COMPARISON OF INTRA ARTICULAR DELIVERY OF HYALURONIC ACID BETWEEN ACTIVATED AND NON-ACTIVATED QUADRICEPS FOR OSTEOARTHRITIS KNEE

BY

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MASTER OF SURGERY
IN
ORTHOPAEDICS

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I hereby declare that this dissertation entitled **"COMPARISON OF INTRA ARTICULAR DELIVERY OF HYALURONIC ACID BETWEEN ACTIVATED AND NON-ACTIVATED QUADRICEPS FOR OSTEOARTHRITIS KNEE"** is a bonafide and genuine research work carried out by me under the guidance of Dr. PRABHU ETHIRAJ, Professor, Department of Orthopaedics, Sri Devaraj Urs Medical College, Kolar, in partial fulfilment of University regulation for the award "**MASTER OF SURGERY IN ORTHOPAEDICS**", the examination to be held in April/May 2022 by SDUAHER. This has not been submitted by me previously for the award of any degree or diploma from the university or any other university.

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ABSTRACT

Background: Intra articular hyaluronic acid injections are non-surgical effective treatment options for osteoarthritis of knee. One of the main criteria for effectiveness of this injection is accurate placement of needle into suprapatellar bursa of knee. Delivery into other surrounding tissues is found to increase pain. The best approach to locate suprapatellar bursa for insertion of needle is ultrasound guidance. But ultrasound imaging may not be available in low resource settings. Hence an approach without ultrasound guidance but improving accuracy of needle placement is desirable. Activated quadriceps method is found to be one such approach which results in expansion of suprapatellar bursa.

Material and Methods: A prospective, comparative and hospital-based study conducted at R. L. Jalappa Hospital and Research Centre, SDUMC, Tamaka on patients with OA knee from December 2019 to July 2021. Clinical data is collected and evaluated with pre-injection and post-injection suprapatellar pouch distension and VAS scoring.

Results: A total of 46 subjects were included in the final analysis. Out of these 50% were injected in activated quadriceps and 50% were injected in non-activated quadriceps position. The mean age was 52.35 ± 9.82 in activated quadriceps group and it was 54.04 ± 7.68 in non-activated quadriceps. The mean Suprapatellar pouch expansion measured using USG pre-injection was 2.49 ± 0.55 in activated quadriceps group and it was 2.54 ± 0.58 in non-activated quadriceps. The mean Suprapatellar pouch expansion measured using USG post-injection was 3.55 ± 0.67 in activated quadriceps group and it was 3.06 ± 0.68 in non-activated quadriceps. There was no difference noted in pain scale after injection.

Conclusion: This study concludes that activated quadriceps method results in greater expansion of suprapatellar bursa there by facilitating accurate intra articular injection without use of ultrasound guidance. This method can be used in low resource settings for accurate delivery of intra articular knee injections.

Keywords: Osteoarthritis, Knee, intra articular injection, superolateral approach, activated quadriceps, VAS

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LIST OF ABBREVIATIONS

GLOSSARY	ABBREVIATIONS
ACL	Anterior cruciate Ligament
ACR	American college of rheumatology
BA	Betamethasone Acetate
BMI	Body mass index
CS	Corticosteroids
ECM	Extracellular matrix
HA	Hyaluronic acid
IA	Intra articular
KL	Kellgren Lawrence
LCL	Lateral collateral Ligament
MA	Methylprednisolone Acetate
MCL	Medial collateral Ligament
MMP	Matrix metalloproteinases
MSC	Mesenchymal stem cells
NSAID	Non-steroidal anti-inflammatory drugs
OA	Osteoarthritis
OAI	Osteoarthritis initiative
PCL	Posterior cruciate Ligament
PFJ	Patellofemoral joint
PMN	Polymorphonuclear
PRP	Platelet-rich plasma

STZ	Superficial tangential zone
TA	Triamcinolone Acetate
TFJ	Tibiofemoral joint
TH	Triamcinolone Hexacetonide
VAS	Visual analogue scale
WBC	White blood cell

INTRODUCTION

INTRODUCTION:

Osteoarthritis (OA) is the most common form of the arthritis and amongst the leading causes of disability. This degenerative and progressive joint disease affects around 250 million people worldwide.[1] With the rising incidence of obesity and the ageing of the population, societal burden (both in terms of human suffering and usage of health resources) is expected to rise.

OA is defined as idiopathic, slowly progressive disease of diarthrodial (Synovial) joints, occurring late in life and characterized pathologically by focal degeneration of cartilage, underlying subchondral bone thickening (Sclerosis), marginal osteochondral outgrowths (Osteophytes) and joint deformity.

Clinically it can be defined as recurring episodes of pain, synovitis with effusion, stiffness, and progressive limitation of motion; and radiographically by narrowing of joint interval, increased density and thickening of subchondral bone, subchondral cysts, and marginal bony excrescences.

The pathogenesis involves an imbalance between normal cartilage derivative and repair mechanisms.

OA usually affects finger joints, knees, hips, shoulders, and the spine. The knee is the most commonly affected joint with osteoarthritis. The heterogeneity of OA arises from many factors that can contribute to cartilage damage. It initially appears to affect the surface and progressively extends deeply throughout the entire cartilage thickness.

Alterations of the physiochemical characteristics diminish cartilage resistance to compressive and tensile forces, it develops fibrillations, deep clefts, shredding, and finally complete erosion, exposing the subchondral bone.[2]

When assessing patients with early knee OA and identifying disease progression, combining biochemical markers with clinical and radiographic data is most helpful in improving diagnostic and prognostic values.[3]

In India, 22 percent to 39 percent of people have symptomatic OA knee, which is defined as pain on most days of the month and radiologic evidence of arthritis.[4] Intra-articular injections of corticosteroids, hyaluronic acid, or other medicines can be used to treat knee osteoarthritis and rheumatoid arthritis. However, it has been observed that medication is injected into the surrounding synovium, suprapatellar fat pad, or prefemoral fat pad erroneously in some situations.[5-7]

Patients who receive incorrect injections may experience excruciating agony. In such circumstances, it's probable that the injection was made into the synovial tissue, which contains numerous nerve endings, rather than the suprapatellar bursa.[8,9] Patients with a lot of subcutaneous fat and little effusion have a higher risk of extra-articular injections, which makes it difficult for doctors to identify if the needle has pierced the suprapatellar bursa.[10] A reliable method to inject into the joint should be created to prevent pain associated with extra-articular injections[11] and to assure that an injected medicine is effective.

NEED FOR STUDY:

Intra-articular injection is an important technique for treating osteoarthritis of knee. However, medication is often inaccurately injected outside the joint. To prevent pain associated with extra-articular injections and to ensure that an injected drug is effective. The activated quadriceps contraction method is therapeutically effective and could reduce the risk of injection pain due to inaccurate injections into the synovial membrane, which has a large number of nerve endings. In big cities and towns, the intra articular injections are performed under ultrasound guidance. However, in the rural settings like large parts of India where ultrasound is not available, this technique can be utilised and intra articular knee injections can be given. So far activation of quadriceps has not been considered for intra articular injection of knee. It has been recently suggested that activated quadriceps enhance the drug delivery in intra articular injections. A similar study has so far not been done in India and very few literatures are available on activated quadriceps in intra articular knee injections.

AIMS & OBJECTIVES

AIMS & OBJECTIVES:

1. To document the amount of drug delivery in intra articular injection in activated quadriceps by measuring antero-posterior diameter of suprapatellar pouch pre intra articular injection with ultrasound and post intra articular injection with ultrasound.
2. To document the amount of drug delivery in intra articular injection in non-activated quadriceps by measuring antero-posterior diameter of suprapatellar pouch pre intra articular injection with ultrasound and post intra articular injection with ultrasound.
3. To compare amount of drug delivery in intra articular injection in activated and non-activated quadriceps groups.
4. To document the pain in activated and non-activated quadriceps groups by using visual analogue scale pre intra articular injection and post intra-articular injection.

REVIEW OF LITERATURE

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.[12] 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, hence it is susceptible to injuries.[13,14]

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.[15]

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.[15]

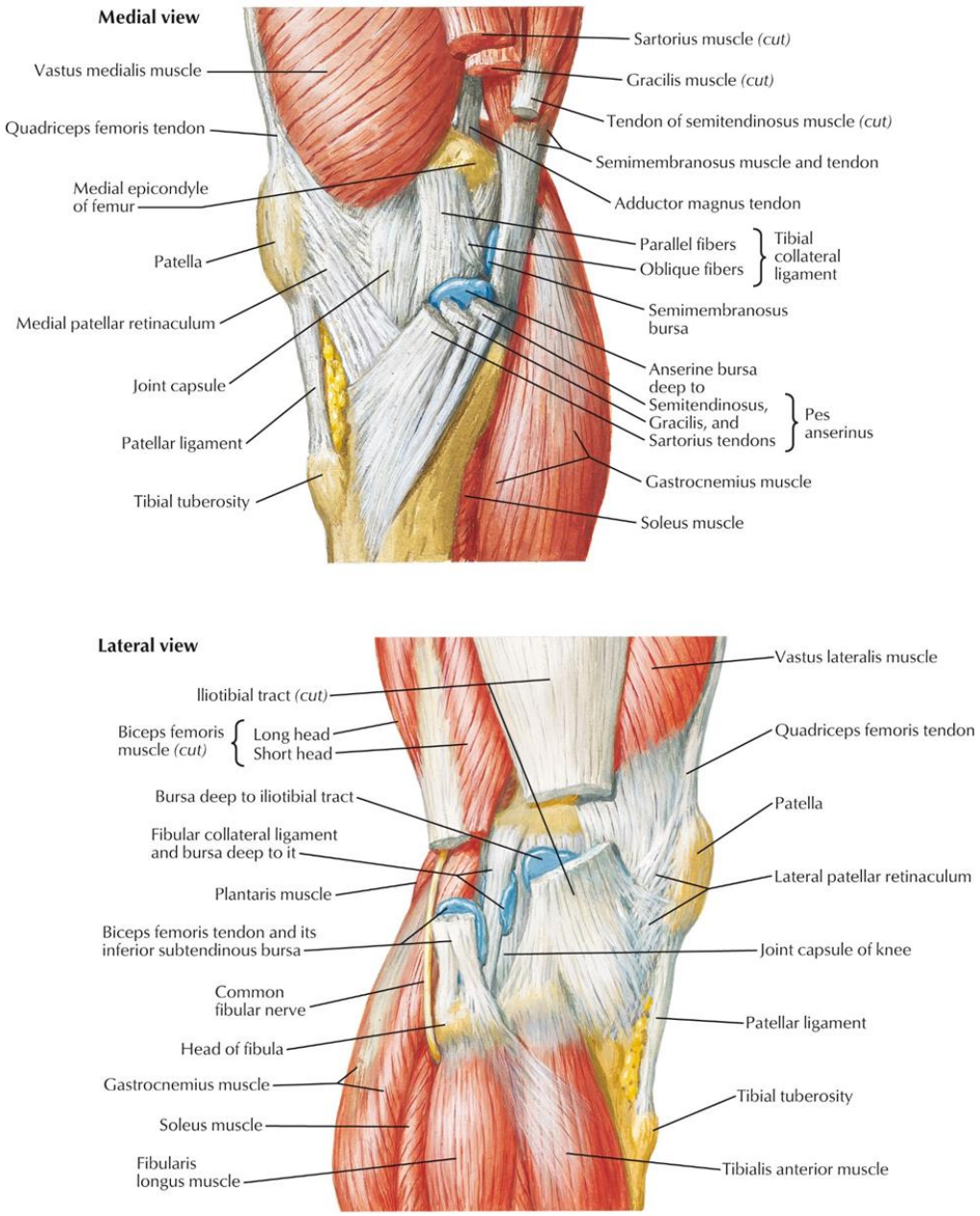

Figure 1: Knee medial & lateral view[16]

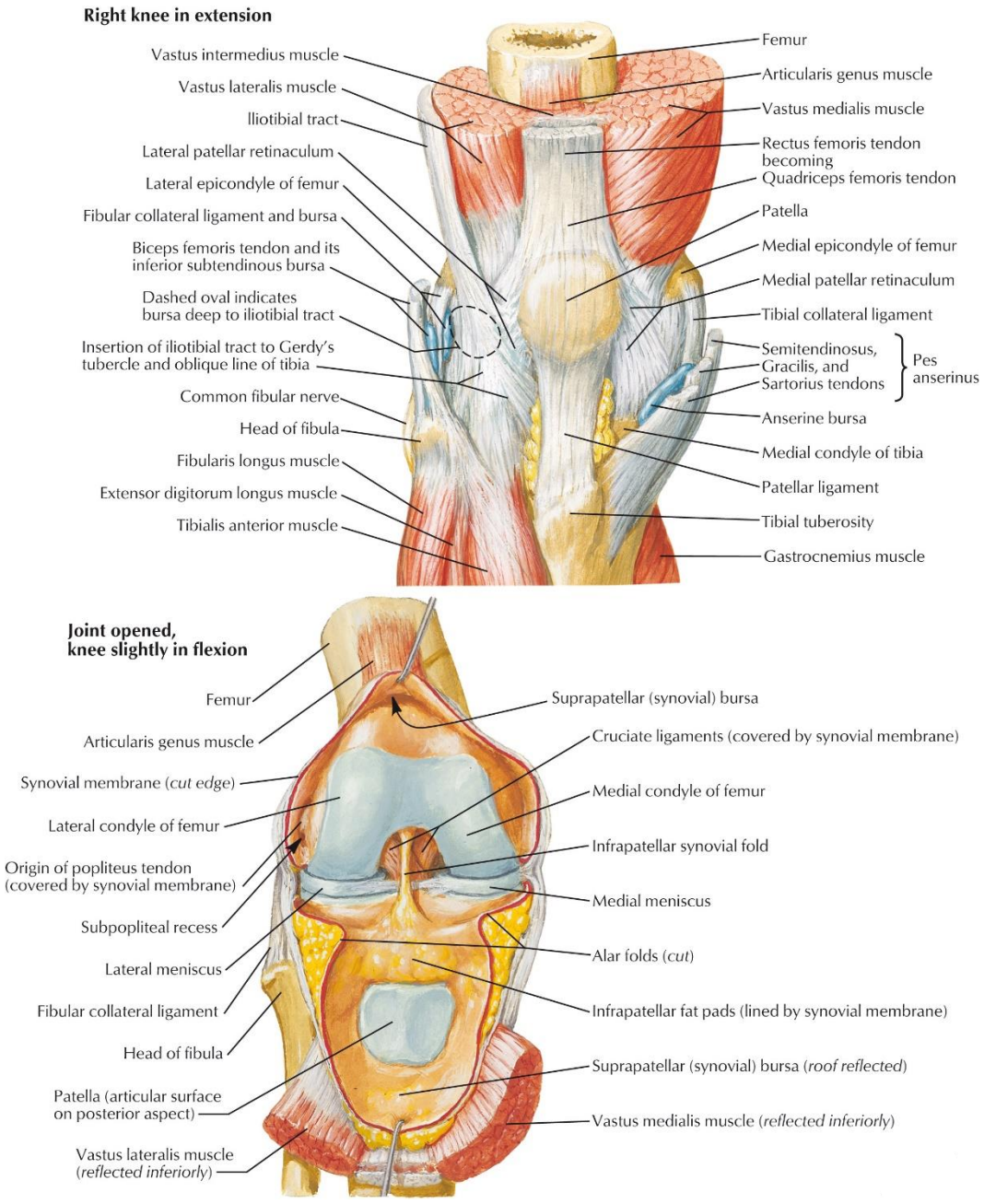

Figure 2: Knee anterior view[16]

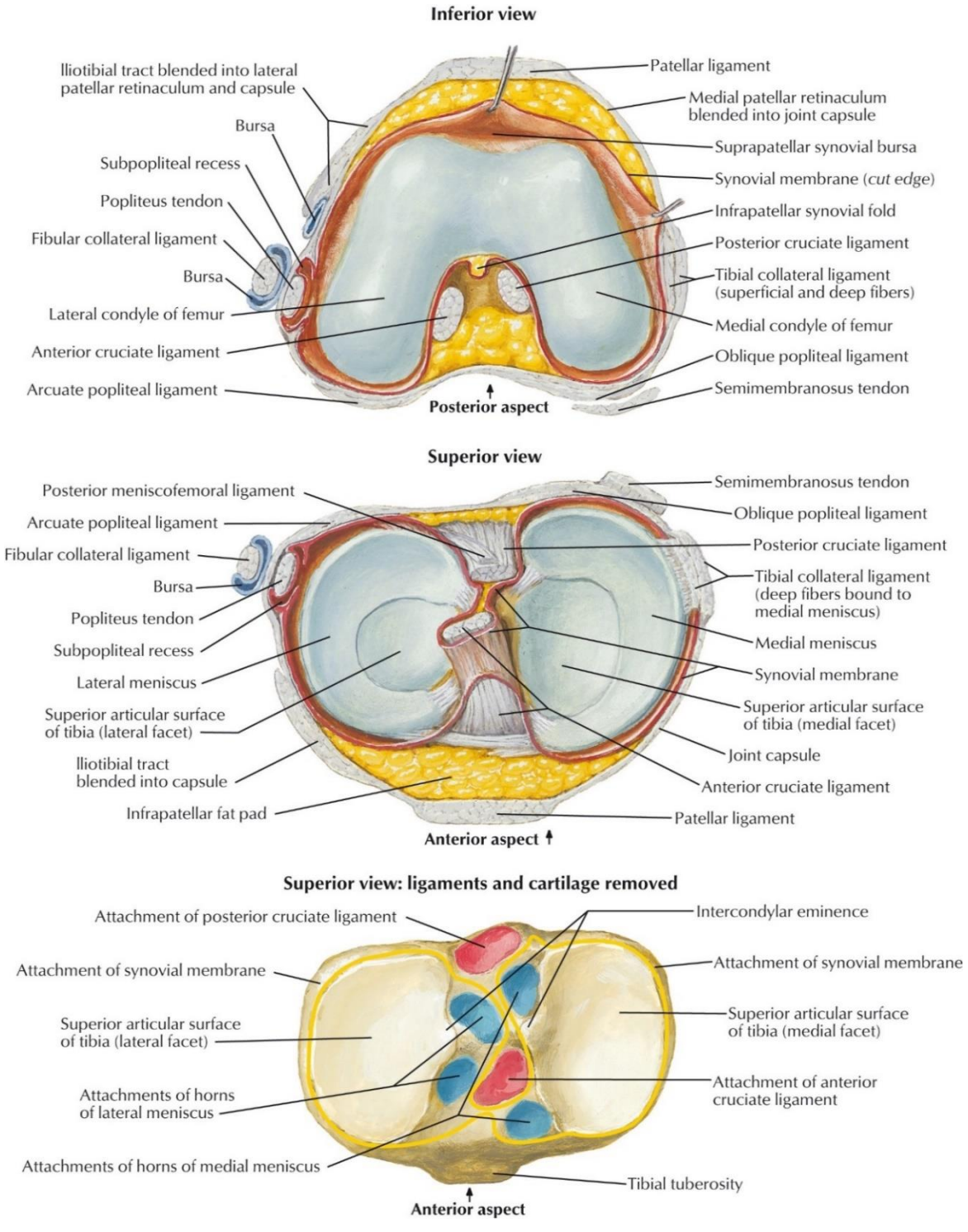

Figure 3: Knee interior view[16]

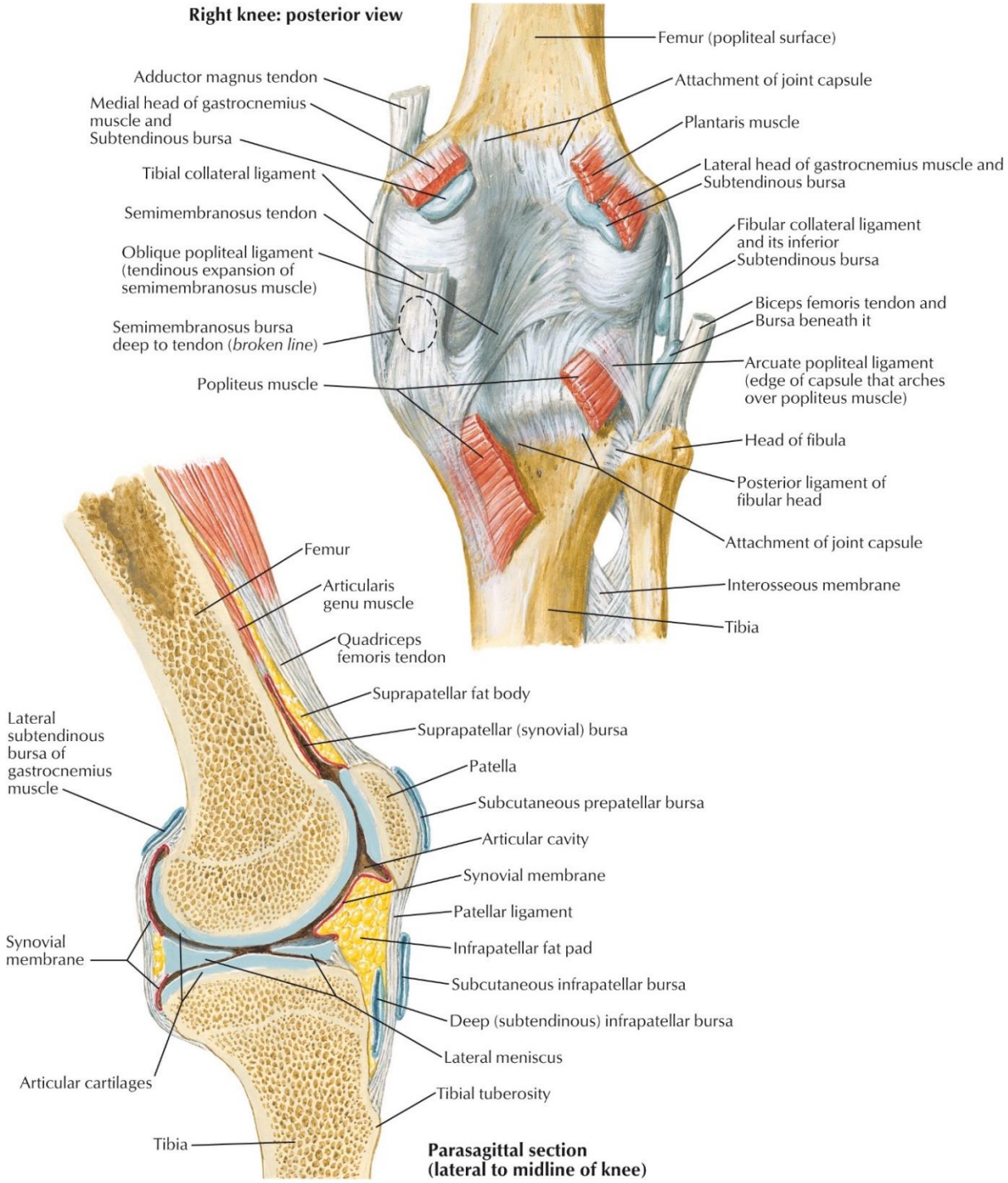

Figure 4: Knee posterior view[16]

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.[17]

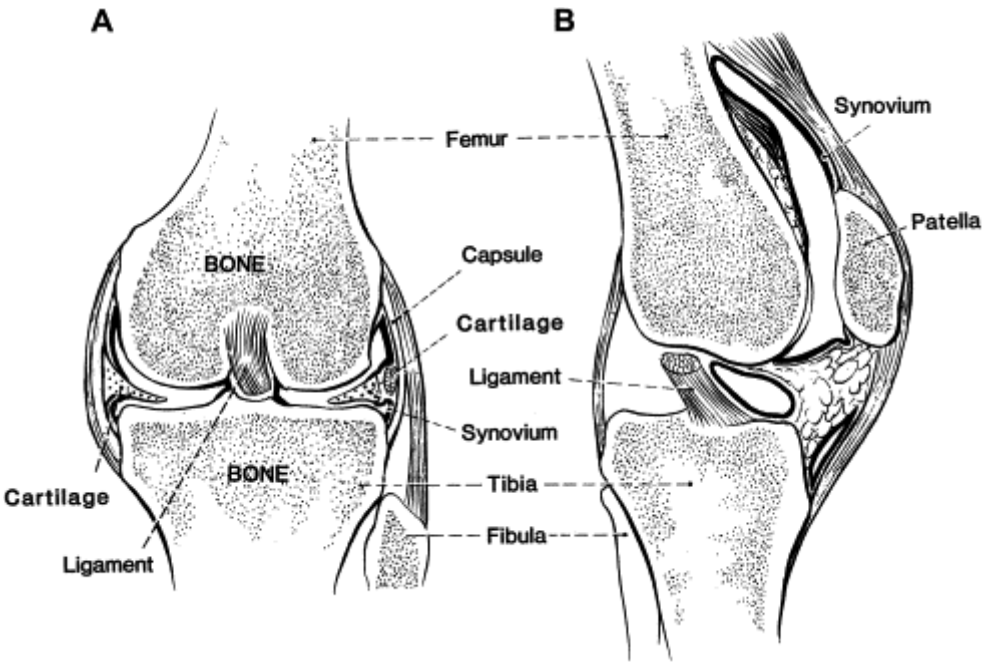

Figure 5: Coronal & Sagittal illustrations depicting relationship between Knee Capsule and Synovium[18]

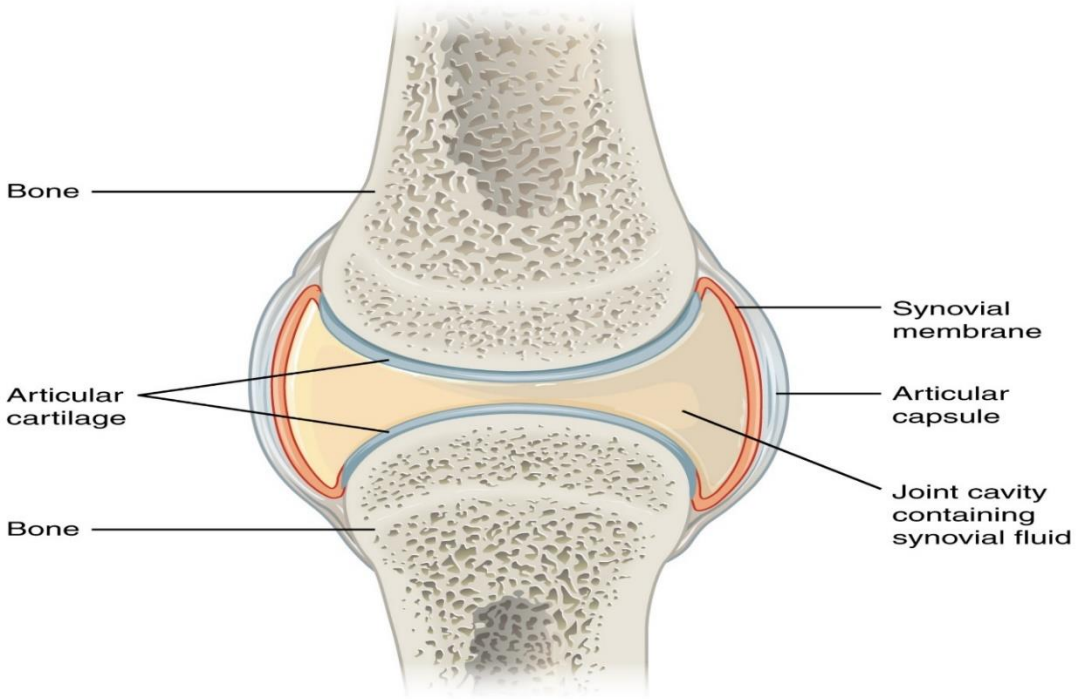

Figure 6: Synovial joint[19]

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.[17]

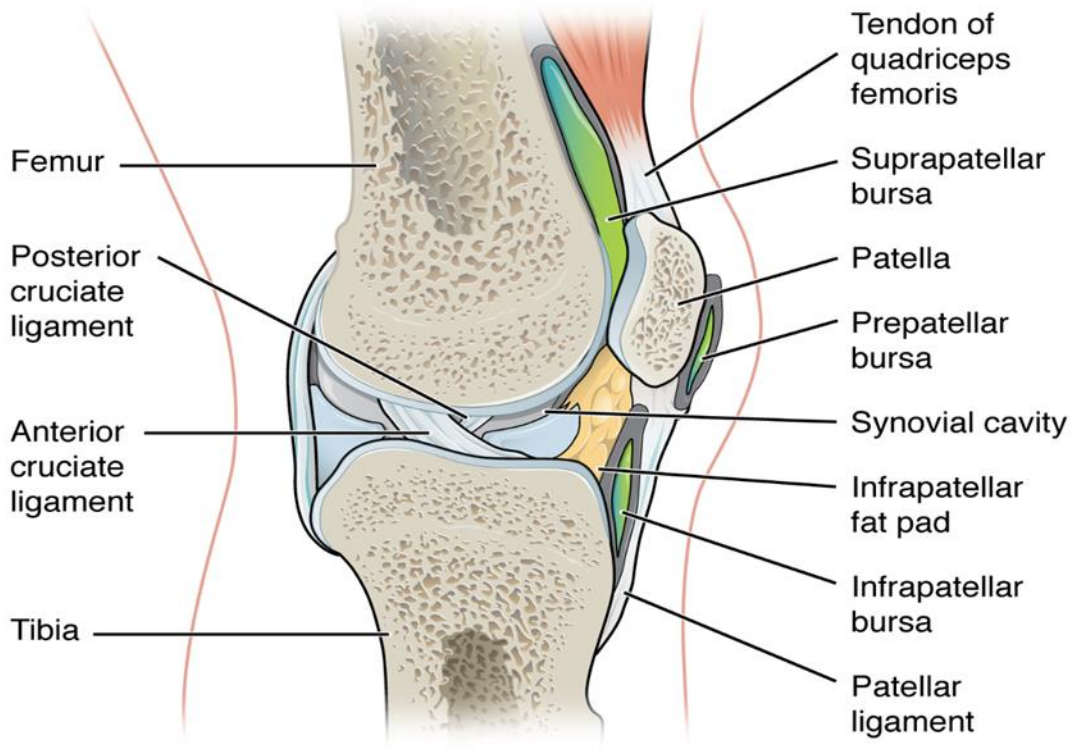

Figure 7: Bursae[20]

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.[20]

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.[20] 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.[20]

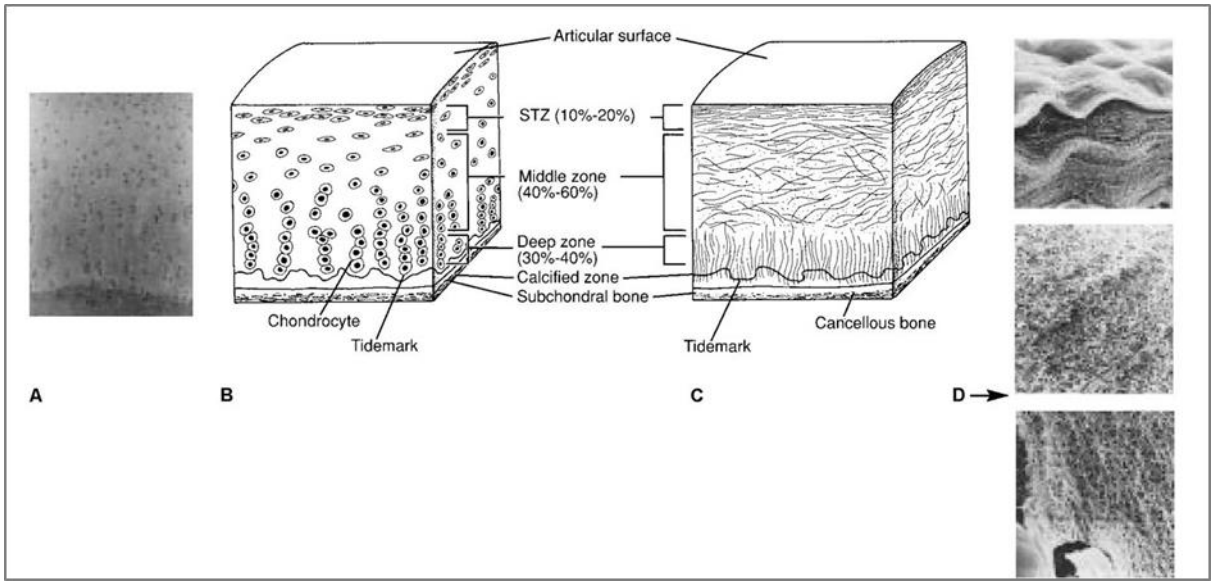

Figure 8: Structure of articular cartilage[17]

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.[21] 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.[22] 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.[23] 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.[23]

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

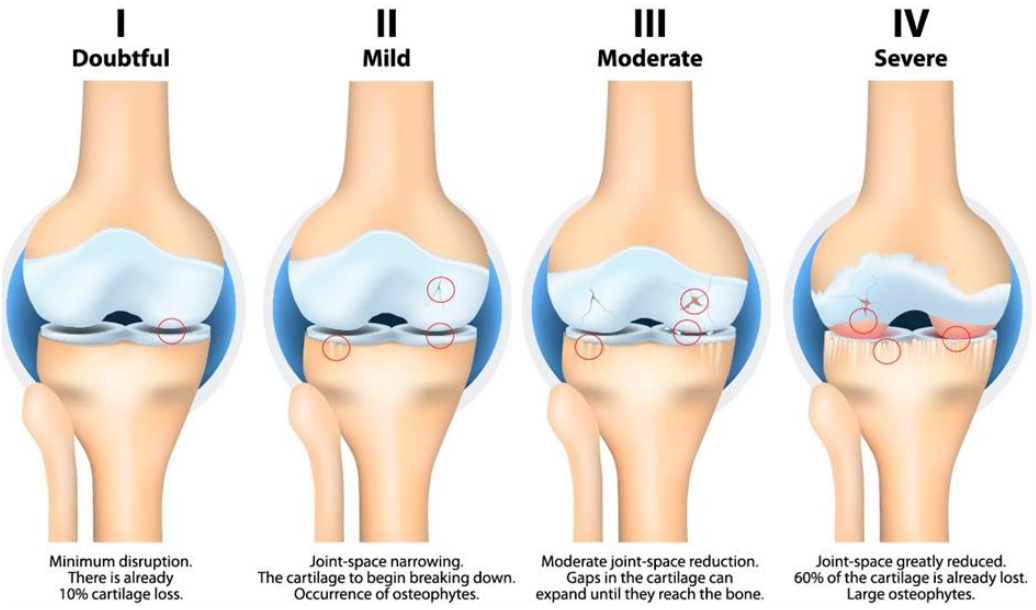

Figure 9: Stages of knee OA[24]

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

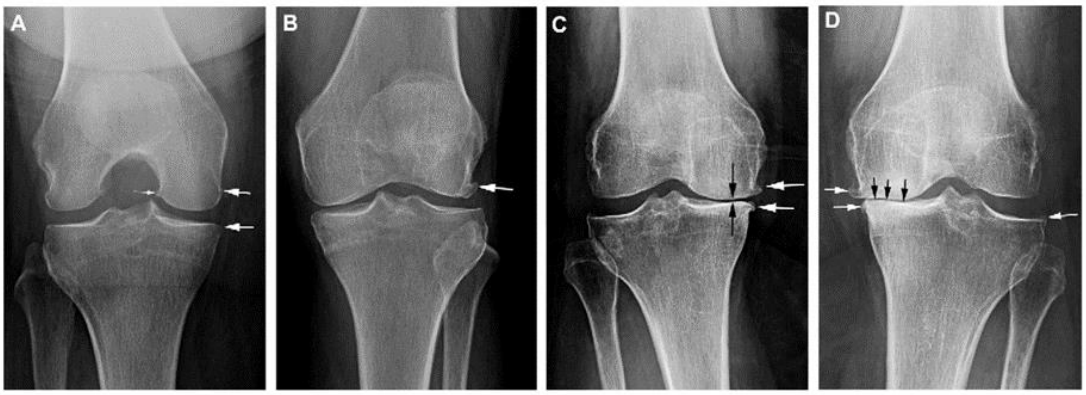

Figure 10: The Kellgren-Lawrence classification is a composite scale of OA severity, taking into account primarily the radiographic OA features of marginal osteophytes and joint space narrowing in the AP radiograph.[25]

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).

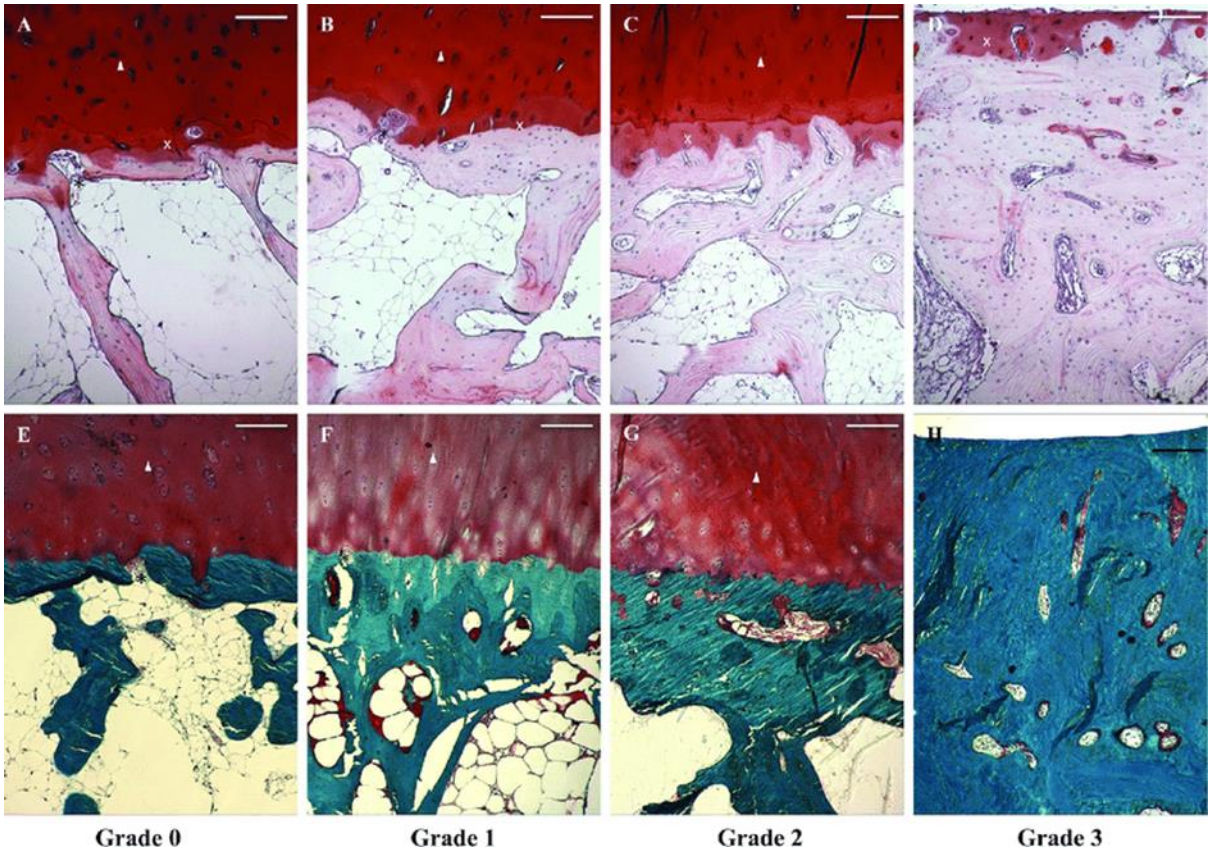

Figure 11: Safranin O (A-D) and Masson's trichrome stained histological samples of subchondral bone grades.[26]

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.[26]

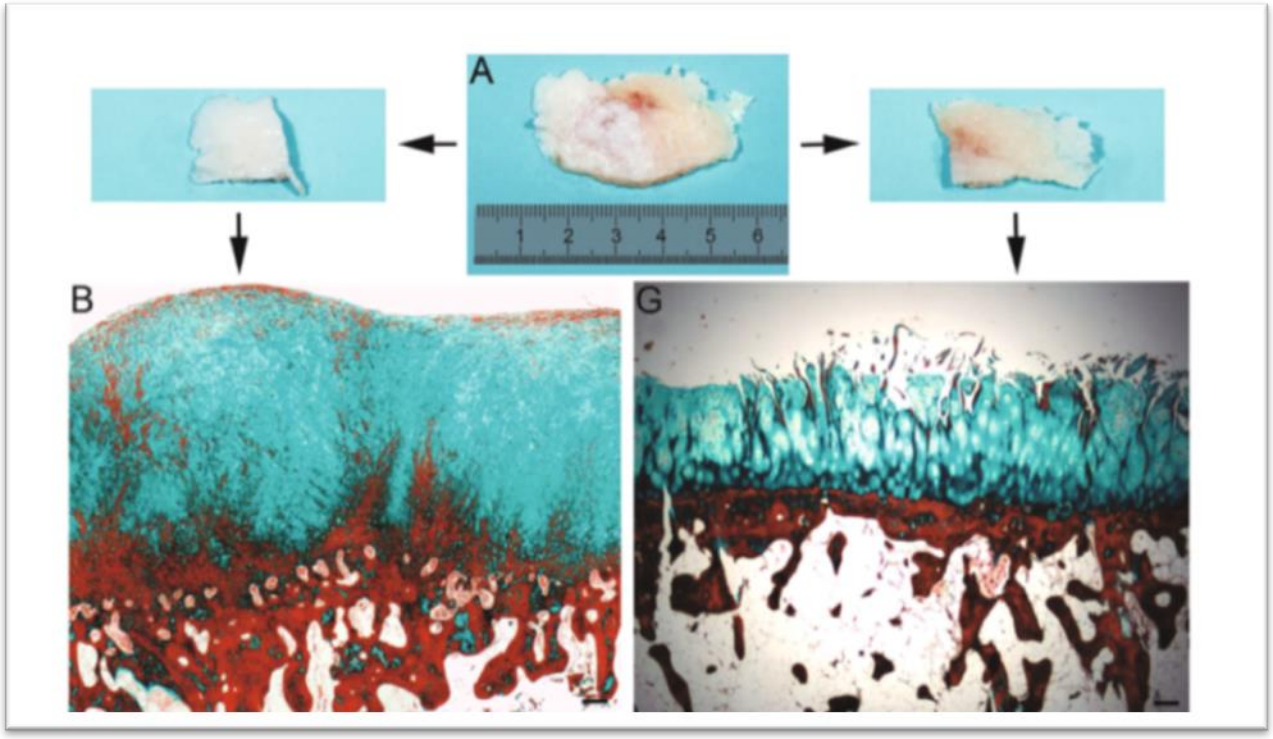

Figure 12: (A) Macroscopic morphology of the sample B and G show panoramic images of the sample (Masson's trichrome staining). comparison of a healthy (left) and OA knee joint (right).[27]

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.[28] National Health Interview Survey estimated that 14 million people in the US have symptomatic knee OA, including >3 million racial/ethnic minorities. 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.[29] 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.[27] Overall prevalence of knee OA in India was found to be 28.7%.[30]

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.[31] 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.[32]

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.[33] 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.[34] 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.[35]

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.[36] 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.[37]

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. With the advancement of OA, the joint capsule, synovium subchondral bone, ligaments and peri-auricular 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.[36] 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. Multiple inflammatory mediators are found in synovial fluid in OA such as plasma proteins, prostaglandins, leukotrienes, cytokines, growth factors, nitric oxide, and complement components.

Prolonged and dysregulated degree of inflammation due to white blood cells as immune response also can lead to tissue destruction.[38] 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.[38,39]

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[40]

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.	❖ 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.

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.[22]

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.[41]

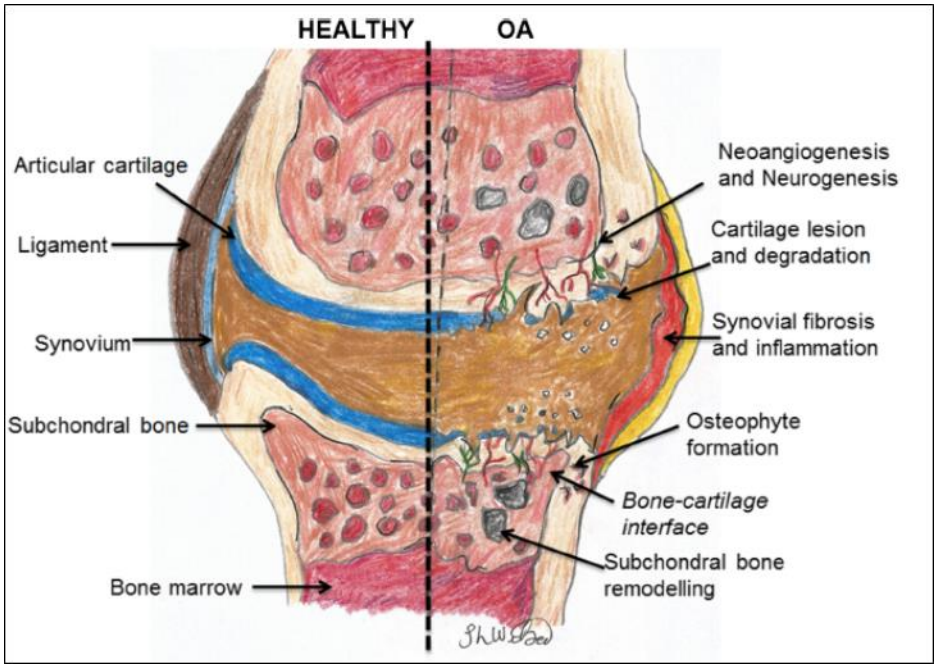

Figure 13: Comparison of a healthy (left) and OA knee joint (right).[42]

DIAGNOSIS:

To diagnose knee OA, the main criteria are patient history, physical examination, and radiologic and laboratory findings.[23] The most common physical examination findings are a reduced range of motion, crepitus, and intra-articular joint swelling, also called an effusion.[43]

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.[36]

Table 2 : 1986 Criteria for classification of osteoarthrosis (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/mm^3).

Diagnostic criteria have been developed for osteoarthritis by Altman et al (1986).[23]

The American College of Rheumatology (ACR) defined three classification criteria for knee OA, mostly used research purposes.[21] 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.

2016 ACR revised criteria for early diagnosis of knee OA[21]

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.[44] 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.[45]

SEQUELAE OF OA KNEE

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.[46] 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.[47]

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.

NON-PHARMACOLOGICAL MANAGEMENT:

With increasing in the age of population and with increasing obesity, OA arises as a major public health problem and an important financial burden for the global economy. For the knee OA, various conservative treatment modalities are recommended by clinical guidelines. The non-pharmacological modalities include patient education regarding self-management, exercises, weight reduction, walking supports (crutches), bracing, shoe and insoles modification, local cooling/heating, acupuncture and electromagnetic therapy.

The primary aim of OA management is to control the noxious signals originating from joints. Likewise, it serves in such a way to improve quality of life. Non-pharmacological therapy was the preferred first line of treatment.

A sedentary lifestyle is detrimental to the knee joint health. Significantly, the mechanical stimuli lack will lead to swift cartilage degeneration due to thinning of cartilage, decreased glycosaminoglycan content, impairment of joint mechanics and flexibility. Light-to-moderate physical activity is highly beneficial in addition to reduced risk of diabetes, cardiovascular disease, disability, and a sense of wellbeing and self-efficacy.[48,49]

Exercise routines should be customized to every patient's needs and preferences and long-term adherence should be increased to increase success. There are different exercise modalities have proved a favorable effect on OA knee patients, the exercise regimes should be performed thrice each week. To assess the response, these patients should complete a minimum of 12 sessions.[50,51]

Aquatic therapies offer an alternative to patients who are reluctant to start land-based exercises, as these activities are gentler on the joint. Some patients can tolerate aquatic therapy better and decrease the exacerbation of symptoms. Some physicians use this model as a bridge to land based modalities once the patient has gained more confidence in movement.[48,49] Weight management plays an important role in management of symptoms, and it has been noted that the benefit of exercise is potentiated by the reduction of weight. Obesity has detrimental molecular and mechanical effects. The cytokines adipokine, IL6, TNF alfa, and C-reactive protein are elevated in obese patients and are known to be associated with alteration of cartilage degeneration.[52,53]

The different exercise modalities recommended for OA knee patients include

1. Aerobic/endurance Exercise modalities
2. Balance/proprioceptive Stretching
3. Resistance/strength training

Cycling has always been a favorite amongst patients as it involves low impact on their joints. Isotonic, isokinetic and dynamic modalities target the quadriceps, hip abductors, hamstrings, and calf muscles. They improve strength and physical function just as aerobic exercises. This includes Tai Chi, in which movements are gentle and slow to adopt different weight baring postures along with breathing techniques. This helps in improving patient's flexibility and range of motion.[48] With respect to myriad non-pharmacological interventions, patients might

benefit from thermal modalities, but there is insufficient evidence to advice therapeutic ultrasound.[54]

PHARMACOLOGICAL MANAGEMENT:

Pharmacologic therapies can be summarized as Non-Steroidal Anti-Inflammatory Drugs, Opioid analgesics. If orally administered drugs are ineffective, intra articular (IA) injection (corticosteroids, visco-supplements, blood-derived products) is the last non-surgical treatment option that could be preferred. In OA knee there will be both qualitative and quantitative decrease in HA content. i.e., chain length is halved from 4-5mD in normal individual to 2-3mD in affected individual.

Given that the vast majority of OA patients are elderly and have several comorbidities, systemic medicines must be considered in this population. The most widely utilized drugs have been cyclooxygenase inhibitors (acetaminophen and NSAIDs). However, extended use of these drugs is limited due to their gastrointestinal, renal, and cardiac side effects. Acetaminophen, a pain reliever, has been shown to be inferior to NSAIDs.[55]

Because of their similar efficacy, topical NSAIDs are considered to be safer than systemic NSAIDs. Some studies have shown that they are more effective than placebo at controlling pain during the first week of treatment, but that they are ineffective after two weeks.[55,56]

Over the last few years, there has been a growing understanding of the dangers of long-term opiate usage. Opioids are not superior to NSAIDs in relieving pain according to many researches, and the hazards of using them obviously exceed the benefits. However, if the patient has failed to respond to other treatments and needs to be treated with an opioid, Tramadol is more effective in the treatment of worsening OA. This medicine has a lower risk of addiction and respiratory depression than others.[57]

INTERVENTIONAL MANAGEMENT:

The delivery of multiple substances via intra-articular (IA) injections have been explored in the past. The concept behind this is that local treatments will have less systemic adverse effects and deposition of the medication inside the joint will have a direct effect. Studies have illustrated that in general IA therapies are way better than NSAIDs and other systemic pharmacologic treatments, but they also revealed that a percentage of that benefit might be secondary to IA.[1]

Corticosteroid injections: - Corticoids (CS), derive their immunosuppressive and anti-inflammatory effects by directly acting on nuclear receptors, thus interrupting the inflammatory cascade at multiple levels. They decrease the production and action of IL-1, leukotrienes, prostaglandins, and metalloproteinases.[53,58] Currently, FDA approved Immediate Release (IR) corticosteroids for IA usage are: Methylprednisolone Acetate (MA), Triamcinolone Acetate (TA), Triamcinolone Hexacetonide (TH), Betamethasone Acetate (BA), Betamethasone Sodium Phosphate (BSP), and Dexamethasone. There have been attempts to define which is the best option in the past. Dosages higher than 50 mg of prednisone (equivalent to 40 mg of TA and MA) are linked to a relief of pain extending 12–24 weeks compared to 2-4 weeks of pain relief that has been reported with lower dosages.[59,60] There might be small differences between approved IR corticosteroid preparations with regards to pain relief, but present evidence is equivocal. Yavuz et al stated that a higher degree of relief of pain can be achieved within the first 6 weeks with MA when compared to the various corticosteroids used but all of them provide equivalent analgesia from week six to week twelve.[60] Pyne et al recommended that TA acts more swiftly and provides better pain relief for the first 3 weeks than MA, but its resulting effect is not immediate and thus might provide better analgesia after the eighth week.[61]

A recent study by Buyuk et al showed that both MA and TH were equally effective until 24 weeks and showed an upsurge in action by second week thus confirming similar findings by Lomonte et al.[62] Various studies have stated questions regarding IA CS, such as its mode of action, its duration, indications, effect on cartilage structure/intra-articular space and its negative effects. Some of the studies showed several variabilities in their design, depicting contradictory results and hindering the creation of a strong consensus. This has been reflected in the guidelines of various associations. Other possible variables like the degree of knee tenderness, baseline pain, BMI, gender, and anxiety or depression, have failed to show reliable predictors of response.[63] In contrast, a low degree of radiographic changes on the KL system (0–1) shows a good response as opposed to patients with severe radiographical changes. Earlier several techniques of Intraarticular injection have been described, including the anterolateral and anteromedial, as well as the mid-lateral and superolateral approaches (performed with the knee extended). Studies agree that using ultrasound guidance with a superolateral approach provides the best chance to inject the CS accurately.

Research regarding CS and knee cartilage integrity has also provided significant results, with some studies suggesting that there is no alteration in the structure of cartilage, while others recommend that CS can promote chondrocyte destruction and increase the necessity for joint replacement. The damage to the cartilage could possibly be reduced by vitamin C supplements.[64]

A minor part of the IA CS is absorbed systemically, with the possibility to produce hypoglycemia and hence, transiently affect the hypothalamic-pituitary-adrenal (HPA) axis in up to 25% of the patients. Cortisol levels may reduce after injection, but they return to baseline after 1–4 weeks.[65]

NON-CORTICOSTEROID INTERVENTIONAL THERAPIES

As an alternative to the IA CS, in the recent years, new products and therapies have been used that target different factors other than inflammation. However, some research is required to determine their efficacy, applicability, and safety profile. Viscosupplementation with hyaluronic acid (HA), is a natural glycosaminoglycan which is synthesized by type B synovial cells, chondrocytes, and fibroblasts and later secreted into the synovial fluid. It acts as a shock absorbent and provides a viscous lubricating property and a possible anti-inflammatory function have also been described.[53,58] In an osteoarthritic knee, concentration of HA decreases significantly and hence formulated a proposal of viscosupplementation of the joint so as to reinstate the HA benefits. The current evidence regarding efficacy is conflicting and consequently, there is variation regarding recommendations from the societies. The AAOS does not recommend its usage, the ACR has no recommendations about it, and the OARSI has an "uncertain recommendation.[56] A recent European consensus mentioned that HA had a good level of tolerance for low and moderate grade OA. Lastly, this treatment might be more effective in patients with higher levels of knee pain.[66]

REGENERATIVE MEDICINE

With the intention to stop and revert the degeneration, Intra articular injections of autologous conditioned serum (ACS), platelet rich plasma (PRP), mesenchymal stem cell (MSC) were experimented.[53,58] Their mechanism is reduction of inflammatory reactions mediated by cytokines in addition to inducing anabolism and chondrocyte differentiation through stem cells and growth factors present in it. These methods have proven to be quite promising and certain studies mentioned their safety, well tolerated and superior to IA placebo and HA with respect to relief of pain and function.[67,68]

It is a developing field and certainly more research is needed so as to define the optimal retrieval, preparation and storage methods of these products.

HYALURONIC ACID:

Hyaluronic acid (HA) produced by B cells of synovial membrane is biochemically a high viscosity polysaccharide also classified in glycosaminoglycan (GAG) group. [69] In physiological conditions HA acts as a salt also named as sodium hyaluronate or hyaluronan.[70] High viscosity solution formed by interlinking high molecular weight molecules. This high viscosity acts as both lubricant as well as shock absorber.[71]

HA on interaction with the CD44 receptors will acts as an important modulator that helps in decreasing pressure due to body weight and promotes the better force distribution.[72]

USES OF HYALURONIC ACID:

Diminishes prostaglandin production, degradation of type 2 collagen and also had analgesic action by diminishing nociceptor sensitivity and the nerve impulses.[73]

It stimulates the proliferation of chondrocytes by this way it increases aggrecan and type 2 collagen production.[74,75]

Sodium hyaluronate has an intra-articular half-life of 13 hours, while the hylan G-F 20 has a half-life of 1.5 days (liquid phase) and 8.8 days (solid phase), probably because of the cross-links. This may explain why the good results are obtained with only one application.[76]

ADVERSE REACTION:

Adverse reaction accounts about 4.2% of the patients presented with effusions, arthralgia, heat and the joint erythema.[77] In such cases, as occurring in any acute arthritis crisis, the treatment should consist of ice, rest, limb elevation and use of anti-inflammatory medication, if not contraindicated.

Hyaluronic acid, a naturally available non-sulfated glycosaminoglycan (GAG) non-protein compound with a distinct physico-chemical properties with repeating b-1,4-D-glucuronic acid and b-1,3-N-acetylglucosamine units.[76,78,79,80] HA is known for its good biocompatibility, excellent viscoelasticity, hygroscopic properties and high moisture retention capacity.[79] HA behaves like a great lubricant, joint structure stabilizer, shock absorber. Moreover, it is also known for its water balance property and flow resistance regulation properties.[71,72]

HA forms the major component of the extracellular matrix (ECM) and is a major component of synovial fluid, bone marrow and articular cartilage. Hyaluronic acid is required in proliferation of cells, migration, and morphogenesis.[81] Inside the cavity of the knee joint, HA molecules are predominately synthesized by type B synoviocytes. HA is synthesized by hyaluronan synthase. HA is catabolized by hyaluronidases, with increase in age there is decrease in Hyaluronic acid molecular weight with in the knee cartilage.[82,83]

HISTORY:

Balazs in 1993 visco-supplementation with intraarticular HA injections has emerged as a viable treatment modality for nonoperative care of symptomatic osteoarthritis.[72] Hyaluronic Acid, has wide range of usage like in managing osteoarthritis, cosmetic surgery, ophthalmological surgeries and also in healing of wound. The production and recovery of HA, has attained its great importance. Injecting exogenous intra articular HA, there will be restoration of the articular cartilage and the synovial fluid; and also, to achieve certain biological effects.

In OA knee, the cartilage is subjected to mechanical, structural and matrix changes of the articular surface and a decrease in PG monomer size and aggregation. Aging, oxidative stress and the inflammation acts as a major contributor to the development of OA and its

progression. Apoptosis (programmed cell death) of chondrocytes are the cause of failure and articular cartilage degeneration OA.[84]

Rheological qualities of Hyaluronic acid in formulation and mode of administration (such as molecular weight, concentration, and viscoelasticity) are significant determining factors for successful OA therapy.[80,85]

Intra articular (IA) administration is more efficacious than parenteral or enteral route because it avoids systemic exposure and its potential side effects. Intraarticular injection of HA into OA joints could reinstate the Synovial Fluid rheological properties, promote the endogenous production of a higher Molecular Weight HA.

The molecular weight of the Hyaluronic acid appears lower in Osteoarthritis patient Synovial fluid. so, IA Hyaluronic acid injections are thought to be a good choice for treating OA knee patients.

Normal adult knee has approximately 2mL of SF and 2.5–4.0 mg/mL of hyaluronic acid. Synovial HA is depolymerized (MW, 2,700–4,500 kDa) and removed at a faster rate (11–12 h) in OA than in healthy people (20 h).[86,87]

Osteoarthritis knee there will be cartilage degeneration due to oxidative/nitrosative stress and inflammation. The NO production of the HA group was significantly less than without the HA treatment. These results recommended that there is an inhibition of Nitric Oxide production in meniscus and synovium as part of the therapeutic effect of Hyaluronic acid in OA.[88,89]

Actions of hyaluronic acid:

HA action is by inhibition of the actions of pro-inflammatory mediators and pain producing neuropeptides released by activated synovial cells.

HA specific effects:

1. Antioxidative/Antinitrosative, and anti-inflammatory

HA decreased PGE2 and increased cAMP in Synovial fluid binging about Anti-inflammatory, anti-chondroptosis, and anti-OA.[90] HA down-regulates aggrecanase-2, cytokines (TNF-a, and IL-8) and iNOS through interaction of CD44 in FLS.[91] HA protected mitochondria from oxidative stress, and chondrocytes from apoptosis. HA reduced IL-1-induced PGE2 and NO concentrations and decreases apoptosis in OA chondrocytes.[92]

2. Analgesics

HA relived joint pain by inhibiting PGE2 production.[93] HA produces reduction of the sensitivity of mechanosensory ion channels of nociceptive nerve terminals.[94] HA decreased cytokines, leptin in serum and synovial fluid of OA patient.[95] In a dose-dependent manner, HA interacts with HA receptors on or surrounding the free nerve endings that detect pain in the joint tissue.[96]

3. Structure of bone and cartilage with functions

HA ameliorated IL-1b-induced expression of genes of matrix degrading enzymes (MMP1), inflammatory mediators (IL6, PTGS2) by chondrocytes and fibroblasts.[97] The production of MMP-13 via CD44 and p38 in chondrocytes/articular cartilage is inhibited by HA.[98] Higher-Molecular weight HA also inhibits cartilage degeneration and loss of chondrocytes. The downregulation of MMP-3 and IL-1b by HA. HA inhibits PPAR-g mRNA being expressed and exerts anti-chondroptosis.[99] HA regulates the function and distribution of sulphated GAG.[100] HA suppressed IL-1b-induced-transcriptional activity of type a2(VI) collagen.

4. Rheological properties of Hyaluronic acid and Synovial Fluid

HA increased viscoelasticity, anti-inflammatory potential, increased proliferation of chondrocytes.[101,102] HA stimulated synoviocytes of high MW HA synthesis, and reduced synovial hyperplasia.[103,104] IA viscosupplementation promoted endogenous HA production in Synovial fluid of OA knee. Increased HA concentration and viscoelasticity.[105]

5. Pharmacokinetics of HA

After oral administration of 99mTc-HA, it readily absorbed, distributed and excreted suggesting a rapid uptake of HA. There is Short half-life of the Hyaluronic acid in humans. Hyaluronic acid also distributes to lymphatics suggesting Rapid distribution and elimination of HA.[106,107]

Evidence for disease-modifying activity of HA stems from the complex molecular and cellular effects of the HA in the ECM of articular cartilage, including interactions between exogenously administered HA and articular cartilage, subchondral bone, matrix PGs, and collagens. IA injections of HA help slow the course of cartilage deterioration and prevent the narrowing of joint space shown on X-rays.[108,109]

TOXICITY AND SAFETY EVALUATION

HA as a physiological component, will not produce adverse reactions even after repeated usage. In various clinical trials, Hyaluronic acid is safe and well-tolerated in Osteoarthritis patients, when given IA.[110,111] After administration, minor side effects can occur, like pain at the injection site (in 1–30% of patients), swelling (in 1–30%), and local skin reactions (in 3–21%). These effects are transient. In rare cases, treated joints may become infected.[112]

CONTRAINDICATIONS:

HA treatment is contraindicated in individuals who are hypersensitive to HA products, woman who are pregnant or nursing, pediatric patients, patients with bacteremia, or patients with infections in or around the target knee.[113]

INTRA-ARTICULAR HA TECHNQUIES

The use of an intra-articular injection of HA as a treatment for pain associated with OA of the knee has lately gained traction. However, an incorrect placement of extra-articular HA injection causes discomfort to the patient and declination of the effect of the HA.

Different techniques have been described:

1. Anterolateral injection technique: Patient in supine or sitting position with knee flexion in 90°. The landmark is the intersection between 2 imaginary lines; the horizontal line from lower border the patella and the vertical line from Gerdy tubercle. The direction of needle tip is 10° parallel to posterior tibial slope, to avoid cartilage and meniscus injury with the needle tip aimed toward the lateral tibial plateau.

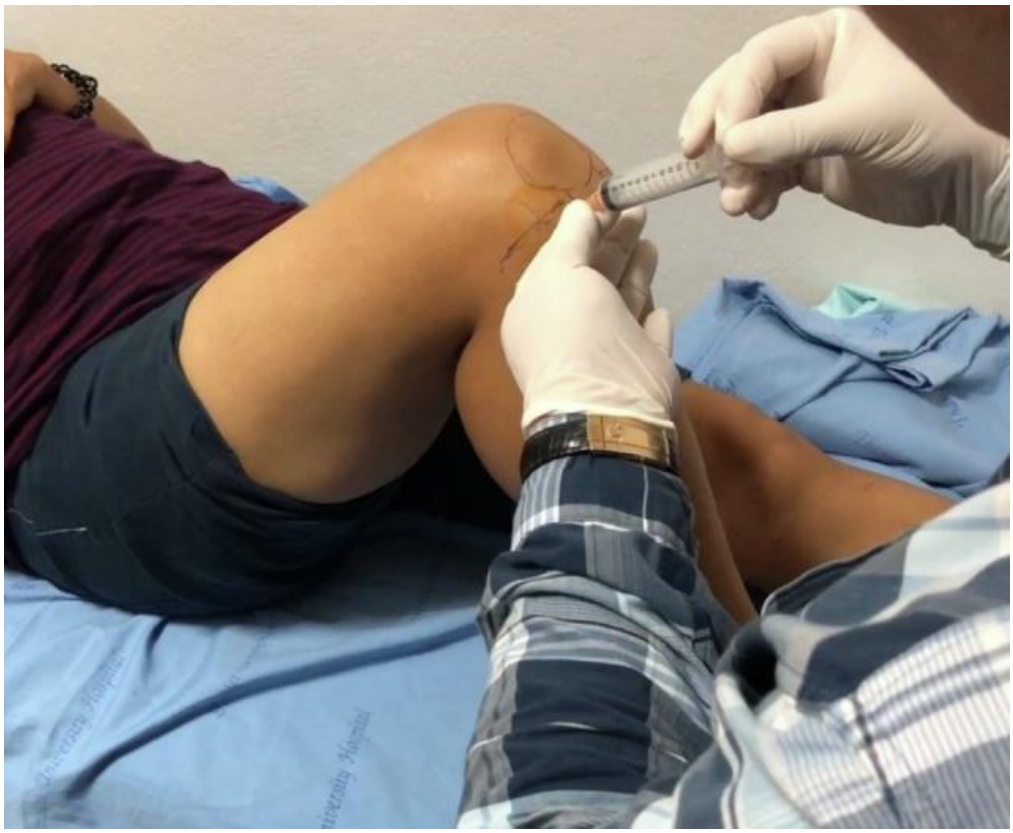

Figure 14: Anterolateral approach to intra-articular injection to knee

2. Superolateral injection technique: the patient is positioned supine on the examination table, with the legs extended. The patella and soft spot are palpated. The landmark is the intersection of 2 imaginary lines; horizontal line from the superior border of the patella, and another line intersecting the lateral border of the patella. The needle is aimed parallel to the anterior femoral cortex.

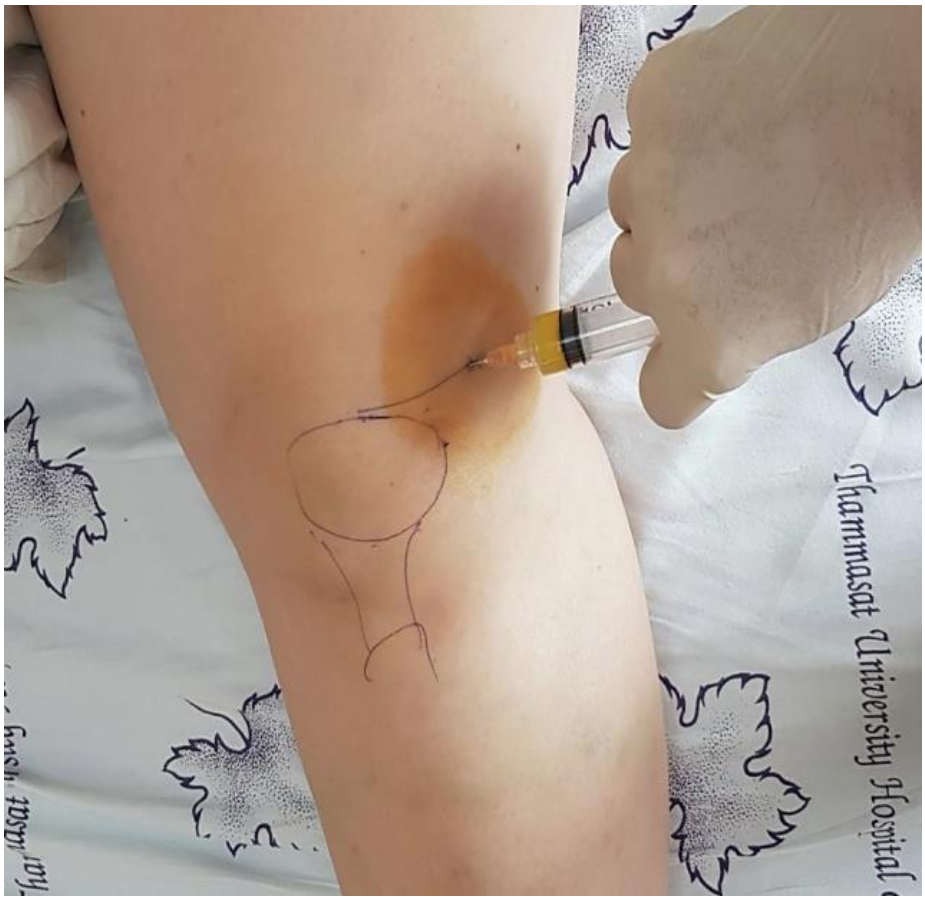

Figure 15: Superolateral approach to intra-articular injection to knee

3. Mid-patellar injection technique: This technique is performed with the knee in extension. The patella is pulled medially or laterally and a needle is advanced under the patella. The lateral midpatellar (LMP) approach is the most commonly used.[115] The patellofemoral joint can then be aspirated and/or injected using the LMP and MMP methods. The needle is directed at a 45° angle towards the middle of the medial aspect of the joint while performing a surgery using the LMP method. The needle enters the medial aspect of the knee joint under the middle of the patella (midpole) and is directed towards the lateral patellar midpole when using the MMP method.[116]

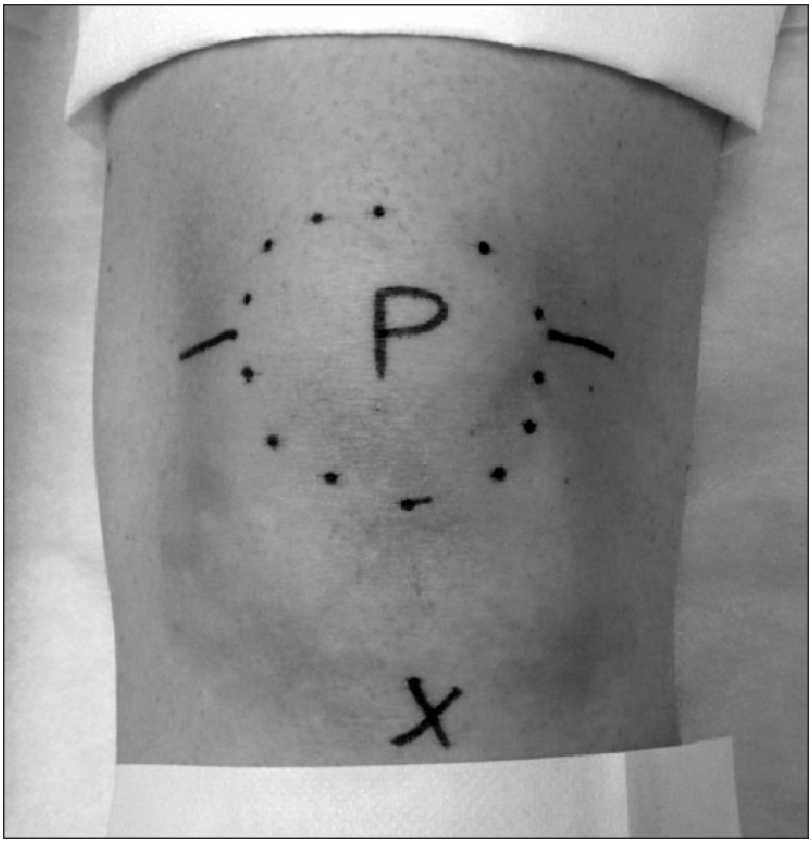

Figure 16: The tibial tuberosity is marked with a cross. Lines indicate the access points for medial and lateral midpatellar approaches to injection of the knee joint.

4. Anteromedial injection technique: This technique is an infrapatellar approach. With the knee flexed, the needle is introduced medial to the patella tendon, and is directed upwards towards the femoral notch. There is no need to manipulate the patella. These approaches traverse only Hoffa's fat pad and they avoid the extensor mechanism and major blood vessels.[117]

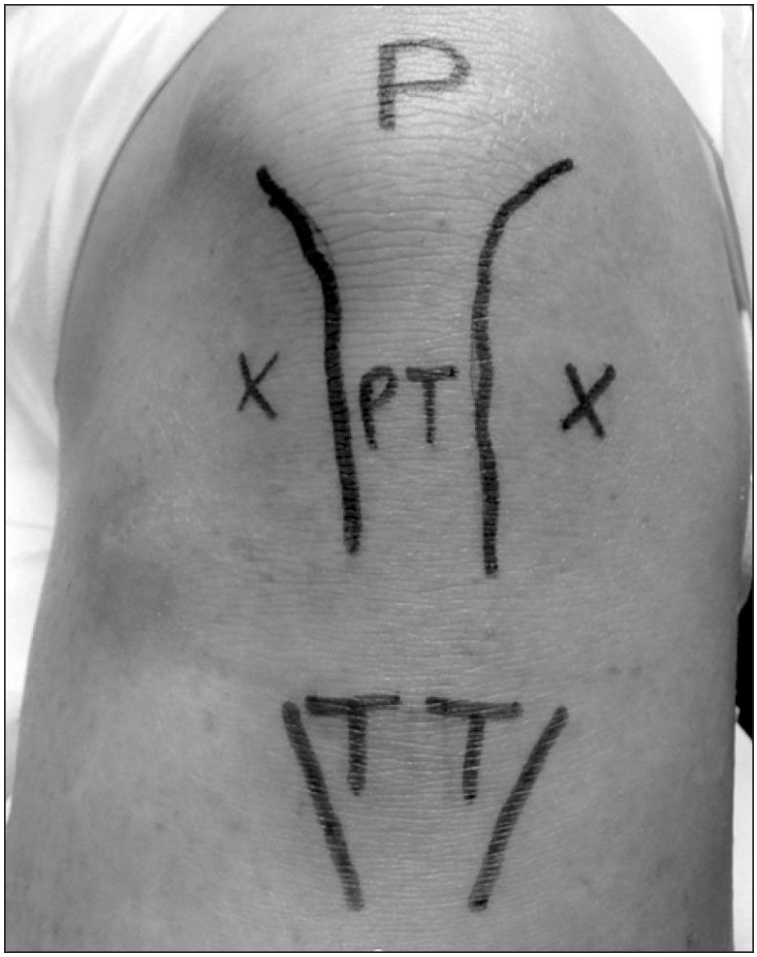

Figure 17: anteromedial approaches to injection of the knee joint. P: patella, PT: patellar tendon, TT: tibial tuberosity

SCORING SYSTEM

Visual Analogue Scale (VAS) SCORING

The Visual Analogue Scale (VAS) is a typical type of pain scale used in health outcome studies. It is presented as a single 100-mm line with anchor statements on the left (no pain) and right (pain) (extreme pain). The VAS system was first published in the early 1920s, although it was not widely used at the time.[136] In 1923, Freud was the first to apply this method in psychology. The Visual Analogue Scale (VAS) is a straight line with ends that define extreme boundaries like "no pain at all" and "worst pain." The patient is instructed to draw a line between the two endpoints and mark his pain level. The subject's suffering is defined by the distance between 'no pain at all' and the mark.

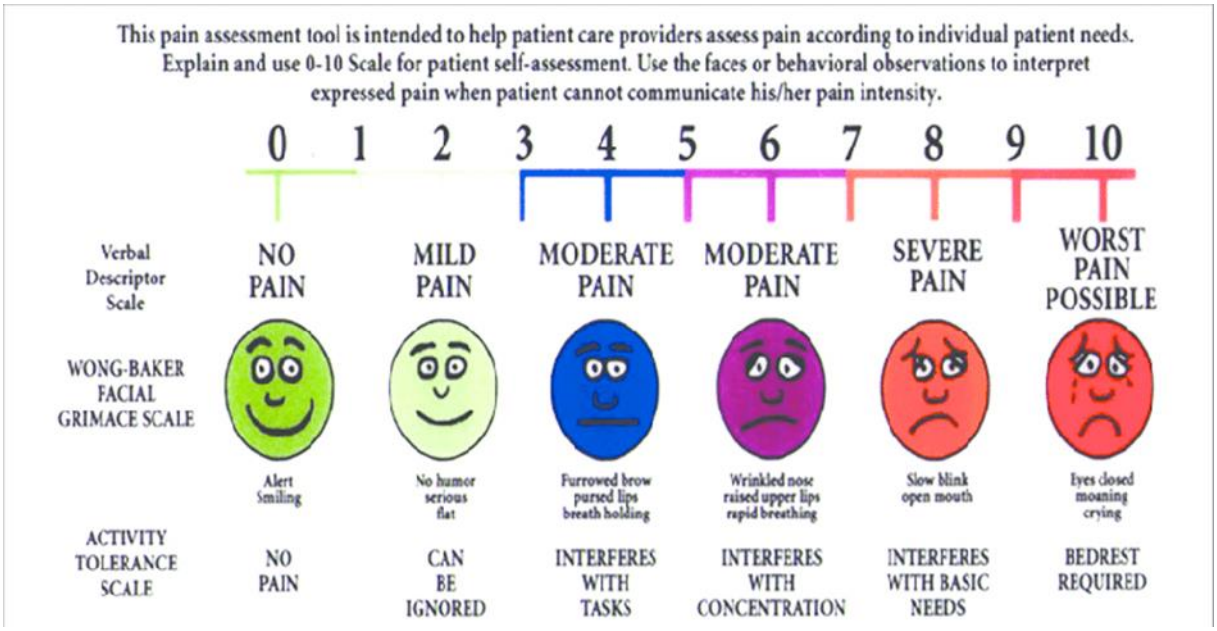

Figure 18: Visual analogue scale pain assessment tool[137]

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.[138] 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.[136] 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.[138]

In a study conducted by Lussier et al. in 1996, they observed patients had higher incidence of adverse events when intra-articular HA injection was given by medial approach when compared to lateral or anterior approach.[111]

In a study conducted by Bliddal et al. in 1999, they assessed the intra-articular knee injection accuracy by air arthrogram in osteoarthritis knee without effusion. They concluded that superolateral approach had 95% accuracy into knee injection when compared to medial and lateral parapatellar approach.[139]

In a study conducted by Douglas et al. in 2002, they recommend using the lateral midpatellar portal with the knee extended as it is the most accurate approach for intra-articular needle placement in a knee with no effusion.[140]

In a study conducted by Glattes et al in 2004, they compared needle placement into knee joint with aid of arthrogram amongst 2 approaches. They concluded that in superolateral approach needle placement is more accurate into knee joint when compared with anterolateral approach where there was higher frequency of seepage of dye into soft tissues rather than knee joint. [141]

In a study conducted by Luc et al. in 2006, concluded that appropriate positioning of needle for intra-articular hyaluronic acid injection is very difficult without assistance of fluoroscopic image guidance in a dry knee i.e., a knee without any evidence of effusion.[142]

In a study conducted by Esenyel et al in 2007, they compared the accuracy rate amongst different intra articular knee injection technique. They concluded that anterolateral approach has the maximum accuracy rate accounting to 85% delivery of medications and medial midpatellar approach to be the least accounting to only 55% delivery into the knee joint.[115]

In a study conducted by Toda et al in 2008, they compared accuracy of intra articular hyaluronic acid injection delivery into knee joint amongst four approaches. They concluded that the superolateral approach to the knee joint had the maximum accuracy in the needle placement in knee joint when compared to seated anteromedial, lateral parapatellar and Waddell's (anterolateral) approach.[117]

In a study conducted by Lopes et al in 2008, they compared accuracy of intra articular injection given blindly in patients with rheumatoid arthritis. They observed 100% accuracy into knee joint when given by superolateral approach.[143]

In a study conducted by Shortt et al in 2009, they evaluated different techniques which would lead to better needle placement into the joint and confirmed arthrographically. In their study, they concluded that in superolateral approach needle placement is in patellofemoral joint when compared to anterolateral approach where the needle is placed in the trochlea of femur.[144]

In a study conducted by Hermans et al in 2011, they compared various approaches in intra-articular delivery of hyaluronic acid injection for osteoarthritis knee. They observed that superolateral approach had maximum accuracy into knee joint when compared to anterolateral, anteromedial and lateral midpatellar approach.[145]

In a study conducted by Maricar et al in 2013, they compared blind intra articular knee injection approaches with image guided intra articular knee injection accuracy rates. They concluded that with bony landmark guided knee intra articular injection superolateral approach has the best accuracy followed by medial midpatellar and then anterolateral approach.[146]

In a study conducted by Lee et al in 2015, they compared VAS score amongst superolateral approach and anterolateral approach to intra-articular knee injection. They observe that anterolateral approach had less VAS score compared to superolateral approach.[147]

In a study conducted by Wagner et al in 2015, they compared pain post injection and drug delivery into knee joint amongst anterolateral, anteromedial and superolateral approaches. They observed no statistically significant difference amongst three groups.[148]

In a study conducted by Wada et al in 2018, they compared the drug delivery into knee joint between isometrically contracted quadriceps with non-contracted quadriceps given in superolateral approach for osteoarthritis knee. They observed increased drug delivery when quadriceps are contracted and knee is flexed to 25° when compared to a non-contracted quadriceps and extended knee.[149]

In a study conducted by Chernchujit et al in 2019, they compared the accuracy of modified anterolateral approach and superolateral approach in intra articular delivery of medications in OA knee without effusion. They concluded from the study that anterolateral approach had better drug delivery into the intra-articular space.[114]

In a study conducted by D'Alessandro et al in 2021, they compared the accuracy and VAS score amongst patients who underwent intra articular hyaluronic acid injection between two approaches i.e., anterolateral and superolateral for osteoarthritis knee in overweight patients. They concluded that post injection pain is less in superolateral approach along with better drug delivery when compared to anterolateral approach which had more pain and less accurate drug delivery into intra articular knee joint.[150]

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 Orthopaedics, R. L. Jalappa Hospital and Research Centre, Kolar, Karnataka were considered as the study population.

STUDY DESIGN:

The current study is prospective, comparative and hospital-based study.

SAMPLE SIZE:

Sample size was calculated based on mean difference observed in 2 methods i.e. activated vs non activated quadriceps in suprapatellar bursa expansion in a study by Wada et al. [149] The observed variance estimates of 1.05 SD with 90% power with α error of 5% expecting at least 50% difference in the mean suprapatellar bursa expansion between the groups.

The required sample size per group will be 23.

Formula:

$$n = \frac{2s_p^2[z_{1-\alpha/2} + z_{1-\beta/2}]^2}{\mu_{d\,2}}$$

$$S_P^2 = \frac{S_1^2 + S_2^2}{2}$$

- S_1^2 : Standard deviation in first group
- S_2^2 : Standard deviation in second group
- μ_d^2 : Mean difference between the samples
- α : Significance level
- 1-β: Power

STUDY DURATION:

The data collection for the study was done between December 2019 to July 2021.

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.

SAMPLING METHOD:

All the eligible subjects were recruited into the study consecutively by simple randomization till the sample size is reached.

INCLUSION CRITERIA:

Patients above 40 years of age and diagnosed with Kellgren and Lawrence grade 1 to 3 osteoarthritis were included in the study.

EXCLUSION CRITERIA:

Patients with ultrasound knee measuring >4mm anterior-posterior dimension of suprapatellar bursa when in supine position with knees extended indicating effusion in knee joint and Fixed flexion deformity of knee >10° were excluded from the study.

DATA COLLECTION TOOLS:

All the relevant parameters were documented in a structured study proforma.

METHODOLOGY:

- All patients were evaluated by detailed history, clinical examination and documenting antero-posterior diameter of suprapatellar pouch pre intra articular injection using ultrasound – Philips epiq 5G (5-12MHz).
- A sample of size 46 was be selected meeting the inclusion and exclusion criteria.
- Patients were divided into two groups by simple randomization.
- Both groups pre injection VAS scores were documented
- Group A underwent intra articular injection for Osteoarthritis knee with activated quadriceps (23 patients).
- Group B underwent intra articular injection for Osteoarthritis knee with non-activated quadriceps (23 patients).
- Post injection both groups antero-posterior diameter of suprapatellar pouch documented using ultrasound
- Both groups post injection VAS scores were documented

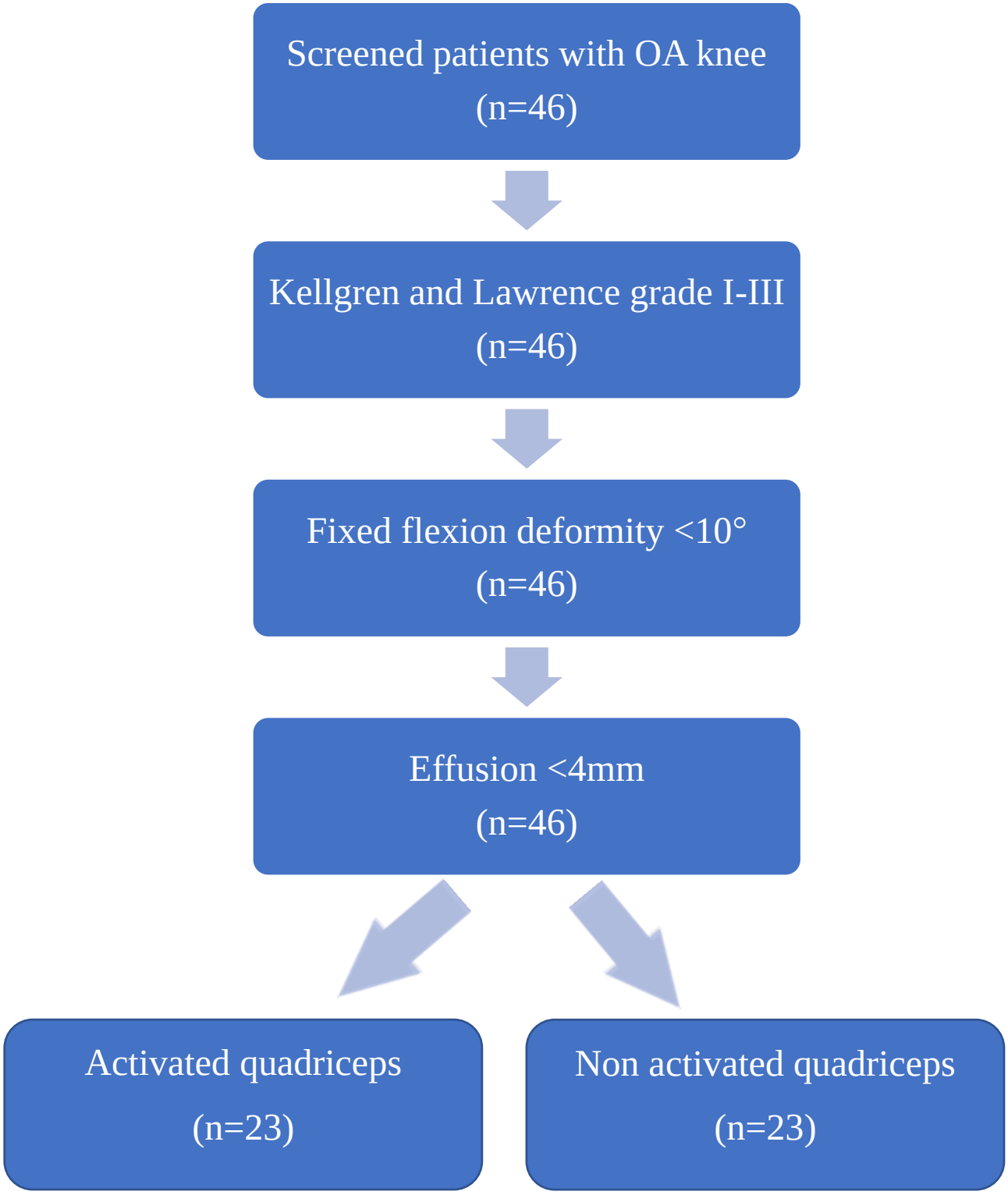

Figure 19: Illustrating eligibility criteria flowchart

Ultrasound Observation of the Suprapatellar Bursa and Anterior-Posterior Dimension Measurements:

"All patients in both groups (46 knees) were told to relax the muscles surrounding the knees, the injection condition used in the non-activated quadriceps method. The anterior-posterior dimension of the suprapatellar bursa on the longitudinal axis along the midline of the quadriceps tendon was measured. The measurement site was the point proximal to the suprapatellar fat pad, which is the area with the smallest amount of soft tissue between the suprapatellar bursa and the quadriceps."

Group A- Activated quadriceps group:

After meeting inclusion criteria 23 patients with OA knee, were selected for intra articular HA injection with activated quadriceps via superolateral approach. Pre injection suprapatellar bursa anterior-posterior dimension was documented using ultrasound. Pre injection VAS score was also documented.

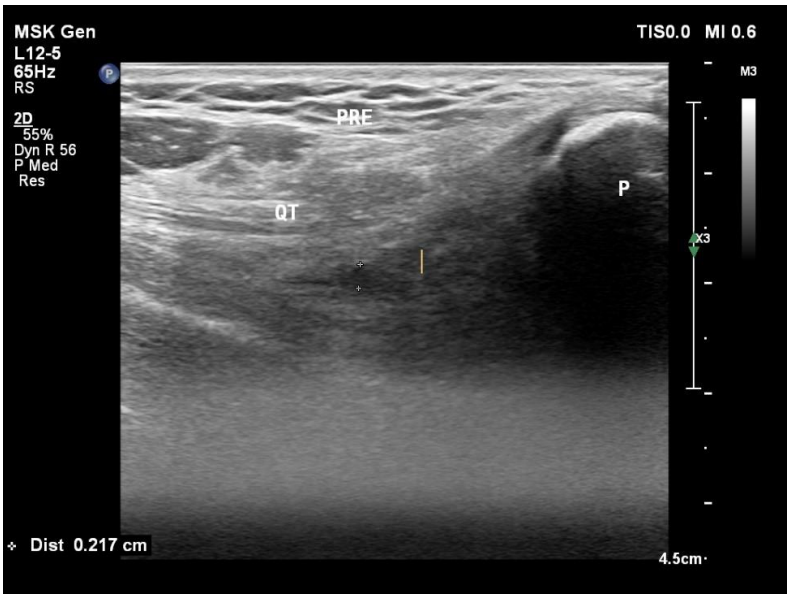

Figure 20: Pre injection suprapatellar pouch anterior-posterior dimension measurement using ultrasound

“Patients were taken to Operation theatre in supine position, parts painted and draped. Patients were instructed to place the knees at an angle of approximately 25° on a pillow and were then instructed to extend the knees, as follows: “Please extend your knee firmly and keep your heel off the bed.” Subsequently, we touched the quadriceps and said, “Please contract this muscle firmly.” There were no subjects who could not follow these instructions. After manually confirming that the quadriceps muscle was in a state of isometric contraction with the knee extended and the heel off the surface of the bed”.

“A 25-G needle and 1% hyaluronic acid (low molecular weight, approximately 900 kDa) solution at a dose of 8 mL/injection were employed. The skin was pierced at a point on the lateral side of the quadriceps tendon approximately 1 cm proximal to the superior margin of the patella. The needle tip was angled toward the suprapatellar bursa. Once the drug solution was injected, an ultrasound probe was used parallel to the needle to capture its image and confirm whether the solution diffused within the joint”. Post injection suprapatellar bursa anterior-posterior dimension and VAS score documented.

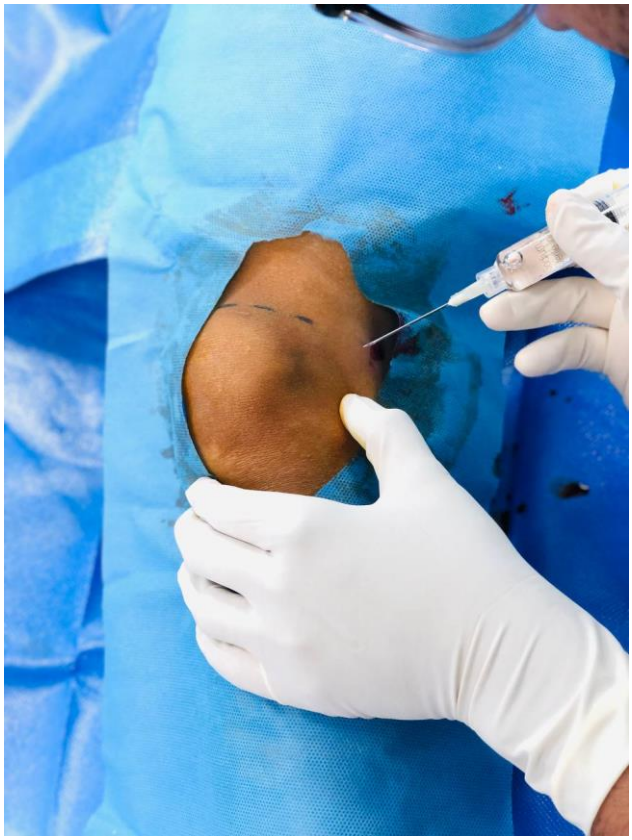

Figure 21: Intra-articular HA injection with activated quadriceps via superolateral approach

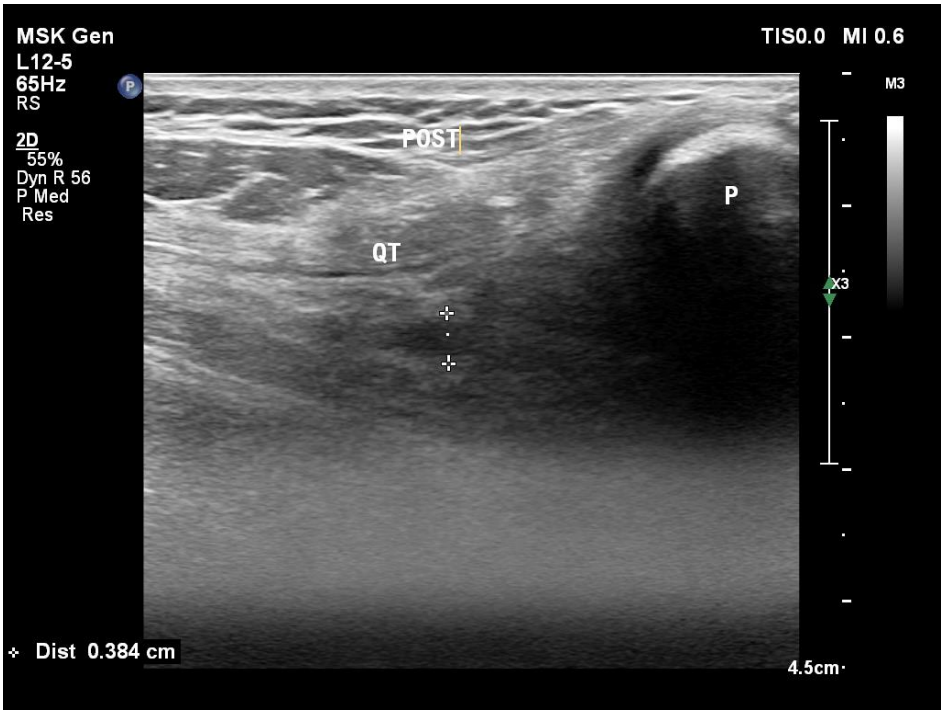

Figure 22: Post injection suprapatellar pouch anterior-posterior dimension measurement using ultrasound

Group B - Non-Activated quadriceps group:

After meeting inclusion criteria 23 patients with OA knee, were selected for intra articular HA injection with non-activated quadriceps via superolateral approach. Pre injection suprapatellar bursa anterior-posterior dimension was documented using ultrasound. Pre injection VAS score was also documented.

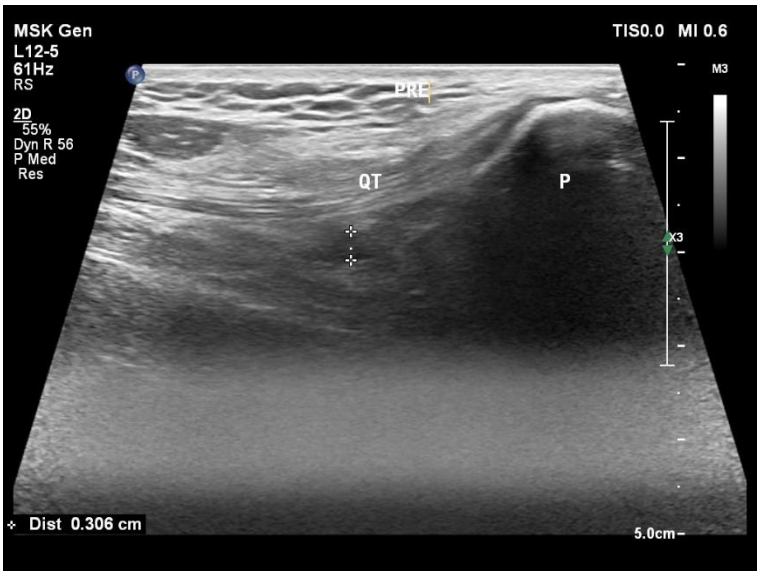

Figure 23: Pre injection suprapatellar pouch anterior-posterior dimension measurement using ultrasound

"Patients were taken to Operation theatre, supine position, parts painted and draped. Patients were instructed to extend the knees on flat surface and relax the surrounding muscles of knee. Manually confirmed that the quadriceps muscle was in a state of relaxation with the knee. A 25-G needle and 1% hyaluronic acid (low molecular weight, approximately 900 kDa) solution at a dose of 8 mL/injection were employed. The skin was pierced at a point on the lateral side of the quadriceps tendon approximately 1 cm proximal to the superior margin of the patella. The needle tip was angled toward the suprapatellar bursa. Once the drug solution was injected, an ultrasound probe was used parallel to the needle to capture its image and

confirm whether the solution diffused within the joint". Post injection suprapatellar bursa anterior-posterior dimension and VAS score documented.

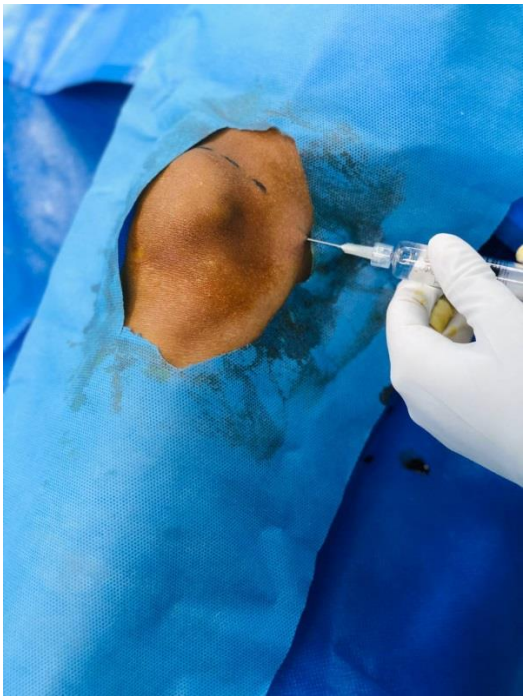

Figure 24: Intra-articular HA injection with non-activated quadriceps via superolateral approach

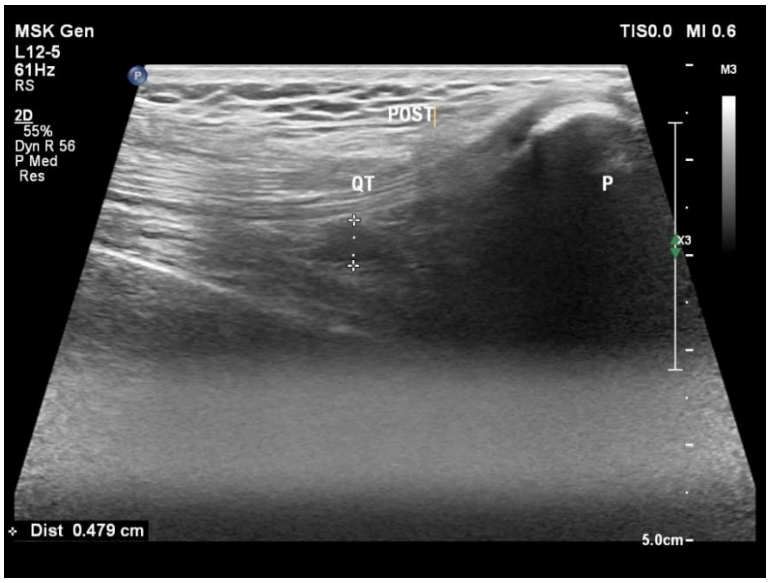

Figure 25: Pre injection suprapatellar pouch anterior-posterior dimension measurement using ultrasound

STATISTICAL METHODS

Suprapatellar pouch expansion and VAS pre and post injection and Kellgren & Lawrence grade were considered as primary outcome variables. Age, gender, side and comorbidities were considered as other study relevant variables. Study group (activated quadriceps Vs non-activated quadriceps) was considered as primary explanatory variable.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non normally distributed quantitative variables were summarized by median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagram, pie diagram.

All Quantitative variables were checked for normal distribution within each category of 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 normal distribution.

For normally distributed Quantitative parameters the mean values were compared between study groups using Independent sample t-test (2 groups). For non-normally distributed Quantitative parameters, Medians and Interquartile range (IQR) were compared between study groups using Mann Whitney u test (2 groups). The change in the quantitative parameters, before and after the intervention was assessed by paired t-test. For non-normally distributed parameters, before and after the intervention was assessed by Wilcoxon singed rank test.

Categorical outcomes were compared between study groups using Chi square test /Fisher's Exact test

P value < 0.05 was considered statistically significant. Data was analyzed by using SPSS software, V.22.[151]

OBSERVATIONS AND RESULTS

RESULT:

A total of 46 subjects were included in the final analysis.

Table 3: Descriptive analysis of study group in the study population (N=46)

Study Group	Frequency	Percentages
Activated quadriceps	23	50.00%
Non-activated quadriceps	23	50.00%

Among the study population, 23 (50%) participants were activated quadriceps and remaining 23 (50%) were non- activated quadriceps group. (Table 3)

Table 4: Comparison of mean of age between study group (N=46)

Parameter	Study group (Mean± SD)		P value
	Activated quadriceps (N=23)	Non-activated quadriceps (N=23)	
Age (in years)	52.35 ± 9.82	54.04 ± 7.68	0.518

The mean age was 52.35 ± 9.82 in activated quadriceps group and it was 54.04 ± 7.68 in non-activated quadriceps, the mean difference between two groups was statistically not significant (P value 0.518). (Table 4 & Figure 26)

Figure 26: Error bar chart of mean of age between study group(N=46)

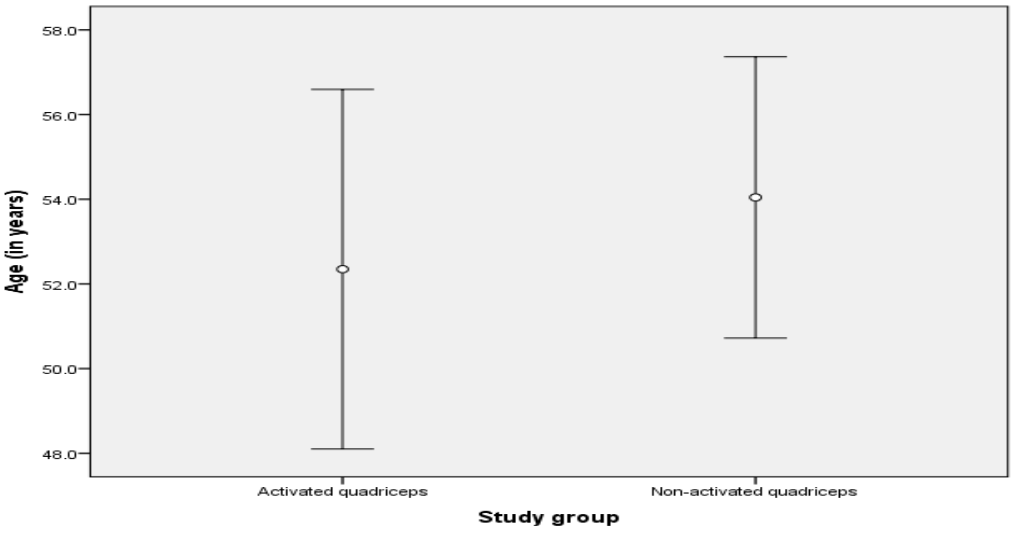

Table 5: Comparison of gender between study group (N=46)

Gender	Study Group		Chi square	P value
	Activated Quadriceps (N=23)	Non-Activated Quadriceps (N=23)		
Male	7 (30.43%)	10 (43.48%)	0.840	0.359
Female	16 (69.57%)	13 (56.52%)		

In activated quadriceps group, 7 (30.43%) participants were male and 16 (69.57%) were female. In non-activated quadriceps group, 10 (43.48%) participants were male and 13 (56.52%) were female. The difference in the proportion of gender between the study group was statistically not significant (P value 0.359). (Table 5 & Figure 27)

Figure 27: Cluster bar chart of comparison of gender between study group (N=46)

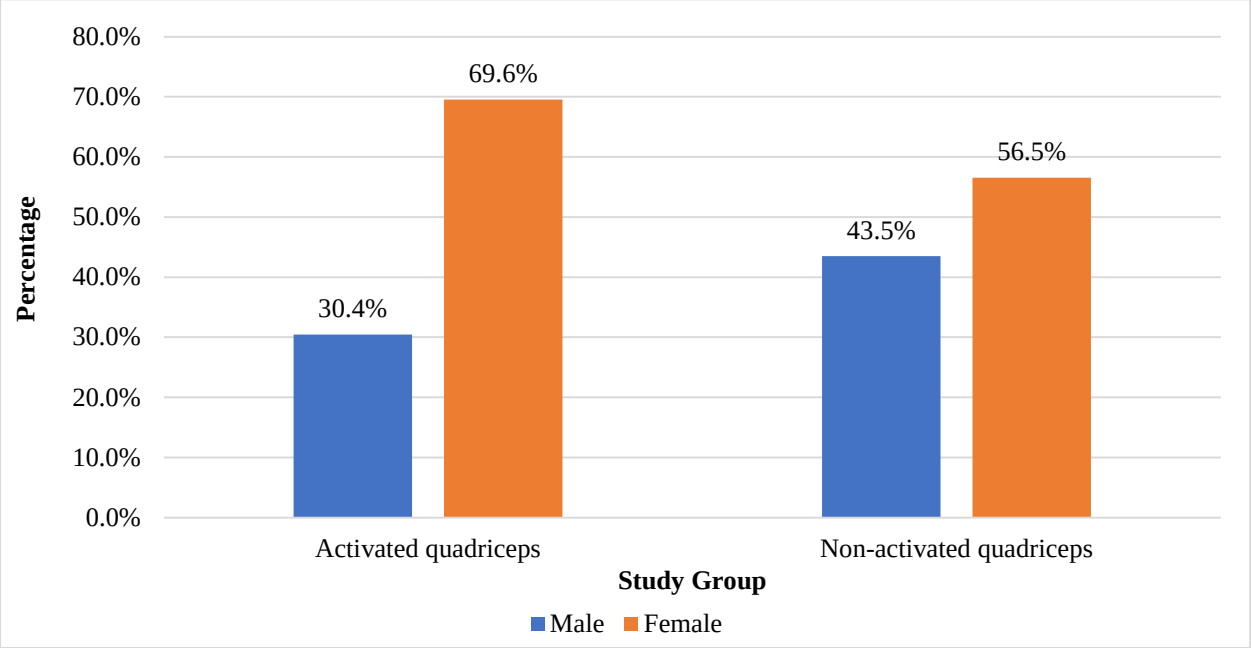

Table 6: Comparison of side between study group (N=46)

Side	Study Group		Chi square	P value
	Activated Quadriceps (N=23)	Non-Activated Quadriceps (N=23)		
Right	11 (47.83%)	11 (47.83%)	0.000	1.000
Left	12 (52.17%)	12 (52.17%)		

In activated quadriceps group, 11 (47.83%) participants were reported right side and 12 (52.17%) were reported left side. In non-activated quadriceps group, 11 (47.83%) participants were reported right side and 12 (52.17%) were reported left side. The difference in the proportion of side between the study group was statistically not significant (P value 1.000). (Table 6 & Figure 28)

Figure 28: Cluster bar chart of comparison of side between study group (N=46)

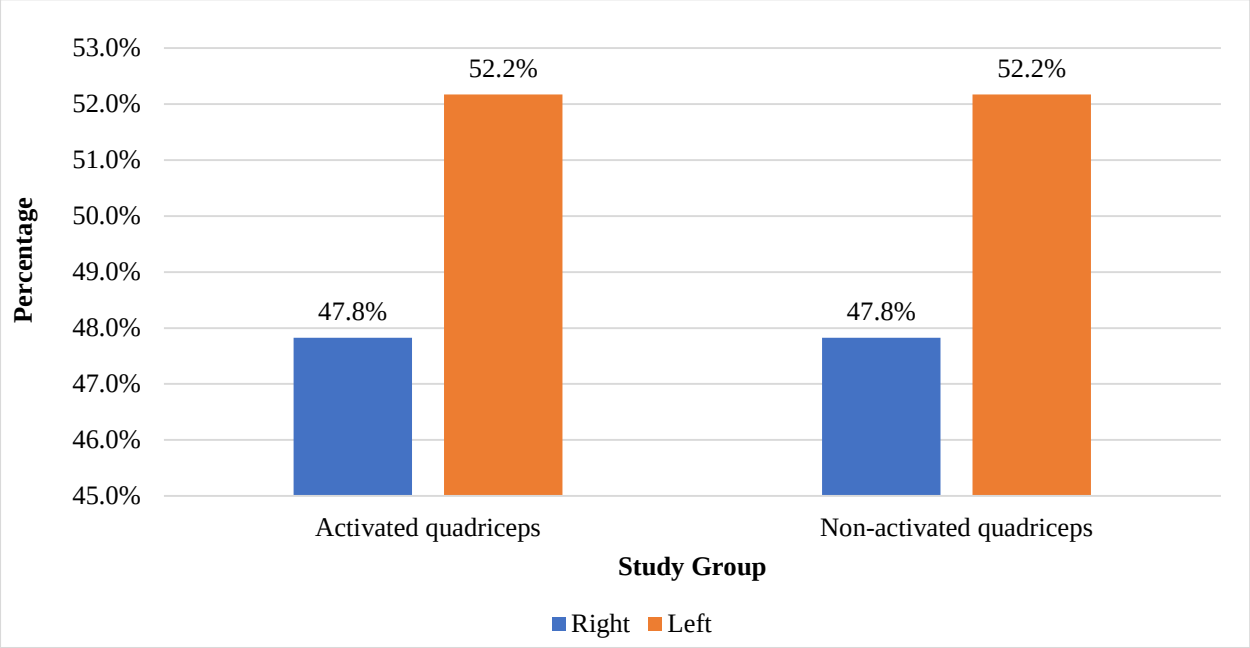

Table 7: Comparison of diabetes between study group (N=46)

Diabetes	Study Group		Fisher exact P value
	Activated Quadriceps (N=23)	Non-Activated Quadriceps (N=23)	
Yes	3 (13.04%)	6 (26.09%)	0.459
No	20 (86.96%)	17 (73.91%)	

The difference in diabetes between the study groups is found to be insignificant with a P-value of 0.459, the majority of 6 (26.09%) diabetes participants were non-activated quadriceps group. (Table 7 & Figure 29)

Figure 29: Cluster bar chart of comparison of diabetes between study group (N=46)

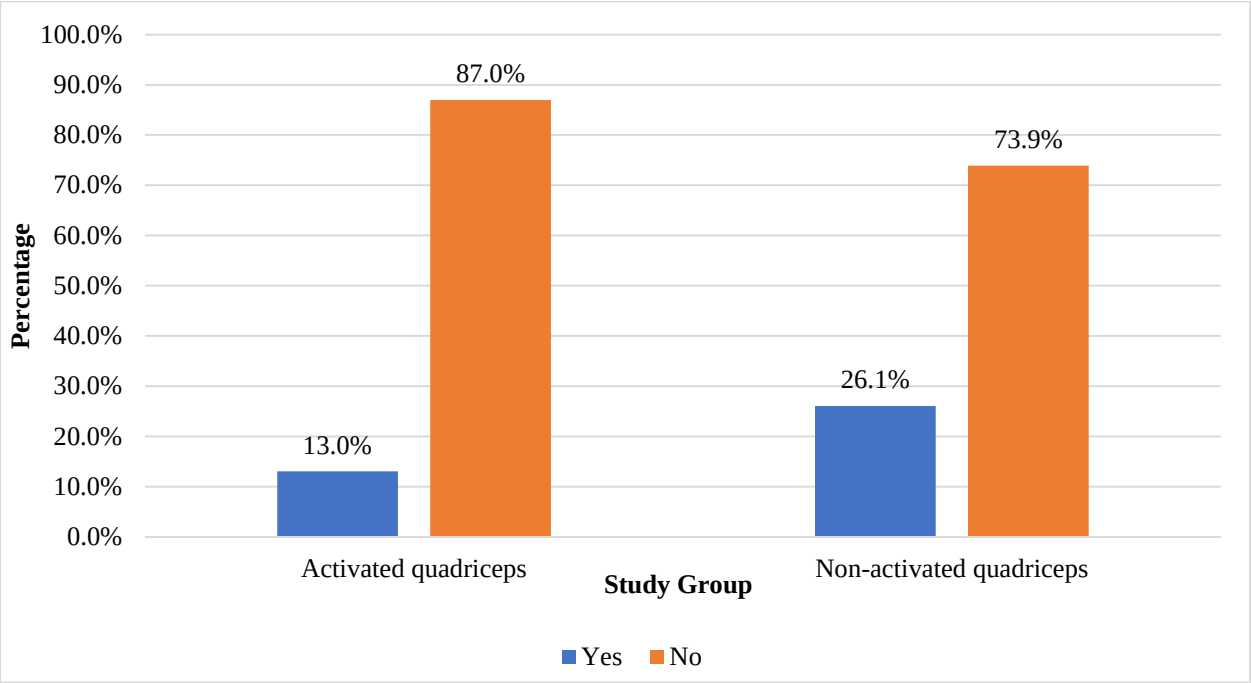

Table 8: Comparison of hypertension between study group (N=46)

Hypertension	Study Group		Chi square	P value
	Activated Quadriceps (N=23)	Non-Activated Quadriceps (N=23)		
Yes	5 (21.74%)	5 (21.74%)	0.000	1.000
No	18 (78.26%)	18 (78.26%)		

The difference in hypertension between the study groups is found to be insignificant with a P-value of 1.000. (Table 8 & Figure 30)

Figure 30: Cluster bar chart of comparison of hypertension between study group (N=46)

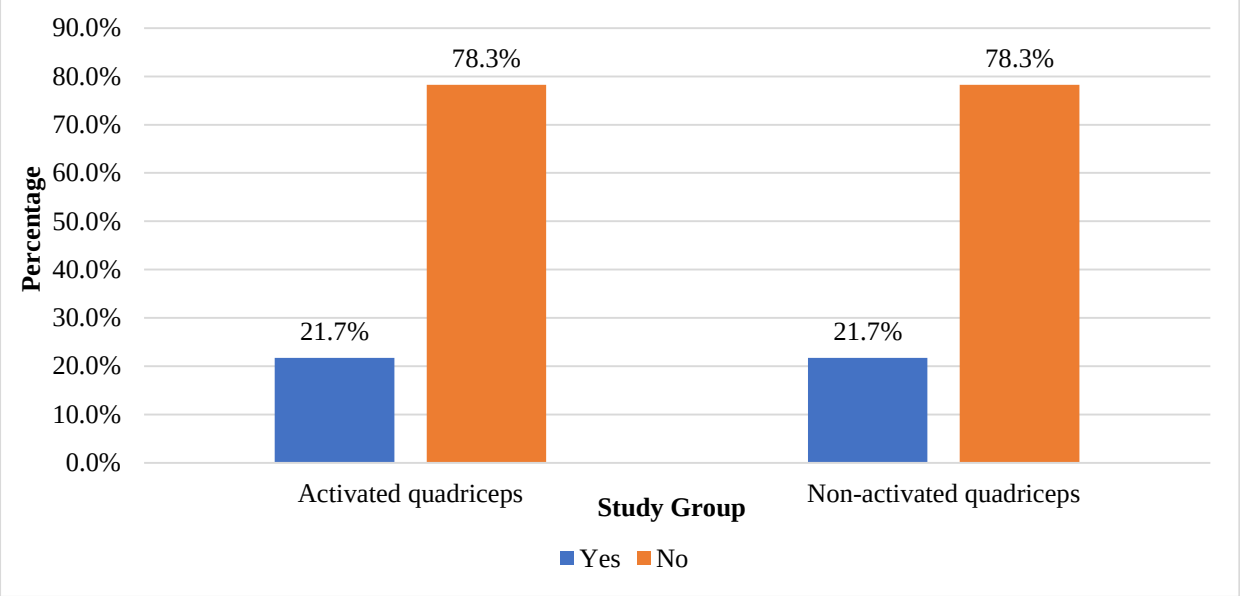

Table 9: Comparison of Kellgren & Lawrence grade between study group (N=46)

Kellgren & Lawrence Grade	Study Group	
	Activated Quadriceps (N=23)	Non-Activated Quadriceps (N=23)
1	10 (43.48%)	10 (43.48%)
2	12 (52.17%)	13 (56.52%)
3	1 (4.35%)	0 (0%)

No statistical test was applied- due to 0 subjects in the cells

In activated quadriceps group, 10 (43.48%) participants were Kellgren & Lawrence grade 1, 12 (52.17%) were Kellgren & Lawrence grade 2 and only 1 (4.35%) participant was Kellgren & Lawrence grade 3. In activated quadriceps group, 10 (43.48%) participants were Kellgren & Lawrence grade 1 and 13 (56.52%) were Kellgren & Lawrence grade 2. (Table 9)

Table 10: Comparison of mean of Suprapatellar pouch expansion- pre and post injection between study groups (N=46)

Parameter	Study group (Mean± SD)		Independent sample t test (P value)
	Activated quadriceps (N=23)	Non-activated quadriceps (N=23)	
Suprapatellar pouch expansion - Pre-Injection	2.49 ± 0.55	2.54 ± 0.58	0.777
Suprapatellar pouch expansion - Post Injection	3.55 ± 0.67	3.06 ± 0.68	0.019

The mean USG pre-injection was 2.49 ± 0.55 in activated quadriceps group and it was 2.54 ± 0.58 in non- activated quadriceps, the mean difference between two groups was statistically not significant (P value 0.777). The mean USG post-injection was 3.55 ± 0.67 in activated quadriceps group and it was 3.06 ± 0.68 in non- activated quadriceps, the mean difference between two groups was statistically significant (P value 0.019). (Table 10)

Table 11: Comparison of median VAS score between the two groups at pre and post-operative time periods (N=46)

VAS	Study Group		Mann Whitney U test (P value)
	Activated Quadriceps Median (IQR)	Non-Activated Quadriceps Median (IQR)	
Pre-Injection (N=46)	2 (2,3)	2 (2,3)	0.803
Post Injection (N=46)	5 (4,6)	5 (5,6)	0.085

Among the people with activated quadriceps, the median VAS pre-injection was 2 (IQR 2 to 3) and it was 2 (IQR 2 to 3) in people with non-activated quadriceps. The difference in the VAS pre-injection between study groups was statistically not significant (P Value 0.803). Among the people with activated quadriceps, the median VAS post-injection was 5 (IQR 4 to 6) and it was 5 (IQR 5 to 6) in people with non-activated quadriceps. The difference in the VAS post-injection between study groups was statistically not significant (P Value 0.085). (Table 11)

Table 12: Comparison of mean Suprapatellar pouch expansion in Pre and post injection among activated quadriceps and non- activated quadriceps individually

Study group	Suprapatellar pouch expansion Pre-Injection	Suprapatellar pouch expansion Post Injection	(Paired t test) P-value
Activated quadriceps	2.49 ± 0.55	3.55 ± 0.67	<0.001
Non-activated quadriceps	2.54 ± 0.58	3.06 ± 0.68	<0.001

Among activated quadriceps group, the mean of suprapatellar pouch expansion pre-injection was 2.49 ± 0.55 and it was to 3.55 ± 0.67 in post injection, the difference in pre and post-injection was statistically significant (p value <0.001). Among non-activated quadriceps group, the mean of suprapatellar pouch expansion pre-injection was 2.54 ± 0.58 and it was to 3.06 ± 0.68 in post injection, the difference in pre and post- injection was statistically significant (p value <0.001). (Table 12)

Table 13: Comparison of mean VAS in Pre and post injection among activated quadriceps and non- activated quadriceps individually

Study group	VAS Pre-Injection (Median IQR)	VAS Post Injection (Median IQR)	(Wilcoxon singed rank test) P-value
Activated quadriceps	2 (2,3)	5 (4, 6)	<0.001
Non-activated quadriceps	2 (2, 3)	5 (5, 6)	<0.001

Among the people with activated quadriceps group, the median VAS pre-injection was 2 (IQR 2 to 3) and it was 5 (IQR 4 to 6) in VAS post injection. The difference in between pre and post-injection within activated quadriceps group was statistically significant (p value <0.001). Among the people with activated quadriceps group, the median VAS pre-injection was 2 (IQR 2 to 3) and it was 5 (IQR 5 to 6) in VAS post injection. The difference in between pre and post-injection within non-activated quadriceps group was statistically significant (p value <0.001). (Table 13)

DISCUSSION

DISCUSSION:

Osteoarthritis of the knee can be effectively treated with intra-articular hyaluronic acid injections.[149] There is a need for accurate delivery of hyaluronic acid through injection into the suprapatellar bursa of the knee joint for its efficacy in reducing osteoarthritis-related symptoms. The best method for ensuring precise placement of the needle is ultrasound guidance.[152] But in many low-resource hospital settings, ultrasound guidance may not be available. The other techniques used include changing the position of the knee and anatomical landmarks.[153] Activated quadriceps that induce expansion of suprapatellar bursa by activation of quadriceps are methods believed to aid in the accurate delivery of intraarticular knee injections in low-resource settings.

Hyaluronic acid mitigates pro-inflammatory mediators and pain-producing neuropeptides released by activated synovial cells. Intraarticular injection of hyaluronic acid into knee joints is believed to restore rheological properties of synovial fluid, promote the endogenous synthesis of higher molecular weight and more functional hyaluronic acid, improve articular mobility function and reduce pain.[87] Chondrocytes are found to lose the ability to maintain cartilage homeostasis with progressing osteoarthritis due to decline in mitotic and synthetic activity, decreased response to anabolic growth factors, and decreased synthesis of cartilage-specific PG core proteins.[40] Hyaluronic acid prevents the degradation of cartilage and proteolytic enzymes in synovial fluid.[93]

In activated quadriceps method the quadriceps tendon becomes tense under isometric contraction increasing the space between femoral bone and tendon. Along with quadriceps contraction there will be contraction of articular genus muscle which lifts suprapatellar bursa to proximal position so that it is not entrapped in patella-femoral joint.[154] Tension on patellar tendon and patellar retinaculum moves Hoffa fat pad towards femoral condyles and

intercondylar space reducing lumen of tibiofemoral joint and patellofemoral joint. This will move joint fluid to suprapatellar bursa and contraction of articularis genus muscle puts synovium under tension making accurate administration of injection even in obese people. It is shown that using activated quadriceps contraction method, which focuses on the expansion of the suprapatellar bursa by inducing isometric contraction of the quadriceps and the articularis genus muscle would enable greater accuracy in delivering intra-articular injections to patients with arthritis without effusion.[155] Based on all the above considerations this study aims to compare amount of drug delivery in intra articular injection in activated and non-activated quadriceps groups and to document the pain in activated and non-activated quadriceps groups by using visual analogue scale pre intra articular injection and post intra-articular injection. Suprapatellar pouch expansion and VAS pre and post injection and Kellgren & Lawrence grade were considered as primary outcome variables. Age, gender, side and comorbidities were considered as other study relevant variables. Study group (activated quadriceps Vs non-activated quadriceps) was considered as primary explanatory variable.

A total of 46 subjects were included in the final analysis. Out of these 50% were injected in activated quadriceps and 50% were injected in non-activated quadriceps position. The mean age was 52.35 ± 9.82 in activated quadriceps group and it was 54.04 ± 7.68 in non- activated quadriceps. Mean age being more than 50 in both the groups correlates with the fact that risk of osteoarthritis of knee increases with age. In activated quadriceps group, (30.43%) participants were male and (69.57%) were female. In non-activated quadriceps group, (43.48%) participants were male and (56.52%) were female. Majority of participants in both the groups are female. There is evidence in literature that osteoarthritis of knee is more prevalent in women than men. The prevalence was found to be 51% in women and 33.09% in men.[31] The increased risk of osteoarthritis of knee in women is multifactorial including anatomic differences, genetic and hormonal issues. A difference in knee kinetics is also

noticed in women. Women have greater anterior and posterior shear forces, greater extension, increased valgus movements which puts stress on knee increasing risk of osteoarthritis.[156]

There is evidence that ultrasound is a valid imaging technique for detecting structural pathology of knee and hence ultrasound measurement of expansion of suprapatellar bursa used in study is an effective means of evaluation. The mean Suprapatellar pouch expansion measured using USG pre-injection was 2.49 ± 0.55 in activated quadriceps group and it was 2.54 ± 0.58 in non- activated quadriceps. The mean Suprapatellar pouch expansion measured using USG post-injection was 3.55 ± 0.67 in activated quadriceps group and it was 3.06 ± 0.68 in non- activated quadriceps. When there is expansion of suprapatellar bursa as reported in this study in activated quadriceps group there will be more probability of accurate administration of injection. This observation was similar to that reported in a similar study by Wada, M., et al. in which there was expansion of suprapatellar bursa in activated quadriceps individuals.[149]

In clinical trials investigating knee osteoarthritis, disease severity is most commonly assessed by the Kellgren–Lawrence (KL) criteria. This system grades osteoarthritis into five categories of severity, from 0 to 4, with lower grades representing greater joint space and less disease severity. The results of a meta-analysis by Nicholls, M., et al.[157] suggest that intraarticular hyaluronic acid injection is most efficacious in reducing pain in patients with early-moderate knee osteoarthritis, but not in the late osteoarthritis subgroup. In activated quadriceps group, (43.48%) participants were Kellgren & Lawrence grade 1, (52.17%) were Kellgren & Lawrence grade 2 and only (4.35%) participant were Kellgren & Lawrence grade 3. In non-activated quadriceps group, (43.48%) participants were Kellgren & Lawrence grade 1 and (56.52%) were Kellgren & Lawrence grade 2. In the study majority of participants belonged had early stages of osteoarthritis as shown by percentage of patients with Kellgren &

Lawrence grades of 1 and 2 being more in both groups. Visual analogue scale (VAS) is used for pain assessment in knee osteoarthritis with the following cut points on the pain. been: no pain (0–4 mm), mild pain (5–44 mm), moderate pain (45–74 mm), and severe pain (75– 100 mm)

Among the people with activated quadriceps, the median VAS pre-injection was 2 and it was 2 in people with non-activated quadriceps. Among the people with activated quadriceps, the median VAS post-injection was 5 and it was 5 in people with non-activated quadriceps. The pain appears to be moderate in all groups which can be supported by the fact that all of them had early stage osteoarthritis. There was no difference noted in pain scale after injection rather it is shown to be increased to 5. In metanalysis by Nicholls, M., et al.[157] it was showed that significant pain relief with hyaluronic acid injections can occur within 4–13 weeks post-injection and remain beneficial up to approximately 6 months. Since the pain measurements were taken immediately after injection the effect may not have been shown. The increase in pain observed is also not significant both in terms of number on scale and also since VAS is analysed based on patients' self-reporting there might be mistakes on part of patients in reporting pain post-injection due to anxiety of injection.

This study shows that the accuracy of articular injection increases in activated quadriceps group due to expansion of suprapatellar bursa as measured by ultrasound. There are various approaches used for administration of intraarticular injections. Among these a review by Maricar et al. [146] reported that superolateral patellar approach without ultrasound guidance had a success rate of 87%, medial midpatellar approach had a success rate of 64%, anterolateral approach had a success rate of 70%. Superolateral approach was reported to have an accuracy of 91% in a study by Hermans, et al.[145] Another study by Park et al. [158] reported 83.7% accuracy of superolateral patellar approach without ultrasound guidance and

96% with ultrasound guidance. In a study by Wada, M., et al.[149] the success rate of activated quadriceps method was found to be 93.3%. Another study by Toda, Y., et al. [117] in which the accuracy rates of three different methods of administration of intraarticular injections were confirmed with a single radiograph after injections of a mixture of radiographic contrast medium. In the K-L grade IV cases (n=11), the accuracy rates through the modified Waddell approach was found to be 100% higher than those through the seated anteromedial approach and the lateral patellar approach both of which had 55% accuracy rate. Among all the methods studied in different studies the success rate of activated quadriceps is found to more after Waddell approach.

LIMITATION:

The generalization of results of this study require support from other similar large studies as the study sample used in this study was of small size. Ultrasound measurements were done by 3 different sonologist so there was inter observer bias noted in the study.

RECOMMENDATION:

This study recommends use of activated quadriceps method for patients with knee osteoarthritis while administration of intraarticular injections because more accuracy noted by this method and simplicity of method.

CONCLUSION

CONCLUSION:

This study concludes that activated quadriceps method results in greater expansion of suprapatellar bursa there by facilitating accurate intra articular injection without use of ultrasound guidance. This method can be used in low resource settings for accurate delivery of intraarticular knee injections.

SUMMARY

SUMMARY:

Intraarticular hyaluronic acid injections are non-surgical effective treatment options for osteoarthritis of knee. One of the main criteria for effectiveness of this injection is accurate placement of needle into suprapatellar bursa of knee. Delivery into other surrounding tissues is found to increase pain. The best approach to locate suprapatellar bursa for insertion of needle is ultrasound guidance. But ultrasound imaging may not be available in low resource settings. Hence an approach without ultrasound guidance but improving accuracy of needle placement is desirable. Activated quadriceps method is found to be one such approach which results in expansion of suprapatellar bursa. We studied 46 patients diagnosed with Osteoarthritis clinico-radiologically selected from the Department of Orthopedics, R L Jalappa Hospital and Research Centre, Kolar, Karnataka. This study compared the expansion of the suprapatellar bursa and the accuracy rate of intra-articular injections between the activated quadriceps method and the non-activated quadriceps method. The study concluded that activated quadriceps method results in greater expansion of suprapatellar bursa there by facilitating accurate injection of articular injection without use of ultrasound guidance.

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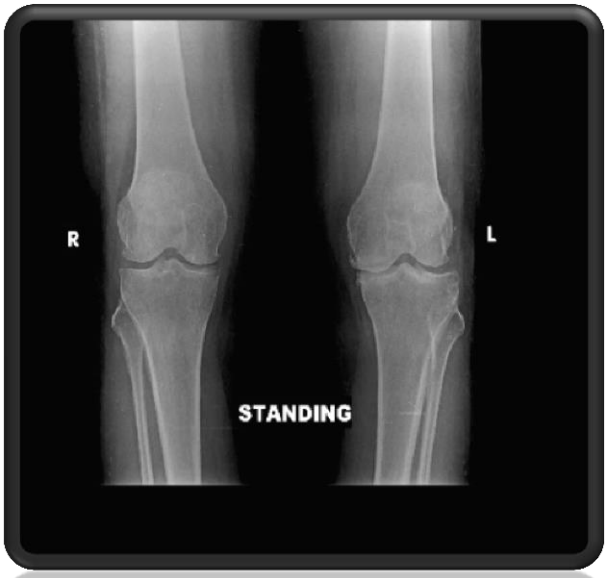
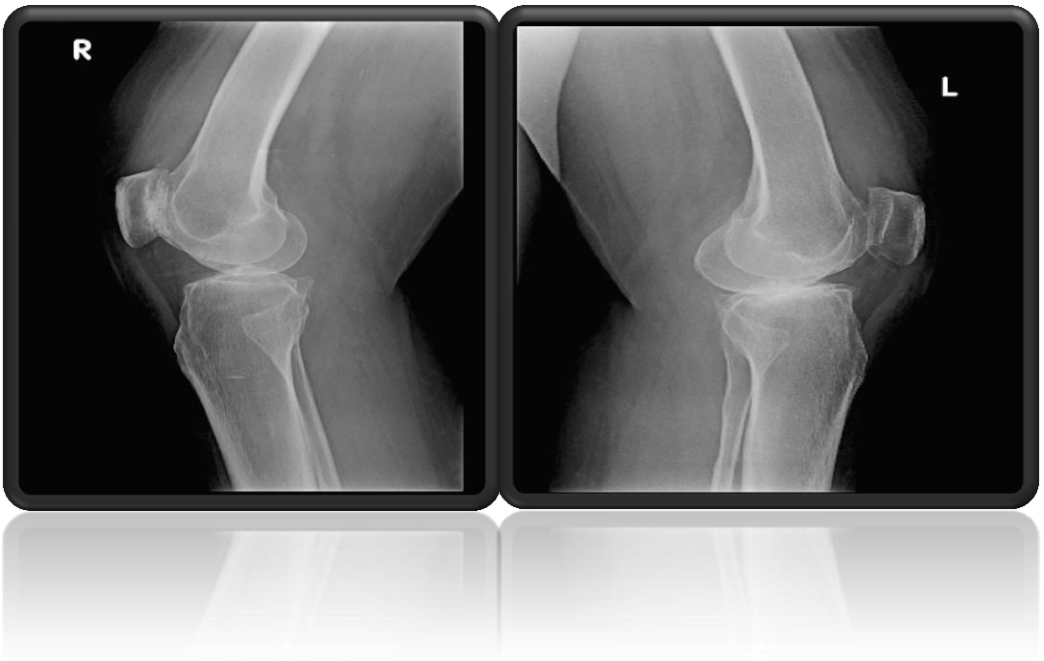
ANNEXURES-I

ANNEXURES

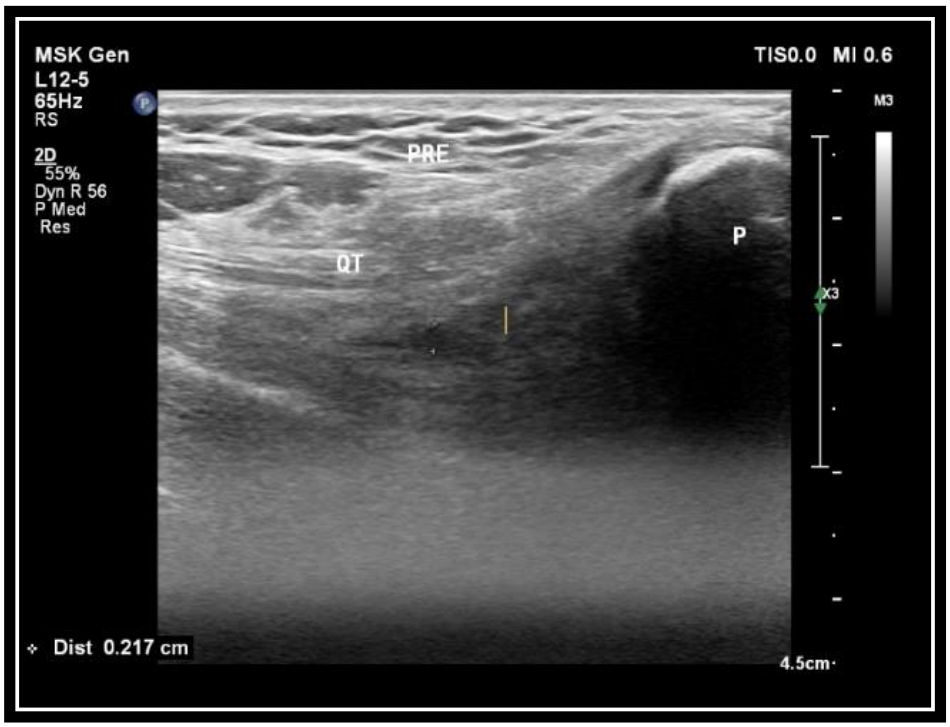
CASE ILLUSTRATIONS

CASE 11 (ACTIVATED QUADRICEPS GROUP):

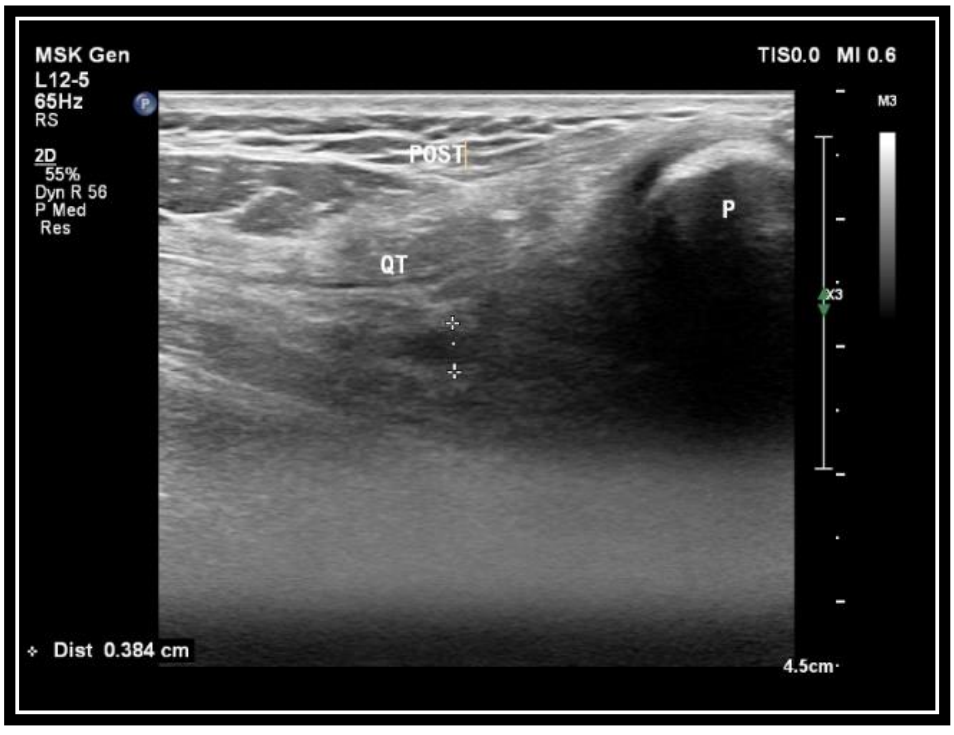




PRE-INJECTION SUPRAPATELLAR POUCH DISTENSION

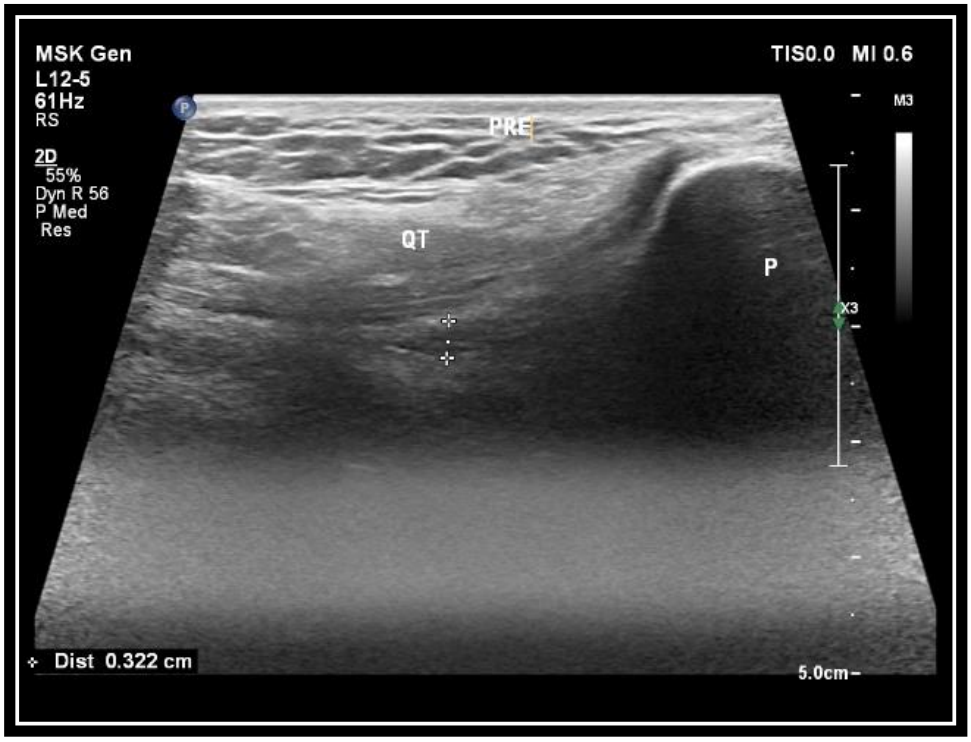


POST INJECTION SUPRAPATELLAR POUCH DISTENSION

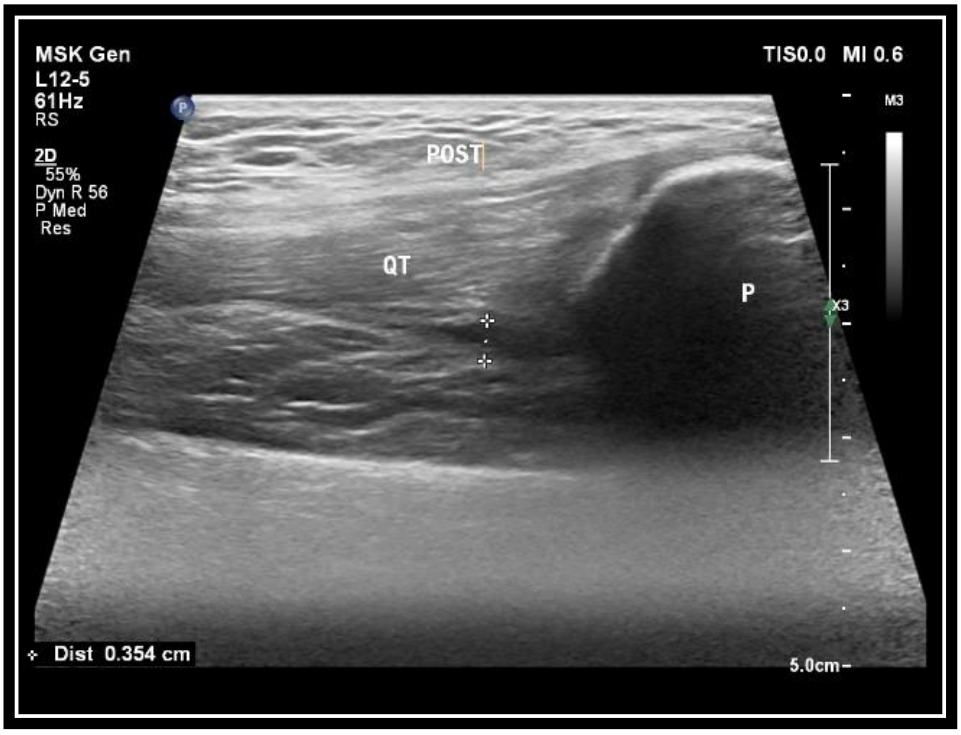


CASE 26 (NON-ACTIVATED QUADRICEPS GROUP):

PRE-INJECTION SUPRAPATELLAR POUCH DISTENSION



POST-INJECTION SUPRAPATELLAR POUCH DISTENSION



ANNEXURES-II

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.

PROFORMA

Case no:

UHID no:

TITLE:
"COMPARISON OF INTRA ARTICULAR DELIVERY OF HYALURONIC ACID BETWEEN ACTIVATED AND NON ACTIVATED QUADRICEPS FOR OSTEOARTHRITIS KNEE"

1. BASIC DATA

Name Age/Sex

Address

Mobile No.

Date of Admission

Date of Discharge

History :

General physical examination :

Vitals: Pulse- B.P-
RR- Temp-

Systemic examination:

CVS-

RS-

PS-

CNS-

Pre existing systemic illness :

Diabetes/Thyroid disorder/ Cervical Spine/ CVS/RS/ CNS/locomotor/ TB/ anaemia/

Hypertension/ malnutrition/others

Local examination:

Side : Left/Right
Deformity : Present/Absent
Swelling : Present/Absent
Tenderness : Present/Absent
Patellar tap : Present/absent
ROM @knee flexion :
Retropatellar crepitus : Present/Absent
Retropatellar tenderness : Present/Absent

2. DIAGNOSIS:

3. INVESTIGATIONS:

X ray knee joint AP and Lateral views

USG knee

Visual analogue scale:

4. PROCEDURE :

5. POST PROCEDURE:

USG knee:

Visual analogue scale:

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.

INFORMED CONSENT FORM

Case no:

UHID no:

TITLE:
"COMPARISON OF INTRA ARTICULAR DELIVERY OF HYALURONIC ACID BETWEEN ACTIVATED AND NON ACTIVATED QUADRICEPS FOR OSTEOARTHRITIS KNEE"

- I, _____ aged _____ ,after being explained in my own vernacular language about the purpose of the study and the risks and complications of the procedure, hereby give my valid written informed consent without any force or prejudice for Intra articular injection of osteoarthritis knee which is a therapeutic procedure to be performed on me. The nature and risks involved in the procedure have been explained to me to my satisfaction.

  I have been explained in detail about the Clinical Research on "COMPARISON OF INTRA ARTICULAR DELIVERY OF HYALURONIC ACID BETWEEN ACTIVATED AND NON ACTIVATED QUADRICEPS FOR OSTEOARTHRITIS KNEE" being conducted. *I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.* I hereby give consent to provide my history, undergo physical examination, undergo the injection/ operative procedure, undergo investigations and provide its results and documents etc to the doctor / institute etc.

  For academic and scientific purpose the operation / procedure, etc may be video graphed or photographed. All the data may be published or used for any academic purpose. I will not hold the doctors / institute etc responsible for any untoward consequences during the procedure / study.

  A copy of this Informed Consent Form and Patient Information Sheet has been provided to the participant.

Signature/Thumb impression & Name of patient

Signature & Name of Pt. Attender

Relation with patient:

Signature & Name of Research person /doctor:

ಶ್ರೀ ದೇವರಾಜ್ ಯುಆರ್ಎಸ್ ಅಕಾಡೆಮಿ ಆಫ್ ಹೈಯರ್ ಎಜುಕೇಶನ್

ಅಂಡ್ ರಿಸರ್ಚ್, ತಮಕಾ, ಕೋಲಾರ್ - 563101.

ಮಾಹಿತಿ ಕಾನ್ಸೆಂಟ್ ಫಾರ್ಮ್

ಪ್ರಕರಣ ಸಂಖ್ಯೆ:

ಐಪಿ ಸಂಖ್ಯೆ:

ಶೀರ್ಷಿಕೆ:"ಸಕ್ರಿಯ ಮತ್ತು ಸಕ್ರಿಯಗೊಂಡಿಲ್ಲ ಹೈಲಾರಾನಿಕ್ ಆಸಿಡ್ನ ಇಂಟ್ರಾ ಆರ್ಟಿಕ್ಯುಲರ್ ವಿತರಣೆಯ ಹೋಲಿಕೆ ಅಸ್ಥಿಸಂಧಿವಾತ ಮೊಣಕಾಲು ಗಾಗಿ"

 ನಾನು, _____ ವಯಸ್ಸಿನ _____, ಅಧ್ಯಯನದ ಉದ್ದೇಶ ಮತ್ತು ಕಾರ್ಯವಿಧಾನದ ಅಪಾಯಗಳು ಮತ್ತು ತೊಡಕುಗಳ ಬಗ್ಗೆ ನನ್ನ ಸ್ವಂತ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಿದ ನಂತರ, ಅಸ್ಥಿಸಂಧಿವಾತ ಮೊಣಕಾಲಿನ ಒಳಗಿನ ಕೀಲಿನ ಚುಚ್ಚುಮದ್ದಿನ ಯಾವುದೇ ಬಲ ಅಥವಾ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ನನ್ನ ಮಾನ್ಯ ಲಿಖಿತ ತಿಳುವಳಿಕೆಯುಳ್ಳ ಸಮ್ಮತಿಯನ್ನು ಈ ಮೂಲಕ ನೀಡುತ್ತದೆ. ನನ್ನ ಮೇಲೆ ಮಾಡಬೇಕಾದ ಚಿಕಿತ್ಸಕ ವಿಧಾನವಾಗಿದೆ. ಕಾರ್ಯವಿಧಾನದಲ್ಲಿ ಒಳಗೊಂಡಿರುವ ಸ್ವರೂಪ ಮತ್ತು ಅಪಾಯಗಳನ್ನು ನನ್ನ ತೃಪ್ತಿಗೆ ವಿವರಿಸಲಾಗಿದೆ. ಕ್ಲಿನಿಕಲ್ ರಿಸರ್ಚ್ ಬಗ್ಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ "ಆಕ್ಟಿವೇಟೆಡ್ ವರ್ಸಸ್ ನ ಹೋಲಿಕೆ ಅಧ್ಯಯನವು ಸಕ್ರಿಯವಾದ ಕ್ವಾಡ್ರಿಸೆಪ್ಸ್ ಇನ್ ಇಂಟ್ರಾ ಆರ್ಟಿಕಲ್ ಇಂಜೆಕ್ಷನ್ಸ್ ಇನ್ ಓಸ್ಟಿಯೊಆರ್ಥ್ರಿಟಿಸ್ ಫಾರ್ ಕೆನೆ" ನಡೆಸಲಾಗುತ್ತಿದೆ. ನಾನು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಯಾವುದೇ ಪ್ರಶ್ನೆ ಕೇಳುವ ಅವಕಾಶ ನನಗೆ ಸಿಕ್ಕಿದೆ. ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪುತ್ತೇನೆ. ನನ್ನ ಇತಿಹಾಸವನ್ನು ಒದಗಿಸಲು, ದೈಹಿಕ ಪರೀಕ್ಷೆಗೆ ಒಳಗಾಗಲು, ಇಂಜೆಕ್ಷನ್ / ಆಪರೇಟಿವ್ ಕಾರ್ಯವಿಧಾನಕ್ಕೆ ಒಳಗಾಗಲು, ತನಿಖೆಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಅದರ ಫಲಿತಾಂಶಗಳು ಮತ್ತು ದಾಖಲೆಗಳನ್ನು ವೈದ್ಯರಿಗೆ / ಸಂಸ್ಥೆಗೆ ಒದಗಿಸಲು ನಾನು ಈ ಮೂಲಕ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ. ಶೈಕ್ಷಣಿಕ ಮತ್ತು ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಕಾರ್ಯಾಚರಣೆ / ಕಾರ್ಯವಿಧಾನ ಇತ್ಯಾದಿಗಳನ್ನು ವೀಡಿಯೊ ಗ್ರಾಫ್ ಮಾಡಬಹುದು ಅಥವಾ hed ಾಯಾಚಿತ್ರ ಮಾಡಬಹುದು. ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಯಾವುದೇ ಶೈಕ್ಷಣಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಪ್ರಕಟಿಸಬಹುದು ಅಥವಾ ಬಳಸಬಹುದು. ಕಾರ್ಯವಿಧಾನ / ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ಅಹಿತಕರ ಪರಿಣಾಮಗಳಿಗೆ ನಾನು ವೈದ್ಯರು / ಸಂಸ್ಥೆ ಇತ್ಯಾದಿಗಳನ್ನು ಹೊಣೆಗಾರರನ್ನಾಗಿ ಮಾಡುವುದಿಲ್ಲ. ಭಾಗವಹಿಸುವವರಿಗೆ ಈ ತಿಳುವಳಿಕೆಯುಳ್ಳ ಒಪ್ಪಿಗೆ ನಮೂನೆ ಮತ್ತು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯ ನಕಲನ್ನು ಒದಗಿಸಲಾಗಿದೆ.

ಸಹಿ / ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕ ಸಹಿ

ರೋಗಿಯ ಹೆಸರು ರೋಗಿಯೊಂದಿಗೆ ಸಂಬಂಧಸಾಕ್ಷ

ಸಹಿ

ಸಂಶೋಧನಾ ವ್ಯಕ್ತಿ / ವೈದ್ಯರ ಹೆಸರು

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.

PATIENT INFORMATION SHEET

STUDY TITLE: "COMPARISON OF INTRA ARTICULAR DELIVERY OF HYALURONIC ACID BETWEEN ACTIVATED AND NON ACTIVATED QUADRICEPS FOR OSTEOARTHRITIS KNEE"

Study location: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

Details- Patients diagnosed with fracture distal end of radius admitted in orthopaedics ward from opd and casualty at R.L.J. HOSPITAL AND RESEARCH CENTRE, attached to SRI DEVARAJ URS MEDICAL COLLEGE,TAMAKA,KOLAR

- Patients in this study will have to undergo routine Blood Investigations: CBC, HIV, HBsAg status. Radiological investigation: Plain x-ray of knee joint in antero-posterior & lateral views. Ultrasound knee to measure antero-posterior diameter of suprapatellar pouch pre and post intra articular knee injection.

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 the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.
All information collected from you will be kept confidential and will not be disclosed to any outsider. Your 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.

CONFIDENTIALITY

Your medical information will be kept confidential by the study doctor and staff and will not be made publicly available. Your original records may be reviewed by your doctor or ethics review board. For further information/ clarification please contact

Dr.SAIGANESH D SHETTY (Post Graduate),
Department Of ORTHOPAEDICS,
SDUMC ,Kolar
CONTACT NO : 9448714808

ಶ್ರೀ ದೇವರಾಜ್ ಆರ್ಎಸ್ ಅಕಾಡೆಮಿ ಆಫ್ ಹೈಯರ್ ಎಜುಕೇಶನ್ ಅಂಡ್

ರಿಸರ್ಚ್, ತಮಾಕಾ, ಕೋಲಾರ್ - 563101

ರೋಗಿಯ ಮಾಹಿತಿ ಫಾರ್ಮ್

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: "ಸಕ್ರಿಯ ಮತ್ತು ಸಕ್ರಿಯಗೊಂಡಿಲ್ಲ ಹೈಲಾರಾನಿಕ್ ಆಸಿಡ್ನ ಇಂಟ್ರಾ ಆರ್ಟಿಕ್ಯುಲರ್ ವಿತರಣೆಯ ಹೋಲಿಕೆ ಅಸ್ಥಿಸಂಧಿವಾತ ಮೊಣಕಾಲು ಗಾಗಿ"

ಅಧ್ಯಯನದ ಸ್ಥಳ: ಕೋಲಾರ್‌ನ ತಮಾಕಾದ ಶ್ರೀ ದೇವರಾಜರ್ಸ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜಿಗೆ ಲಗತ್ತಿಸಲಾದ ಆರ್ ಎಲ್ ಜಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ.

ವಿವರಗಳು- ಆರ್.ಎಲ್.ಜೆ.ಯಲ್ಲಿ ಆಪ್ತ ಮತ್ತು ಅಪಘಾತದಿಂದ ಮೂಳೆಚಿಕಿತ್ಸಕ ವಾರ್ಡ್‌ನಲ್ಲಿ ದಾಖಲಾದ ತ್ರಿಜ್ಯದ ಮುರಿತದ ಡಿಸ್ಟಲ್ ಎಂಡ್ ರೋಗನಿರ್ಣಯ. ಹಾಸ್ಪಿಟಲ್ ಮತ್ತು ರಿಸರ್ಚ್ ಸೆಂಟರ್, ಶ್ರೀ ದೇವರಾಜ್ ಯುಆರ್ಎಸ್ ಮೆಡಿಕಲ್ ಕಾಲೇಜ್, ತಮಕಾ, ಕೋಲಾರ್ಗೆ ಲಗತ್ತಿಸಲಾಗಿದೆ

ಸ್ಪಡಿ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ರೋಗಿಗಳು ದಿನನಿತ್ಯದ ರಕ್ತ ತನಿಖೆಗೆ ಒಳಗಾಗಬೇಕಾಗುತ್ತದೆ: ಎಚ್‌ಬಿ%, ಒಟ್ಟು ಡಬ್ಲ್ಯೂಬಿಸಿ ಎಣಿಕೆ, ಭೇದಾತ್ಮಕ ಎಣಿಕೆ, ಇಎಸ್ಆರ್, ಬಿಟಿ, ಸಿಟಿ, ಬ್ಲಡ್ ಯೂರಿಯಾ, ಸೀರಮ್ ಕ್ರಿಯೇಟಿನೈನ್, ಆರ್‌ಬಿಎಸ್, ಎಚ್‌ಐವಿ, ಎಚ್‌ಬಿಎಸ್‌ಎಜಿ ಸ್ಥಿತಿ, ಇಸಿಜಿ, ಎದೆಯ ಕ್ಷ ಕಿರಣ ಅಗತ್ಯವಿದ್ದಾಗ. ವಿಕಿರಣಶಾಸ್ತ್ರದ ತನಿಖೆ: ಆಂಟೀರೋ-ಹಿಂಭಾಗದಲ್ಲಿ ಮೊಣಕಾಲಿನ ಸರಳ ಎಕ್ಸರೆ. ಅಲ್ಟ್ರಾಸೌಂಡ್ ಮೊಣಕಾಲು ಸುಪ್ರಪಟೆಲ್ಲರ್ ಪೌಚ್ ಪೂರ್ವ ಮತ್ತು ನಂತರದ ಕಾರ್ಯವಿಧಾನದ ಆಂಟೀರೋ-ಹಿಂಭಾಗದ ವ್ಯಾಸವನ್ನು ಅಳೆಯಲು. ದಯವಿಟ್ಟು ಈ ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಒಪ್ಪಿದರೆ ನಾವು ನಿಮ್ಮಿಂದ ಅಥವಾ ನಿಮ್ಮಿಂದ ಅಥವಾ ಇಬ್ಬರಿಗೂ ಜವಾಬ್ದಾರರಾಗಿರುವ ವ್ಯಕ್ತಿಯಿಂದ ಮಾಹಿತಿಯನ್ನು (ಪ್ರೊಫಾರ್ಮಾದ ಪ್ರಕಾರ) ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಸಂಬಂಧಿತ ಇತಿಹಾಸವನ್ನು ತೆಗೆದುಕೊಳ್ಳಲಾಗುವುದು. ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರಬಂಧ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತು ಬಹಿರಂಗಗೊಳ್ಳುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನವನ್ನು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯು ಪರಿಶೀಲಿಸಿದೆ ಮತ್ತು ನೀವು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತರಾಗಿದ್ದೀರಿ. ಈ ಅಧ್ಯಯನವನ್ನು ಒಪ್ಪಿಕೊಳ್ಳಲು ಯಾವುದೇ ಬಲವಂತವಿಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಕಾಳಜಿ ಬದಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಕೊಂಡರೆ ಮಾತ್ರ ನೀವು ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆಗೆ ಸಹಿ / ಒದಗಿಸುವ ಅಗತ್ಯವಿದೆ

ಗೌಪ್ಯತೆ

ನಿಮ್ಮ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯನ್ನು ಅಧ್ಯಯನ ವೈದ್ಯರು ಮತ್ತು ಸಿಬ್ಬಂದಿ ಗೌಪ್ಯವಾಗಿಡುತ್ತಾರೆ ಮತ್ತು ಸಾರ್ವಜನಿಕವಾಗಿ ಲಭ್ಯವಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಮೂಲ ದಾಖಲೆಗಳನ್ನು ನಿಮ್ಮ ವೈದ್ಯರು ಅಥವಾ ನೈತಿಕ ಪರಿಶೀಲನಾ ಮಂಡಳಿಯು ಪರಿಶೀಲಿಸಬಹುದು. ಹೆಚ್ಚಿನ ಮಾಹಿತಿಗಾಗಿ / ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ದಯವಿಟ್ಟು ಸಂಪರ್ಕಿಸಿ

ಡಾ.ಸೈಗನೇಶ್ ಡಿ ಶೆಟ್ಟಿ (ಸ್ನಾತಕೋತ್ತರ),

ಆರ್ಥೋಪೆಡಿಕ್ಸ್ ಇಲಾಖೆ,

ಕೋಲಾರ

ಸಂಪರ್ಕ ಸಂಖ್ಯೆ: 9448714808

KEYS TO MASTER CHART

A- Serial Number

B- Name

C- Age

D- Gender

E- UHID No.

F- Side (Left/Right)

G- Co-morbidity

H- Kellgren & Lawrence grade

I- Activated quadriceps vs Non activated quadriceps

J- USG pre injection (suprapatellar anterior-posterior dimension)

K- USG post injection (suprapatellar anterior-posterior dimension)

L- VAS pre injection

M- VAS post injection

SL. No.	NAME	AGE	GENDER	UHID No.	SIDE	CO-MORBIDITIES	KELLGREN & LAWRENCE GRADE	AQ VS NAQ	USG- PRE INJECTION	USG- POST INJECTION	VAS PRE INJECTION	VAS POST INJECTION
1	MAHADEVAIAH	56	M	704693	RIGHT	NIL	3	AQ	3.7	5.1	3	6
2	MAHADEVAIAH	56	M	704693	LEFT	NIL	2	NAQ	3.9	4.3	3	7
3	JAYAMMA	40	F	827511	LEFT	NIL	2	AQ	3.2	4.2	2	6
4	KRISHNAMMA	70	F	835352	LEFT	DM	2	AQ	2.5	3.6	4	7
5	KRISHNA	50	M	834981	LEFT	NIL	1	NAQ	3	2	4	5
6	BALAMMA	48	F	843990	RIGHT	NIL	1	NAQ	2.1	2.5	2	6
7	RAMESH	45	M	849838	RIGHT	NIL	1	AQ	2.8	3.4	2	6
8	RAMESH	45	M	849838	LEFT	NIL	2	NAQ	2.7	3.1	3	7
9	VENKATASWAMY	58	M	852814	RIGHT	NIL	2	AQ	3.1	3.8	3	5
10	VENKATASWAMY	58	M	852814	LEFT	NIL	1	NAQ	3	3.6	3	6
11	HASEENA	44	F	860306	LEFT	HYPERTENSION	1	AQ	2.1	3.8	4	6
12	HASEENA	44	F	860306	RIGHT	HYPERTENSION	2	NAQ	3.5	4.7	3	6
13	JEENATH	68	F	893116	LEFT	NIL	1	NAQ	3.2	3.5	2	5
14	JEENATH	68	F	893116	RIGHT	NIL	2	AQ	2.8	4.6	2	4
15	NANJUNDASWAMY	47	M	899532	LEFT	NIL	1	AQ	1.6	4.7	2	4
16	NANJUNDASWAMY	47	M	899532	RIGHT	NIL	1	NAQ	3.2	4	2	5
17	BHARATHI	46	M	900647	LEFT	NIL	2	AQ	2.8	3.7	4	6
18	CHOWDAMMA	70	F	894781	LEFT	HYPERTENSION	2	AQ	2.8	4.2	3	4
19	CHOWDAMMA	70	F	894781	RIGHT	HYPERTENSION	1	AQ	1.7	2.7	2	4
20	LAKSHMAMMA	50	F	845466	LEFT	NIL	1	NAQ	2.1	3	3	5
21	LAKSHMAMMA	50	F	845466	RIGHT	NIL	2	AQ	2.3	3.5	2	5
22	SHAHAZAD	50	M	899589	LEFT	NIL	1	NAQ	2.3	2.9	3	5
23	SHAHAZAD	50	M	899589	RIGHT	NIL	2	AQ	2.1	3	2	5
24	NETHRAVATI	44	F	899339	RIGHT	NIL	1	NAQ	3	3.5	2	6
25	NETHRAVATI	44	F	899339	LEFT	NIL	2	AQ	3.2	3.7	3	5
26	VENKATLAKSHMAMMA	60	F	799426	LEFT	HYPERTENSION	1	NAQ	3.1	3.9	2	5
27	VENKATLAKSHMAMMA	60	F	799426	RIGHT	HYPERTENSION	1	AQ	3	3.8	3	5
28	MUNIYAMMA	66	F	899068	RIGHT	HYPERTENSION	2	NAQ	2.5	3.2	3	6
29	MUNIRAJU	56	M	940568	LEFT	NIL	1	AQ	2.1	3.1	3	5
30	SATHYAPPA	60	M	944105	RIGHT	DM	2	NAQ	2	2.6	3	5
31	YASHODAMMA	50	F	905612	LEFT	DM	2	NAQ	1.8	2.4	2	5

SL. No.	NAME	AGE	GENDER	UHID No.	SIDE	CO-MORBIDITIES	KELLGREN & LAWRENCE GRADE	AQ VS NAQ	USG- PRE INJECTION	USG- POST INJECTION	VAS PRE INJECTION	VAS POST INJECTION
32	RATHNAMMA	46	F	944517	RIGHT	NIL	1	AQ	2	2.9	2	4
33	KASTHURAMMA	45	F	904157	RIGHT	NIL	2	NAQ	2.1	2.6	2	5
34	VENKATLAKSHMAMMA	50	F	915762	LEFT	HYPERTENSION	2	AQ	2	2.8	2	5
35	CHATURVI	51	F	951071	LEFT	NIL	2	NAQ	2	2.4	2	2
36	AYESHA	60	F	950008	RIGHT	DM	1	NAQ	2.1	2.5	2	5
37	MUNIRAJU	65	M	954091	RIGHT	HYPERTENSION,DM	2	NAQ	2.5	2.9	2	5
38	SANA	55	F	950176	LEFT	DM	1	AQ	2	2.8	2	4
39	LAKSHMI	50	F	987512	LEFT	HYPERTENSION	2	NAQ	2.1	2.6	2	5
40	SARASWATHAMMA	49	F	902542	RIGHT	NIL	1	AQ	2.3	3.1	2	5
41	FATHIMA	48	F	925641	LEFT	NIL	2	AQ	2.2	2.9	2	4
42	SANTHOSH	56	M	958714	RIGHT	DM	2	NAQ	2.1	2.8	2	6
43	GIRIJA	48	F	962541	LEFT	DM	2	AQ	3	3.4	3	5
44	PATRALEKHA	44	F	985741	RIGHT	NIL	1	AQ	2	2.8	2	4
45	GOVINDAPPA	67	M	895741	RIGHT	DM	2	NAQ	2.1	2.8	2	5
46	REKHA	53	F	952104	LEFT	NIL	2	NAQ	2	2.6	3	5