clinical score ($P<0.001$) compared to the other two groups. Patients underwent PRP postoperative administration reported significant higher score than those undergoing arthroscopic microfracture alone ($P<0.005$), but lesser than Intraoperative PRF group at 6 months and 1 year follow up. Treatment of osteochondral lesions of the knee using microfracture technique significantly improved functional and pain scores from the pre- to postoperatively time in the overall cohort. Intraoperative application of PRF shows a significantly better outcome than postoperative PRP injections. However, additional treatment with intra-articular PRP injection as an adjunct to microfracture technique may offer better clinical outcomes over microfracture technique alone.

Manunta et al¹²¹ (2014), studied the efficacy of microfracture technique combined with PRP injections for treatment of chondral lesions in patients aged 30–55 years. They all had medial femoral chondral lesions of the knee and a pain duration ranging from 8 to 12 months. They randomized the patients into two groups. Group A had microfracture and three intra-articular PRP injections. Group B had microfractures alone. At periodic clinical follow-ups, group A had a mean VAS score of 8.2 ± 0.6 at baseline, 5.7 ± 0.8 at 6 months, and 1.4 at 12 months. Group B had a mean VAS score of 8.1 ± 0.6 at baseline, 6.2 ± 0.8 at 6 months, and 2 ± 0.7 at 12 months. The study concluded that functional recovery and resolution of pain are obtained more quickly in PRP-treated patients and a better functional outcome in the patients treated with the combination of PRP and microfractures, even at 12 months, although the difference was not statistically significant.

Patel et al¹²² (2013), in a randomized controlled trial of patients with bilateral OA divided randomly into 3 groups studied the effects of PRP. Group A received a single injection of PRP, group B received 2 injections of PRP 3 weeks apart, and group C received a single injection of normal saline. Statistically significant improvement in all WOMAC parameters was noted in groups A and B within 2 to 3 weeks and lasting until the final follow-up at 6 months, with slight worsening at the 6-month follow-up. The mean WOMAC scores (pain, stiffness, physical function, and total score) for group A at baseline were 10.18, 3.12, 36.56, and 49.86, respectively, and at final follow-up were 5.00, 2.10, 20.08, and 27.18, respectively, showing significant improvement. Similar improvement was noted in group B (mean WOMAC scores at baseline: 10.62, 3.50, 39.10, and 53.20, respectively; mean WOMAC scores at final follow-up: 6.18, 1.88, 22.40, and 30.48, respectively). In group C, the mean WOMAC scores deteriorated from baseline (9.04, 2.70, 33.80, and 45.54, respectively) to final follow-up (10.87, 2.76, 39.46, and 53.09, respectively). The 3 groups were compared with each other, and no improvement was noted in group C as compared with groups A and B ($P < .001$). There was no difference between groups A and B, and there was no influence of age, sex, weight, or body mass index on the outcome. Knees with Ahlback grade 1 fared better than those with grade 2. Mild complications such as nausea and dizziness, which were of short duration, were observed in 6 patients (22.2%) in group A and 11 patients (44%) in group B. The study concluded that a single dose of WBC-filtered PRP in concentrations of 10 times the normal amount is as effective as 2 injections to alleviate symptoms in early knee OA. The results, however, deteriorate after 6 months. Both groups treated with PRP had better results than did the group injected with saline only.

Lee et al⁸³ (2013), conducted a study to find the efficacy of PRP in combination with arthroscopic microfracture for patients over 40 years of age with early OA of the knee with cartilage lesion less than 4 cm² in size.

The control group had only arthroscopic microfracture, and the study group was treated with arthroscopic microfracture and PRP. They evaluated the patients with VAS, IKDC score at preoperative and postoperative 1, 6, 12, and 24 months. A second arthroscopy showed significant improvements in clinical results between preoperative evaluation and postoperative 2 years in both groups ($p = 0.017$). In the postoperative 2 years, clinical results showed significantly better in the study group than in the control group ($p = 0.012$). In post-arthroscopic finding, hardness and elasticity degree were better in the study group. The PRP injection with arthroscopic microfracture would be improved the result.

Lee et al²¹ (2013), conducted a double-blind, randomized controlled pilot study of knee OA patients allocating participants randomly to receive three injections of either PA-PRP or HA. 32 % received PA-PRP, and 30 % received HA. At four and 12 weeks follow up the PA-PRP group showed significant improvements in the VAS score ($p < 0.01$), KOOS Pain ($p < 0.05$), KQoL Physical ($p < 0.05$) and KQoL Emotional subscales ($p < 0.05$). AT 12 weeks, there was improvement only on the KOOS Function subscale in the HA group ($p < 0.01$). There were no significant difference between-groups at both the time points. The study reported PA-PRP improved pain and lower extremity function; however, no differences between-groups were found.

Gobbi et al¹²³ (2012), studied fifty patients with knee OA treated with 2 intra-articular injections of autologous PRP among which 25 had previous cartilage shaving or microfracture. All the patients are evaluated at periodically pretreatment and at 6 and 12-months posttreatment. Statistical analysis did not reveal any significant difference in improvement in Tegner, Marx, and KOOS sports scores between subgroups. The VAS score in patients with previous surgery was 3.2 ± 1.4 pretreatment, 1.9 ± 1.7 at 6-month follow up

post-treatment, 1.2 ± 1.1 at 12-month follow-up. VAS in patients with no previous surgery was 4.4 ± 2.7 pretreatment, 2.4 ± 1.9 at 6-month follow-up, 1.3 ± 1.4 at 12-month follow-up. The study concluded that PRP treatment showed positive effects in patients with knee OA. Operated and non-operated patients showed significant improvement by means of diminishing pain and improved symptoms and quality of life.

Wang-Saegusa et al¹²⁴ (2011), treated patients with OA of the knee (Outer bridge grades I-IV) with PRGF (plasma rich in growth factors). Three intra-articular injections of autologous PRGF were administered at 2-week intervals in outpatient surgery. There was a statistically significant difference ($P < 0.0001$) noted in pain, stiffness, functional capacity in the WOMAC Index, the VAS pain score between pre-treatment and follow-up values. The study concluded that following intra-articular infiltration of PRGF patients with OA of the knee; there is an improvement in function and quality of life as documented by OA-specific and general clinical assessment instruments. These favorable findings point to consider PRGF as a therapy for OA.

Laupattarakasem et al¹²⁵ (2010), conducted a study to identify the effectiveness of AD in knee OA on pain and function from randomized controlled trials (RCT) or controlled clinical trials (CCT) assessing the effectiveness of AD compared to another surgical procedure, including sham or placebo surgery and other non-surgical interventions, in patients with a diagnosis of primary or secondary OA of the knees, who did not have other joint involvement or conditions requiring long term use of non-steroidal anti-inflammatory drugs (NSAIDs). The main outcomes were pain relief and improved function of the knee. Three RCTs were included with a total of 271 patients. They had different comparison groups and a moderate risk of bias. One study compared AD with lavage and sham surgery. Compared to lavage, the

study found no significant difference. Compared to sham surgery placebo, the study found worse outcomes for AD at two weeks (WMD for pain 8.7, 95% CI 1.7 to 15.8, and function 7.7, 95% CI 1.1 to 14.3; NNTH=5) and no significant difference at two years. The second trial, at higher risk of bias, compared AD and arthroscopic washout and found that AD significantly reduced knee pain compared to a washout at five years (RR 5.5, 95% CI 1.7 to 15.5; NNTB=3). The third trial, also at higher risk of bias, compared AD to closed-needle lavage, and found no significant difference.

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LACUNAE OF LITERATURE

Osteoarthritis (OA) of the knee is common, and its treatment initially is nonoperative with physical therapy and pharmacology. If conservative therapy fails, surgery is considered, and the surgical treatments include arthroscopy, cartilage repair, osteotomy, and knee arthroplasty. Arthroscopic techniques are lavage and debridement of the knee. Microfracture is a cartilage restoration technique that has proven to provide clinical benefits in the osteoarthritic knee, which is a relatively simple procedure that can be concurrently performed with other arthroscopic procedures and require minimal equipment. Autologous PRP can stimulate the natural healing cascade, and tissue regeneration and the anti-inflammatory properties of PRP have been investigated as an associate effect in promoting tissue healing. There are studies investigating the potential of debridement, microfracture and PRP for knee OA as separate procedures but there are no studies exploring the possibility of using PRP as an adjunct at the end of the debridement and microfracture procedure for knee cartilage defects. The current study is an attempt to explore the potential benefits of combining intraoperative autologous PRP injection with debridement and microfracture for knee OA.

MATERIALS AND METHODS



MATERIALS AND METHODS:

Study site: This study was conducted in the department of at R.L. Jalappa Hospital and Research Centre attached to Sri Devaraj URS Medical College, Tamaka, Kolar.

Study population: All patients diagnosed with Osteoarthritis clinico-radiologically selected from the Department of Orthopedics, R L Jalappa Hospital and Research Centre, Kolar, Karnataka were considered as the study population.

Study Design: The current study prospective, observational and hospital-based was a study.

Sample size: Sample size was estimated based on mean difference in VAS scores pre and postoperative in a study by Manco A et al⁸⁴, in 2016 reported an average variance estimate of 3.09 in VAS scores, with 99%CI, with 80 Power to detects the difference of 25% in the VAS score pre and postoperatively. The resigned sample size will be 29, expecting a dropout rates of 20 % during follow up the final sample size calculated as 35.

Formula

$$n = \frac{2s_p^2 [Z_{1-\alpha/2} + Z_{1-\beta}]^2}{\mu_d^2}$$
$$s_p^2 = \frac{s_1^2 + s_2^2}{2}$$

Where,

s_1^2 : Standard deviation in the first group

s_2^2 : Standard deviation in the second group

μ_d^2 : Mean difference between the samples

α : Significance level

$1 - \beta$: Power

Sampling method: All the eligible subjects were recruited into the study consecutively by convenient sampling till the sample size is reached.

Study duration: The data collection for the study was done between November 2018 to November 2020.

Ethical considerations: Study was approved by the institutional human ethics committee. Informed written consent was obtained from all the study participants, and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

Inclusion criteria:

- ❖ The age group of 40- 60 years.
- ❖ Early osteoarthritis (classified as Grade I, II and III according to Kellgren and Lawrence Classification).

Exclusion Criteria:

- ❖ Major axis deviation (valgus/ Varus deformity-5 degree).
- ❖ Hematological diseases/coagulopathies.
- ❖ (Hb11.3gm/dl, platelet< 1lac/microliters).
- ❖ Tumor / Infection/ Crystal arthropathies.
- ❖ Neuropathic arthropathy.
- ❖ Metabolic bone diseases.
- ❖ Ligament instability.

Data collection tools: All the relevant parameters were documented in a structured study proforma.

Methodology:

- ❖ 35 patients diagnosed with Osteoarthritis clinic-radiologically selected from the Department of Orthopaedics, R L Jalappa Hospital and Research Centre, Kolar, Karnataka are included meeting inclusion and exclusion criteria after informed consent.
- ❖ Clinical examination and X rays of the knee joints in standing position anteroposterior views and lateral views were done, and the blood sample of the patients was collected, and PRP prepared in the Blood bank of the same institute.
- ❖ Baseline VAS and WOMAC scores will be assessed, and the patient will be taken up for the surgical procedures, i.e. Arthroscopic Debridement, Microfracture (Steadman's technique). At the end of the microfracture procedure, Ca-gluconate activated Platelet-rich plasma injection will be injected into the joint, around the site of the lesion under arthroscopic at the same setting.

Steadman's technique:

Involves the removal of unstable cartilage and cartilage lesion are prepared with debridement of the subchondral bone. After measuring the length and width of the lesion using a probe, its area is calculated in centimetres squared. Angled awls were used to make holes perpendicularly through the subchondral bone measuring 2-4mm deep and were placed 3-4 mm apart.

PRP preparation: Under aseptic precautions, 20 ml of the patient's peripheral whole blood will be obtained using an 18-gauge needle. Then Ca-gluconate is added to the collected blood (in the ratio of 1:10-15) and around 5 ml. PRP is extracted by a double centrifugation technique at 1000 rpm for 15 minutes to separate erythrocytes and then again at 3000 rpm for 5 minutes to concentrate platelets by centrifugation.

Procedure:

Arthroscopy was performed with the subject placed in a supine position on the operating table. “Spinal anesthesia was given, and the tourniquet was applied. Anatomical landmarks for the medial patellar approach was palpated and marked on the skin. The anterolateral portal was introduced a centimeter above the joint line just next to the patellar tendon in a palpable soft spot. The anteromedial portal (working or instrumentation portal) was placed 1 cm above the joint line and 1 cm medial to the patellar tendon, also in a palpable soft spot. This is confirmed with a spinal needle using the arthroscope. “Then using a no. 15 or 11 blades, facing away from the patellar tendon, a 4- to 5-mm portal is made with incising the skin and the joint capsule, taking care not to damage the ligaments or cartilage and to stay above the meniscus.”

“The arthroscopic cannula with a blunt obturator is then brought into the field and held with the index finger along the cannula, and the cannula is inserted into the anterolateral portal at an angle parallel to the tibial plateau and directed between the condyles. The cannula is then pushed into the intercondylar notch. This motion is repeated a few times until the cannula is moving freely through the portal and fat pad and then it is pulled back just enough to be outside of the intercondylar notch. The knee is straightened into full extension, and the cannula is advanced under the patella into the suprapatellar pouch. The obturator is removed,

and the arthroscopic camera is locked into the cannula. The arthroscopic procedure is initiated by starting the fluid flow.”

“Through the previously marked portal, a spinal needle is inserted into the medial compartment and needle held toward the tip so as not to over-penetrates and damage the cartilage. The needle is inserted just above the meniscus. After an optimal position is found, the needle is removed and the No. 15 or 11 blades are used again to cut the skin approximately 5 mm. Using the knife an inline capsulotomy is performed, and after an adequate capsulotomy has been performed, fluid is seen to escape from the portal.”

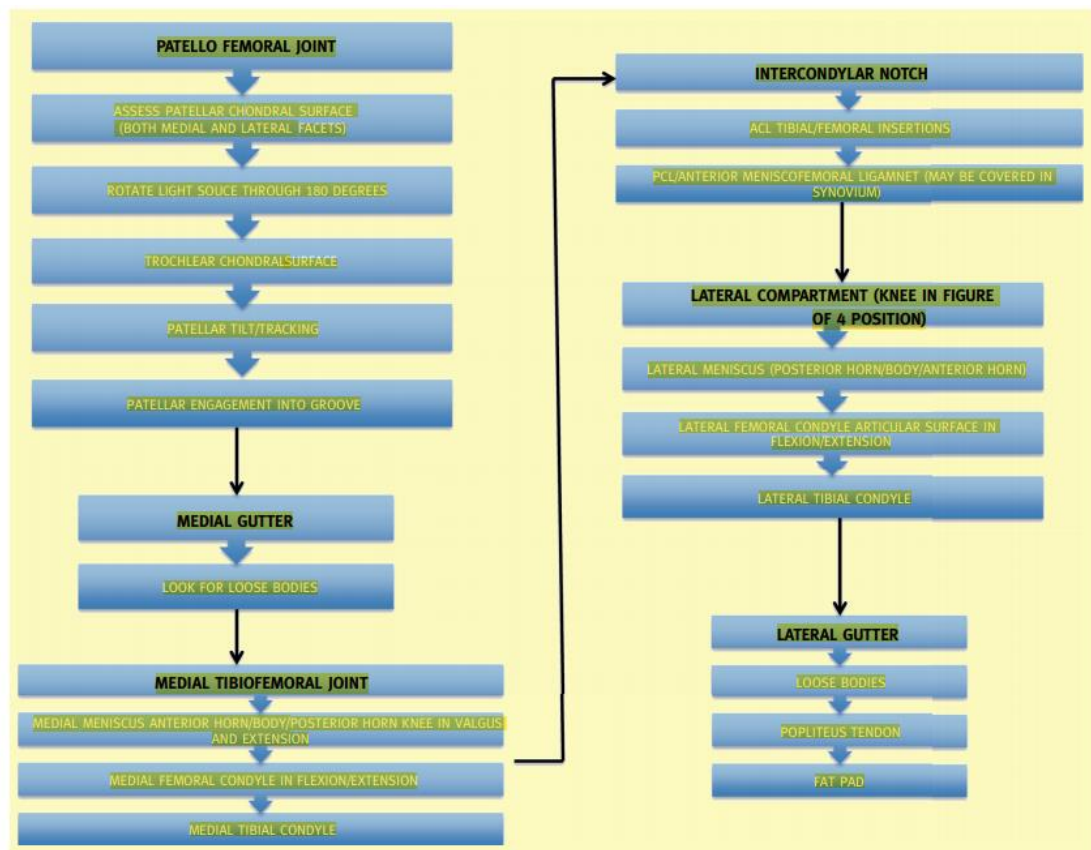


Figure 23: Systemic flowchart for basic knee arthroscopy.

“Through the anterolateral portal, the arthroscope is placed into the suprapatellar pouch. Rotating the light cord downward, the patella is examined, and then the light cord is raised to examine the trochlear groove to evaluate for cartilage injury. The arthroscope is then moved

medially into the medial gutter to checking for loose bodies. The knee is straightened using valgus force on the leg to open the medial compartment, and the arthroscope is brought into the medial compartment. The medial meniscus is inspected and probed for tears. The cartilage on the tibial plateau and the medial femoral condyle is evaluated.”

“The knee is then bent to 90, and the arthroscope is brought into the intercondylar notch. The anterior cruciate ligament and posterior cruciate ligament are examined and checked for the presence of loose bodies, and the ligaments are probed to check for integrity. “

“After identifying the triangle between the lateral meniscus, the lateral femur, and the anterior cruciate ligament, the lateral compartment is entered. The light cord is turned to look laterally, and the arthroscope is advanced into the triangle. Applying varus force to the knee either using the figure-of-4 position or directly using the circumferential leg holder, the lateral meniscus and articular cartilage are examined. The popliteal hiatus and popliteal tendon are also evaluated. Next, the arthroscope is brought directly into the lateral gutter to check for loose bodies.”

MICROFRACTURE AND PRP:

“Unstable cartilage flap and calcified cartilage bed are debrided with an open curette. Subchondral bone is punctured circumferentially from the periphery to Centre with a Microfracture angled awl. The length and width of the lesion are measured using a probe, and its area is calculated in centimeters squared. The subchondral bone is penetrated 3 to 4 mm deep and apart. Mesenchymal blood can be seen to egress from bone marrow through subchondral

holes. After completion of knee arthroscopy, the water is turned off. The cannula is left in the knee to allow for any arthroscopic fluid to drain out of the joint to facilitate faster recovery. The arthroscope is removed, and the portals are closed with skin stapler. The knee is bent at

45-90 degrees of flexion, and 5 mL PRP is injected into the knee joint with an 18- gauge needle without local anesthetic. Post injection of PRP passive knee flexion and extension are performed. Jones compression bandage is applied at the end of the procedure.”

FOLLOW UP:

Patients were assessed with WOMAC (Western Ontario McMaster Universities Arthritis Index) scoring and VAS (visual analogue scale) for pain, pre-procedure and post-procedure period of 1 month, 3 month and 6 months. A reduction in WOMAC score and VAS score for pain is suggestive of improvement in the patient’s condition.

STATISTICAL METHODS:

VAS score and WOMAC score were considered as primary outcome variables. Age, gender etc., were considered as Primary explanatory variable.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like a pie diagram, bar chart. All Quantitative variables were checked for normal distribution within each category of an explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro- wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as a normal distribution.

The association between non-normal quantitative outcome was assessed by comparing the median values. Wilcoxon signed test was used to assess statistical significance. P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.¹²⁶

RESULTS



OBSERVATIONALS AND RESULTS

35 people included in the final analysis.

Table 4: Descriptive analysis of age in study population (N=35)

Parameter	Mean $\pm$ SD	Minimum	Maximum	95% C. I	
				Lower	Upper
Age	55.97 $\pm$ 4.93	40.00	60.00	54.28	57.67

Among the study population, the mean age was 55.97 $\pm$ 4.93 (40 to 60). (Table 4)

Table 5: Descriptive analysis of age in the study population (N=35)

Age	Frequency	Percentages
40 to 45	1	2.86%
46 to 50	4	11.43%
51 to 55	9	25.71%
56 to 60	21	60.00%

Among the study population, 21(60%) of the age was between 56 to 60, 9(25.71%) of the age was between 51 to 55 and 4(11.43%) of the age was between 46 to 50. (Table 5 and Figure 24)

Figure 24: Pie chart of age in the study population (N=35)

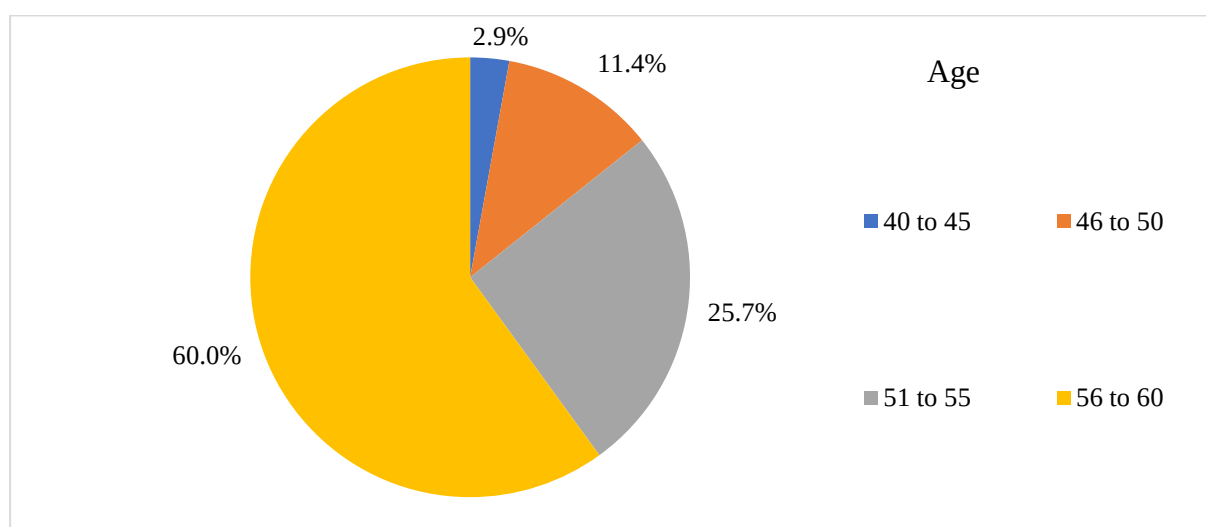


Table 6: Descriptive analysis of gender in the study population (N=35)

Gender	Frequency	Percentages
Male	13	37.14%
Female	22	62.86%

Among the study population, 22(62.86%) of them were female, and 13(37.14%) of them were male. (Table 6 and Figure 25)

Figure 25: Pie chart of sex in the study population (N=35)

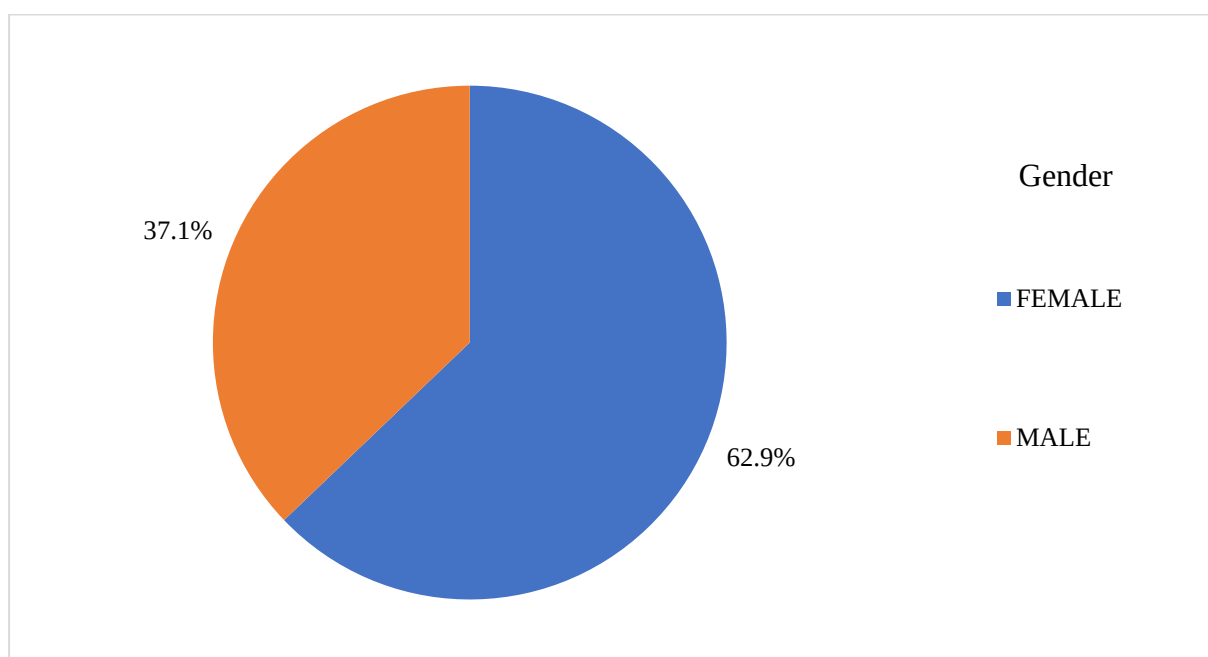


Table 7: Descriptive analysis of side in the study population (N=35)

Side	Frequency	Percentages
RIGHT	24	68.57%
LEFT	11	31.43%

Among the study population, 24(68.57%) of them had the right side, and 11(31.43%) of them had left side. (Table 7 and Figure 26)

Figure 26: Pie chart of side in the study population (N=35)

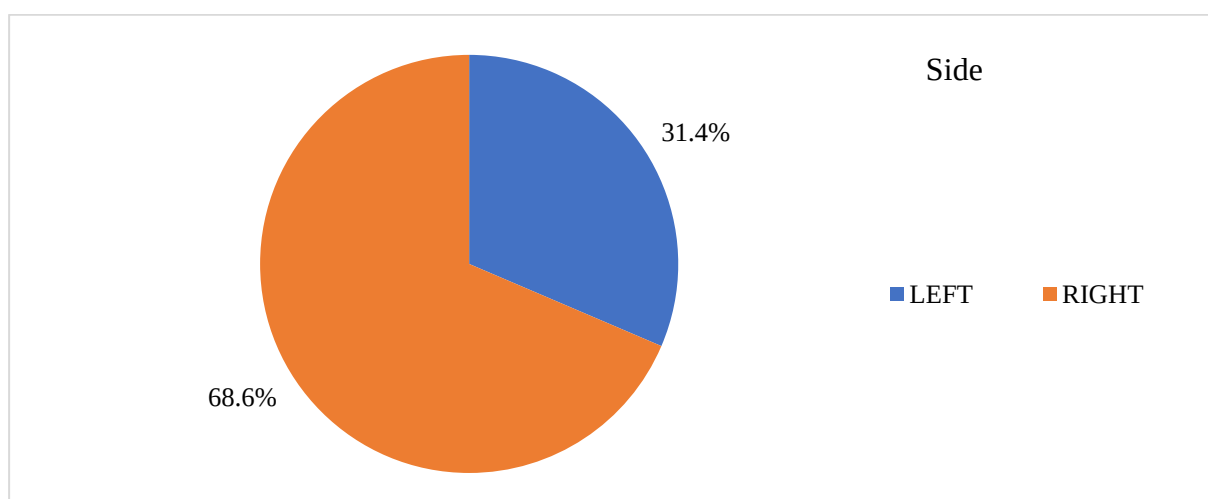


Table 8: Descriptive analysis of grade kellegren-lawrence in the study population (N=35)

Grade Kellegren-Lawrence	Frequency	Percentages
Grade II	9	25.71%
Grade III	26	74.29%

Among the study population, Grade Kellegren-Lawrence was 26(74.29%) of them had grade III, and 9(25.71) of them had grade II. (Table 8 and Figure 27)

Figure 27: Pie chart of grade kellegren-lawrence in the study population (N=35)

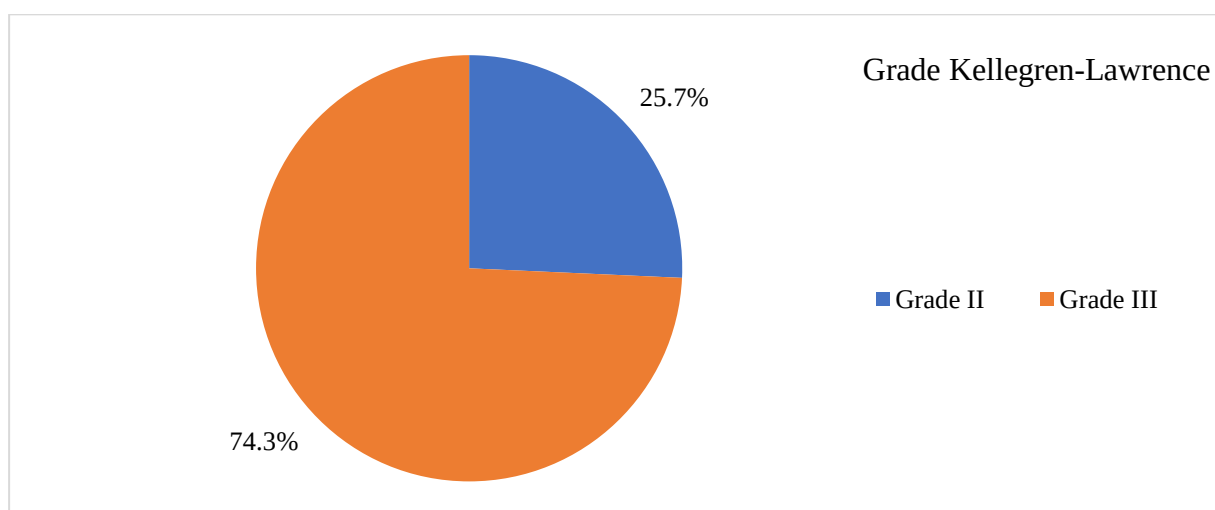


Table 9: Descriptive analysis of VAS score (pre-op and post-op at 1month, 3 months, 6 months) in study population (N=35)

Parameter	Mean $\pm$ SD	Minimum	Maximum	95% C.I	
				Lower	Upper
VAS score (Pre-Op)	7.91 $\pm$ 0.74	7.00	9.00	7.66	8.17
VAS score (1 Month)	5.71 $\pm$ 0.99	4.00	7.00	5.38	6.05
VAS score (3 Months)	4.51 $\pm$ 0.66	3.00	6.00	4.29	4.74
VAS score (6 Months)	3.17 $\pm$ 1.07	2.00	6.00	2.80	3.54

Among the study population, the mean VAS score at pre-op was 7.91 ± 0.74 , it was 5.71 ± 0.99 Post-op 1 month, it was 4.51 ± 0.66 Post-op 3 months, and it was 3.17 ± 1.07 Post-op 6 months. (Table 9 and Figure 28)

Figure 28: Bar chart for VAS score (pre-op and post-op at 1 month, 3 months, 6 months) in study population (N=35)

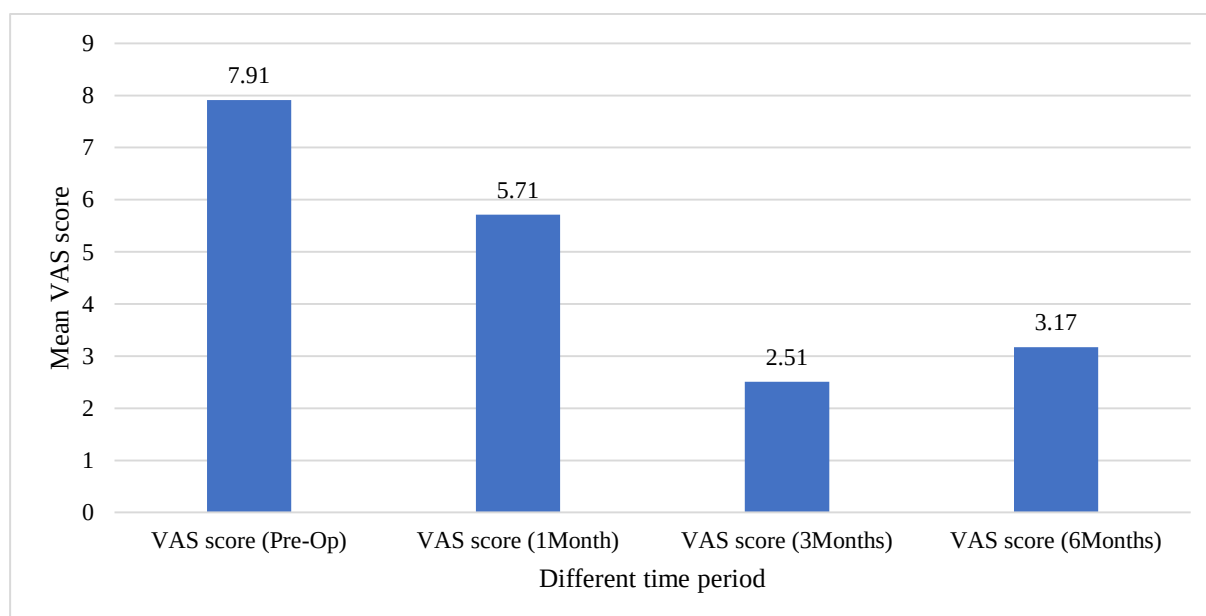


Table 10: Descriptive analysis of WOMAC score (pre-op and post-op at 1month, 3 months, 6 months) in study population (N=35)

Parameter	Mean $\pm$ SD	Minimum	Maximum	95% CI	
				Lower	Upper
WOMAC (Pre-Op)	67.11 $\pm$ 8.73	57.00	80.00	64.12	70.11
WOMAC (1 Month)	50.14 $\pm$ 9.99	37.00	63.00	46.71	53.58
WOMAC (3 Months)	40.83 $\pm$ 7.8	32.00	57.00	38.15	43.51
WOMAC (6 Months)	31.66 $\pm$ 5.28	25.00	51.00	29.84	33.47

Among the study population, the mean WOMAC score at pre-op was 67.11 ± 8.73 , it was 50.14 ± 9.99 post-op 1 month, it was 40.83 ± 7.8 post-op 3 months, and it was 31.66 ± 5.28 post-op 6 months. (Table 10 and Figure 29)

Figure 29: Bar chart for WOMAC score (pre-op and post-op at 1 month, 3 months, 6 months) in study population (N=35)

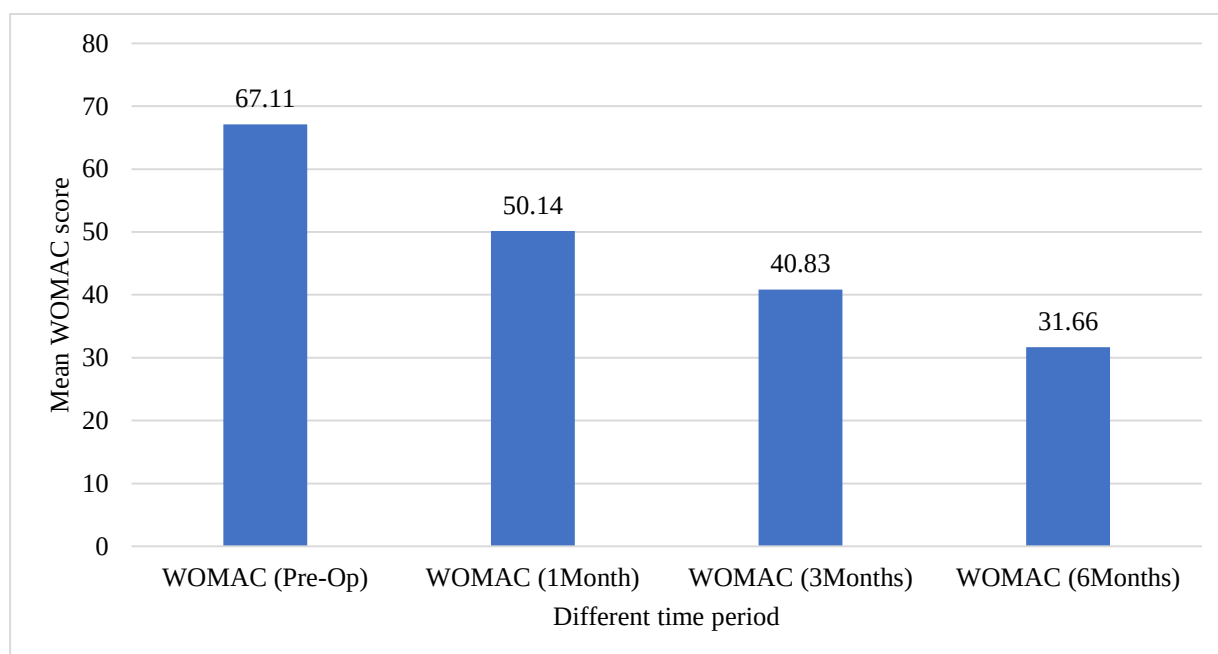


Table 11: Comparison of pre-op VAS score and post-op at 1 month, 3 months, 6 months

VAS score (N=35)

Parameter	Median (IQR)	P value (Wilcoxon signed -Test)
Pre-operative VAS score (Baseline)	8 (7 to 8)	
VAS score (Post-op 1 month)	6 (5 to 7)	<0.001
VAS score (Post-op 3 months)	5 (4 to 5)	<0.001
VAS score (Post-op 6 months)	3 (2 to 4)	<0.001

Among the study population, the median VAS score at pre-op was 8 (7 to 8), it was 6 (5 to 7) post-op 1 month, it was 5 (4 to 5) post-op 3 months, and it was 3 (2 to 4) post-op 6 months. The median difference between pre-op and post-op (at 1 month, 3 months, 6 months) was statistically significant. P value (<0.001). (Table 11 and Figure 30)

Figure 30: Bar plot for pre-op VAS score and post-op at 1 month, 3 months, 6 months

VAS score (N=35)

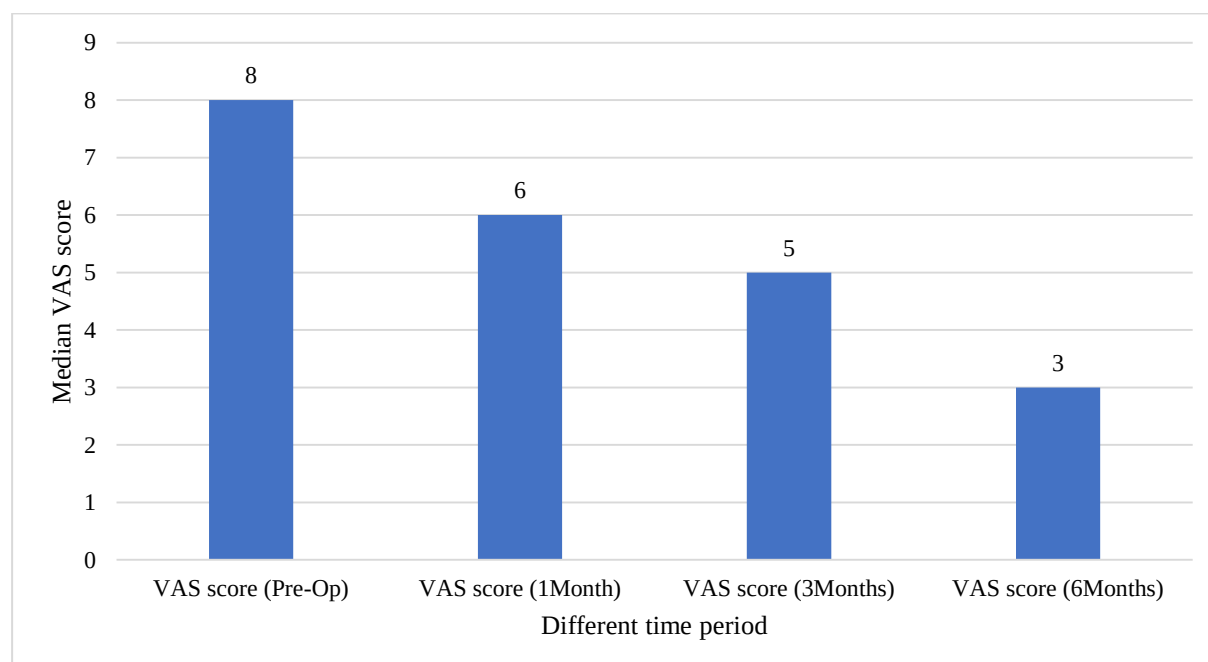


Table 12: Comparison of pre-op WOMAC score and post-op at 1 month, 3 months, 6 months WOMAC score (N=35)

Parameter	Median (IQR)	P value (Wilcoxon signed - Test)
Pre-operative WOMAC score (Baseline)	65 (58 to 76)	
WOMAC score (Post-op 1 month)	51 (39 to 62)	<0.001
WOMAC score (Post-op 3 months)	37 (34 to 46)	<0.001
WOMAC score (Post-op 6 months)	31 (28 to 35)	<0.001

Among the study population, the median WOMAC score at pre-op was 65 (58 to 76), it was 51 (39 to 62) post-op 1 month, it was 37 (34 to 46) post-op 3 months, and it was 31 (28 to 35) post-op 6 months. The median difference between pre-op and post-op 1month, Post-op 3 months, Post-op 6 months) was statistically significant. P value (<0.001). (Table 12 and Figure 31)

Figure 31: Bar chart for pre-op WOMAC score and post-op at 1 month, 3 months, 6 months WOMAC score (N=35)

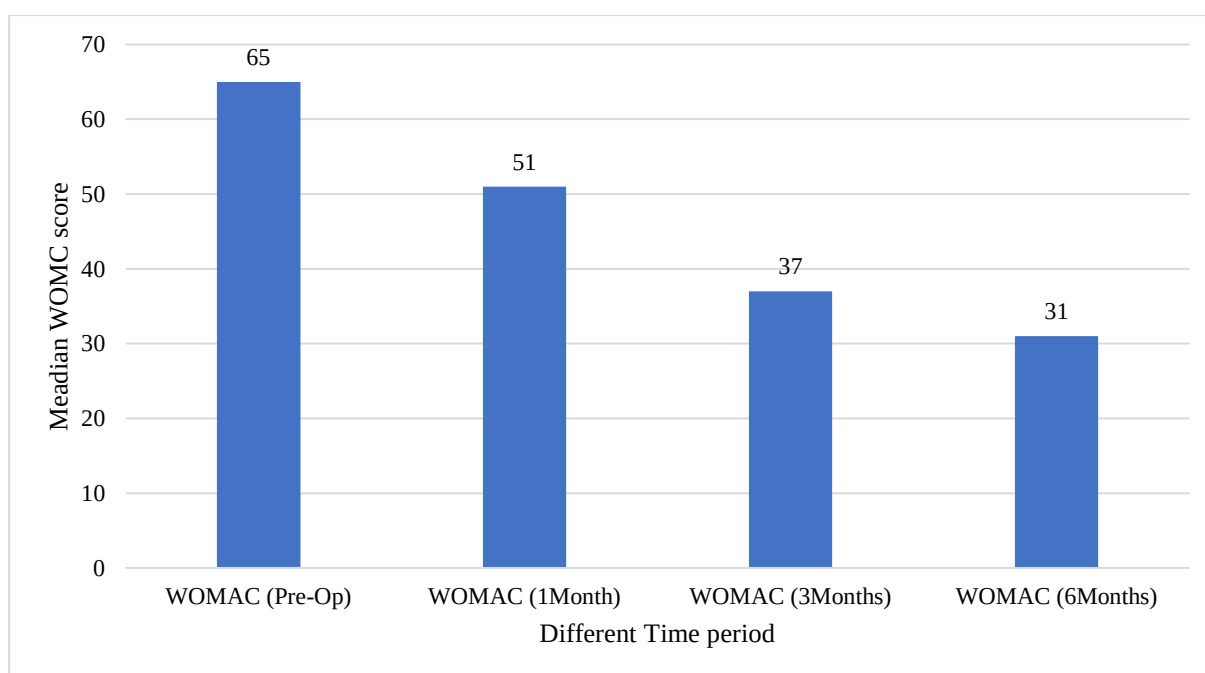


Table 13: Frequency distribution of VAS score outcome in the study population (N=35)

VAS score outcome	Frequency	Percentages
Good (VAS score ≥ 5)	24	68.57%
Poor (VAS score <5)	11	31.43%

Among the study population, 24(68.57%) of them had good VAS outcome, and 11(31.43%) of them had poor VAS outcome. (Table 13 and Figure 32)

Figure 32: Pie chart for VAS score outcome in the study population (N=35)

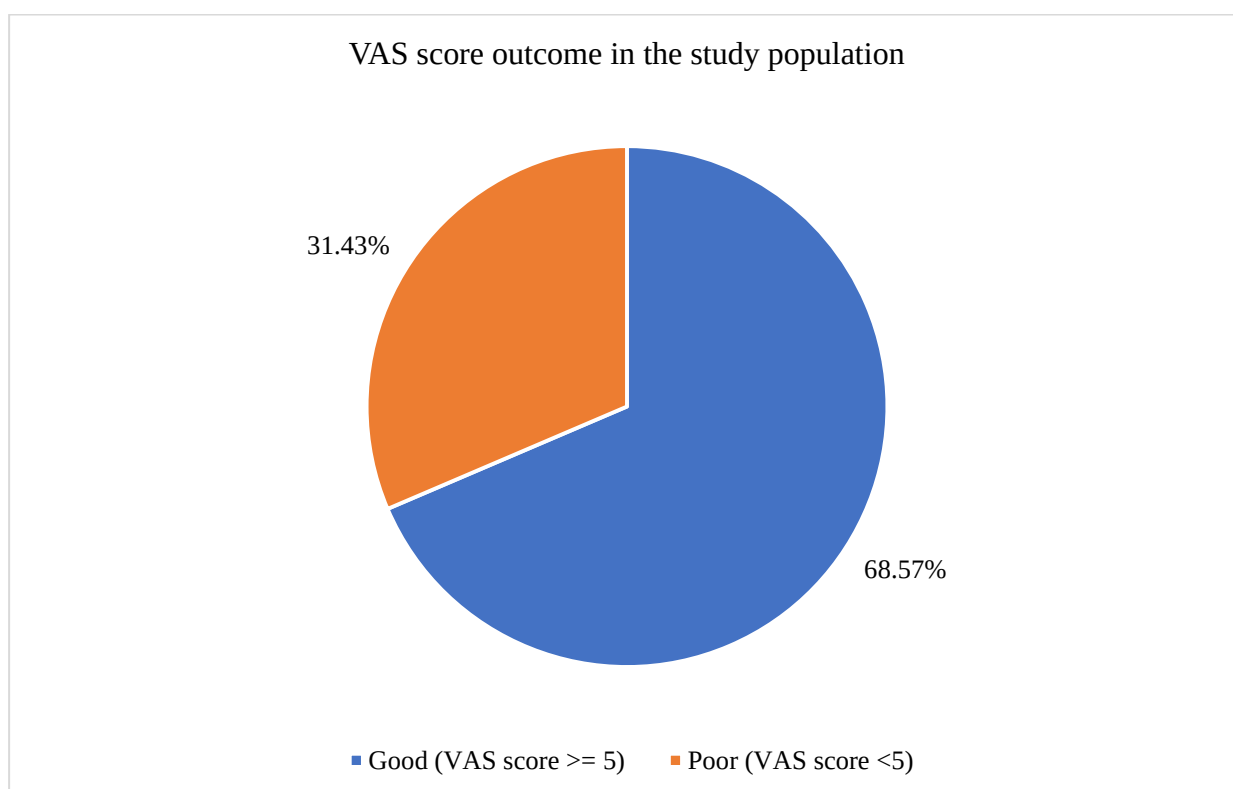
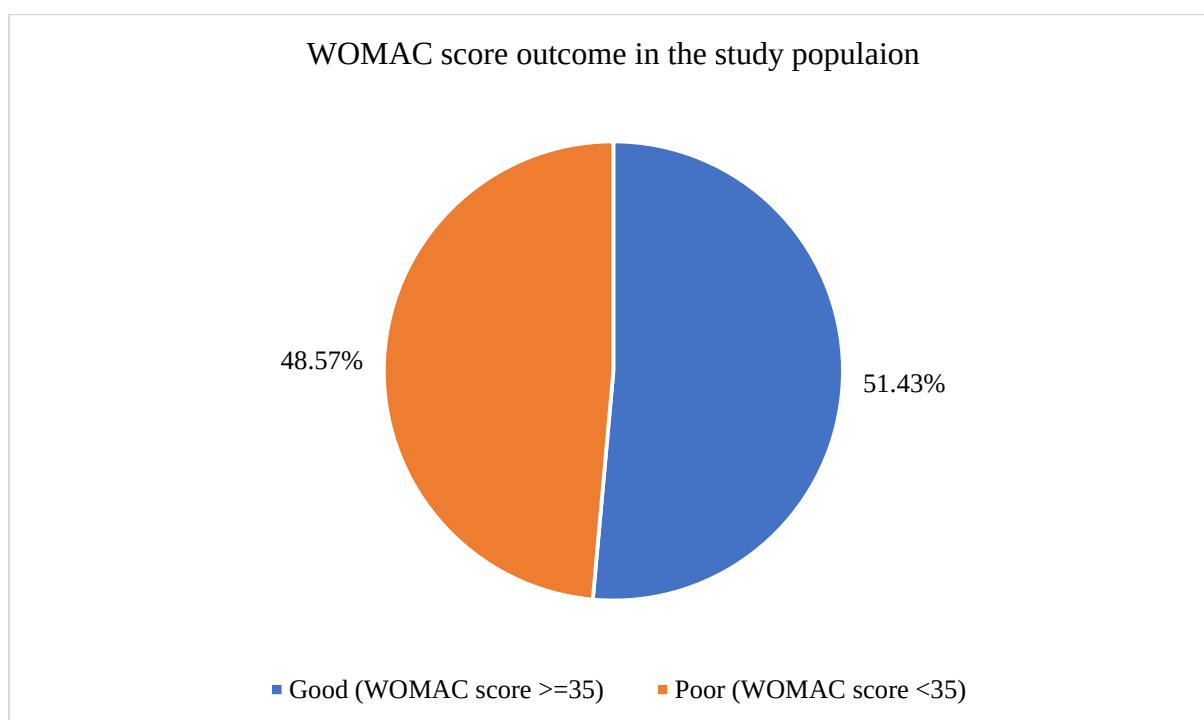


Table 14: Frequency distribution of WOMAC score outcome in the study population (N=35)

WOMAC score outcome	Frequency	Percentages
Good (WOMAC score ≥ 35)	18	51.43%
Poor (WOMAC score < 35)	17	48.57%

Among the study population, 18(51.43%) of them had good WOMAC outcome, and 17(48.57%) of them had poor WOMAC outcome. (Table 14 and Figure 33)

Figure 33: Pie chart for WOMAC score outcome in the study population (N=35)



DISCUSSION



DISCUSSION:

The pathology of OA involves the whole joint in a disease process that includes focal and progressive hyaline articular cartilage loss with concomitant changes in the bone underneath the cartilage, including the development of marginal outgrowths, osteophytes, and increased thickness of subchondral bone.¹²⁷ Arthroscopic procedures for osteoarthritis of the knee include lavage, partial meniscectomy, chondroplasty, synovectomy, removal of loose body, removal of offending osteophytes, and adhesiolysis, which are performed in a proper combination according to the articular lesion type. Arthroscopic debridement consists of lavage, removal of loose body, partial meniscectomy, chondroplasty, synovectomy, removal of offending osteophytes, adhesiolysis, and joint insufflation. These procedures are helpful for short-term symptom relief in early arthritis, but ineffective for halting the progression of the disorder.⁶ Arthroscopic microfracture is indicated as a routine treatment for OA. However, meta- and systematic analyses indicate that although AM initially improves OA symptoms,^{128,129} this effect is only short term.¹²⁸ As an alternative approach, OA has been treated using platelet- rich plasma (PRP). PRP contains the pool of cytokines and growth factors stored in platelets.¹³⁰ Some studies have shown that PRP improves OA symptoms.^{123, 23} Kon et al. noted a short-term efficacy in reducing pain and improving both knee function and quality of life.²³ A prospective, randomized, double-blind study evaluating the clinical efficacy of PRP in early OA compared to placebo (saline) noted, despite a general deterioration of the results after six months, better results, in terms of the effects on pain, stiffness and knee function, in patients treated with PRP.¹²²

The aim of this study is to evaluate the functional outcomes of arthroscopic debridement with micro-fracture with PRP injection in mild to moderate OA of the knee using Western Ontario and McMaster Universities Score (WOMAC) and visual analogue scale.

This is a prospective, observational and hospital-based study of 35 patients diagnosed with knee OA clinico-radiologically. WOMAC (Western Ontario McMaster Universities Arthritis Index) scoring and VAS (visual analogue scale) for pain are considered as the primary outcome variables. Age, gender etc., were considered as Primary explanatory variable. Based on the VAS score and WOMAC score, it is observed that intra-articular PRP injection after debridement and microfracture has more benefit in pain relief and functional improvement in patients with symptomatic knee OA at 6 months post-injection. It is noted that the PRP injection significantly improved and prolonged the treatment efficacy of microfracture for OA.

The mean age of the study group is 55.97 ± 4.93 years ranging from 40 to 60 years. This is a slightly older age group compared to those in Manco et al⁸⁴, study where the mean age was 52.4 years. King et al¹¹⁴, had a younger age group in their study with a mean age of 44.56 ± 12.74 years. Nguyen et al¹¹², study had a slightly older age group with a mean age of 58.60 ± 6.48 in the treatment group, and 58.20 ± 5.71 in the placebo group and Vasavilbaso et al¹¹³, had a mean age of 64.4 years in their study. Manunta et al¹²¹, study had patients with ages ranging from 30 and 55 years. Lee et al⁸³, had a relatively younger age group with patients aged between 40 and 50 years, as did Gobbi et al¹²³, with a mean age of 47.7 ± 2.52 years. Majority of the patients in our study are in the 56 to 60 age group followed by 51 to 55 age group. Ours is a predominantly female population group with 62.86% of them being female and 37.14% males which are in contrast to Gobbi et al¹²³, study who had 62% males and King et al¹¹⁴, study who had 69% males. Vasavilbaso et al¹¹³, had 52% males in their study, which

is similar to Manunta et al¹²¹, who also had an almost equal gender distribution with 55% females in their study. Nguyen et al¹¹², study had a predominantly female population with 80% females.

In our study, 68.57% had right side knee OA, and 31.43% had left side knee OA. King et al¹¹⁴, reported 48% had left knee pain and 52% had right knee pain in their study while Gobbi et al¹²³, study group had 60% with left knee pain and 40% with right knee pain.

Clinical examination and X rays of the knee joints in standing position anteroposterior views and lateral views are taken and the severity is classified as per Kellegren-Lawrence system. Non-operative treatment of OA is useful for patients with Kellegren-Lawrence grade 1–3, which are early stages of OA. In our study, the majority with 74.29% had Kellegren-Lawrence grade III knee OA, and 25.71% had grade II knee OA which is similar to Nguyen et al¹¹², study group where 70% Kellegren-Lawrence grade III knee OA and 30% had grade II knee OA. King et al¹¹⁴, study group had 51.9% with Kellegren-Lawrence grade III knee OA followed by 21.2% with Kellegren-Lawrence grade 1, 13.5% with grade 2, and 13.5% with grade 4. Manco et al⁸⁴, had a relatively early osteoarthritis group classed as grade 1–2 according to the Kellgren-Lawrence classification. In Gobbi et al¹²³, study, 40% had with Kellegren-Lawrence grade 1II followed by 38% with grade II and 22% grade I knee OA.

Table 15: Kellegren-Lawrence classification of knee OA across studies:

Kellegren-Lawrence	Grade I	Grade II	Grade III
Our study	-	25.71%	74.29%
Nguyen et al. ¹¹²	-	30%	70%
King et al. ¹¹⁴	21.2%	13.5%	51.9%
Gobbi et al. ¹²³	22%	38%	40%

After arthroscopic debridement and microfracture (Steadman's technique) and Ca-gluconate activated Platelet-rich plasma injection is injected into the joint, around the site of the lesion under arthroscopic at the same setting. Patients are evaluated using WOMAC, VAS SCORE for levels of pain and knee function prior to the procedure, and after 1 month, 3 months and 6-month post-procedure. It was observed that the mean VAS score had decreased gradually from pre-op which was at 7.91 ± 0.74 to 5.71 ± 0.99 at 1 month, further down to 4.51 ± 0.66 at 3 months and it was 3.17 ± 1.07 at 6 months showing the good functional outcome of the procedure in terms of pain and quality of life. The median VAS score at pre-op was 8 (IQR 7 to 8), it was 6 (IQR 5 to 7) at 1 month, it was 5 (IQR 4 to 5) at 3 months, and it was 3 (IQR 2 to 4) at 6 months. The median difference between pre-op and post-op (at 1 month, 3 months, 6 months) was statistically significant with a p value <0.001 . It is observed that 68.57% of the study population had good VAS outcome while 31.43% had a poor VAS outcome. This is in congruence with Nguyen et al¹¹², study where they reported VAS scores in the group treated with microfracture and PRP gradually increased post- treatment showing that PRP not only maintained and prolonged the effects of AM but also increased overall treatment efficacy. In the microfracture group, VAS scores significantly increased after 6 months compared with those at pretreatment and gradually decreased at 12 and 18 months showing that microfracture resulted in significantly reduced pain and improved knee function 6 months after the procedure, and these persisted for up to 12 months, but 18 months post- AM, the symptoms of OA in the majority of patients reverted back to pretreatment levels. Increase in the VAS score is due to the left to the right-oriented scale used. Similarly, Manco et al⁸⁴, noted the VAS score decreased from a pre-operative value of 6.62 ± 1.26 to 3.54 ± 2.26 at 24 months in the microfracture group ($p < 0.001$), and from 6.43 ± 1.91 to 3.36 ± 2.84 in microfracture + PRP injection group ($p < 0.001$). Their study observed that the use of autologous PRP in association with the microfracture technique gave better clinical and functional results in short-term

follow-up, above all as regards pain but at two-year follow-up, the clinical results were similar to that of microfracture group. This finding is supported in a study by Elik et al¹⁰⁴, who reported that in the first and sixth months after the treatment, the VAS scores of the PRP group were significantly low ($p < 0.001$). Manunta et al¹²¹, noted that the difference between the VAS values in microfracture and PRP group and microfracture alone group was not significant at any evaluation (p -values of 0.714, 0.182 and 0.126 at baseline, 6 months and 12 months, respectively) but suggested that functional recovery and resolution of pain are obtained more quickly in PRP-treated patients. In another study, Gobbi et al¹²³, noted the use of PRP in knee OA after cartilage shaving or microfracture had good short-term results without provoking local or systemic adverse events. The mean VAS pre-procedure was 3.2 ± 1.4 , which decreased to 1.9 ± 1.7 at 6-month follow up and further down to 1.2 ± 1.1 at 12 months follow up. The PRP injection with arthroscopic microfracture would be improved the results in the early osteoarthritic knee with cartilage lesion in 40-50 years old as demonstrated by the VAS score at preoperative and postoperative 1, 6, 12, and 24 months in Lee et al⁸³, study.

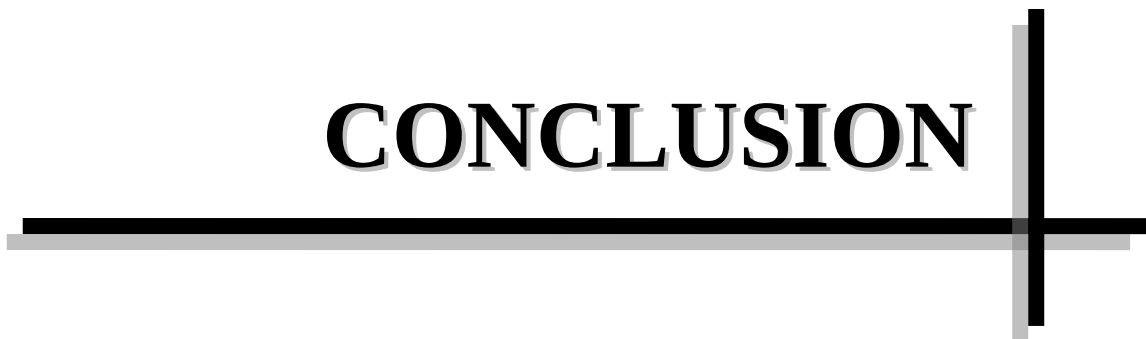
Table 16: VAS pre-procedure and at 6-month follow up:

VAS	Pre-procedure	6-month follow up
Our study	7.91 ± 0.74	3.17 ± 1.07
Manunta et al. ¹²¹	8.2 ± 0.6	5.7 ± 0.8
Gobbi et al. ¹²³	3.2 ± 1.4	1.9 ± 1.7

Supporting the change seen in the VAS score post-treatment, when assessed by the WOMAC score, there is a statistically significant improvement ($p < 0.001$) with a decrease in the WOMAC score from pre-op 67.11 ± 8.73 to 50.14 ± 9.99 at 1 month, and 40.83 ± 7.8 at 3 months and further reduced to 31.66 ± 5.28 at 6 months. The median WOMAC score at pre-

op was 65 (IQR 58 to 76), 51 (IQR 39 to 62) at 1 month, 37 (IQR 34 to 46) at 3 months and 31 (IQR 28 to 35) at 6 months. Good WOMAC outcome is noted in 51.43%, and 48.57% had poor WOMAC outcome. Similar findings were noted in Nguyen et al's study where the WOMAC scores demonstrated that at 18 months post- treatment, all patients in the treatment group had significantly improved pain, movement, and capacity for physical activity.¹¹² In another study, Vasavilbaso et al¹¹³, reported that patients treated with PRP in their study constitute a diverse group who seemed to follow the rule of all or nothing, as those who improved did so in a very significant way, and this improvement is maintained until the end of follow-up, whereas something similar occurred with non-responder patients and by the end of the study, only 60% of patients achieved the minimal clinically important improvement threshold. In a meta-analysis, Dai et al¹¹⁷, reported that when compared with saline, PRP was more effective for pain relief (WOMAC pain score) and functional improvement (WOMAC function score) at 6 months and 12 months post-injection.

CONCLUSION



CONCLUSIONS:

A total of 35 patients diagnosed with knee OA with a mean age of 55.97 ± 4.93 years are included in the study. This is a predominantly female population group, with 62.86% of them being female and 37.14% males. Majority of the patients with 74.29% are diagnosed as having Kellegren-Lawrence grade III knee OA and 25.71% grade II knee OA. 68.57% had right side knee OA, and 31.43% had left side knee OA. After arthroscopic debridement and microfracture (Steadman's technique) and Ca-gluconate activated Platelet-rich plasma injection is injected into the joint, around the site of the lesion under arthroscopic at the same setting. Patients are evaluated using WOMAC, VAS SCORE for levels of pain and knee function prior to the procedure and after 1 month, 3 months and 6-month post-procedure. It was observed that the mean VAS score has decreased gradually from pre-op which was at 7.91 ± 0.74 to 5.71 ± 0.99 at 1 month, further down to 4.51 ± 0.66 at 3 months and it was 3.17 ± 1.07 at 6 months showing the good functional outcome of the procedure in terms of pain. When assessed by the WOMAC score, there is a statistically significant improvement ($p < 0.001$) with a decrease in the WOMAC score from pre-op 67.11 ± 8.73 to 50.14 ± 9.99 at 1 month, and 40.83 ± 7.8 at 3 months and further reduced to 31.66 ± 5.28 at 6 months.

The study concludes that intra-articular PRP injection after debridement and microfracture has shown more benefit in terms of pain relief and functional improvement. It also prolongs the treatment efficacy of microfracture in patients with symptomatic knee OA.

LIMITATIONS & RECOMMENDATIONS

- ❖ Limitations of the study are small sample size and short follow-up period.
- ❖ Patients with Kellegren-Lawrence grade II and III knee OA are studied hence cannot draw conclusions for more severe cases of OA.
- ❖ No second-look arthroscopy was performed for documenting the evidence of Cartilage healing.
- ❖ Long term follow-up is recommended to analyze the long-term efficacy of PRP with debridement and microfracture.

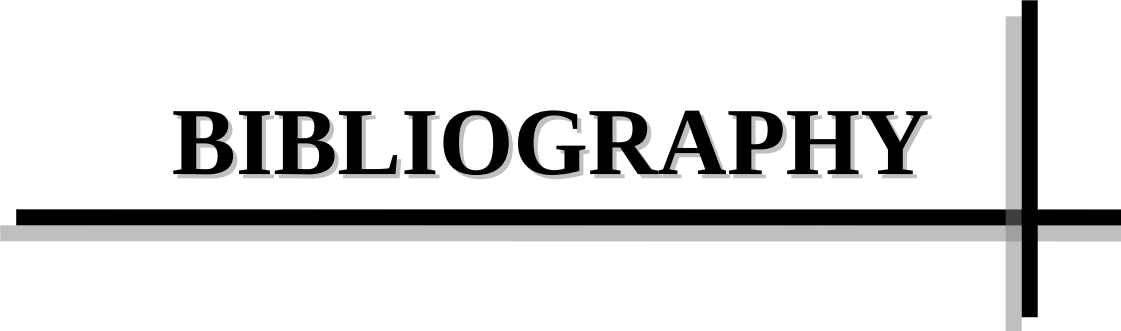
SUMMARY

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SUMMARY

Arthroscopic procedures for osteoarthritis of the knee include arthroscopic debridement and lavage, which is helpful for short-term symptom relief in early arthritis, but ineffective for halting the progression of the disorder. Arthroscopic microfracture is indicated as a routine treatment for OA, developed by Steadman in 1997, which involves penetration of the subchondral bone plate with an arthroscopic awl to allow bone marrow cells to repopulate defects, filling them with repair tissue. PRP is thought to stimulate the proliferation of chondrocytes and the differentiation of mesenchymal cells of the subchondral bone into the chondrogenic line. Combining microfracture with PRP injections helps in promoting early clinical improvement. We studied 35 patients diagnosed with Osteoarthritis clinic-radiologically selected from the Department of Orthopedics, R L Jalappa Hospital and Research Centre, Kolar, Karnataka. VAS score and WOMAC score were considered as primary outcome variables. Age, gender etc., were considered as Primary explanatory variable. After arthroscopic debridement and microfracture (Steadman's technique) and Calcium gluconate activated Platelet-rich plasma injection is injected into the joint, around the site of the lesion under arthroscopic at the same setting. Patients are evaluated using WOMAC, VAS SCORE for levels of pain and knee function prior to the procedure and after 1 month, 3 months and 6-month post-procedure. The study concludes that intra-articular PRP injection after debridement and microfracture has more benefit in pain relief and functional improvement, and it also prolongs the treatment efficacy of microfracture in patients with symptomatic knee OA.

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A decorative graphic consisting of a thick horizontal black line and a thick vertical black line intersecting at the right end of the horizontal line. The vertical line extends both above and below the horizontal line.

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ANNEXURES

A decorative graphic element consisting of a thick horizontal line and a thick vertical line intersecting at a right angle. The intersection is located at the bottom right of the page, below the word 'ANNEXURES'. The lines are black and have a slight shadow effect.

ANNEXURES-I

ARTHROSCOPIC INSTRUMENT AND PORTALS



ARTHROSCOPIC INSTRUMENTS



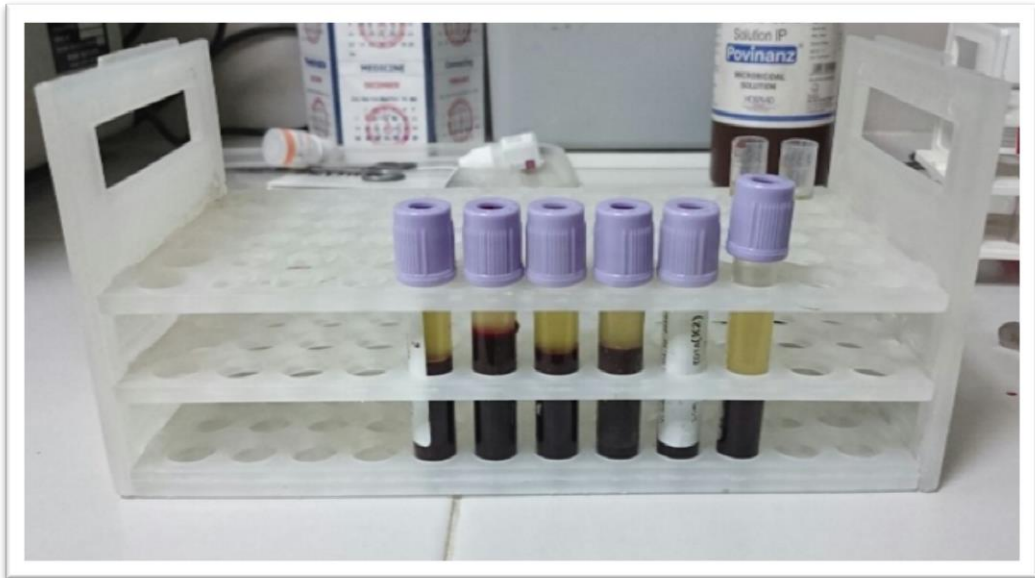
PLATELET RICH PLASMA COLLECTION AND PROCESSING



CENTRIFUGE FOR PRP SEPARATION WITH TIMER : FRONT VIEW



VACUTAINERS INSIDE THE CENTRIFUGE



VACUTAINERS AFTER DOUBLE CENTRIFUGATION

- 1) 15 MINUTES OF CENTRIFUGATION WITH 1000 RPM
- 2) 5 MINUTES OF CENTRIFUGATION WITH 3000 RPM



CA-GLUCONATE ACTIVATED PRP IN SYRINGE

RADIOGRAPHS

CASE 1



CASE 3



CASE 11



CASE 17

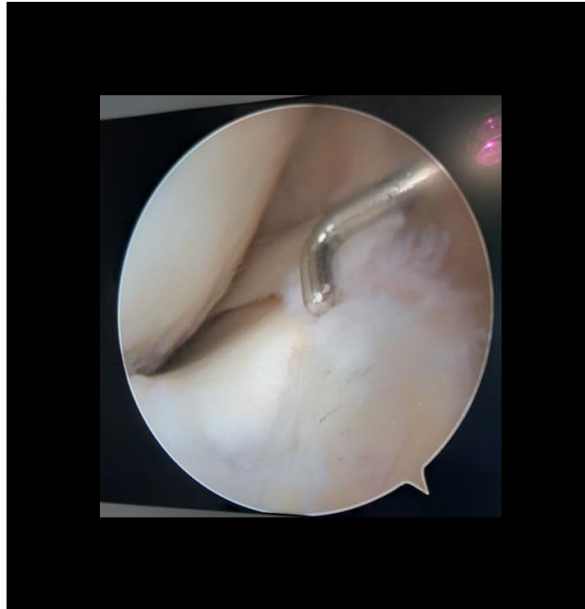


CASE 35

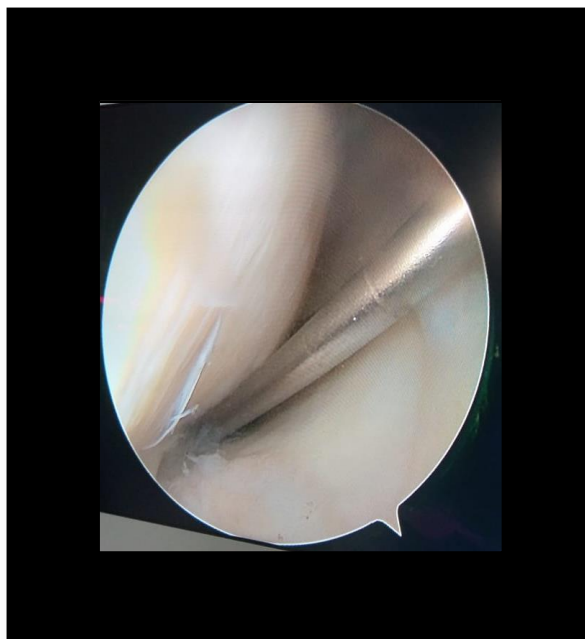


INTRA-OPERATIVE IMAGES

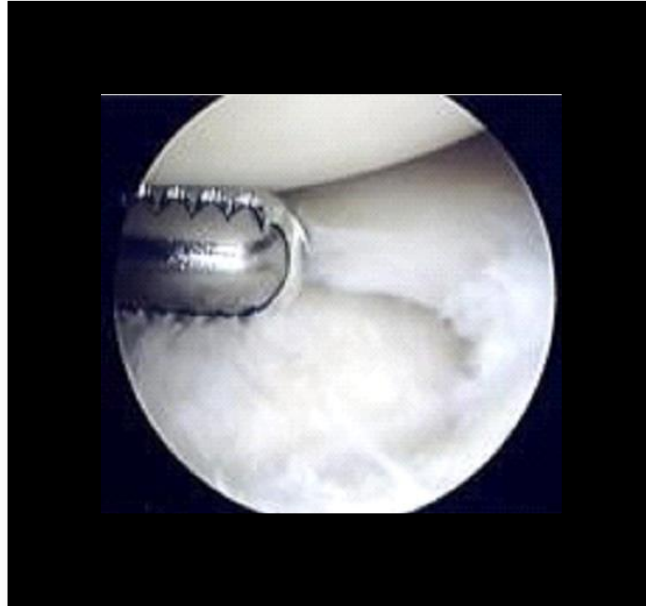
CASE 3 : SHOWS MENISCAL FRAYING



CASE 11: SHOWS FEMORAL CONDYLE CARTILAGE FRAYING



CASE 17: SHOWS INTACT MENISCI AFTER DEBRIDEMENT



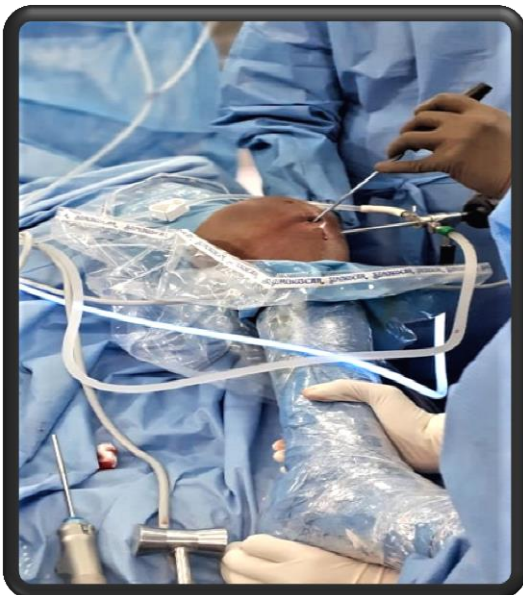
CASE 35: OUTER-BRIDGE GRADE-IV PATELLAR CHONDROMALACIA



PLAN FOR ARTHROSCOPIC DEBRIDMENT



MICROFACTURE AWL



PRP INJECTION



ANNEXURES-II

PROFORMA

Name:

I.P. No.:

Age:

Date of Admission:

Sex:

Date of Surgery:

Address:

Date of Discharge:

PRESENTING COMPLAINTS

- ❖ Pain:
- ❖ Swelling:
- ❖ Locking:
- ❖ Deformity:
- ❖ Inability to bear weight / walk:
- ❖ Morning stiffness:

H/O OF PRESENTING ILLNESS

PAIN

Onset, Progression, aggravating and relieving factors

SWELLING

Mode of onset, progress, impairment of function

LOCKING

Degree of locking, nature of locking, amount of flexion

VARUS DEFORMITY

INABILITY TO WALK

On a flat surface, going up or downstairs, going on and off the toilet

MORNING STIFFNESS

Duration

PAST HISTORY

Diabetes mellitus

Hypertension

Tuberculosis

Trauma to knee

PERSONAL HISTORY

FAMILY HISTORY

GENERAL EXAMINATION

- ❖ CARDIOVASCULAR SYSTEM
- ❖ CENTRAL NERVOUS SYSTEM
- ❖ RESPIRATORY SYSTEM
- ❖ PER ABDOMEN

LOCAL EXAMINATION

INSPECTION

- ❖ Skin over knee
- ❖ Swelling
- ❖ Muscle wasting
- ❖ Deformity
- ❖ Gait – antalgic

PALPATION

- ❖ Tenderness
- ❖ Bony irregularity
- ❖ Patellar tap
- ❖ Synovial thickening
- ❖ Crepitus

INVESTIGATION (PRE-OP ASSESSMENT)

- ❖ Radiography of weight-bearing bilateral knee joint
- ❖ AP, lateral.
- ❖ Routine blood investigation

SURGICAL TREATMENT

- ❖ Type of anesthesia
- ❖ Position of patient
- ❖ Prophylactic antibiotics
- ❖ Tourniquet application
- ❖ Duration of surgery
- ❖ Per operative findings

POSTOPERATIVE CARE

- ❖ Analgesics
- ❖ Antibiotics
- ❖ Physiotherapy

COMPLICATIONS

DURATION OF STAY IN HOSPITAL

FOLLOW UP

VISUAL ANALOGUE SCALE

PRE -OP	
POST OP: 1 MONTH	
3MONTHS	
6 MONTHS	

WESTERN ONTARIO MACMASTER OSTEOARTHRITIS INDEX

PRE -OP	
POST OP: 1 MONTH	
3 MONTHS	
6 MONTHS	

CONSENT FORM

STUDY TITLE: “FUNCTIONAL OUTCOME FOLLOWING ARTHROSCOPIC DEBRIDEMENT WITH MICROFRACTURE AND PLATELET RICH PLASMA INJECTION IN OSTEOARTHRITIS OF KNEE –A PROSPECTIVE STUDY”.

CHIEF RESEARCHER/ PG GUIDE’S NAME: DR. SANDESH AGARWAL
UNDER THE GUIDANCE OF DR. PRABHU.E

NAME OF THE SUBJECT:

AGE:

ADDRESS

- a) I have been informed in my own vernacular language the purpose of the study, the necessity of relevant investigations to be carried out, and photographs to be taken.
- b) I understand that the medical information produced by this study will become part of the institutional record and will be kept confidential by the said institute.
- c) I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
- d) I agree not to restrict the use of any data or results that arise from this study provided such use is only for the scientific purpose(s).
- e) I confirm that _____ (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that I may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant’s signature

Signature of the witness:

Date:

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature

Date:

PATIENT INFORMATION SHEET

STUDY TITLE: “FUNCTIONAL OUTCOME FOLLOWING ARTHROSCOPIC DEBRIDEMENT WITH MICROFRACTURE AND PLATELET RICH PLASMA INJECTION IN OSTEOARTHRITIS OF KNEE –A PROSPECTIVE STUDY”.

STUDY SITE: R.L Jalapa Hospital and Research Centre, Tamaka, Kolar.

AIM:

- ❖ To assess the pain using **Visual Analogue scale** prior to surgery
- ❖ To evaluate functional outcome following arthroscopic debridement with Micro-fracture and platelet rich plasma injection on a patient with mild to moderate osteoarthritis of the knee using **WOMAC score and Visual Analogue Scale**

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in this study, we will collect information (as per proforma) from you. This information collected will be used for dissertation and publication. All information collected from you will be kept confidential and will not be disclosed to any outsider. Subject's identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee, and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For any further clarification, you can contact the study investigator:

Dr. SANDESH AGARAWAL

Mobile no: 8668672697

E-mail id: preciouss333@gmail.com

ರೋಗಿಯ ಮಾಹಿತಿ ಮತ್ತು ಸಮ್ಮತಿ ಪತ್ರ

ಕ್ರಮ ಸಂಖ್ಯೆ:

ರೋಗಿಯ ಹೆಸರು:

ಮೊಬೈಲ್ ನಂಬರ್:

ಶೀರ್ಷಿಕೆ: “FUNCTIONAL OUTCOME FOLLOWING ARTHROSCOPIC DEBRIDEMENT WITH MICROFRACTURE AND PLATELET RICH PLASMA INJECTION IN OSTEOARTHRITIS OF KNEE –A PROSPECTIVE STUDY”.

ಈಕೆಳಗೆ ರುಜು ಮಾಡಿರುವ ನಾನು, ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು, ಅಧ್ಯಯನ ನಡೆಸಲು ಮತ್ತು ಈ ಸಮ್ಮತಿ ನಮೂನೆಯ ಅಂಶಗಳಂತೆ ನನ್ನ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯನ್ನು ಬಹಿರಂಗಪಡಿಸುವ ಒಪ್ಪಿಗೆ ನೀಡಿರುತ್ತೇನೆ.

ನನಗೆ ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶ ಹಾಗೂ ಗೋಪ್ಯತೆಯ ವಿಚಾರವನ್ನು ನನ್ನ ಭಾಷೆಯಾದ ಕನ್ನಡದಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದ ಕುರಿತಾದ ನನ್ನ ಎಲ್ಲ ಪ್ರಶ್ನೆಗಳಿಗೂ ಸಮಾಧಾನಕರ ಉತ್ತರ ನನಗೆ ದೊರಕಿರುತ್ತದೆ. ಎಲ್ಲ ಮಾಹಿತಿಗಳು ಸಂಶೋಧನೆಗಾಗಿಯೇ ಬಳಸಲಾಗುವುದು.

ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿ ಇಡಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರ ಬಹಿರಂಗ ಮಾಡಲಾಗುವುದಿಲ್ಲ.

ಈ ಅಧ್ಯಯನದಿಂದ ನನ್ನ ಜೀವಕ್ಕೆ ಯಾವುದೇ ಹಾನಿ ಇರುವುದಿಲ್ಲ ಮತ್ತು ಹೆಚ್ಚು ಅನುಕೂಲಕರವಾಗಿದೆ ಎಂದು ನನಗೆ ಅರ್ಥವಾಗಿರುತ್ತದೆ.

ನಾನು ಯಾವಾಗ ಬೇಕಾದರೂ ಈ ಅಧ್ಯಯನದಿಂದ ಹೊರನಡೆಯಬಹುದು ಮತ್ತು ನನಗೆ ಯಾವುದೇ ರೀತಿಯ ಅಧಿಕ ಖರ್ಚಾಗಿರುವುದಿಲ್ಲವೆಂದು ನಾನು ಒಪ್ಪಿಕೊಂಡಿರುತ್ತೇನೆ.

ರೋಗಿಯ ಹೆಸರು ಮತ್ತು ರುಜು/ಬೆರಳುಗುರುತು

ಸಾಕ್ಷಿಗಳ ಹೆಸರು ಮತ್ತು ರುಜು

1.

2.

ಪ್ರಮುಖ ಸಂಶೋಧಕರ ಹೆಸರು ಮತ್ತು ರುಜು: ಡಾ|| DR SANDESH AGARAWAL

MASTER SHEET

A	B	C	D	E	F	G	H	I	J	H	I	J
S.N O	AG E	GEND ER	SID E	GRADE KELLEGR EN- LAWRENC E	VAS PRE OP	VAS POST OP 1MON TH	VAS POST OP 3MON TH	VAS POST OP 6MON TH	WOM AC PREO P	WOMA C POST OP 1MON TH	WOMA C POST OP 3MON TH	WOMA C POST OP 6MON TH
1	50	2	2	III	8	6	5	5	57	38	37	33
2	60	2	1	III	7	5	5	4	59	40	33	31
3	58	1	1	II	9	7	5	4	73	56	38	38
4	60	1	1	III	9	5	5	5	80	62	41	40
5	55	2	2	II	8	4	4	3	57	37	33	33
6	60	1	1	III	8	5	5	3	58	38	36	30
7	60	1	1	III	7	6	5	3	57	39	37	35
8	60	2	1	II	8	6	5	6	63	51	46	51
9	60	2	1	III	9	7	5	3	79	63	55	31
10	60	2	1	III	7	6	5	2	76	62	57	28
11	55	2	1	II	7	5	3	2	57	51	46	36
12	56	1	1	III	9	7	5	4	73	56	48	32
13	60	2	1	III	9	5	5	5	80	62	41	40
14	59	2	1	III	8	4	4	3	67	37	33	30
15	52	2	2	II	8	6	3	2	71	62	32	25
16	60	2	2	III	8	7	4	3	76	57	34	26
17	55	2	1	III	7	5	4	2	62	52	41	31
18	47	1	1	II	9	7	4	2	69	46	36	30
19	46	1	2	III	8	5	4	2	74	57	33	26
20	55	1	1	III	7	5	5	4	57	39	37	29
21	52	2	2	II	8	5	4	3	64	42	36	30
22	60	1	2	III	8	6	6	4	63	51	46	35
23	57	1	2	III	8	7	4	3	76	57	34	26
24	40	1	2	II	7	4	4	3	65	51	46	35
25	60	2	1	III	8	4	4	3	57	37	33	33
26	60	2	1	III	8	5	4	2	58	38	36	25
27	52	2	2	III	7	6	5	2	76	62	57	28
28	59	2	1	III	8	7	4	3	76	57	34	26
29	57	2	1	III	9	7	5	3	79	63	55	31
30	50	1	1	III	8	6	4	2	63	51	46	26
31	52	2	1	III	8	5	4	3	58	38	36	30
32	60	1	1	III	7	6	5	5	57	39	37	35
33	57	2	2	II	7	6	5	3	57	39	37	30
34	60	2	1	III	9	7	5	3	79	63	55	35
35	55	2	1	III	7	6	5	2	76	62	47	28

Key to Master Chart:

- A- SERIAL NUMBER
- B- AGE IN YEARS
- C- GENDER: 1=MALE, 2=FEMALE
- D- SIDE: 1=RIGHT, 2=LEFT
- E- KELLEGGREN-LAWRENCE GRADE
- F- VAS PRE-OP
- G- VAS POST-OP 1 MONTHS
- H- VAS POST-OP 3 MONTHS
- I- VAS POST-OP 6 MONTHS
- J- WOMAC PRE-OP
- K- WOMAC POST-OP 1 MONTHS
- L- WOMAC POST-OP 3 MONTHS
- M- WOMAC POST-OP 6 MONTHS