“Comparison of the functional outcome and pain relief of Intra articular Hylan GF-20 Vs. Methyl Prednisolone Acetate for Grade II Osteo Arthritis – Knee.”

Dissertation submitted to The Tamil Nadu Dr.M.G.R. medical University, Chennai, Tamil Nadu, in partial fulfillment of the requirements for MD (Physical Medicine and Rehabilitation)., – University Examinations, April-2017.

Submitted by

Dr.S.Suganthi

(Reg.No: 201429001)

Under the guidance of

Prof.Dr.C.Ramesh

Director & Head of the Department, Department of physical medicine and rehabilitation, Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai.

&

Prof.Dr.T.Jayakumar

Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.S.Suganthi
Postgradaute M.D.(Physical Medicine & Rehabilitation)
Madras Medical College
Chennai 600 003

Dear Dr.S.Suganthi,

The Institutional Ethics Committee has considered your request and approved your study titled **"Comparitive study of functional outcome of intra articular hylan GF-20 Vs Methyl Prednisolone Acetate in Grade II Osteoarthritis knee" No.27062015.**

The following members of Ethics Committee were present in the meeting held on 09.06.2015 conducted at Madras Medical College, Chennai-3.

1. Prof.C.Rajendran, M.D.,	: Chairperson
2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.B.Vasanthi, M.D., Prof. of Pharmacology, MMC	: Member
5. Prof.P.Raghumani, M.S., Professor of Surgery, MMC	: Member
6. Prof.Md.Ali, M.D., DM., Prof. & HOD of MGE, MMC	: Member
7. Prof.Baby Vasumathi, Director, Inst.of O&G, Ch-8	: Member
8. Prof.Ramadevi, Director, Inst.of Bio-chemistry, MMC	: Member
9. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
10. Prof.K.Srinivasagalu, M.D.,Director, I.I.M. MMC, Ch-3	: Member
11. Thiru S.Rameshkumar, B.Com., MBA	: Lay Person
12. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
13. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

15/6/15

Member Secretary, Ethics Committee

"Comparison of the functional outcome and pain relief of Intra articular Hylan GF-20 Vs Methyl Prednisolone Acetate for Grade II Osteo Arthritis – Knee"

17

Dissertation submitted to The Tamil Nadu Dr.M.G.R. medical University, Chennai, Tamil Nadu, in partial fulfillment of the requirements for M.D.(Physical Medicine and Rehabilitation) – University Examinations, April, 2017

Submitted by

Dr.S.Suganthi (Reg.No.:201429001)

Under the guidance of

Comparison of the functional outcome and pain...

By Suganthi S

"Comparison of the functional outcome and pain relief of Intra articular Hylan GF-20 Vs Methyl Prednisolone Acetate for Grade II Osteo Arthritis – Knee"

Dissertation submitted to The Tamil Nadu Dr.M.G.R. medical University, Chennai, Tamil Nadu, **in partial fulfillment of the requirements for** 16

M.D.(Physical Medicine and Rehabilitation) – University Examinations, April, 2017 Submitted by Dr.S.Suganthi (Reg.No.:201429001) Under the guidance of Prof. Dr. C. Ramesh Director & Head of the Department, Department of physical medicine and rehabilitation, Government

Institute of Rehabilitation **Medicine, Madras Medical College, Chennai.** 22

& Prof. Dr. T. Jayakumar Government

Institute of Rehabilitation **Medicine, Madras Medical College, Chennai.** 22

Introduction: Osteoarthritis is mainly concerned with disease of synovial joints and its surrounding soft tissues. The main pathology involves progression

of articular cartilage and the formation of bone at the margins of the 20

Jyothish AN EXPERIMENTAL STUDY TO ASSESS THE EFFECTIVENESS OF STRUCTURED TEACHING PROGRAMME ON ASSESSMENT OF CHRONIC WOUNDS, IN TERMS OF KNOWLEDGE AND SKILL AMONG STAFF NURSES WORKING IN A SELECTED HOSPITAL IN MADURAI. Jyothish .P. Ipe A

DISSERTATION SUBMITTED TO THE TAMIL NADU DR M.G.R MEDICAL UNIVERSITY, CHENNAI, IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR

THE DEGREE OF MASTERS OF SCIENCE IN NURSING SEPTEMBER 2001. Acknowledgement I the investigator of this study owe deep sense of gratitude to all those who have contributed to the successful completion of this endeavor. First of all, I praise and thank Lord Almighty for His abundant grace and blessing throughout this study. My sincere thanks to Prof. K.R.Arumugam Head of The Institution, Sacred Heart Nursing College, Ultra

DECLARATION

I declare that, this dissertation entitled **"COMPARISON OF FUNCTIONAL OUTCOME AND PAIN RELIEF OF INTRA ARTICULAR HYLAN GF-20 Vs. METHYL PREDNISOLONE ACETATE FOR GRADE II OSTEOARTHRITIS - KNEE"** is the original work done by **DR.S.SUGANTHI, Reg.No:201429001** in the Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai under the direct guidance and supervision of **Prof.Dr.C.Ramesh**, and **Prof.Dr.T.Jayakumar**, Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai as co-guide and is submitted to The Tamil Nadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the board regulations for the award of the degree of MD (Physical Medicine and Rehabilitation).,

DR.S.SUGANTHI

(Reg.No: 201429001)

CERTIFICATE

This is to certify that this dissertation entitled **"COMPARISON OF FUNCTIONAL OUTCOME AND PAIN RELIEF OF INTRA ARTICULAR HYLAN GF-20 Vs. METHYL PREDNISOLONE ACETATE FOR GRADE II OSTEOARTHRITIS - KNEE"** is the original work done by **DR.S.SUGANTHI, Reg.No:201429001** in the Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai from March-2015 to August-2016 under my guidance submitted in partial fulfillment of the regulation for the degree of MD(Physical Medicine and Rehabilitation).,

Prof.Dr.C.Ramesh DA., D.Phys.Med., MD(PMR)., DNB(PMR).,

(Guide)

Director & Head of the Department,

Government Institute of Rehabilitation Medicine,

Madras Medical College, Chennai.

CERTIFICATE

This is to certify that this dissertation entitled **"COMPARISON OF FUNCTIONAL OUTCOME AND PAIN RELIEF OF INTRA ARTICULAR HYLAN GF-20 Vs. METHYL PREDNISOLONE ACETATE FOR GRADE II OSTEOARTHRITIS - KNEE"** is the bonafide work carried out by **DR.S.SUGANTHI, Reg.No:201429001** in the Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai under my co-guidance submitted in partial fulfillment of the regulation for the degree of MD(Physical Medicine and Rehabilitation).,

Prof.Dr.T.Jayakumar D.Ortho., DPMR., DNB(PMR)., MD(PMR).,

(Co-Guide)

Professor,

Government Institute of Rehabilitation Medicine,

Madras Medical College, Chennai.

CERTIFICATE

This is to certify that this dissertation entitled **"COMPARISON OF FUNCTIONAL OUTCOME AND PAIN RELIEF OF INTRA ARTICULAR HYLAN GF-20 Vs. METHYL PREDNISOLONE ACETATE FOR GRADE II OSTEOARTHRITIS - KNEE"** is the bonafide work carried out by **DR.S.SUGANTHI, Reg.No:201429001** in the Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai submitted in partial fulfillment of the regulation for the degree of MD(Physical Medicine and Rehabilitation).,

Dean

Madras Medical College, Chennai.

Director & HOD

Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai.

ACKNOWLEDGEMENT

I owe my special thanks to **Prof.Dr.C.Ramesh and Prof.Dr.Sampath Kumar**, who were instrumental in conceptualization of this topic and has been my constant support and encouragement. They has been very kind and helped me academically. Their wisdom in solving problems has been inspirational. If not for them I would have not been able to complete this thesis work for which I am deeply indebted to them and I am proud to have them as my mentors.

I also like to thank **Prof.Dr.M.K.Muralidharan**, Dean, Madras Medical College and **Prof.Dr.Sudha Sesaiyan**, Vice Principal, Madras Medical College for their support.

I owe my thanks to **Prof.Dr.T.Jayakumar, Prof.Dr.C.Priyadharshini** for their help and guidance and allowing me to use the facilities of the Department.

I also extend my thanks to **Prof.Dr.Thirunavukkarasu, Dr.A.Rajakumar, Dr.B.Jayanthi, Dr.C.Premalatha** for their help and constant support.

I am grateful to **Dr.Padma Priya, Dr.Padma Rani, Dr.Uma, Dr.Prince Rajinikanth and other colleagues** for their help. I am grateful to the Medical Records Department and Department of Physiotherapy of Government Institute of Rehabilitation Medicine, Chennai for their support.

I am indebted to all my patients who form an integral part of this study for their cooperation without which this dissertation could not been possible. Finally I thank my **parents**, my **husband**, my **daughter** and my **brother** for being a source of constant support and inspiration.

Dr.S.Suganthi

ABSTRACT

Introduction:

Osteoarthritis (OA) of the knee is characterized by chronic pain, cartilage matrix degradation, deterioration of the mechanical properties of the synovial fluid, bony osteophyte formation, and episodic inflammation. Compared to healthy joints, the synovial fluid in joints affected by OA can be characterized by both diminished molecular weight and concentration of its primary functional constituent, hyaluronan.

Hyaluronan is a polysaccharide consisting of repeating linear dimers of N-acetylglucosamine and glucuronic acid. It is physiologically ubiquitous in the animal kingdom, in particular existing as a large molecular weight substance in bony joints where small quantities serve as both a lubricant and a transport medium for nutrients, proteins, and degradation products related to joint tissue metabolism. Lower molecular weight hyaluronan found in osteoarthritic joints fails to retain its viscoelasticity and ability to withstand shear forces, both small (normal joint movement) and large (high impact forces). As a result, joint surfaces can become progressively damaged when endogenous hyaluronan production is reduced by disease.

Corticosteroids may work through influencing levels of collagenase and aggrecan, as well as matrix metalloproteinases and proinflammatory cytokines.

No single cause of OA found no far. Multiple factors that might cause OA includes, genetic predisposition, age, injury prior to adulthood, microtrauma, body weight, stress on the joint, occupational task i.e., repetitive knee bending, heavy lifting and previous surgery of joint.[1-3]

Aims and Objectives:

To compare the functional outcome and pain relief of Intra articular Hylan GF-20 Vs. Methyl Prednisolone Acetate for Grade II Osteo Arthritis – Knee.

Study Centre:

Government Institute of Rehabilitation Medicine, KK Nagar, Chennai-600 083.

Duration of study:

18 months (March-2015 to August-2016)

Study design:

Prospective Single blinded Cohort study

- Subjects will be randomized by systematic random sampling, according to registration number of the study
- Odd numbers (Group A)will be treated with Hylan GF-20
- Even numbers (Group B) will be treated with Methyl Prednisolone Acetate.

Methodology:

- Patients will be given test dose of 0.5ml of Lignocaine 2%
- They will be taken to Operation theatre and parts will be cleaned with Betadine and drapped with sterile towel
- Under aseptic precautions, Lignocaine 2% will be injected to anesthetise the injection site
- By following randomization procedure, either Hylan-GF20(48mg)/methyl prednisolone acetate(40mg) will then be infiltrated into the knee joint space after confirmation by aspiration technique by infero lateral approach
- After infiltration the subjects will be observed for 15 minutes for adverse reactions
- Subjects will be asked to report immediately in case of adverse reactions like post injection flare (increased pain, swelling)/hypersensitivity reactions etc.,
- Also they will be given 3 days of analgesics and antibiotics.

Inclusion criteria:

- Age > 45 years
- Grade II osteoarthritis knee by Kellgren-Lawrence grading
- Knee pain with failed conservative treatment for 1 month
- Stiffness:<30mts
- Crepitus

- Bony tenderness
- Bony enlargement
- No palpable warmth.

Exclusion criteria:

- Post Operative cases
- Cellulitis / Infections
- Any implants inside.
- Associated with DVT calf muscles
- Non co-operative patient
- Low I.Q Patients /psychiatric patient
- Trauma
- Meniscal injury
- Anterior/Posterior cruciate ligament injury
- Medial/Lateral collateral ligament injury
- Bursitis
- Rheumatoid arthritis
- Pseudogout
- Other grades of osteo arthritis knee

Sample size:

Approx 30+30

Product/Investigation details:

Investigations:

FBS, PPBS, X-ray knee-AP and Lateral

Product details:

Methylprednisolone acetate – 80mg

Hylan-GF 20 – 48mg

Data collection and Methods:

- Subjects will be randomized according to registration number of the study
- Odd numbers (Group A) will be treated with Hylan GF-20
- Even numbers (Group B) will be treated with Methyl Prednisolone Acetate
- Case History age, sex, duration of pain will be collected. Anthropometric measurements height and weight of the patient will be collected.
- They will be assessed with pre procedural and post procedural
    - pain score using Visual Analog Score (VAS)
    - WOMAC-C score
    - Range of Movements of Knee
- The assessment will be analysed using SPSS software (version 21)

Results:

- There were 23 males and 37 females enrolled in the study, among which 14 males (60.9% of total males) and 16 females (43.2% of total females) were enrolled in Hylan group and 9 males (29.1% of total males) and 21 females (56.8% of total females) were enrolled in the steroid group.
- 49 patients had pain along anterior aspect of knee joint and 11 patients had pain along medial joint line. Among hylan group, 25 patients had pain along anterior aspect and 5 had pain along medial joint line. In steroid group, 24 had pain along anterior aspect and 6 had pain along medial joint line.
- Pain was assessed using Visual Analog Scoring (VAS) in this study. It showed significant pain relief with hylan group over due course of time. In steroid group, there was initial pain response till 8 weeks after the treatment, but later the pain score started to show upward trend in later weeks. In conclusion, pain relief was better in hylan group than steroid group with p value <0.05 in all the follow up period except 8^{th} week.
- Functional assessment after the treatment was done using WOMAC score (The Western Ontario and McMaster Universities Arthritis Index) and improvement in range of movements of the knee in this study. It showed significant functional improvement with hylan group over due course of time. In steroid group, there was initial better response till 8 weeks, but later the functional ability started to reduce in later weeks. In

conclusion, functional improvement as per WOMAC score was better in hylan group than steroid group with p value <0.05.

- Functional assessment after the treatment was also done using range of movements (ROM). It showed significant improvement in ROM with hylan group over due course of time and remained stable in 12^{th} and 26^{th} weeks. In steroid group, there was initial better response around 4^{th} and 8th weeks, but later ROM got reduced and did not show any further change in later weeks. In conclusion, functional improvement as per ROM was better in hylan group than steroid group with p value <0.05.

Conclusions:

- Intra articular Hylan GF-20 shows statistically significant improvement in Pain in analyzing the patients with Visual Analog Score (VAS)
- Similarly, there is improvement in range of movements and WOMAC score (C domain) in hylan group
- For steroid group, there is initial statistical improvement upto 8 weeks in pain and other functional components, but after 8 weeks, there is no clinical improvement
- Hence Hylan GF-20 can be considered as an important therapeutic measure in the management of OA knee.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF CHARTS

LIST OF ABBREVIATION

OA	–	Osteo Arthritis
VAS	–	Visual Analog Score
WOMAC	–	Western Ontario McMaster Universities of Osteoarthritis Index
ROM	–	Range of Motion
TGF	–	Transforming Growth Factor
PDGF	–	Platelet Derived Growth Factor
TNF	–	Tumor Necrosis Factor
IL	–	Interleukin
MRI	–	Magnetic Resonance Imaging
USG	–	Ultrasonography
NSAIDs	–	Non Steroidal Anti Inflammatory Drugs.

INTRODUCTION

Osteoarthritis is mainly concerned with disease of synovial joints and its surrounding soft tissues. The main pathology involves progression of articular cartilage and the formation of bone at the margins of the joint.[1]

EPIDEMIOLOGY:

Osteoarthritis is an extremely common condition after 40 yrs of age. It is wide spreading in adults older than 65 and affects men more than women before the age of 50 and reverses after the age of 50. More than 20 million people are affected by OA in U.S. It is the most common leading cause of chronic disability[1]. In India, studies show that the prevalence of osteoarthritis is as high as in any other part of the world. WHO Technical Report Series – 919 shows prevalence of osteoarthritis of the knee per 1,00,000 population in India. Indian statistics revealed that 4644 males and 6587 females in 45-59 age group and 2247 females in 35-44 age group has osteoarthritis based on clinical Epidemiology.

In United States, osteoarthritis is second only to ischemic heart disease as a cause of work disability in men over age 50. It has been estimated that about 1,00,000 people in United States are unable to walk independently because of osteoarthritis of hip or knee. Data from arthritis research campaign show that upto 5,50,000 people in United Kingdom has severe osteoarthritis of knee.[2,3]

ETIOLOGY:

No single cause of OA found no far. Multiple factors that might cause OA includes, genetic predisposition, age, injury prior to adulthood, microtrauma, body weight, stress on the joint, occupational task i.e., repetitive knee bending ,heavy lifting and previous surgery of joint.[1,4,5]

Progression of OA includes following factors:

1. Loss of cartilage matrix which makes the joint most susceptible to injury
2. Alterations to underlying bone associated with wear on the cartilage
3. Formation of osteophytes
4. Release of debris of cartilage or bony fragments into the joint
5. Cartilage breakdown with synovial inflammation leads to release of cytokines and enzymes which exacerbate the cartilage damage.

Signs and symptoms:

Pain, swelling loss of ROM, bony deformity.

OA is not associated with systemic features like RA

Stiffness and crepitus.

Management:

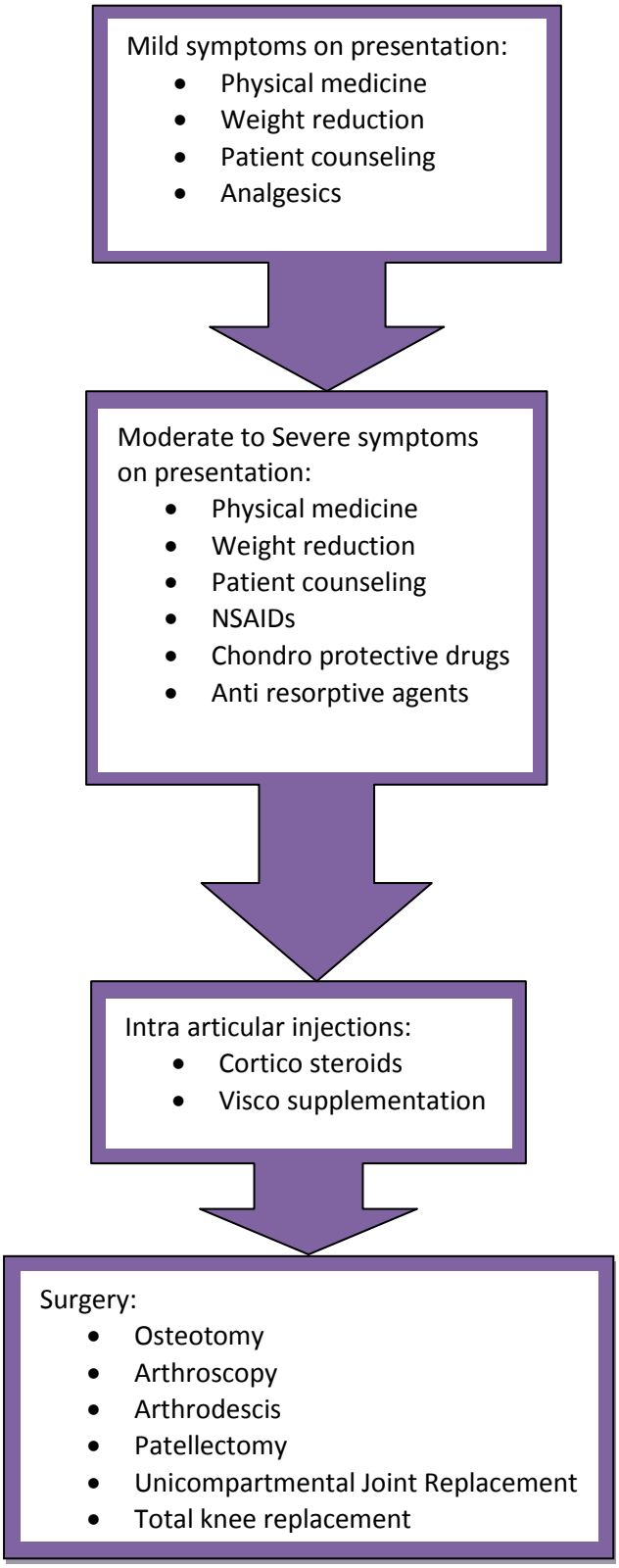


Chart 1: Management **of** Osteo Arthritis – knee.

AIMS AND OBJECTIVES

- To compare the functional outcome and pain relief of Intra articular Hylan GF-20 Vs. Methyl Prednisolone Acetate for Grade II Osteo Arthritis – Knee.

REVIEW OF LITERATURE

Knee joint anatomy

Knee is the largest and most complex joint of the body. It is a compound synovial joint, incorporating two condylar joints between the condyles of femur and tibia and one saddle joint between femur and patella. The stability of the joint is maintained by number of factors:

1. Cruciate ligaments maintain antero posterior stability
2. The collateral ligaments maintain side to side stability
3. The weak capsular ligament was strengthened anteriorly by the medial and lateral patellar retinacula from vastusmedialis and lateralis, laterally by the iliotibial tract, medially by tendons of Sartorius and Semimembranosis and posteriorly by the oblique popliteal ligament
4. The role of iliotibial tract in stabilizing a partially flexed knee cannot be over emphasized

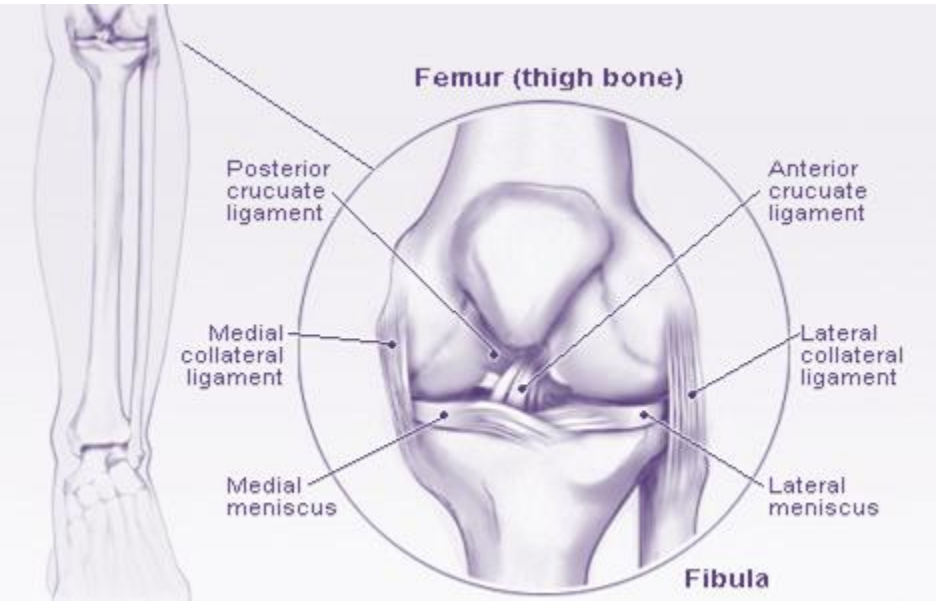


Figure 1: Anatomy of knee joint – AP view.

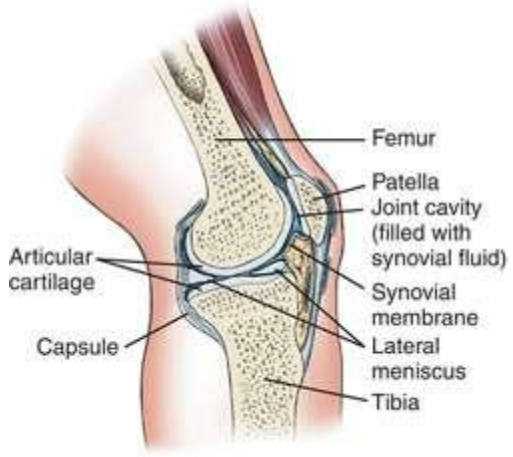


Figure 2: Anatomy of knee joint – Lateral view.

The anatomical axes of the bone runs between the shaft of the femur and tibia, which is normally about 170-175 degree (obtuse, physiologic valgus angle). If any deviation in this angle results varus or valgus deformity, which predisposes to osteoarthritis knee while joint over loads.

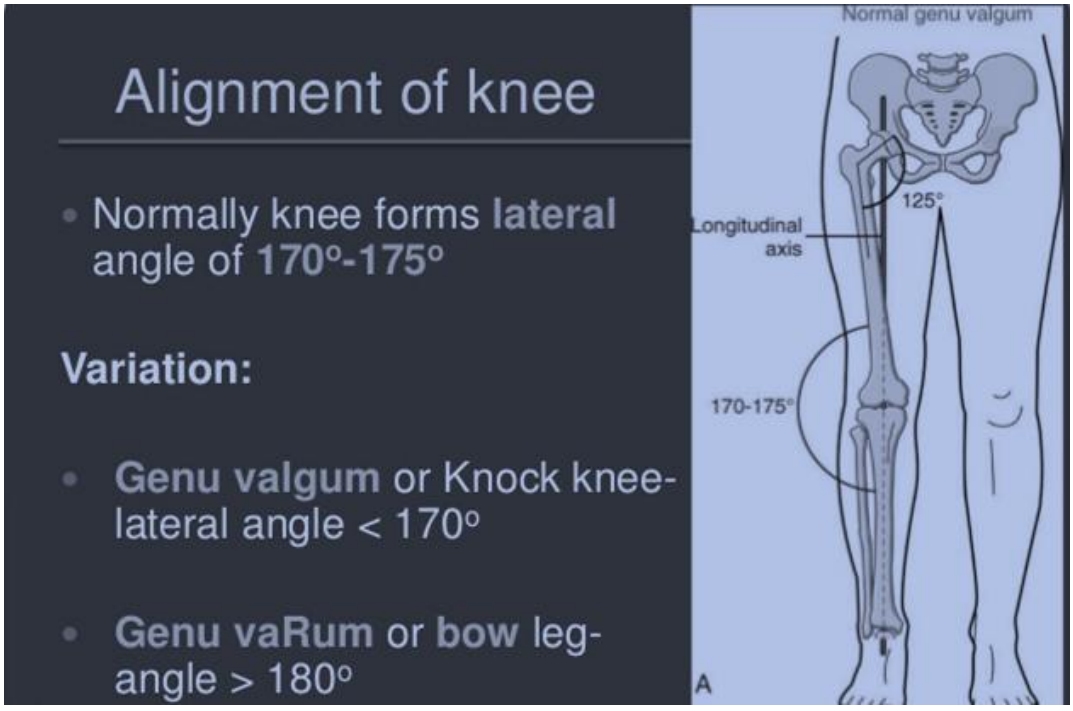


Figure 3: Axes of knee joint.

Osteo Arthritis (OA) Knee:

OA knee is a degenerative joint disease occurring primarily in older persons, characterized by erosion of the articular cartilage, hypertrophy of bone at the margins, subchondral sclerosis and a wide range of biomechanical & morphological alterations of the synovial membrane and the joint capsule. The main clinical symptoms are pain &stiffness after prolonged activity. In industrialized societies OA knee was the leading cause of physical chronic disability, increase in health care utilization & impaired quality of life.[6]

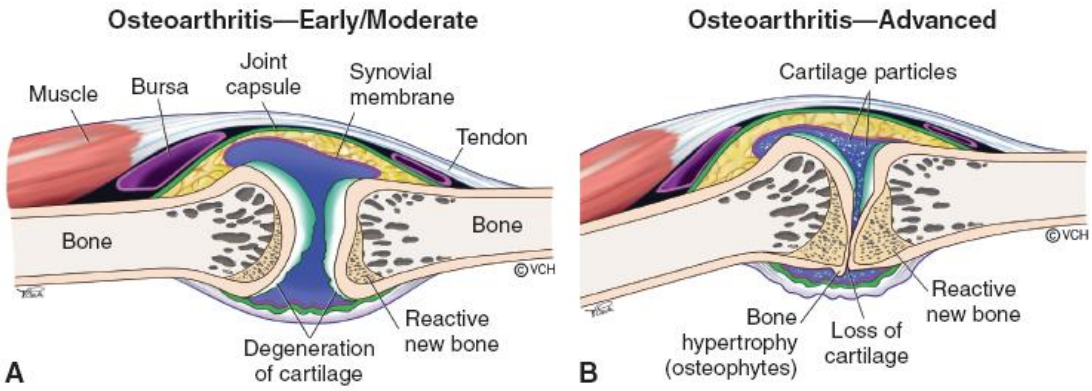


Figure 4: Pathological Changes in OA knee.

Major risk factors affecting degree of risk for developing OA knee include age, joint location, obesity, genetic predisposition, joint malalignment, trauma & gender.

Risk Factors for Osteoarthritis

Systemic Factors	Local Factors
Age	Obesity
Gender	Major joint trauma (e.g., ACL rupture)
Race	Repetitive stress (occupation)
Genetics	Muscle weakness
Metabolic/endocrine	Altered joint biomechanics
High bone density	Joint malalignment
Nutritional status (e.g., vitamin D deficiency)	Proprioceptive impairments
Congenital/ developmental	
Obesity	

Table 1: Risk factors for OA knee.[6]

The impact of arthritic conditions was expected to grow as the population both increases & ages in the coming decades.[6]

Definition:

According to Harrison's Principles of Internal Medicine, osteoarthritis represents failure of the diarthrodial (movable, synovial lined) joint. Definitions which erroneously described it as a degenerative disease are no longer acceptable. Osteoarthritis differs from simple wear and tear of joints innumerous ways.

- It is not necessarily age related.
- It is asymmetrically distributed and often localized only in one part of the joint
- It is more clearly related to impact loading than to frictional wear.
- It progresses steadily, often resulting in pain and dysfunction of the joint.
- It is not necessarily accompanied by any systemic illness.
- Although there are sometimes signs of inflammation, it is not primarily an inflammatory disorder.
- It is more a process than disease, occurring in almost any condition that causes disparity between the mechanical stress applied to articular cartilage and the ability of the cartilage to withstand that stress.

In addition to these primary processes, there are "modifiers" that influence the rate of pathlogic and clinical progression like recurrent synovitis, avascular necrosis of

subchondral bone, joint instability and prolonged use of powerful anti inflammatory preparations, which may depress bone healing[7].

Classification:

Clinically, osteoarthritis may be classified as Primary or idiopathic and secondary.

Primary (idiopathic)

Knee (medial, lateral, patellofemoral)

Secondary

- Dysplastic
- Post-traumatic
- Structural failure
- Post-inflammatory
- Endocrine and metabolic
- Connective tissue
- Etiology obscure.

Race

Prevalence of osteoarthritis of knee is similar among Europeans and Americans. Whether these differences are genetic or due to differences in joint usage related to lifestyle or occupation is unknown.[8]

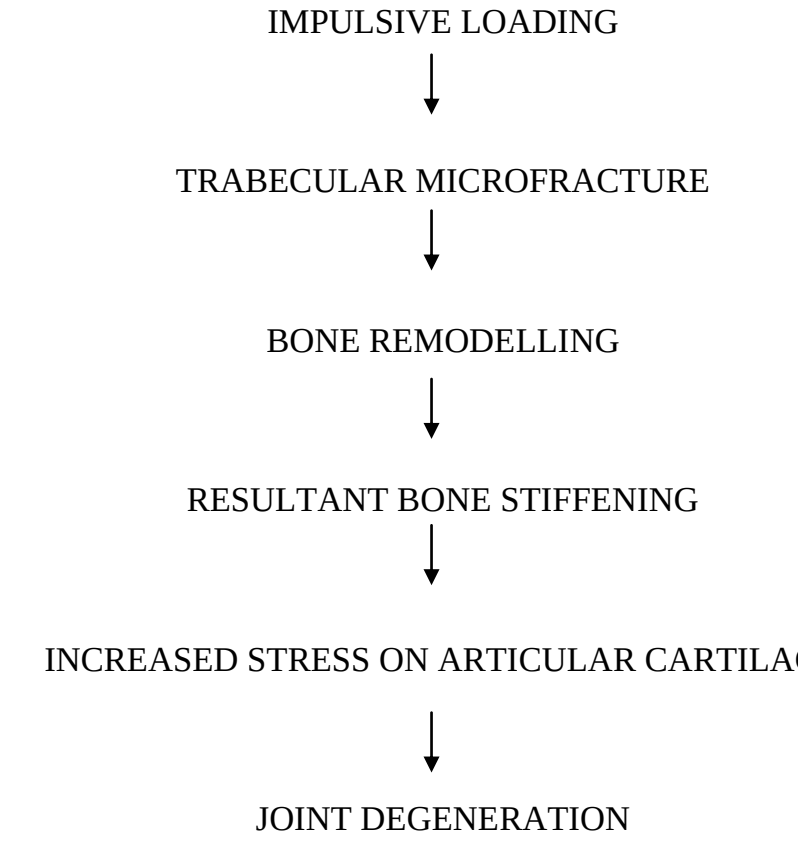
Genetic factors

The relation of heredity to osteoarthritis is less ambiguous. First-degree relatives of diseased females are two to three times likely to develop osteoarthritis, due to the similarity in the genes encoding structural proteins of extracellular matrix of cartilage. Mercer is of the opinion that joint laxity may also be a feature in familial predisposition to osteoarthritis. According to Kelley, a positive family history was often elicited in patients with generalized osteoarthritis and it was a polygenic disorder. At least four genetically determined mechanisms have been postulated:

- A genetic defect in type II collagen may directly affect cartilage structure.
- A heritable trait, as in alkaptonuric ochronosis may indirectly alter the mechanical properties of articular cartilage.
- Inherited forms of epiphyseal dysplasia may result in joint incongruity and eccentric articular stresses.
- Generalized characteristics such as obesity and excessive joint laxity, may adversely affect joint loading.

Evidence from various studies shows that, there is increased concordance for osteoarthritis in monozygotic twins compared with dizygotic twins, indicating the increased genetic susceptibility to the disease.[9,10]

In 1972 Radin et al., proposed a hypothetical model to explain the mechanical basis for osteoarthritis. The model, still quite controversial, accounts for changes observed in joints with signs of osteoarthritis, and was based on wolff's law, outlining the response of skeletal tissue to imposed stress.[11]



Impulsive loading is an external force that reaches a high magnitude in a short time. According to Wolff's law, bone remodels in response to the imposed stress.

In summary, a variety of indirect evidence supports the view that physical changes in the subchondral bone may be important in osteoarthritis and that at least a portion of this issue is related to an alteration in a hydraulic factor in the trabecular tissue.

Normal cartilage

Normal healthy articular cartilage is composed of extra cellular matrix and chondrocytes. Water content is about 65-80% of matrix by weight, type 2 collagen (10%), proteoglycans, non collagenous protein and glycoproteins the remainder. Chondrocytes secrete matrix and present through matrix and concentrated in deep layers. The superficial layer contains highest amount of the water and collagen and giving this zone the greatest tensile stiffness and strength and ability to resist shearing force. Proteoglycans contain protein core and glycosaminoglycans (hyaluronic acid and chondroitin sulfate). Proteoglycans are concentrated in middle and deep zones. Cartilage contains no nerves, blood vessels or lymphatics. It receives its nutrition and elimination of waste via diffusion through synovial fluid by facilitated imbibitions.

Role of cartilage

It decreases friction between articular joint surfaces distributing static and dynamic joint forces to underlying bone and absorbing shock.

Cartilage's shock absorbing effect is minimal (1%), subchondral bone (30%) and also peri articular muscles[11,12]. These joint structures with ligaments, menisci, capsule, synovium and synovial fluid give protection to joint from regular wear and tear and damaging forces[11-14]. Cyclical loading of joint enhances proteoglycan synthesis and concentration.[15]

Biomechanics and disease mechanisms of OA:

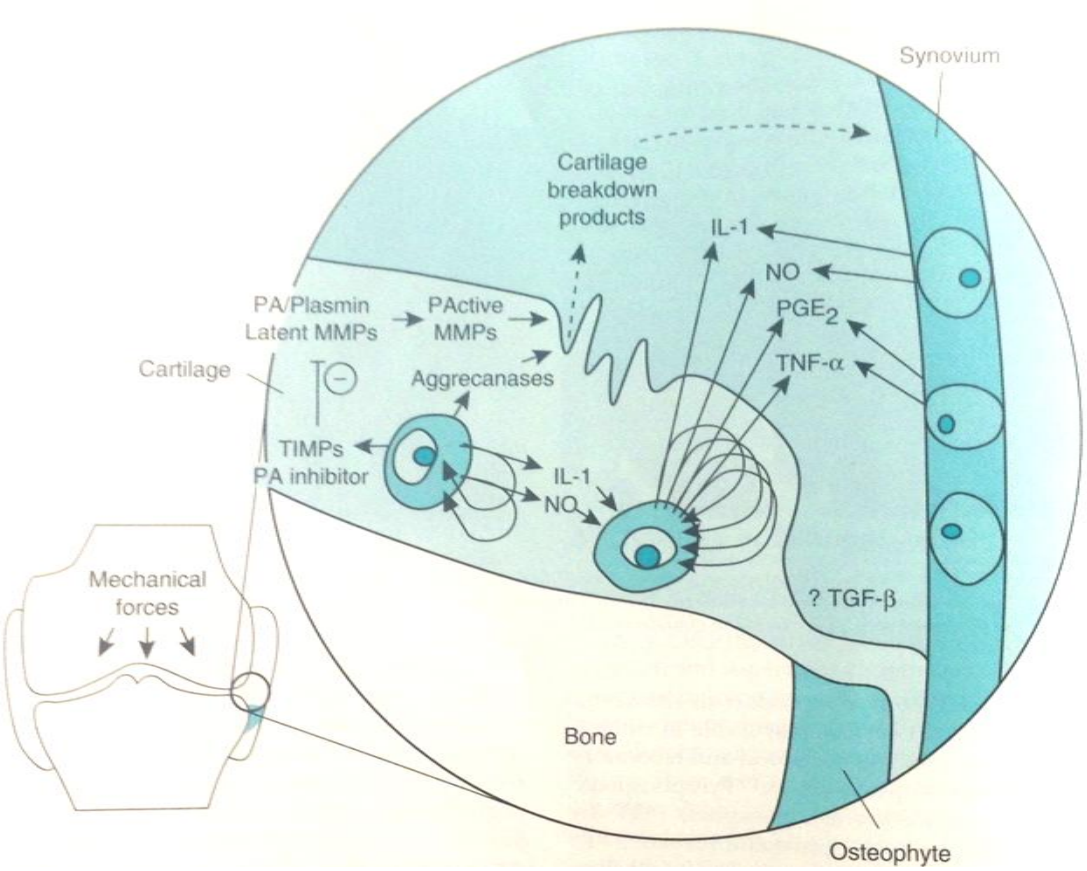


Figure 5: Pathogenesis of OA knee.

The reparative process of cartilage differs from other vascularised tissues was that it was avascular. The healing response has three phases in vascularised tissues.[16,17]

Necrosis

Inflammation

Repair

Cartilage undergoes the initial phase of necrosis in response to injury was less, because it was insensitive to hypoxia.[16,17]

In partial thickness injuries the inflammatory phase was absent because that don't cross the tidemark and the repair phase was severely limited given the lack of vascularity and a preceeding inflammatory response and no local hyperemia, no fibrosis network was produced, no subsequent clot develops to act as a scaffold for the ingrowth of repair tissue, no mediators, nor cytokines were released, that enhances the cell migration, proliferation and no inflammatory cells(which has mitotic and reparative potential) were recruited.[17,18]

In lesions with partial thickness injuries, the burden of repair process was mainly depending upon the chondrocytes, called intrinsic repair.[19]

In full thickness injuries, chondrocytes undergo extrinsic repair via differentiation and proliferation of mesenchymal stem cells from para articular

connective tissues and forms fibrocartilage with inadequate biomechanical properties.

Three categories

Micro damage or repetitive blunt trauma to the matrix and cells.

Repetitive blunt trauma produces a surface loss of proteoglycans and increased chondrocyte metabolic activity.

Early stages: increased hydration, cellular degeneration, disruption of the collagen ultrastructure resulting in marked variation in the size and arrangement of fibers, fissuring and ulceration of articular surface, thickening of subchondral bone & softening of the cartilage with loss of its compressive and tensile stiffness. Micro injury releases enzymes, proinflammatory mediators- nitric oxide, TNF, IL1. It causes further degradation of surrounding matrix tissue. Eventually the material properties of cartilage were altered, which in accelerates the degenerative process. If discontinue the repetitive trauma which restores the matrix components and reverses all the degradative process.[18,20]

Partial thickness injuries or superficial injuries or chondral fractures (that do not cross the subchondral plate). Osteochondral (full thickness or deep, penetrating) injuries. If damage that cross the articular cartilage tidemark disrupts the subchondral plate, it induces three phases of repair response, in which the

defect will be filled by hematoma. Then it causes organization of fibrin clot with the use of TGF-B, PDGF, IGF, BMPS and later converted into fibrocartilage.[17,20,21]

After 6-8 weeks of injury the repair tissue contains increased amount of chondrocyte like cells surrounded by matrix consisting of proteoglycan and type II collagen with lesser amount of type I collagen.[22]

Cells in deeper layer differentiate into osteoblast & subsequently undergo enchondral ossification to heal the subchondral defect[18].

One year after injury there was a transition of type I collagen from type II[23,24].

The repair tissue consists of mixture of fibro & hyaline cartilage. Fibro cartilaginous repair is susceptible to early degenerative changes because it lacks the biomechanical properties to withstand joint loads.[25]

Subchondral cysts:

It contains myxoid, fibrous or cartilaginous tissue along with bone marrow. These lesions identified by MRI and associated painful OA knee.

OSTEOPHYTE FORMATION:

Osteophytes are fibrous, cartilaginous, or bony in composition and marginal prominences are palpable and often tender in patients with OA knee.

Theories are;

1. Due to increased vascularity in degenerated cartilage
2. Venous congestion from subchondral cyst
3. Thickened subchondral trabeculae
4. Continued sluffing of articular cartilage

Osteophytes contributes the production of pain and functional loss.

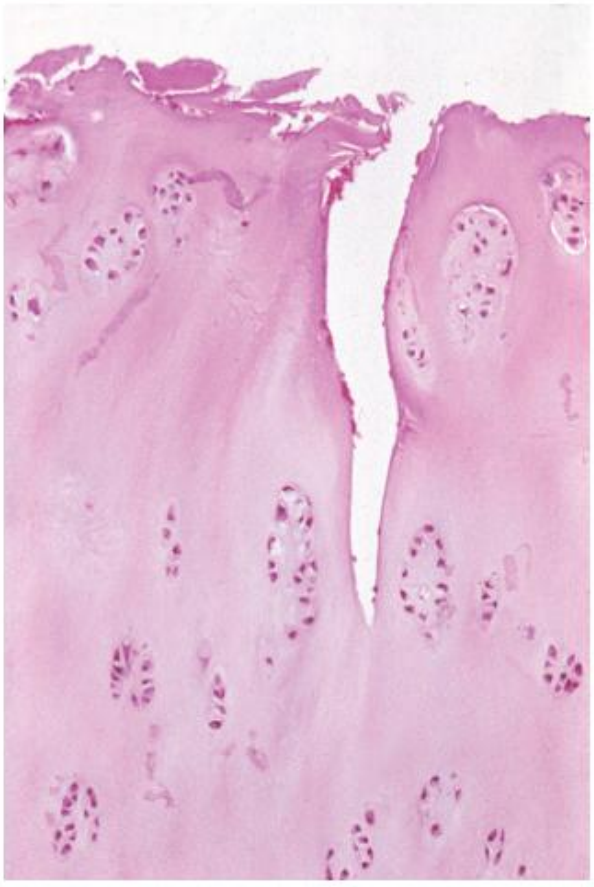


Figure 6: Histopathological feature of Osteoarthritis: Cartilage, Cleft and fibrillation.

Signs and symptoms:

Pain, swelling loss of ROM, bony deformity.

OA is not associated with systemic features like Rheumatoid Arthritis.

Stiffness for less than 30 mts

Crepitus.

Knee OA more commonly affects the medial joint due to the higher weight bearing load on that compartment. As a result, narrowing of joint space leads to pseudolaxity of medial collateral ligament, stretching of the lateral collateral ligament counterpart, and genu varus deformity. Valgus deformity occurs in lateral compartment involvement.

A flexion deformity of knee occurs due to pain, leads to functional leg length discrepancy, decreased step length and quadriceps muscular fatigue and strain.

Functional difficulties:

Climbing stairs and squatting:

Over all OA knee can impose functional limitations equal to heart disease, CHF, COPD and accounts for the substantial proportion of the burden of disability among community living elders. OA is a leading cause of disability and major contributor to work related disability, productivity and absenteeism.

Pain generators

- Focal Synovitis
- Synovial effusion
- Subchondral bone pain receptors
- Periarticulars tendons
- Bursae
- Loose bodies
- Varus or valgus deformity
- Weight issues
- Emotional impact of chronic pain

CLASSIFICATION & CRITERIA OF OA KNEE:

No standard definition of OA has been used. OA knee is diagnosed by radiographic evidence by Kellgren-Lawrance grading and clinical diagnosis by ACR (American College of Rhematologic criteria). Kellgren-Lawrance grading is the most commonly used system for research activities in OA knee.[11,26]

KELLGRAN-LAWRANCE GRADING

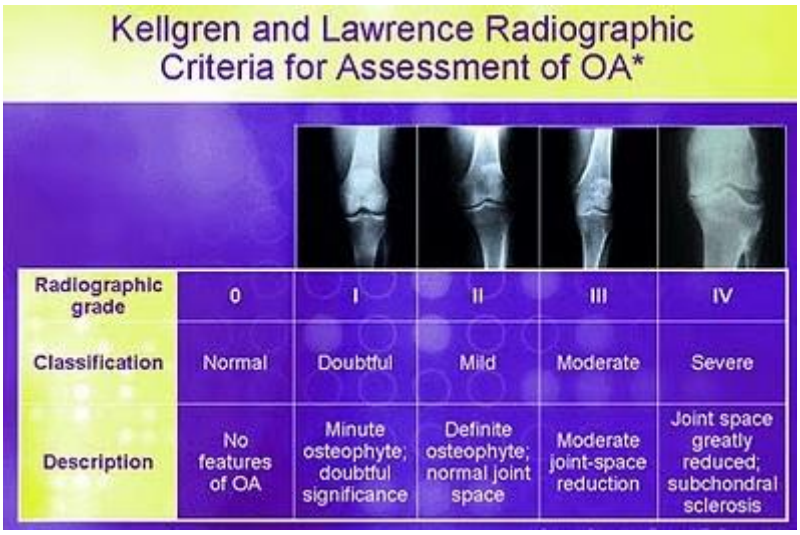


Table 2: Kellgren – Lawrence Grading of OA knee.

ACR CRITERIA:

CLINICAL & LABORTARY:

Knee pain with atleast 5 of the following (92% sensitive, 75% specific)

1. Age > 50 years

2. Stiffness less than 30 minutes

3. Bony tenderness

4. Bony enlargement

5. No palpaple warmth

6. ESR (Westergren method < 40 mm/hr)

7. Rhematoid factor (<1:40 ratio)

8. Synovial fluid signs- clear, viscous, WBC count <2000 cu.mm.

CLINICAL AND RADIOGRAPHIC:

Knee pain plus atleast one of the following (91% sensitive, 81% specific)

1. Age >50 years

2. Stiffness <30 minutes

3. Ccrepitus Plus osteophytes.

CLINICAL CRITERIA:

Knee pain plus atleast 3 of the following (95% sensitive, 69% specific)

1. Age >50 years

2. Stiffness < 30 minutes

3. Crepitus

4. Bony enlargement

5. No palpable warmth

6. Bony tenderness.

There is no association between radiological findings and patient symptoms (pain). Muscles strength and pain are the most common reason of functional loss than radiological findings.[13,27]

Investigations:

Plain X ray – antero posterior and lateral view is the investigation of choice for OA knee.

Ultrasound is used to visualize the bony and soft tissue structures and is more sensitive in diagnosing in effusion, synovitis and early osteophytes in OA knee[28].

High resolution MRI is used to early structural changes and pathology in pain sensitive structures.[11,28]

Radio nuclide scanning:

Scanning with TC 99M shows increased activity during the bone phase in the subarticular region of any affected joint. It may be apparent, years before the typical Xray changes appear and reflects the vascular reaction and osteoblastic activity that are present even in the early stages of cartilage loss.[29]

Complications of OA knee:

1. Capsular herniation (stretching by effusion) encountered most commonly as a Baker's cyst.
2. Loose bodies (cartilage / bone fragments occasionally resulting in locking of the joint).
3. Genu varus or valgus deformities.
4. Joint instability.

Disease onset and course

OA starts in insidious onset, and usually asymptomatic in individuals with only aneural cartilage is involved. Pain is initially episodic and aggravated by specific activity. In later stage pain becomes chronic, dull ache and accentuated with episodic severe pain.

Prognosis

OA is a slow progressing disease that can be self limiting or progress to advanced joint damage and soft tissue damage leading to complete failure of that joint.

Management:

Pharmacological treatment

Non pharmacological treatment

Pharmacological management:

Goals:

Relieve pain and decrease inflammation and maintain or improve mobility and minimize disability.

1. Oral analgesic
2. NSAIDs

3. Corticosteroid injection-used for acute episodes with moderate pain relief. Those above said drugs are used as primary medications in OA knees.

4. Visco supplementation-used in mild to moderate OA knee, which improves pain, stiffness and improves physical functions.
5. Chondroprotectives-glucosamine sulfate and chondroitin sulfate. Long term follow up study with 1500mg/day for 12 months revealed in OA knees patients less likely to undergo total knee replacement at 5 years.
6. Topical analgesics-contains capsaicin (decrease pain about 33% if applied to joints 4 times daily).Other topical agent contains Diclofenac - an alternate adjunctive treatment in OA knee.

Acetaminophen is an oral analgesic, is the drug of first choice. It has no toxicity in recommended doses up to 4gm/day. However it has no anti inflammatory effect. In patients with symptomatic OA knee it has minimal effect on pain and no significant effect on stiffness or physical function. Further, acetaminophen use can lead to liver toxicity and less commonly kidney toxicity in patients who is an alcoholic and also there is increasing evidence of hospitalization due to GI perforation, peptic ulceration and bleeding with acetaminophen use of more than 3 gm/day.[30-34]

NSAIDs –who are not responding to acetaminophen and non pharmacological therapy, NSAIDs may be used in combination with acetaminophen, and should be kept lower doses to avoid GI problem.[11,33]

Non pharmacological treatment:

The chronic nature of the disease (arthritis) plans the treatment by plan of care that includes patient education and self management. Hence rehabilitation of arthritis requires comprehensive and coordinated efforts by physiatrist and physiotherapist.[35]

Currently no studies that revealed such programmes improve the psychologic health, symptoms of health related quality of life or that they significantly alter health care use.[36-38]

Rehabilitative management:

General goals and outcomes of OA knee:

Reduction of impact of impairments by

- Decreasing the pain
- Improvement in joint ROM for functional activities
- Improve the muscle strength for functional activities
- To achieve the joint stability
- Prevention of joint deformity

Reduction of biomechanical stress on affected joints:

- Improve the endurance for functional activities

Physical function by

- To promote the independency in dressing, transfers and self care
- To improve the efficiency and safety of gait pattern and balance
- To maintain the adequate strength of musculoskeletal system, cardio vascular fitness

Improvements in health status and quality of life by

- Educating the patient, family members, and care givers for self management and joint protection

Exercise, Equipment, and education treatment options in OA knee.

Non-pharmacologic measures:

- Reduction of joint loading
- Correction of poor body mechanics
- Correction of poor posture and posture support
- Obese and overweight patients should be counseled to lose weight
- Patellar taping
- Wedged insoles and orthoses.

Lateral wedged insole with an angle 5 to 10 (on a frontal section) is shown to be helpful for treatment of medial compartment knee osteoarthritis providing a "medical osteotomy". Decreased excessive loading on the medial surface and decreased stretching of the lateral collateral ligament obtained by the insole may be effective in reduction of pain. Insole is much more effective for patients with mild osteoarthritis than for those with advanced disease. A polypropylene mesh insole is practical, washable and may last about 2 years (i.e., approximately twice as long as a leather insole).

The use of elastic bandages, neoprene sleeves or canvas braces has been shown to improve proprioception about the knee and to diminish arthrogenous muscle inhibition. Many patients note an increased sense of stability and strength and diminished pain with these knee orthoses.[39,40]

Exercises:

- Aerobic exercises
- Whole body physical activity exercise
- Isometric Quadriceps exercise
- Straight Leg raise exercise
- Hip abductor and adductor strengthening exercise

Exercise helps to keep joints flexible, increase muscle strength, control weight and strengthen bone and ligaments.

Physical Modality:

- Paraffin wax bath
- Infra red radiotherapy (IRR)
- Trans cutaneous electrical nerve stimulation (TENS)
- Short wave diathermy (SWD).

Equipment:

Adaptive for ADL, Assistive for ambulation, Appropriate footwear or insoles

Education:

Self management, weight loss, activity management or joint protection, social support, stress management/relaxation.

Intraarticular cortico steroids:

Hydrocortisone was introduced for intraarticular injection in 1951.[41]

But their use in OA knee was controversial. However early studies in mice, rat & rabbit suggested that multiple corticosteroid injections might alter the cartilage, protein synthesis & consequently damage the cartilage.[42-46]

Methyl prednisolone acetate:

Despite there is no role for systemic steroid in OA knee, local intra articular corticoid preparations can be used. It is intermediate acting cortico steroid. Injection may be repeated 2-3 times a year, but have the potential to cause joint destruction.

MECHANISM OF ACTION:

Down regulate expression of adhesion molecules.

Reduce the cellular infiltration in to the joint and subsequent inflammation. It inhibits the prostaglandin synthesis and decrease the activity of collagenase and other enzymes. Saxne et al study explained about effects on therapy on cartilage metabolism that reduce the production of IL1, TNF alpha & proteases which might degrade the cartilage.[47]

Metabolism:

Injected steroids can be detected in synovial fluid within 48 hours after injection. The rate of absorption of steroid was mainly depending upon the solubility of the compound.[48]

So after injection, we ask the patient to limit their activity as it delays the escape of the steroids and minimize the systemic side effects.

Relative Contraindications:

- Local infection
- Anticoagulant therapy
- Uncontrolled diabetes mellitus
- Severe joint destruction & deformity
- Obesity.

Complications:

Complications of intraarticular therapy are rare even though there were infection, post injection flare (local adverse reactions, reversible), localized subcutaneous or cutaneous atrophy, periarticular calcifications, overuse of steroids giving raise to charcot like arthropathy.[41,49-51]

Methyl Prednisolone has been chosen for intra articular steroid injection in this study as it is more efficacious steroid and has good short term analgesia.[52]

Hylan GF-20:

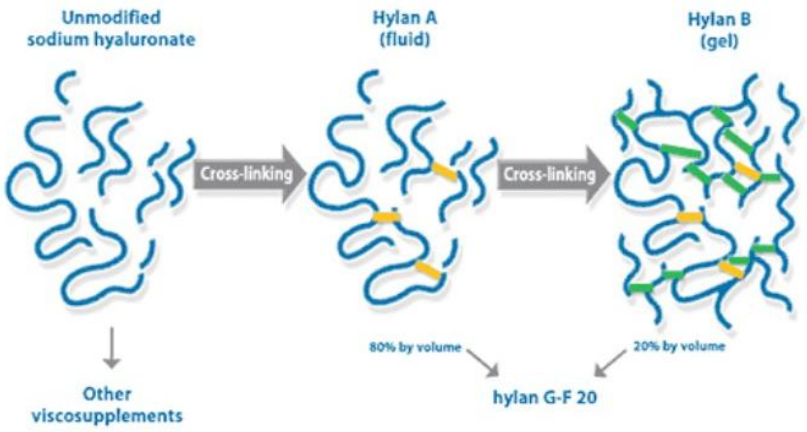


Figure 7: Molecular structure of Hylan GF-20.

Hylan GF-20 is a high molecular visco supplement. It was cross linked derivative of hyaluronan which naturally occurs in synovial fluid. In OA knee, patients have low molecular weight hyaluronan which fails to retain its visco elasticity and ability to with stand shear forces. The mechanism of action of hyaluronan products in humans has not been established. However, a combination of multiple effects proved including restoration of joint rheology, anti nociceptive effects, anti inflammatory effects and normalisation of endogenous hyaluronan synthesis.[53,54]

Hylan GF-20 substance chemically cross linked and formed. It has two different forms – Hylan A and Hylan B. Hylan A is a fluid by volume, comprises

80% of Hylan GF-20, while the other 20% of Hylan Gf-20 is comprised of Hylan B – a gel. This composition makes this, identical to human synovial fluid – both in molecular weight and visco elasticity.

MATERIALS AND METHODS

Study Centre:

This study was conducted at Government Institute of Rehabilitation Medicine, KK Nagar, Chennai-600 083.

Duration of study:

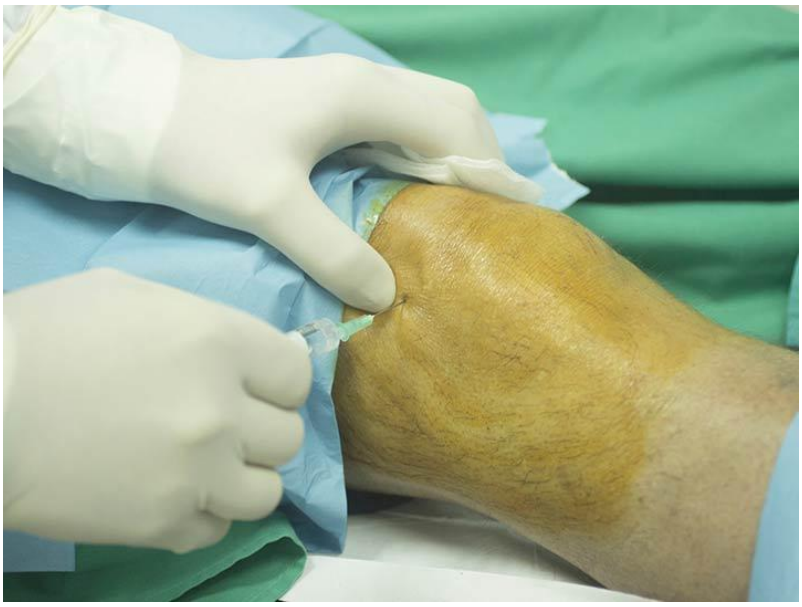
The study period is for 18 months (March-2015 to August-2016), with minimum follow up of 26 weeks.

Study design:

This is a prospective Single blinded Cohort study with

- Subjects will be randomized by systematic random sampling, according to registration number of the study
- Odd numbers (Group A) will be treated with Hylan GF-20
- Even numbers (Group B) will be treated with Methyl Prednisolone Acetate.

Methodology:



- Patients will be given test dose of 0.5ml of Lignocaine 2%
- They will be taken to Operation theatre and parts will be cleaned with Betadine and drapped with sterile towel
- Under aseptic precautions, Lignocaine 2% will be injected to anesthetise the injection site
- By following randomization procedure, either Hylan-GF20(48mg)/methyl prednisolone acetate(80mg) will then be infiltrated into the knee joint space after confirmation by aspiration technique by infero lateral approach
- After infiltration the subjects will be observed for 15 minutes for adverse reactions

- Subjects will be asked to report immediately in case of adverse reactions like post injection flare (increased pain, swelling)/hypersensitivity reactions etc.,
- Also they will be given 3 days of analgesics and antibiotics.

Inclusion criteria:

Patients with the following criteria are included in this study.

- Age > 45 years
- Grade II osteoarthritis knee by Kellgren-Lawrence grading
- Knee pain with failed conservative treatment for 1 month
- Stiffness:<30mts
- Crepitus
- Bony tenderness
- Bony enlargement
- No palpable warmth.

Exclusion criteria:

- Post Operative cases
- Cellulitis / Infections
- Any implants inside.

- Associated with DVT calf muscles
- Non co-operative patient
- Low I.Q Patients /psychiatric patient
- Trauma
- Meniscal injury
- Anterior/Posterior cruciate ligament injury
- Medial/Lateral collateral ligament injury
- Bursitis
- Rheumatoid arthritis
- Pseudogout
- Other grades of osteo arthritis knee

Patients with above criteria were excluded from this study.

Sample size:

A total of 32 patients in hylan group and 36 patients in steroid group were initially enrolled, but 2 patients in hylan group and 6 patients in steroid group lost follow up. Hence 30 patients in each group were finally included in this study according to inclusion, exclusion criteria.

Product/Investigation details:

All the patients who get enrolled in this study will be submitted to the following investigations.

Investigations:

FBS, PPBS, X-ray knee-AP and Lateral

Product details:

Methylprednisolone acetate – 80mg

Hylan-GF 20 – 48mg

Concomitant medications and treatment:

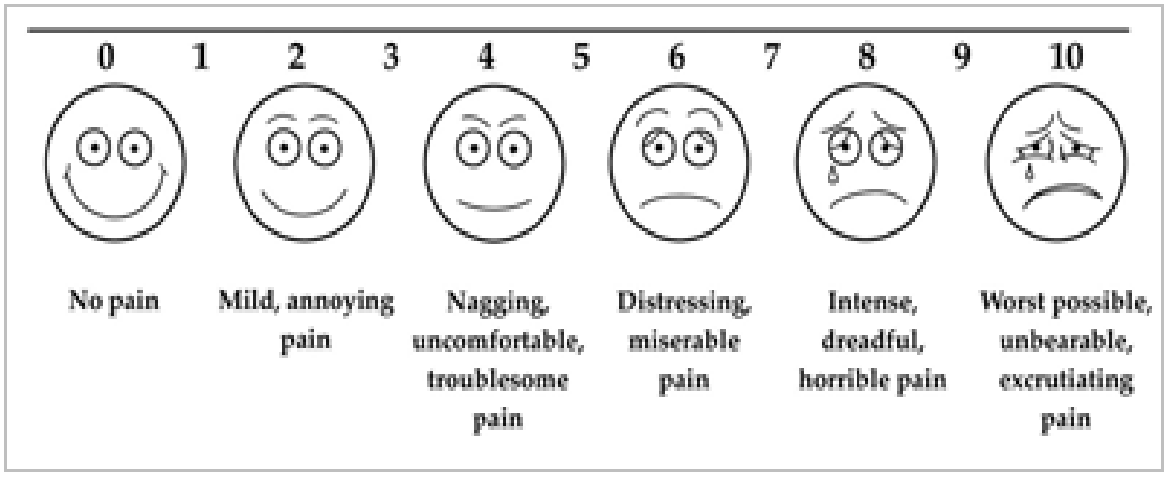
If the patient gets symptoms like pain, they will be treated with oral analgesics (Acetaminophen) for 3 days. The patients are advised not to take analgesic drugs 3 days before follow up. Also they are asked to continue isometric quadriceps program throughout the follow up period.

Data collection and Methods:

- Subjects will be randomized according to registration number of the study
- Odd numbers(Group A) will be treated with Hylan GF-20
- Even numbers(Group B) will be treated with Methyl Prednisolone Acetate

- Case History age, sex, duration of pain will be collected. Anthropometric measurements height and weight of the patient will be collected.
- They will be assessed with pre procedural and post procedural
    - pain score using Visual Analog Score(VAS)
    - WOMAC-C score
    - Range of Movements of Knee
- The assessment will be analysed using SPSS software (version 21).

Visual Analog Pain Score:

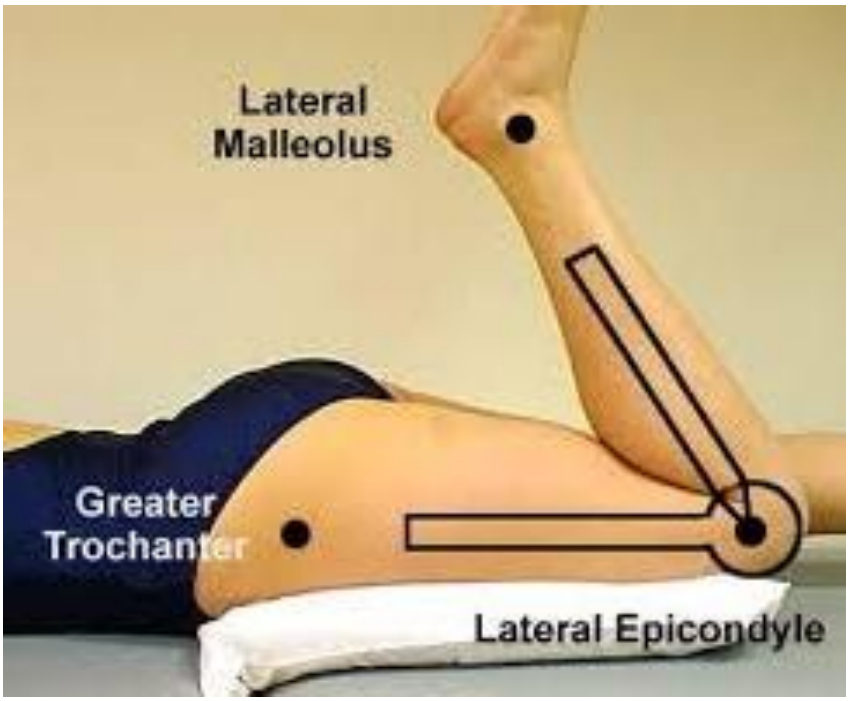


WOMAC-C SCORE:

SL.NO.	WOMAC CRITERIA	NONE(1)	MILD(2)	MODERATE(3)	SEVERE(4)
1	Stair use Ascending				
2	Stair use Descending				
3	Rising from sitting				
4	Standing				
5	Bending				
6	Walking				
7	Getting in-out of a car/bus				
8	Shopping				
9	Putting on socks				
10	Taking off socks				
11	Rising from bed				
12	Lying in bed				
13	Getting in / out of bath				
14	Sitting				
15	Getting on / off toilet				
16	Heavy household duties				
17	Light household duties				

RANGE OF MOVEMENTS:

Range of Movements will be assessed with use of Goniometry.



RESULTS AND DISCUSSION

AGE:

Table 3: Demography – Age.

GROUP		N	Minimum	Maximum	Mean	Std. Deviation
HYLAN GROUP	AGE	30	50	59	53.367	3.2108
STEROID GROUP	AGE	30	46	61	55.4	4.5075

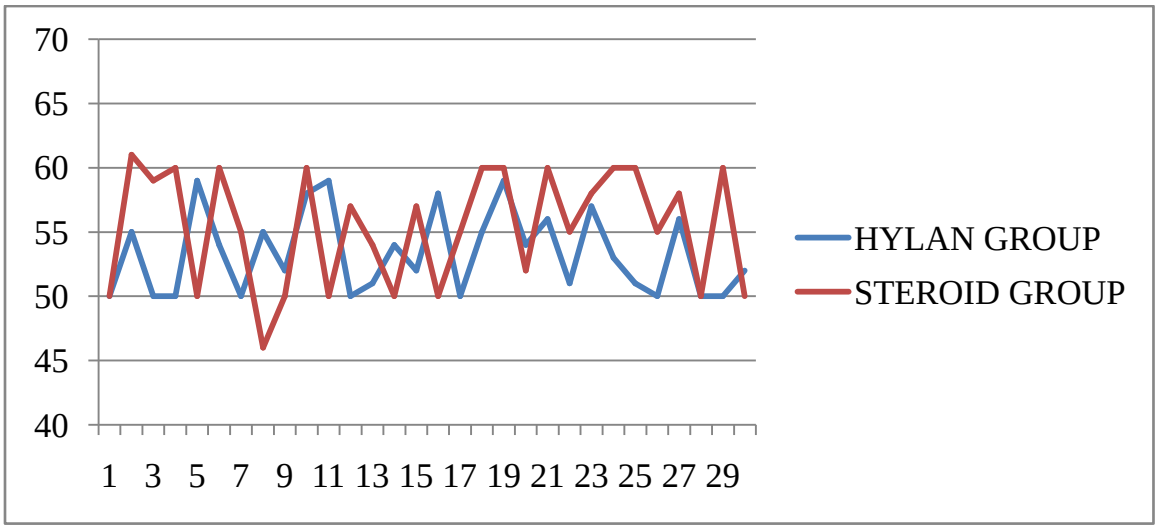


Chart 2: Demography – Age.

The study included patients with age ranging from 46 years to 61 years. After randomisation, the minimum age in the hylan group is 50 years and maximum age is 59 years, with median of 53.37 years. In the steroid group, the minimum age is 46 years and the maximum age is 61 years, with a mean of 55.4 years.

SEX:

Table 4: Demography – Sex.

GROUP		Frequency	Percent	Cumulative Percent
HYLAN GROUP	MALE	14	46.7	46.7
	FEMALE	16	53.3	100
	Total	30	100	
STEROID GROUP	MALE	9	30	30
	FEMALE	21	70	100
	Total	30	100	

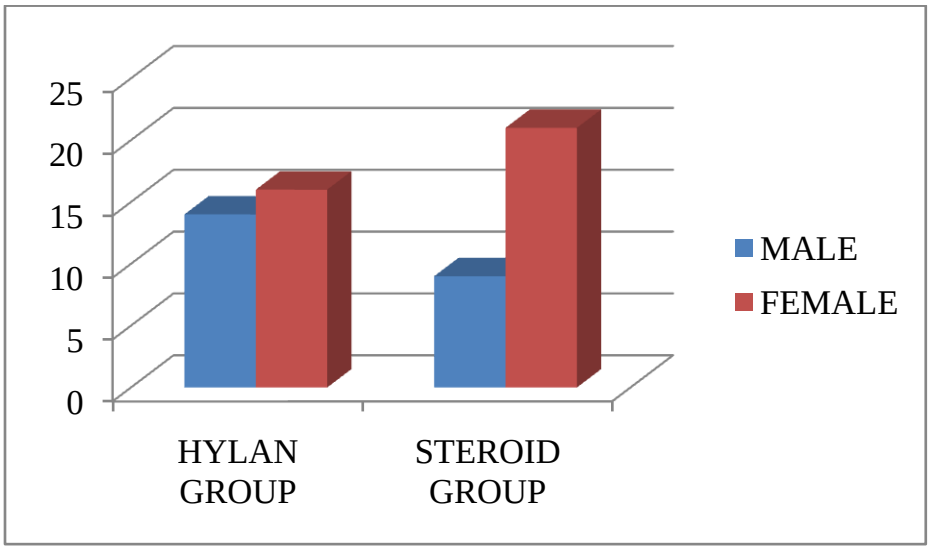


Chart 3: Demography – Sex.

There were 23 males and 37 females enrolled in the study, among which 14 males (60.9% of total males) and 16 females (43.2% of total females) were enrolled in Hylan group and 9 males (29.1% of total males) and 21 females (56.8% of total females) were enrolled in the steroid group.

SIDE OF KNEE PAIN:

Table 5: Side of knee pain.

GROUP	SIDE	Frequency	Percent
HYLAN GROUP	RIGHT	19	63.3
	LEFT	11	36.7
STEROID GROUP	RIGHT	16	53.3
	LEFT	14	46.7

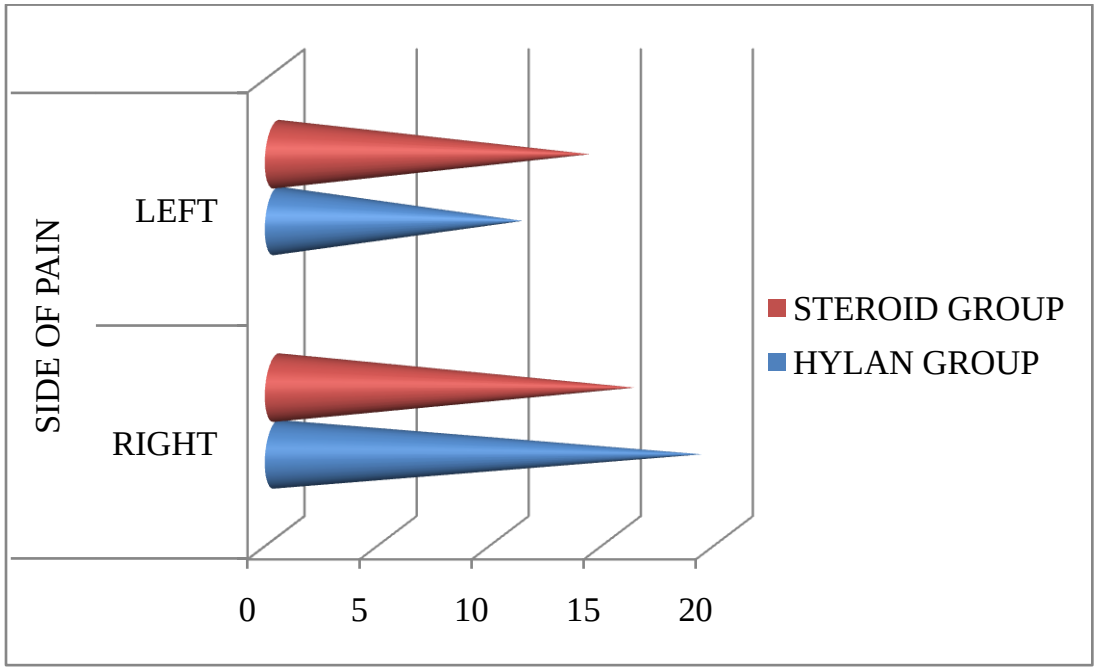


Chart 4: Side of knee pain.

In this study, 35 patients had pain on right knee and 25 patients had pain on left knee. Among the patients, who were enrolled in hylan group, 19 had pain on right side and 11 had pain on left side. And among patients, who were enrolled in steroid group, 16 had pain on right side and 11 had pain on left side.

DURATION:

Table 6: Duration of symptoms.

GROUP	DURATION(MONTHS)	Frequency	Percent
HYLAN GROUP	2	3	10
	3	1	3.3
	4	7	23.3
	5	5	16.7
	6	8	26.7
	7	1	3.3
	8	5	16.7
STEROID GROUP	2	1	3.3
	3	1	3.3
	4	3	10
	5	7	23.3
	6	7	23.3
	7	6	20
	8	5	16.7

Table 7: Duration of symptoms – Mean and Standard deviation

GROUP		N	Minimum	Maximum	Mean	Std. Deviation
HYLAN GROUP	DURATION	30	2	8	5.233	1.7943
STEROID GROUP	DURATION	30	2	8	5.867	1.5477

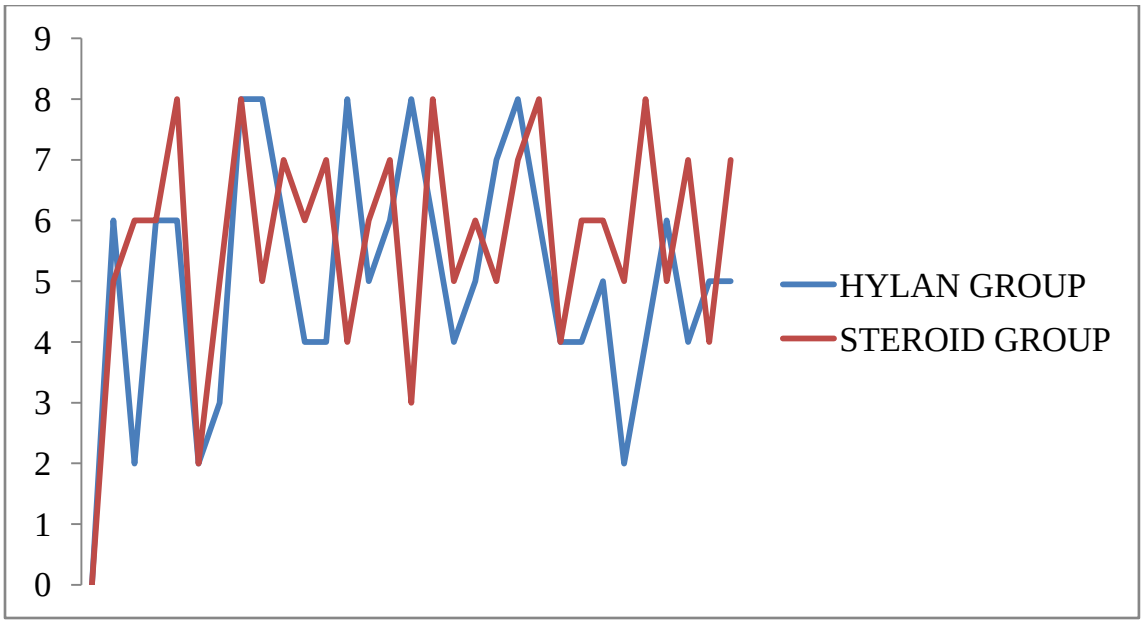


Chart 5: Duration of symptoms.

This study included patients with knee pain for duration ranging from 2 to 8 months, with mean in hylan group is 5.23 months and steroid group is 5.87 months. Majority of the patients had pain for 5 to 6 months.

SITE OF KNEE PAIN:

Table 8: Site of Knee pain.

GROUP		Frequency	Percent
HYLAN GROUP	MEDIAL JOINT LINE	5	16.7
	ANTERIOR	25	83.3
STEROID GROUP	MEDIAL JOINT LINE	6	20
	ANTERIOR	24	80

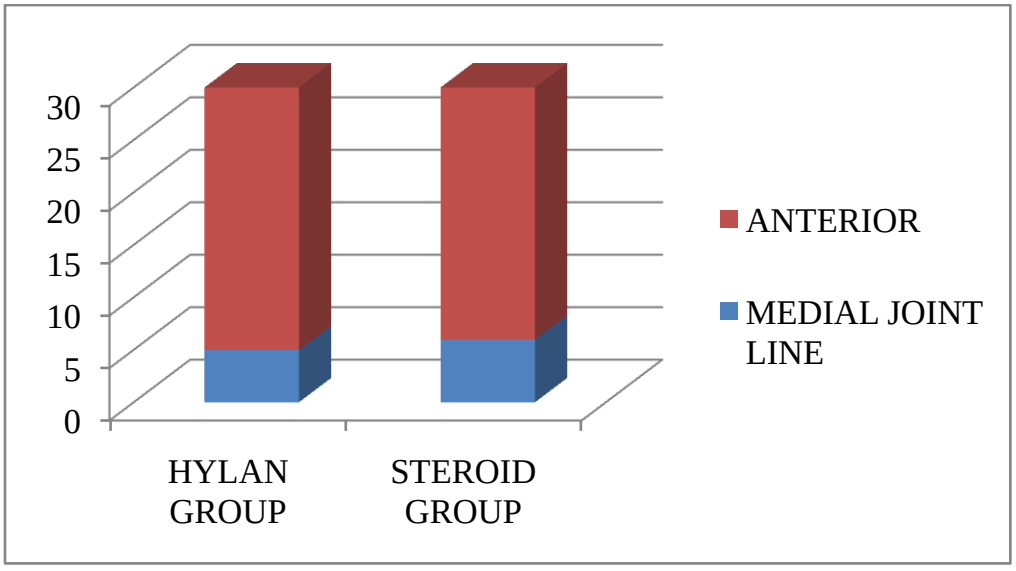


Chart 6: Site of Knee pain

49 patients had pain along anterior aspect of knee joint and 11 patients had pain along medial joint line. Among hylan group, 25 patients had pain along anterior aspect and 5 had pain along medial joint line. In steroid group, 24 had pain along anterior aspect and 6 had pain along medial joint line.

SENSE OF GRINDING/LOCKING OF JOINT:

Table 9: Sense of Grinding/Locking of knee.

GROUP		Frequency	Percent
HYLAN GROUP	PRESENT	3	10
	ABSENT	27	90
STEROID GROUP	PRESENT	7	23.3
	ABSENT	23	76.7

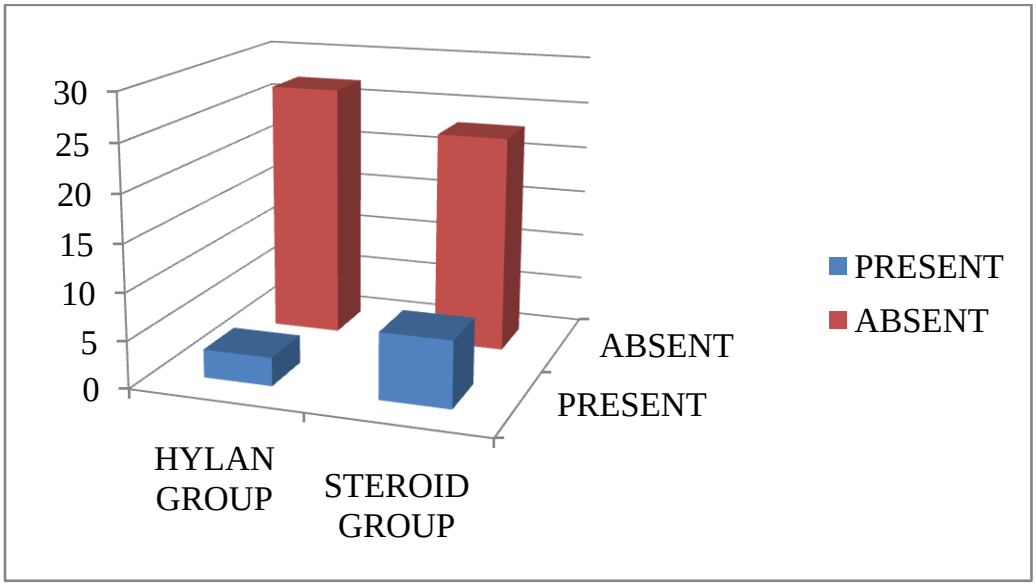


Chart 7: Sense of Grinding/Locking of knee.

In this study, 50 patients (83.3%) did not have sense of grinding or locking of joint. 3 patients (10%) in hylan group and 7 patients (23.3%) had sense of grinding/locking of joint.

STIFFNESS:

Table 10: Stiffness of knee

GROUP		Frequency	Percent
HYLAN GROUP	YES	9	30
	NO	21	70
STEROID GROUP	YES	14	46.7
	NO	16	53.3

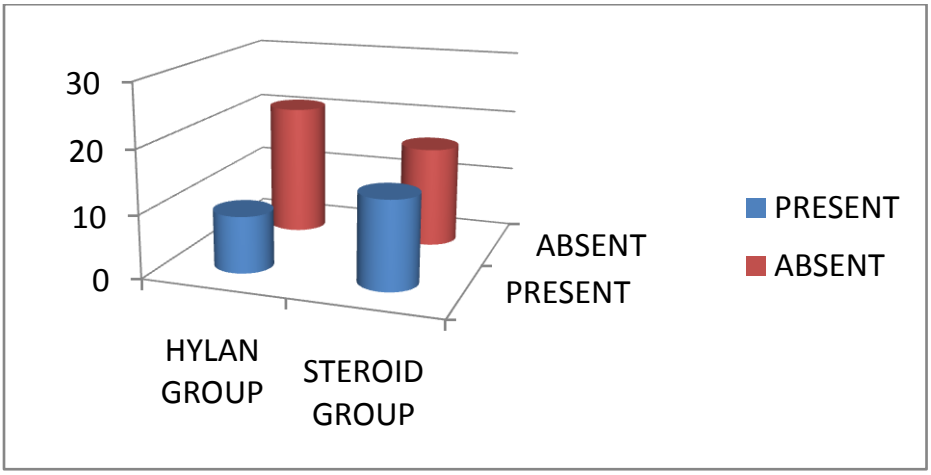


Chart 8: Stiffness of knee.

In this study, stiffness was present in total of 23 patients (9 in hylan group and 14 in steroid group). 37 patients (61.67%) did not have stiffness.

COMORBIDITIES:

Diabetes mellitus-Type 2was the commonest comorbidity seen in this study. 5 patients (16.7% of steroid group) enrolled in steroid group had coronary artery disease associated with diabetes mellitus.

SWELLING OF KNEE JOINT:

Table 11: Swelling of knee.

GROUP		Frequency	Percent
HYLAN GROUP	PRESENT	15	50
	ABSENT	15	50
STEROID GROUP	PRESENT	18	60
	ABSENT	12	40

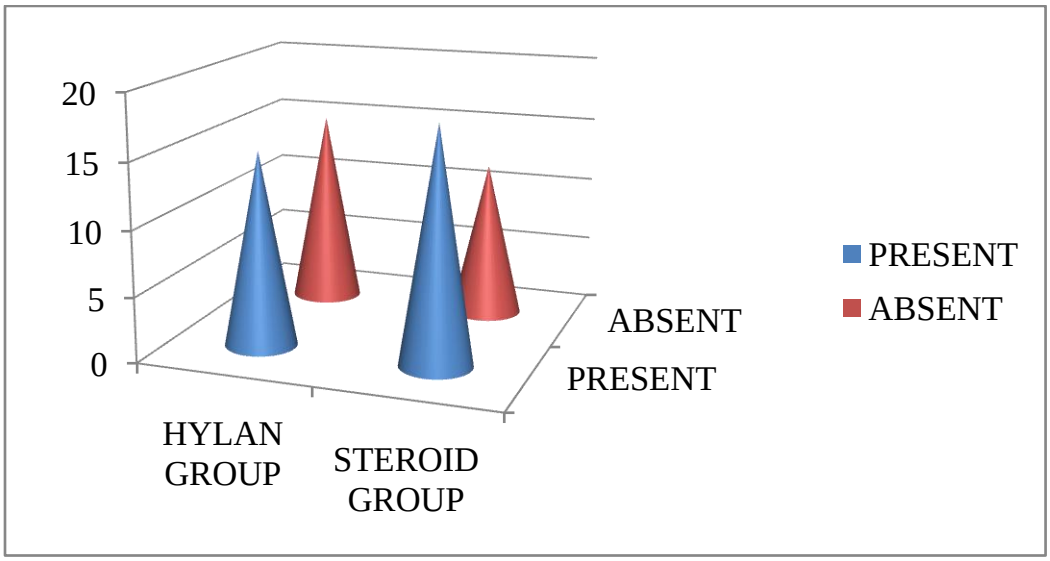


Chart 9: Swelling of knee.

Among the patients in hylan group, 15 patients (50% of hylan group) had swelling over the knee joint and among steroid group, 18 patients(60% of steroid group) had swelling.

TENDERNESS:

Table 12: Tenderness over knee.

GROUP		Frequency	Percent
HYLAN GROUP	PRESENT	23	76.7
	ABSENT	7	23.3
STEROID GROUP	PRESENT	19	63.3
	ABSENT	11	36.7

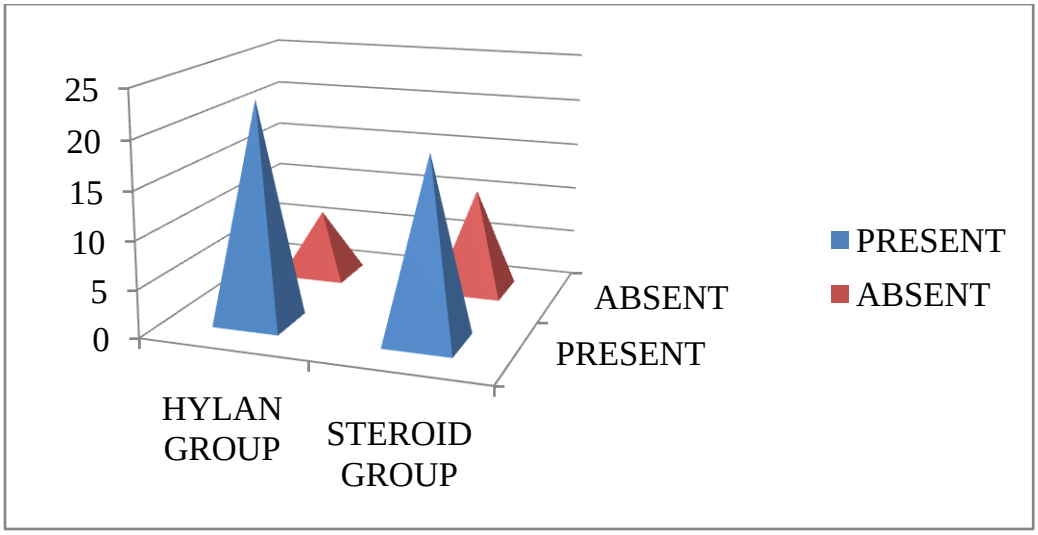


Chart 10: Tenderness over

23 patients in hylan group and 19 patients in steroid group had tenderness over knee joint and 7 patients in hylan group and 11 patients in steroid group did not have tenderness over knee joint.

CREPITUS:

Table 13: Crepitus over knee.

GROUP		Frequency	Percent
HYLAN GROUP	PRESENT	29	96.7
	ABSENT	1	3.3
STEROID GROUP	PRESENT	21	70
	ABSENT	9	30

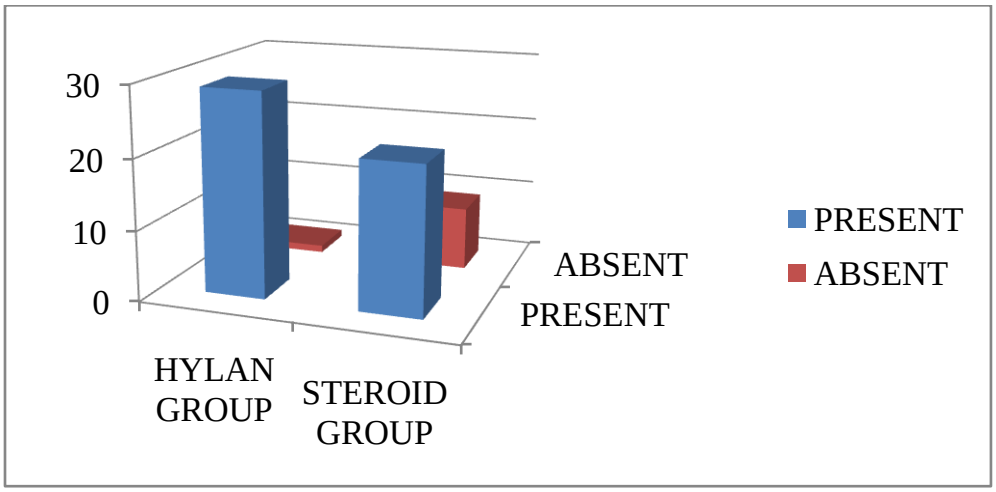


Chart 11: Crepitus over knee.

Crepitus was felt in total of 50 patients – 29 in hylan group and 21 in steroid group. Crepitus was absent in 10 patients – 1 in hylan group and 9 in steroid group.

DEFORMITY:

Deformity was not present in all the patients included in this study.

BONY ENLARGEMENT:

Table 14: Bony Enlargement.

GROUP		Frequency	Percent
HYLAN GROUP	PRESENT	0	0
	ABSENT	30	100
STEROID GROUP	PRESENT	2	6.7
	ABSENT	28	93.3

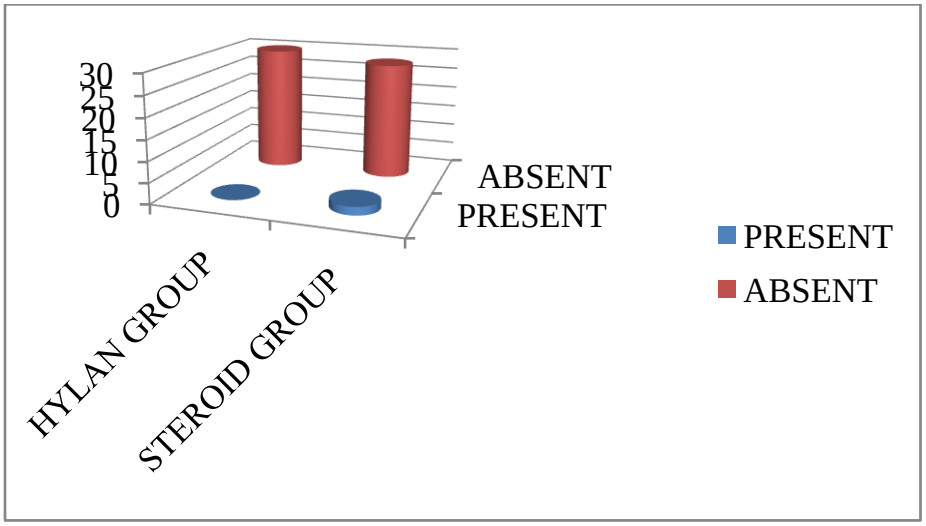


Chart 12: Bony Enlargement.

None of the patients in hylan group and 2 patients (6.7%) in steroid group had bony enlargement felt in the knee joint.

PATELLAR TAP TEST:

Table 15: Patellar Tap test.

GROUP		Frequency	Percent
HYLAN GROUP	POSITIVE	14	46.7
	NEGATIVE	16	53.3
STEROID GROUP	POSITIVE	10	33.3
	NEGATIVE	20	66.7

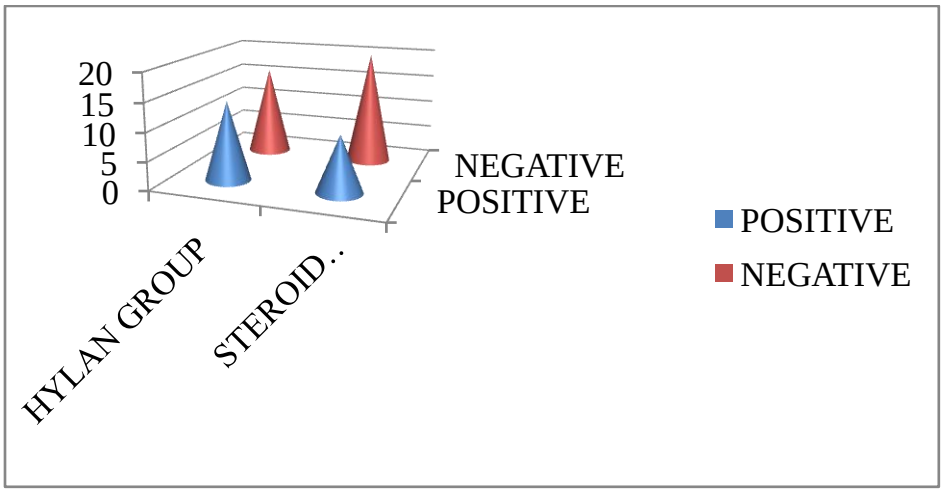


Chart 13: Patellar Tap test .

Patellar tap test was positive in 24 patients – 14 in hylan group and 10 in steroid group. It was negative in 36 patients – 10 in hylan group and 20 in steroid group.

PATELLAR BULGE TEST:

Table 16: Patellar Bulge test.

GROUP		Frequency	Percent
HYLAN GROUP	POSITIVE	3	10
	NEGATIVE	27	90
STEROID GROUP	POSITIVE	11	36.7
	NEGATIVE	19	63.3

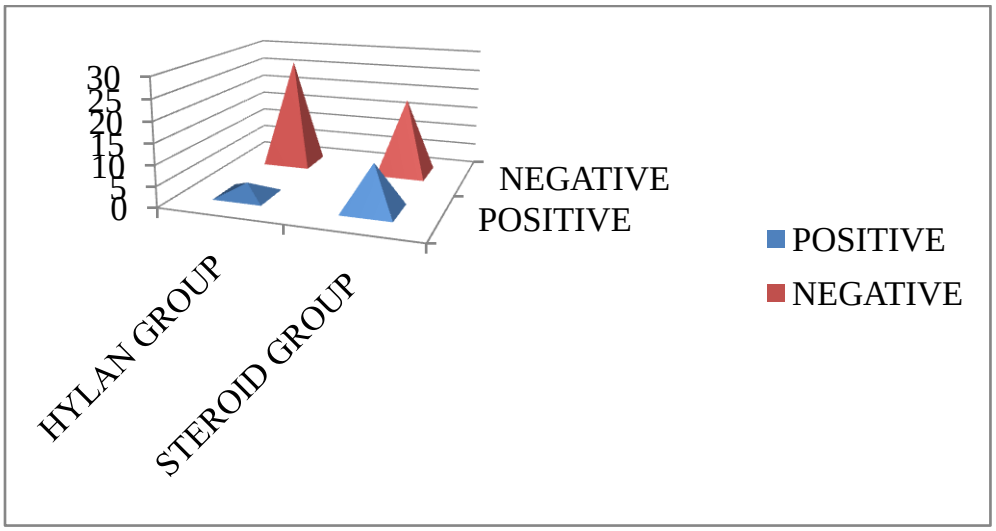


Chart 14: Patellar Bulge test

Patellar bulge test was positive in 14 patients – 3 in hylan group and 11 in steroid group. It was negative in 46 patients – 27 in hylan group and 19 in steroid group.

XRAY – OSTEOPHYTES:

Table 17: Presence of Osteophytes in X-ray.

GROUP		Frequency	Percent
HYLAN GROUP	PRESENT	3	10
	ABSENT	27	90
STEROID GROUP	PRESENT	6	20
	ABSENT	24	80

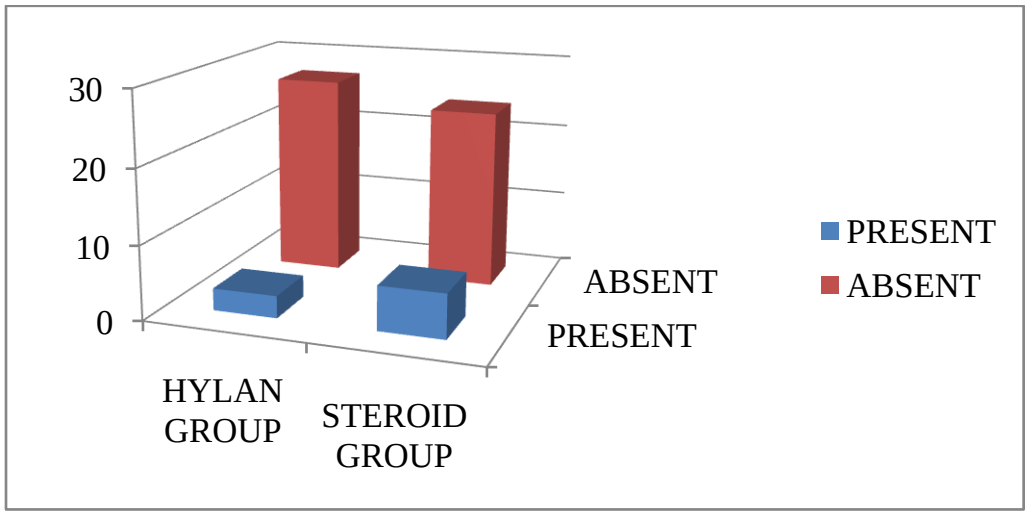


Chart 15: Presence of Osteophytes in X-ray.

Osteophytes were seen in plain x-ray of knee in 9 patients – 3 in hylan group and 6 in steroid group. Osteophytes were not seen in 51 patients – 27 in hylan group and 24 in steroid group.

X-RAY – JOINT SPACE NARROWING:

None of the patients enrolled in this study had significant joint space narrowing radiologically.

ALLERGIC REACTIONS:

None of the patients included in this study developed allergic reactions after the intra articular injection.

PAIN SCORE:

Table 18: Pain score (VAS) in the follow up period.

GROUP	Statistics	PAIN - VAS SCORE						
		0 Day	1 week	2 weeks	4 weeks	8 weeks	12 weeks	26 weeks
HYLAN GROUP	Mean	8.833	8.533	7.333	6.267	3.9	2.8	2.367
	S.D.	1.1167	1.008	0.9589	1.1427	1.3481	0.9248	0.7184
	Median	9	9	8	6	4	2.5	2
STEROID GROUP	Mean	9.667	8.4	6.7	5	3.867	6.567	6.833
	S.D.	0.6065	0.8944	0.9879	0.8305	1.306	1.7555	1.7237
	Median	10	8	7	5	4	7	7

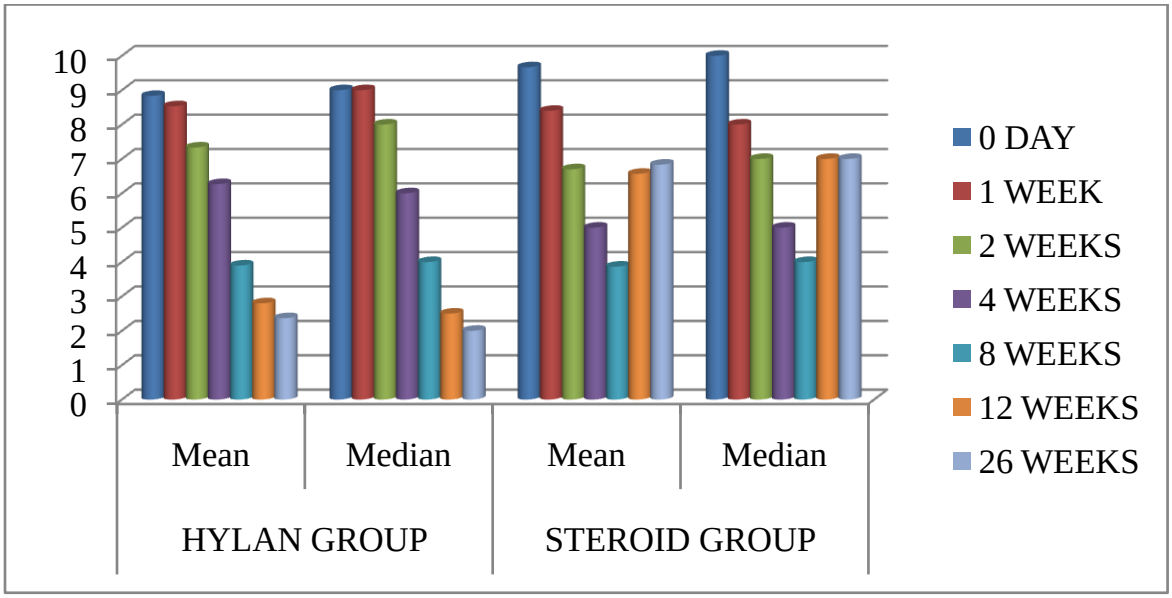


Chart 16: Pain score (VAS) in the follow up.

Pain was assessed using Visual Analog Scoring (VAS) in this study. It showed significant pain relief with hylan group over due course of time. In steroid group, there was initial pain response till 8 weeks after the treatment, but later the pain score started to show upward trend in later weeks. In conclusion, pain relief was better in hylan group than steroid group with p value <0.05 in all the follow up period except 8^{th} week.

WOMAC SCORE:

Table 19: WOMAC-C score in the follow up period.

GROUP	Statistic	WOMAC SCORE						
		0 Day	1 week	2 weeks	4 weeks	8 weeks	12 weeks	26 weeks
HYLAN GROUP	Mean	59.4	58.8	53.8	45.9	29.133	18	15.4
	S.D.	8.3236	8.227	9.5282	9.9874	10.2309	6.7722	6.1341
	Median	63	62	59	50	30	20	17.5
STEROID GROUP	Mean	61.1	54.5	46.2	35.533	28.433	40.3	44.433
	S.D.	5.2807	5.2703	7.5265	9.0848	11.1035	11.3111	13.2318
	Median	62	55	48	40	30	41	48

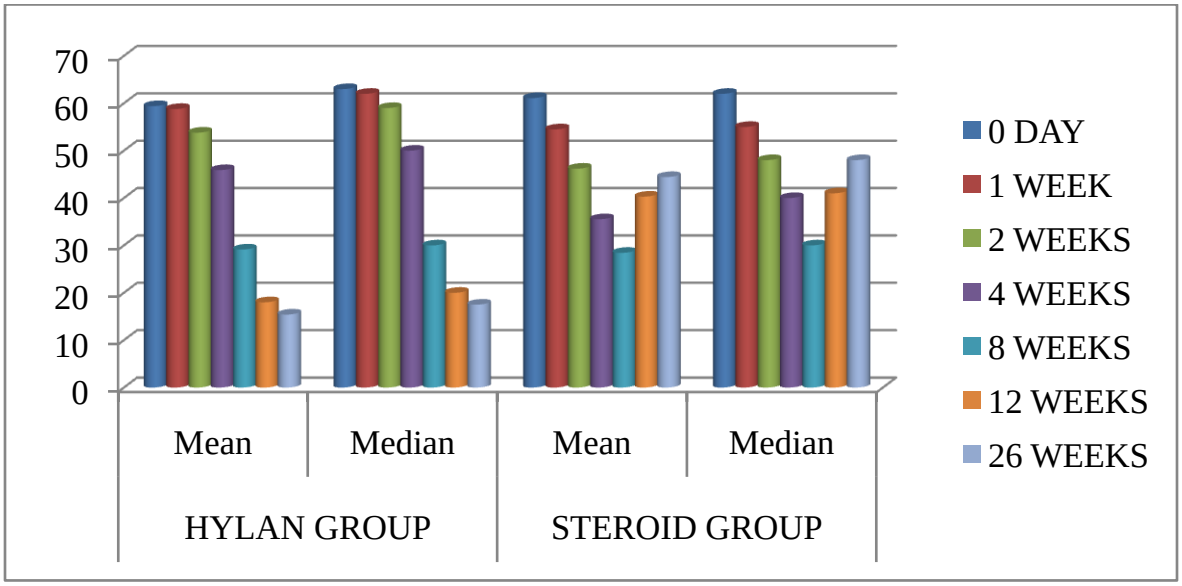


Chart 17: WOMAC-C score in the follow up period.

Functional assessment after the treatment was done using WOMAC score (The Western Ontario and McMaster Universities Arthritis Index) and improvement in range of movements of the knee in this study. It showed significant functional improvement with hylan group over due course of time. In steroid group, there was initial better response till 8 weeks, but later the functional ability started to reduce in later weeks. In conclusion, functional improvement as per WOMAC score was better in hylan group than steroid group with p value <0.05.

RANGE OF MOVEMENTS(ROM) OF KNEE:

Table 20: range of Movements of Knee in the follow up period.

GROUP	Statistic	ROM SCORE						
		0 Day	1 week	2 weeks	4 weeks	8 weeks	12 weeks	26 weeks
HYLAN GROUP	Mean	76.667	76.667	80.333	91.667	102.333	103.333	103.333
	S.D.	8.4418	8.4418	7.6489	5.9209	5.0401	4.7946	4.7946
	Median	70	70	80	90	100	100	100
STEROID GROUP	Mean	79.333	76.8	84.333	93	92	82.333	82.333
	S.D.	9.4443	20.5534	9.3526	9.8786	11.5669	12.5075	12.5075
	Median	80	80	80	90	90	80	80

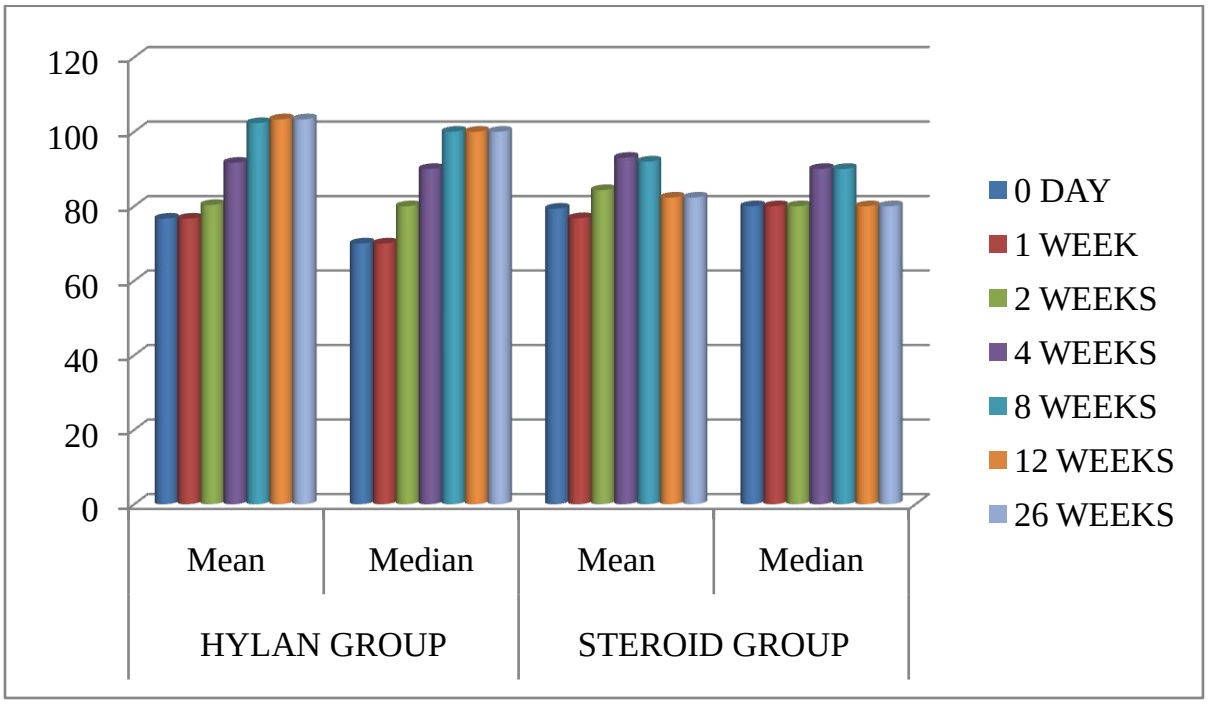


Chart 18: Range of Movements of Knee in the follow up period.

Functional assessment after the treatment was also done using range of movements (ROM). It showed significant improvement in ROM with hylan group over due course of time and remained stable in 12^{th} and 26^{th} weeks. In steroid group, there was initial better response around 4^{th} and 8th weeks, but later ROM got reduced and did not show any further change in later weeks. In conclusion, functional improvement as per ROM was better in hylan group than steroid group with p value <0.05.

DISCUSSION

As we all know about the chronic nature of the disease causing chronic disability with functional impairment, we are concerned about the possible side effects of selective and non selective analgesics, non pharmacological treatment. Hence physicians were increasingly considering intraarticular treatment with steroids or visco supplementation.

The study included patients with age ranging from 46 years to 61 years. After randomisation, the minimum age in the hylan group is 50 years and maximum age is 59 years, with median of 53.37 years. In the steroid group, the minimum age is 46 years and the maximum age is 61 years, with a mean of 55.4 years.

There were 23 males and 37 females enrolled in the study, among which 14 males (60.9% of total males) and 16 females (43.2% of total females) were enrolled in Hylan group and 9 males (29.1% of total males) and 21 females (56.8% of total females) were enrolled in the steroid group.

In this study, 35 patients had pain on right knee and 25 patients had pain on left knee. Among the patients, who were enrolled in hylan group, 19 had pain on right side and 11 had pain on left side. And among patients, who were enrolled in steroid group, 16 had pain on right side and 11 had pain on left side.

This study included patients with knee pain for duration ranging from 2 to 8 months, with mean in hylan group is 5.23 months and steroid group is 5.87 months. Majority of the patients had pain for 5 to 6 months.

49 patients had pain along anterior aspect of knee joint and 11 patients had pain along medial joint line. Among hylan group, 25 patients had pain along anterior aspect and 5 had pain along medial joint line. In steroid group, 24 had pain along anterior aspect and 6 had pain along medial joint line.

In this study, 50 patients (83.3%) did not have sense of grinding or locking of joint. 3 patients (10%) in hylan group and 7 patients (23.3%) had sense of grinding/locking of joint.

In this study, stiffness was present in total of 23 patients (9 in hylan group and 14 in steroid group). 37 patients (61.67%) did not have stiffness.

Diabetes mellitus-Type 2was the commonest comorbidity seen in this study. 5 patients (16.7% of steroid group) enrolled in steroid group had coronary artery disease associated with diabetes mellitus.

Among the patients in hylan group, 15 patients (50% of hylan group) had swelling over the knee joint and among steroid group, 18 patients (60% of steroid group) had swelling.

23 patients in hylan group and 19 patients in steroid group had tenderness over knee joint and 7 patients in hylan group and 11 patients in steroid group did not have tenderness over knee joint.

Crepitus was felt in total of 50 patients – 29 in hylan group and 21 in steroid group. Crepitus was absent in 10 patients – 1 in hylan group and 9 in steroid group.

Deformity was not present in all the patients included in this study.

None of the patients in hylan group and 2 patients (6.7%) in steroid group had bony enlargement felt in the knee joint.

Patellar tap test was positive in 24 patients – 14 in hylan group and 10 in steroid group. It was negative in 36 patients – 10 in hylan group and 20 in steroid group.

Patellar bulge test was positive in 14 patients – 3 in hylan group and 11 in steroid group. It was negative in 46 patients – 27 in hylan group and 19 in steroid group.

Osteophytes were seen in plain x-ray of knee in 9 patients – 3 in hylan group and 6 in steroid group. Osteophytes were not seen in 51 patients – 27 in hylan group and 24 in steroid group.

None of the patients enrolled in this study had significant joint space narrowing radiologically.

None of the patients included in this study developed allergic reactions after the intra articular injection.

Pain was assessed using Visual Analog Scoring (VAS) in this study. It showed significant pain relief with hylan group over due course of time. In steroid group, there was initial pain response till 8 weeks after the treatment, but later the

pain score started to show upward trend in later weeks. In conclusion, pain relief was better in hylan group than steroid group with p value <0.05 in all the follow up period except 8th week.

Functional assessment after the treatment was done using WOMAC score (The Western Ontario and McMaster Universities Arthritis Index) and improvement in range of movements of the knee in this study. It showed significant functional improvement with hylan group over due course of time. In steroid group, there was initial better response till 8 weeks, but later the functional ability started to reduce in later weeks. In conclusion, functional improvement as per WOMAC score was better in hylan group than steroid group with p value <0.05.

Functional assessment after the treatment was also done using range of movements (ROM). It showed significant improvement in ROM with hylan group over due course of time and remained stable in 12th and 26th weeks. In steroid group, there was initial better response around 4th and 8th weeks, but later ROM got reduced and did not show any further change in later weeks. In conclusion, functional improvement as per ROM was better in hylan group than steroid group with p value <0.05.

CONCLUSIONS

From this study, we conclude the following:

- Intra articular Hylan GF-20 (48mg) shows statistically significant improvement in Pain in analyzing the patients with Visual Analog Score (VAS).
- Similarly, there is improvement in range of movements and WOMAC score (C domain) in hylan group.
- For steroid group, there is initial statistical improvement upto 8 weeks in pain and other functional components, but after 8 weeks, there is no clinical improvement.
- Hence Hylan GF-20 can be considered as an important therapeutic measure in the management of OA knee.

LIMITATIONS

- Smaller sample size.
- No long term follow up – more than 26 weeks.
- Radiological follow up not done.
- Pathological improvement/arrest not documented.
- Effect of treatment in severe grades of OA knee not been studied.

SCOPE FOR FUTURE STUDY

- Long term follow up.
- Correlation of clinical improvement to radiological improvement.
- Correlation with arthroscopic analysis.
- Gene therapy – to arrest pathophysiology of OA knee.
- Mesenchymal stem cell therapy – for regeneration of diseased cartilage.

BIBLIOGRAPHY

1. Klippel, JH (ed): Primer on the Rheumatic Diseases. Ed 13. Atlanta: Arthritis Foundation and Springer Publishing; 2011.
2. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. Am J Epidemiol. 1988 Jul;128(1):179-89.
3. Chopra A: The bone and joint decade India. WHO technical report series-919.
4. Valdes AM, Spector TD: The contribution of genes to osteoarthritis. Med Clin North Am 93:45, 2009.
5. Jensen L. Hip osteoarthritis: Influence of work with heavy lifting, climbing stairs or ladders, or combining kneeling/squatting with heavy lifting. Occup Environ Med 65:6, 2008.
6. Herndon JH, Davidson SM, Apazidis A: Recent socioeconomic trends in orthopedic practice. Bone joint surg AM 83-A(7):1097-1105, 2001.
7. Henry J. Mankin, Kenneth D. Brandt: Pathogenesis of osteoarthritis. Text book of Rheumatology, 5th Ed. 2:1370-71.
8. Hochberg MC. Epidemiologic considerations in the primary prevention of osteoarthritis. J Rheumatol. 1991 Oct;18(10):1438-40.
9. Robert B.Duthie: Arthritis and rheumatic diseases. Mercer's Orthopaedic surgery. 9th Ed. PP. 751-859.

10. Felson DT, Zhang YQ. An update on the epidemiology of knee and hip osteoarthritis with aview to prevention. Arthritis Rheumatology. 1998: 41:1343-55.
11. Felson DT. Developments in the clinical understanding of osteoarthritis. Arthritis Res Ther 11:203, 2009. Retrieved May 15, 2011. Available from: http://arthritis-research.com/content/11/1/203.
12. Garstang, SV, and Stitik, TP. Osteoarthritis: Epidemiology, risk factors, and pathophysiology. Am J Phys Med Rehabil 85(11):S2, 2006.
13. Felson DT. Risk factors for osteoarthritis. Understanding joint vulnerability. Clin Orthop Rel Res 427S:S16, 2004.
14. Buckwalter JA, Mankin HJ, Grodzinsky AJ. Articular cartilage and osteoarthritis. American Academy of Orthopedic Surgeons (AAOS) Instr Course Lect. 2005:54:465.
15. Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet.2005:365:965.
16. Chen FS, Frenkel SR, Di cesare PE. Repair of articular cartilage defects. Part I. Basic science of cartilage healing. Am J Orthop 28(1): 31-3, 1999.
17. Coletti JM Jr, Akeson WH, Woo SL. A comparison of the physical behavior of normal articular cartilage and the arthroplasty surface. J Bone Joint Surg Am. 1972 Jan;54(1):147-60.

18. Mankin HJ, Mow VC, Buckwalter JA, et al. Form & function of articular cartilage, in orthopedic basic science, ed. S Simon. American Academy of Orthopedic surgeons, Chicago 1-44, 1994.
19. Grande DA, Singh IJ, Pugh J: Healing of experimentally produced lesions in articular cartilage following chondrocte transplantation. Anat rec. 1987: 218(2):142-8.
20. Buckwalter JA, Mow VC, Ratcliffe A. Restoration of injured or degenerated articular cartilage. J AM Acad Orthop surge.1984:2(4): 192-201.
21. Depalma AF, Mckeever CD, Subin DK. process of repair of articular cartilage demonstrated by histology & autoradigraphy with tritiated thymidine. Clin orthop. 1966:48:229-42.
22. Cheung HS, Lynch KL, Johnson RP, et al. in vitro synthesis of tissue specific type II collagen by healing cartilage. I. Short term repair of cartilage by mature rabbits. Arthritis rheum. 1980:23(2): 211-19.
23. Hamerman D. Prospects for medical intervention in cartilage reair, in joint cartilage degradation: Basic & clinical aspects, ed. JF Woessner, D Howell. Marcel Dekker, Inc Newyork, NY: 1993:p.529-46.
24. Cheung HS, Cottrell WH, Stephenson K, Nimni ME. In vitro collagen biosynthesis in healing and normal rabbit articular cartilage. J Bone Joint Surg Am. 1978 Dec;60(8):1076-81.

25. Shapiro F, Koide S, Glimcher MJ. Cell origin and differentiation in the repair of full-thickness defects of articular cartilage. J Bone Joint Surg Am. 1993 Apr;75(4):532-53.
26. Kellgren, JH, and Lawrence, JS: Atlas of Standard Radiographs: The Epidemiology of Chronic Rheumatism, vol 2. Blackwell Scientific, Oxford: 1963.
27. McAlindon TE, et al. Determinants of disability in osteoarthritis of the knee. Ann Rheum Dis. 1993:52:258.
28. Hayashi D, Guermaziy A, Hunter DJ. Osteoarthritis year 2010 in review: Imaging. Osteoarthr Cartil. 2011;19:354.
29. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum. 1986 Aug;29(8):1039-49.
30. Altman RD. Early management of osteoarthritis. Am J Manag Care. 2010 Mar;16 Suppl Management:S41-7.
31. [No authors listed]. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum. 2000 Sep;43(9):1905-15.

32. American Society of Orthopaedic Surgeons: Treatment of osteoarthritis of the knee (non-arthroplasty), 2008. Retrieved May 2, 2011, from www.aaos.org/research/guidelines/GuidelineOAKnee.asp, 2008.
33. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage. 2008 Feb;16(2):137-62.
34. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage. 2010 Apr;18(4):476-99.
35. Iversen MD, Hammond A, Betteridge N. Self-management of rheumatic diseases—state of the art and future perspectives. Ann Rheum Dis. 2010:69(6):955.
36. Ea HK, Liote'F. Advances in understanding calcium-containing crystal disease. Curr Opin Rheumatol. 2009:21(2):150-57.
37. Kwon YD, Pittler MH, Ernst E. Acupuncture for peripheral joint osteoarthritis: a systemic review and meta-analysis. Rheumatology (oxford). 2006:45(11):1331-37.
38. McCarberg BH, Herr KA. American Academy of pain medicine. Geriatrics. 2001:56(10);14-17.

39. Randall L, Braddom. Physical Medicine and Rehabiliation 2nd ed. Philadelpia, PA: Elsevier:2000.p.743-45.
40. Yasuda K, Sasaki T. The mechanics of treatment of the osteoarthritis knee with a wedged insole. Clin Ortho.1985;215:162.
41. Neustadt DH. Intrarticular therapy. In: Moskowitz RW, Howell DS, Altman RD, Budwalter JA, Goldberg VM, editors. Osteoarthritis Diagnosis and Medical/Surgical Management, 3rd. Philadelphia: W.B. Saunders; 2001:393-411.
42. Steinbrocker O, Neustadt DH. Aspiration and injection therapy in arthritis and musculoskeletal disorders; a handbook on technique and management. Hagerstown, MD: Harper & Row, 1972.
43. Chandler GN, Wright V. Deleterious effect of intra-articular hydrocortisone .Lancet 1958; 2:661–63.
44. Silberberg M, Silberberg R, Hasler M. Fine structure of articular cartilage in mice receiving cortisone acetate. Arch Pathol 1966; 82:569–82.
45. Meyer WL, Kunin AS. Decreased glycolytic enzyme activity in epiphysealcartilage of cortisone-treated rats. Arch Biochem Biophys 1969; 129:431–37.
46. Mankin HJ, Conger KA. The acute effects of intra-articular hydrocortisone on articular cartilage in rabbits. J Bone Joint Surg Am 1966; 48:1383–88.

47. Saxne T, Heinegard D, Wollheim FA. Therapeutic effects on cartilage metabolism in arthritis as measured by release of proteoglycan structures into the synovial fluid. Ann Rheum Dis 1986; 45:491–97.
48. Armstrong RD, English J, Gibson T, Chakraborty J, Marks V. Serum methyl prednisolone levels following intra-articular injections of methyl prednisolone acetate. Ann Rheum Dis 1981; 40:571–74.
49. Fitzgerald RH Jr. Intrasynovial injection of steroids: uses and abuses. Mayo Clin Proc 1976; 51:655–59.
50. McCarty DJ. Treatment of rheumatoid joint inflammation with triamcinolone hexacetonide. Arthritis Rheum 1972; 15:157–73.
51. Sweetnam R. Corticosteroid arthropathy and tendon rupture. J Bone Joint Surg Br 1969; 51:397–98.
52. Shikhar P, Pandey JK, Narayan A, Mahajan R. A prospective clinical evaluation between intra articular injections of methyl prednisolone acetate and triamcinolone in OA knee based on the efficacy, duration and safety. Int J Curr Microbiol Appl Sci 2013; 2:369-81.
53. Carbon D, Rush J, Lanzer W, Parent D, Murray C. A randomized single blind comparison of the efficacy and tolerability of hylan GF 20 AND triamcinolone hexacetonide in patients with osteoarthritis knee. J Rheumatol 2004, 31:333-43.

54. Raman R, Dutta A, Day N, Sharma HK, Shaw CJ, Johnson GV. Efficacy of Hylan G-F 20 and Sodium Hyaluronate in the treatment of osteoarthritis of the knee -- a prospective randomized clinical trial. Knee. 2008 Aug;15(4):318-24.

ANNEXURE-I

STUDY PROFORMA

Name: Age: Sex: Occupation:

OP number: Thesis Registration number:

Address:

Contact number

Height: cm Weight: kg BMI: BP: mmHg

Complaints

Knee pain: Right ⊡ Left⊡

Duration:_____days/months/years Pain Score: VAS ____/10

Site of Pain: Anterior ⊡ MJL ⊡

Aggravating factors: ⊡ If yes, _____ Relieving factors: ⊡If yes, _____

Sense of grinding or locking of a joint: ⊡

Stiffness: ⊡If yes, duration: _____days/months/years

Co-Morbidities: Diabetes mellitus: ⊡ Systemic hypertension: ⊡

Coronary artery disease: ⊡

Examination

Inspection: Swelling ⊡

Palpation on standing /supine: Tenderness⊡ Crepitus ⊡ Deformity: T.Varum⊡ G.varum⊡ G.valgum⊡

Bony enlargement⊡ Patellar tap test⊡ Patellar bulge test⊡

Investigations: FBS:____mg/dlPPBS: _____mg/dl X-ray –Knee: Osteophytes ⊡

Joint space narrowing⊡

Management: Intra articular Hylan-GF-20 Injection⊡
Intra articular steroid (methyl prednisolone acetate)⊡

	0 day	1 weeks	2 weeks	4 weeks	6 weeks	8 weeks	12 weeks	26 weeks
Pain score (VAS)								
WOMAC score								
Knee ROM								

Inclusion criteria:

- Grade II osteoarthritis knee by Kellgren-Lawrence grading
- Knee pain with failed conservative treatment for 1 month associated with
  - Age:>50 years
  - Stiffness:<30mts
  - Crepitus
  - Bony tenderness
  - Bony enlargement
  - No palpable warmth

Exclusion criteria:

- Trauma / Meniscal injury / Ligament Injury
- Bursitis
- Rheumatoid arthritis
- Pseudogout
- Post Operative cases
- Cellulitis / Infections
- Any implants inside
- Associated with DVT - calf muscles
- Non co-operative patient
- Low I.Q Patients /psychiatric patient
- Other grades of osteo arthritis knee

ANNEXURE-II

PATIENT INFORMATION SHEET

TITLE OF THE STUDY: Comparison of functional outcome of Intra articular Hylan GF-20 Vs Methyl Prednisolone Acetate for Grade II Osteo arthritis – knee

We are conducting a study on **"Comparison of functional outcome of Intra articular Hylan GF-20 Vs. on Methyl Prednisolone Acetate for Grade II Osteo arthritis - knee"** among patients in the Government Institute of Rehabilitation Medicine, Madras Medical College, Chennai.

The purpose of this study is to compare the clinical outcome of Intra articular Hylan GF-20 Vs Methyl Prednisolone Acetate for Grade II Osteo arthritis - knee.

We are selecting patients more than 50 years with Grade II Osteo arthritis – knee. We perform intra articular injection with Hylan GF-20 or Methyl Prednisolone Acetate, which in any way do not affect our final report or ;;;; management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.
The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Participant Signature of Investigator
(DR.S.SUGANTHI)

Date :

PATIENT CONSENT FORM

Study Detail : Comparison of functional outcome of Intra articular Hylan GF-20 Vs Methyl Prednisolone Acetate for Grade II Osteo arthritis – knee

Study Centre : Government Institute of Rehabilitation Medicine, Chennai.

Patient's Name :

Patient's Age :

Identification Number :

Check (√) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or wellbeing or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo detailed clinical examination, Radiographs, blood investigations and surgical procedure as required. ☐

Signature/thumb impression
Patient's Name and Address:

Signature of Investigator
Study Investigator's Name: **Dr.S.SUGANTHI**

நோயாளிகள் தகவல் தாள்

கற்கை தலைப்பு: முழங்கால் கீல்வாதம் சிகிச்சைக்கான செயல்பாட்டு முன்னேற்ற ஒப்பீடு(Intra articular Hylan GF-20 Vs Methyl Prednisolone Acetate)

சென்னை மருத்துவக் கல்லூரியின் கீழ் இயங்கி வரும் அரசு புனர் வாழ்வு மருத்துவ நிறுவனத்தில் முழங்கால் கீழ்வாதத்திற்கான சிகிச்சையில் ஆய்வு நடத்தி வருகின்றோம்.

இந்த ஆய்வின் நோக்கம் மூட்டுக்குள் Hylan GF-20 அல்லது மீத்தைல் ப்ரெட்னிசோலோன் (Methyl Prednisolone Acetate) மருந்து செலுத்துவதன் மூலம் ஏற்படும் செயல்பாட்டு விளைவு ஒப்பீடு ஆகும்.

நோயாளிகளின் தனியுரிமை இந்த ஆய்வு முழுவதும் பாதுகாக்கப்படும்.

இந்த சிகிச்சையில் பங்கு கொள்ள முழு மனதுடனும், சுயநினைவுடனும் எந்த வித வற்புறுத்தலின்றி சம்மதிக்கின்றேன்.

இந்த நோய் மற்றும் சிகிச்சை தொடர்பான விளக்கங்கள் மற்றும் பின் விளைவுகளையும் மருத்துவர் மூலம் அறிந்து கொண்டேன்.

பங்கு பெறுபவரின் கையொப்பம் ஆய்வாளரின் கையொப்பம்

(டாக்டர் எஸ். சுகந்தி)

நோயாளிகளின் ஒப்புதல் படிவம்

ஆய்வு : முழங்கால் கீல்வாதம் சிகிச்சைக்கான செயல்பாட்டு முன்னேற்ற ஒப்பீடு

ஆய்வு மையம் : அரசு புனர் வாழ்வு மருத்துவ நிறுவனம், சென்னை மருத்துவக் கல்லூரி, சென்னை.

நோயாளியின் பெயர் :

வயது :

மருத்துவமனை பதிவு எண் :

ஆய்வின் பதிவு எண் :

இந்த கட்டங்களில் (√) இடுக:

நான் இந்த ஆய்வின் நோக்கம் பற்றி அறிந்து கொண்டேன். எனது சந்தேகங்களை தெளிவாக கேட்டு தெரிந்து கொண்டேன்.

இந்த ஆய்வில் பங்கேற்பதும், ஆய்விலிருந்து எந்த நேரத்திலும் விலகிக் கொள்வதும் எனது தனிப்பட்ட உரிமை என்பதையும் தெரிந்து கொண்டேன்.

ஆய்வாளர், நெறிமுறைக் குழு மற்றும் கட்டுப்பாட்டு அதிகாரிகள் எனது மருத்துவ தகவல்களை தெரிந்து கொள்ள அனுமதி அளிக்கின்றேன்.

நோயாளிகளின் தனியுரிமை இந்த ஆய்வு முழுவதும் பாதுகாக்கப்படும் என்பதை தெரிந்து கொண்டேன்.

இந்த ஆய்வில் கலந்து கொள்ள முழு ஒப்புதல் அளிக்கிறேன்.

பங்கு பெறுபவரின் கையொப்பம் ஆய்வாளரின் கையொப்பம்
நோயாளியின் பெயர் மற்றும் முகவரி (டாக்டர். எஸ். சுகந்தி)

தேதி:

ANNEXURE-III

MASTER CHART

Keys to master chart

RANDOM NO:

1 - HYLAN (HYLAN-GF 20 – 48mg) GROUP
2 - STEROID (METHYLPREDNISOLONE ACETATE – 80mg) GROUP

SEX:

1 - MALE
2 - FEMALE

SIDE OF KNEE PAIN:

1 - RIGHT
2 - LEFT

SITE OF PAIN:

1 - MEDIAL JOINT LINE
2 - ANTERIOR

SENSE OF GRINDING/LOCKING OF JOINT:

1 - YES
2 - NO

STIFFNESS:

1 - YES
2 - NO

SWELLING:

1 - YES
2 - NO

TENDERNESS:

1 - YES
2 - NO

CREPITUS:

1 - YES
2 - NO

DEFORMITY:

0 - NO
1 - VARUS
2 - VALGUS

BONY ENLARGEMENT:

1 - YES
2 - NO

PATELLAR TAP TEST:

1 - POSITIVE
2 - NEGATIVE

PATELLAR BULGE TEST:

1 - POSITIVE
2 - NEGATIVE

X RAY-OSTEOPHYTES:

1 - YES
2 - NO

X RAY-JOINT SPACE NARROWING:

1 - YES
2 - NO

MASTER CHART

SL.NO	OP. NO	RANDOM NO.	AGE	SEX	SIDE OF KNEE PAIN	DURATION	SITE OF PAIN	SENSE OF GRINDING/LOCKING OF JOINT	STIFFNESS	SWELLING	TENDERNESS	CREPITUS	DEFORMITY	BONY ENLARGEMENT	PATELLAR TAP TEST	PATELLAR BULGE TEST	FASTING BLOOD SUGAR	POST PRANDIAL BLOOD SUGAR	X RAY-OSTEOPHYTES	X RAY-JOINT SPACE NARROWING	PAIN SCORE(VAS)					WOMAC SCORE						KNEE ROM					
																					0 DAY	1 WEEK	2 WEEKS	4 WEEKS	8 WEEKS	12 WEEKS	26 WEEKS	0 DAY	1 WEEK	2 WEEKS	4 WEEKS	8 WEEKS	12 WEEKS	26 WEEKS	0 DAY	1 WEEK	2 WEEKS	4 WEEKS	8 WEEKS	12 WEEKS	26 WEEKS
1	6351	1	50	2	1	6	1	2	1	1	1	1	0	2	1	2	151	238	1	1	10	9	7	6	4	3	3	60	60	60	50	33	20	10	70	70	70	90	110	110	110
2	2055	2	50	2	1	5	2	2	2	1	2	1	0	2	2	1	92	106	2	1	10	8	7	5	7	7	7	66	60	50	40	48	55	55	70	80	90	90	70	70	70
3	6346	1	55	2	2	2	2	2	1	2	1	1	0	2	2	2	88	121	2	1	9	8	8	6	2	2	2	51	51	50	45	36	25	25	70	70	80	100	110	110	110
4	1631	2	61	1	1	6	2	2	1	1	2	2	0	2	1	2	72	88	2	1	10	9	7	5	6	7	7	64	50	44	36	48	50	55	90	90	90	100	90	90	90
5	6350	1	50	2	2	6	2	2	2	1	2	1	0	2	1	2	95	152	2	1	9	9	8	6	4	2	2	67	67	60	50	30	20	20	90	90	90	100	110	110	110
6	1766	2	59	1	2	6	2	2	1	2	2	1	0	2	2	2	70	88	1	1	9	8	5	5	4	6	6	60	55	50	42	30	30	25	90	90	100	100	100	80	80
7	7986	1	50	2	1	6	2	2	1	1	1	1	0	2	1	2	151	287	1	1	6	6	5	4	2	2	2	47	46	40	30	25	10	10	100	100	100	100	100	100	100
8	1389	2	60	2	2	8	1	1	1	2	1	1	0	2	2	2	100	110	2	1	10	7	6	5	4	8	8	62	55	48	40	20	40	48	80	80	80	110	110	90	90
9	6348	1	59	1	1	2	2	2	1	1	1	1	0	2	1	2	97	145	2	1	7	7	6	5	3	3	2	41	41	30	22	10	10	8	90	90	90	100	100	100	100
10	390	2	50	2	2	2	2	2	2	1	2	1	0	2	2	1	80	96	2	1	10	10	9	7	3	8	9	56	48	36	20	18	32	48	70	7	80	90	90	70	70
11	1394	1	54	1	2	3	2	2	2	2	2	1	0	2	2	2	76	90	2	1	9	8	6	5	4	2	2	60	58	58	54	10	10	8	70	70	70	90	100	100	100
12	1437	2	60	1	2	5	2	2	2	1	1	1	0	1	2	2	92	106	2	1	10	8	7	5	3	7	7	66	60	50	40	30	55	55	70	80	80	90	90	70	70
13	6347	1	50	2	2	8	1	1	1	2	1	1	0	2	2	2	190	360	1	1	10	10	8	6	2	2	2	63	62	60	50	25	10	10	70	70	80	90	100	100	100
14	988	2	55	2	1	8	2	2	2	1	1	1	0	2	1	2	72	88	2	1	10	9	7	5	4	7	7	64	50	44	36	30	50	55	90	90	90	100	90	90	90
15	5121	1	55	1	1	8	2	2	2	2	1	1	0	2	2	2	70	121	2	1	9	9	8	6	4	2	2	63	62	60	50	25	10	10	80	80	80	90	100	100	100
16	4261	2	46	2	1	5	2	2	2	2	1	2	0	2	2	1	79	88	2	1	9	8	5	5	4	6	6	60	55	50	42	30	30	45	90	90	100	100	80	80	80
17	6987	1	52	1	1	6	2	2	2	2	1	1	0	2	2	2	78	101	2	1	9	8	7	6	2	2	2	63	62	60	50	25	10	10	70	70	70	80	100	100	100
18	5950	2	50	2	2	7	2	2	2	1	1	2	0	2	2	1	100	110	2	1	10	7	6	5	4	8	8	62	55	48	40	20	40	48	80	80	80	110	110	90	90
19	7101	1	58	2	1	4	2	2	2	2	2	1	0	2	2	2	108	140	2	1	10	9	7	6	4	3	3	60	60	60	50	33	20	20	70	70	80	90	110	110	110
20	5059	2	60	2	1	6	2	2	1	1	1	2	0	2	2	1	80	96	2	1	8	7	7	3	2	7	7	56	48	36	20	18	32	48	80	80	80	90	100	80	80
21	8200	1	59	1	1	4	2	2	2	1	2	1	0	2	1	2	80	90	2	1	9	9	8	8	6	4	2	63	63	60	55	40	20	20	80	80	80	90	100	100	100
22	3142	2	50	1	1	7	2	2	2	1	1	2	0	2	1	2	92	106	2	1	10	8	6	5	3	6	6	66	60	50	40	48	55	55	70	80	90	90	70	70	70
23	8305	1	50	2	1	8	1	1	1	2	1	1	0	2	2	2	70	100	2	1	9	9	8	7	4	3	3	65	63	55	50	30	20	10	70	70	80	90	100	100	100
24	6177	2	57	2	2	4	2	1	1	2	2	1	0	2	2	2	72	88	1	1	10	9	7	5	4	7	7	64	50	44	36	30	50	55	90	90	90	100	90	90	90
25	8402	1	51	2	2	5	1	2	2	2	2	1	0	2	2	2	72	104	2	1	10	9	7	7	4	2	2	62	60	58	52	30	15	15	70	70	80	80	100	100	100
26	6550	2	54	2	2	6	1	1	1	2	2	1	0	2	2	2	76	90	2	1	10	8	7	5	7	7	7	66	60	50	40	48	55	55	70	70	70	80	70	70	70
27	5105	1	54	2	1	6	2	2	2	2	2	1	0	2	2	2	80	98	2	1	9	9	8	7	3	2	2	64	60	54	40	15	10	10	70	70	90	90	100	100	100
28	3142	2	50	1	1	7	2	2	2	1	1	2	0	2	1	2	90	100	2	1	9	8	6	5	2	4	7	66	55	48	45	50	50	64	90	90	70	70	80	80	80
29	8146	1	52	1	1	8	2	2	2	1	1	1	0	2	1	2	95	152	2	1	9	9	8	6	4	2	2	67	67	60	50	30	20	20	90	90	90	100	110	110	110
30	6170	2	57	2	2	3	1	1	2	2	2	1	0	2	2	1	74	80	1	1	9	8	6	5	2	4	7	66	55	48	45	15	50	64	90	90	70	70	80	80	80

SL.NO	OP. NO	RANDOM NO.	AGE	SEX	SIDE OF KNEE PAIN	DURATION	SITE OF PAIN	SENSE OF GRINDING/LOCKING OF JOINT	STIFFENESS	SWELLING	TENDERNESS	CREPITUS	DEFORMITY	BONY ENLARGEMENT	PATELLAR TAP TEST	PATELLAR BULGE TEST	FASTING BLOOD SUGAR	POST PRANDIAL BLOOD SUGAR	X RAY-OSTEOPHYTES	X RAY-JOINT SPACE NARROWING	PAIN SCORE(VAS)							WOMAC SCORE							KNEE ROM						
																					0 DAY	1 WEEK	2 WEEKS	4 WEEKS	8 WEEKS	12 WEEKS	26 WEEKS	0 DAY	1 WEEK	2 WEEKS	4 WEEKS	8 WEEKS	12 WEEKS	26 WEEKS	0 DAY	1 WEEK	2 WEEKS	4 WEEKS	8 WEEKS	12 WEEKS	26 WEEKS
31	4891	1	58	1	1	6	2	2	2	2	1	1	0	2	2	1	190	360	2	1	10	10	8	6	2	2	2	63	62	60	50	25	10	10	70	70	80	90	100	100	100
32	7255	2	50	2	2	8	1	1	2	2	1	1	0	2	2	1	78	92	2	1	10	9	7	4	4	8	8	60	60	50	30	15	45	50	70	70	80	80	90	70	70
33	6795	1	50	2	1	4	2	2	2	2	1	1	0	2	1	1	95	152	2	1	9	9	8	6	4	2	2	67	67	60	50	30	20	20	70	70	70	100	110	110	110
34	6738	2	55	2	1	5	2	2	2	1	1	2	0	2	1	2	90	108	2	1	10	9	7	4	4	8	8	60	60	50	30	15	45	50	70	70	80	80	90	70	70
35	7543	1	55	1	1	5	2	2	2	1	1	1	0	2	1	2	78	100	2	1	9	9	8	7	4	3	3	65	63	55	50	30	20	10	70	70	80	90	100	100	100
36	7934	2	60	2	1	6	2	2	1	1	1	1	0	2	2	1	78	84	2	1	10	9	7	4	3	9	9	48	48	36	25	20	42	42	70	70	70	80	90	70	70
37	9205	1	59	1	1	7	2	2	2	1	1	1	0	2	2	2	80	90	2	1	9	9	8	8	6	4	2	63	63	60	55	40	20	10	80	80	80	90	100	100	100
38	4002	2	60	1	2	5	2	2	2	2	1	1	0	2	2	2	80	94	2	1	10	9	7	4	3	9	9	48	48	36	25	20	42	42	70	70	70	80	80	70	70
39	8567	1	54	1	1	8	2	2	2	1	1	1	0	2	1	2	100	140	2	1	10	9	7	6	4	3	3	60	60	60	50	33	20	20	70	70	70	90	110	110	110
40	6489	2	52	2	1	7	2	2	1	1	1	1	0	2	1	2	79	88	2	1	8	7	5	4	3	8	8	52	50	30	20	15	47	47	90	90	90	90	110	90	90
41	5579	1	56	2	2	6	2	2	2	2	2	1	0	2	2	2	95	152	2	1	9	9	8	6	4	2	2	67	67	60	50	30	20	20	80	80	90	100	110	110	110
42	8530	2	60	2	1	8	2	2	1	1	1	2	0	2	1	1	80	92	2	1	10	8	7	5	3	7	7	66	60	60	40	38	55	55	70	80	90	90	70	70	70
43	6907	1	51	1	1	4	2	2	2	1	1	1	0	2	1	2	151	287	2	1	6	6	5	4	2	2	2	47	46	40	30	25	10	10	80	80	80	90	100	100	100
44	4836	2	55	2	2	4	2	1	1	2	1	1	0	2	2	2	90	106	1	1	10	9	7	5	6	7	7	64	50	44	36	38	50	55	90	90	90	100	90	90	90
45	7562	1	57	1	1	4	2	2	2	2	1	1	0	2	2	2	97	145	2	1	7	7	6	5	3	2	2	41	41	30	22	10	10	8	90	90	90	100	100	100	100
46	8984	2	58	2	1	6	2	2	2	2	1	1	0	2	2	1	96	103	2	1	10	10	7	6	3	8	9	56	48	36	20	18	32	48	70	70	80	90	90	70	70
47	7998	1	53	2	2	5	2	2	2	2	1	1	0	2	2	2	80	98	2	1	9	9	8	8	6	4	2	63	63	60	55	40	20	20	80	80	80	90	100	100	100
48	8060	2	60	1	1	6	1	2	1	1	1	1	0	2	1	2	151	238	1	1	10	9	7	6	4	3	3	60	60	60	50	33	20	10	70	70	70	90	110	110	110
49	9105	1	51	2	2	2	1	1	2	2	1	2	0	2	2	2	151	238	2	1	10	9	7	6	4	3	3	60	60	60	50	33	20	20	70	70	80	90	110	110	110
50	1792	2	60	2	2	5	2	2	1	1	2	2	0	2	1	2	72	88	2	1	10	9	7	5	6	7	7	64	50	44	36	48	50	55	90	90	90	100	90	90	90
51	8125	1	50	1	1	4	2	2	2	1	1	1	0	2	2	1	85	121	2	1	9	8	8	6	2	2	2	51	51	50	45	36	20	20	70	70	70	90	90	110	110
52	10376	2	55	1	2	8	2	2	2	1	2	1	0	2	1	2	95	152	2	1	9	9	8	6	4	2	2	67	67	60	50	30	20	20	90	90	90	100	110	110	110
53	7559	1	56	1	1	6	2	2	2	1	1	1	0	2	1	2	97	145	2	1	7	7	6	5	3	2	2	41	41	32	22	10	10	8	70	70	70	80	100	110	110
54	10343	2	58	2	1	5	2	2	1	2	2	1	0	2	2	2	70	88	1	1	9	8	5	5	4	6	6	60	55	50	42	30	30	25	90	90	100	100	100	80	80
55	163	1	50	2	2	4	2	2	1	1	1	1	0	2	1	2	84	98	2	1	9	9	8	8	6	4	2	66	66	54	50	45	30	20	80	80	80	90	100	100	100
56	10113	2	50	2	2	7	1	1	1	2	1	1	0	2	2	2	100	110	2	1	10	7	6	5	4	8	8	62	55	48	40	20	40	48	80	80	80	110	110	90	90
57	589	1	50	2	2	5	2	2	1	1	1	1	0	2	1	2	74	96	2	1	9	9	8	8	6	4	2	66	66	54	50	45	30	20	80	80	80	90	100	100	100
58	5310	2	60	2	1	4	2	2	2	1	2	1	0	2	2	1	80	96	2	1	10	10	9	7	3	8	9	56	48	36	20	18	32	48	70	7	80	90	90	70	70
59	590	1	52	2	2	5	2	2	1	1	1	1	0	2	1	2	78	92	2	1	9	9	8	8	6	4	2	66	66	54	50	45	30	20	80	80	80	90	100	100	100
60	6767	2	50	1	1	7	2	2	2	1	1	1	0	1	2	2	92	106	2	1	10	8	7	5	3	7	7	66	60	50	40	30	55	55	70	80	80	90	90	70	70