COMPARISON BETWEEN THE EFFECT OF PLATELET RICH PLASMA (PRP) AND HYALURONIC ACID LOCAL INJECTION IN TREATMENT OF THUMB CARPOMETACARPAL JOINT OSTEOARTHRITIS

Thesis

Submitted for partial fulfillment of Master Degree in Physical Medicine, Rheumatology and Rehabilitation

Presented by

Radwa Yehia Abd El Fattah Ibrahim

M.B., B.Ch. - Faculty of Medicine- Ain Shams University

Supervised by

Prof. Dr. Hanaa Fathy Saad

Professor of Physical Medicine, Rheumatology & Rehabilitation
Faculty of Medicine, Ain Shams University

Prof. Dr. Dina Shawky Al-Zifzaf

Professor of Physical Medicine, Rheumatology & Rehabilitation
Faculty of Medicine, Ain Shams University

Dr. Hala Mohamed Abd El Sabour

Lecturer of Physical Medicine, Rheumatology & Rehabilitation
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2018

مقارنة بين تأثير الحقن الموضعي للبلازما الغنية بالصفائح الدموية و حمض الهيالورونيك في علاج خشونة المفصل الرسغى السنعى للابهام

رسالة

توطئة للحصول علي درجة الماجيستير في الطب الطبيعي و الروماتيزم والتأهيل

مقدمة من

الطبيبة/ رضوي يحيى عبد الفتاح ابراهيم

بكالريوس الطب والجراحة- جامعة عين شمس

تحت إشراف

أ.د/ هناء فتحي سعد

أستاذ الطب الطبيعى والروماتيزم والتأهيل

كلية الطب- جامعة عين شمس

أ.د/ دينا شوقي الزفزاف

أستاذ الطب الطبيعى والروماتيزم والتأهيل

كلية الطب- جامعة عين شمس

د/ هالة محمد عبد الصبور

مدرس الطب الطبيعى و الروماتيزم والتأهيل

كلية الطب- جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٨

بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgement

First and foremost thanks to ALLAH, the Most Merciful.

I wish to express my deep appreciation and sincere gratitude to ***Prof. Dr. Hanaa Fathy Saad,*** *Professor of Physical Medicine, Rheumatology & Rehabilitation, Ain Shams University, for her close supervision, valuable instructions, continuous help, patience, advices and guidance. She has generously devoted much of her time and effort for planning and supervision of this study. It was a great honor to me to work under her direct supervision.*

I wish to express my great thanks and gratitude to ***Prof. Dr. Dina Shawky Al-Zifzaf,*** *Professor of Physical Medicine, Rheumatology & Rehabilitation, Ain Shams University, for her kind supervision, indispensable advice and great help in this work.*

I wish to express my great thanks and gratitude to ***Dr. Hala Mohamed Abd El Sabour,*** *Lecturer of Physical Medicine, Rheumatology & Rehabilitation, Ain Shams University, for her kind supervision, indispensable advice and great help in this work.*

Finally I would present all my appreciations to my patients without them, this work could not have been completed.

Contents

List of Abbreviations

ACR	:	American College of Rheumatology
anti-CCP	:	Anti–cyclic citrullinated peptide
AP	:	Adductor pollicis
APL	:	Abductor pollicis brevis
AUSCAN	:	Australian/Canadian OA Hand Index
CD44	:	Cluster of differentiation 44
CMC joint	:	Carpometacarpal joint
COX	:	Cyclooxygenase
CRP	:	C-reactive protein
CT		Computed tomography
DASH		Disabilities of arm, shoulder and hand
ECM	:	Extracellular matrix
EGF	:	Epidermal Growth Factor
ESR	:	Erythrocyte sedimentation rate
EULAR	:	European League Against Rheumatism European League Against Rheumatism
FDA	:	Food and Drug Administration
FIHOA	:	Functional Index of hand OA
GFR	:	Glomerular filtration rate
GIT	:	Gastro intestinal tract
HA	:	Hyaluronic acid
HMWHA	:	High molecular weight hyaluronic acid
IAHA	:	Intra articular hyaluronic acid
ICAM-1	:	Intercellular adhesion molecule-1
IGF-1	:	Insulin-like growth factor 1
IL	:	Interleukin
iNOS	:	Inducible nitric oxide synthase
IPJs	:	Interphalangeal joints
kDa	:	Kilodaltons
Kg	:	Kilogram
LMWHA	:	Low molecular weight hyaluronic acid
LPS	:	Lipopolysaccharide
MAP	:	Mitogen-activated protein
MDa.	:	Megadaltons
MKP	:	Mitogen-activated protein kinase phosphatase

MMP	:	Metalloproteinase
MMWHA	:	Moderate molecular weight HA
MR	:	Magnetic resonance MR
MSCs	:	Mesenchymal stem cells
MSUS	:	Musculoskeletal ultrasound
NF-κB	:	Nuclear factor kappa-light-chain-enhancer of Activated B cells
NSAIDs	:	Non steroidal anti inflammatory drug
OA	:	Osteoarthritis
PDCD 5	:	Programmed cell death 5
PGE2	:	Prostaglandin E2
PROMs	:	Patient-reported outcome measures
PRP	:	Platelet-rich plasma
RF	:	Rheumatoid factor
SF	:	Synovial fluid
ST	:	Scaphotrapezial
TGFβ,	:	Transforming Growth Factor beta
TLR-2	:	Toll-like receptor 2
TNF-α	:	Tumor necrosis factor α
US	:	Ultra sound
VAS	:	Visual analog scale
VEGF,	:	Vascular Endothelial Growth Factor

List of Table

List of Figures

Abstract

Objectives: to compare the effectiveness of PRP versus hyaluronic acid injection in osteoarthritis of thumb carpometacarpal joint based on clinical and functional outcome measures. **Patients and methods:** Prospective interventional study conducted on thirty patients with thumb CMC OA. Patient was assessed by joint Palpation for tenderness with grading from I-IV, Provocative tests (Grind test and Lever test), VAS for pain, AUSCAN score, grip and pinch strength. The patients were randomly divided into two equal groups, Group 1: received Platelet-Rich Plasma (PRP) intra-articular injection. Group 2 received hyaluronic acid injection. Re-evaluation at 4 and 12 weeks was done for tenderness, VAS, AUSCAN index, Grip and pinch strength. **Results:** This study was conducted on thirty patients with ages ranged from 40 to 70 years (mean: 52.77 ± 8.59). Our results revealed that both groups showed a highly significant improvement after 4 weeks regarding pain relief assessed by VAS, tenderness grading, AUSCAN hand function score, grip and pinch strength after injection in comparison to before injection (P= 0.000). However, these improvement couldn't be sustained for the PRP group after 12 weeks, there was a highly statistically significant increase (deterioration) in hand functional score from 4 to 12 weeks follow up (P=0.000) and total score (P=0.004) , highly statistically increase in VAS(P= 0.000) and decrease in grip & pinch strength (P=0.000) , while HA group showed a highly statistically significant improvement regarding pain, hand function score , grip and pinch strength after 12 weeks of injection. **Conclusion**: We observed clinical improvement in both groups of CMC OA treated either with single dose of HA or PRP at 4 and 12 weeks follow up. However, HA provide a superior improvement with respect to PRP at 12 weeks follow up regarding VAS for pain, joint tenderness, AUSCAN hand function score, grip and pinch strength. So we support the use of a single hyaluronic acid injection as therapy for thumb CMC OA in preference to PRP injection.

Key Words: Thumb CMC, Osteoarthritis, hyaluronic acid, PRP, Intra-articular injection.

Introduction

Osteoarthritis (OA) is a degenerative joint disease that can affect any joint including hands. Among the different subtypes of hand OA, that affecting the base of the thumb represents a particular challenge to clinicians due to limited efficacy of treatment options ***(Bijsterbosch et al., 2010).***

The thumb carpometacarpal (CMC) joint is a biconcave saddle joint between the thumb metacarpal and trapezium that allows for multi planar movement. The thumb is responsible for over 60% of common prehensile function, making it a common subject for over exertion in daily stress and strain scenarios ***(Young & Mikola, 2004)***.

Thumb carpometacarpal joint (CMCJ) is the second most common form of hand OA affecting between 20% and 30% of the general population. Thumb CMC joint OA is more prevalent in females than males, increases with age and has been associated with hand pain and loss of functional hand use ***(Marshall et al., 2009).***

Injury in the thumb CMC joint is normally attributed to repetitive daily tasks that create stress on the joint. High local stresses that result from repetitive, forceful gripping and pinching motions can slowly degrade cartilage layers. A 1 kg load applied at the tip of the thumb is equivalent to a 12 kg force at the CMC joint. Simple activities such as ringing out a towel can produce a force up to 120 kg ***(Zhang & Jordon, 2010).***

OA involves a perturbed joint environment at the cellular level with alteration in the composition of the synovial fluid. As a consequence, chondrocytes become activated with increased proliferation, production of matrix-degrading enzymes, cytokines and cytokines receptors ***(Loeser et al., 2012)***. Finally the inadequate healing response to synovial inflammation result in further structural cartilage degradation ***(Bijlsma et al., 2011)***.

Radiographic thumb CMC OA was reported to affect nearly 21% of the population over 40 years of age and it is usually more frequently related to pain and disability than interphalangeal joint OA. In addition to pain, it can cause deformity, stiffness, decreased range of motion and strength, resulting in difficulty performing common activities such as opening jars, carrying weights and writing ***(Kloppenburg, 2014).***

Conservative therapeutic approaches have been proposed with the aim of reducing pain, maintaining and/ or improving the joint function, mobility and strength such as medication starting from analgesic, non- steroidal anti-inflammatory, exercises, assistive devices and orthosis ***(Zhang et al., 2007).***

It is well known that the pharmacological treatment particularly in the elderly may cause relevant side effects on GIT, renal, hepatic and CVS systems ***(Psaty & Furberg, 2005).***

Surgery for thumb CMC OA have been advocated. Although no procedure has been proven superior, surgical intervention can be effective. However, operative interventions are more prone to complications ***(Vermeulen et al., 2011).***

A well-known, widely used form of local treatment is the injection of corticosteroids into the affected joint, particularly for patients with thumb CMC OA. The local anti-inflammatory effects of corticosteroid injections are hypothesized to decrease inflammation and consequently relieve the symptoms of OA ***(Wolf & Delaronde, 2012*****).**

While Viscosupplementation is based on the physiologic importance of hyaluronan in the synovial fluid, and it is hypothesized that this can restore the reduced viscoelasticity of the synovial fluid in osteoarthritic joints and thus decrease pain, improve mobility and restore the natural protective functions of hyaluronan in the joint ***(Fam et al., 2007)***.

The effect of steroids is achieved faster, but is short lived, compared with hyaluronic acid, which seemed to have a longer-lasting effect but starts more slowly ***(Fuchs et al., 2006)***.

Recent studies indicate that autologous platelet rich plasma (PRP) is an appropriate injectable material with great potential in treating many different muscloskeletal disorders ***(Meheux et al., 2015)***. The positive effect of PRP attributed to various growth factors, cytokines and bioactive proteins. These components play key roles in promoting cell proliferation, matrix regeneration, angiogenesis and an anti- inflammatory effect ***(Kabiri et al., 2014)***.

PRP injection into joints can modify the biological microenvironment inside the joint. Thereby, PRP affects local and infiltrating cells, mainly synovial cells, endothelial cells, immune cells, and cellular components of cartilage and bone. Ultimately, it is believed to reduce the inflammatory process and alter the joint homeostasis of anabolism and catabolism in cartilage ***(Scotti et al., 2016)***.

Aim of the work

The aim of this study is to compare the effectiveness of PRP versus hyaluronic acid injection in treatment of osteoarthritis of thumb carpometacarpal joint based on clinical and functional outcome measures.

Anatomy of thumb carpometacarpal joint

The thumb carpometacarpal (CMC) joint is a biconcave concavo-convex saddle joint between the distal surface of the trapezium and the base of the first metacarpal **(Figure 1).** Thumb CMC joint motion arcs of the metacarpal on the trapezium are flexion-extension and abduction-adduction. Pronation-supination represents composite rotation and translation of this joint based on morphology and muscular activity ***(Ladd et al., 2013)***.The metacarpal base is concave dorso-volarly and convex radio-ulnarly. Conversely, the trapezial concave arc is radioulnar, and the convex arc is dorsovolar ***(Matullo et al., 2007)*** (**Figure 2**)

The concavity of each articular surface is shallow, so the skeleton affords little intrinsic stability. The ligaments and muscles play varying roles in stability, laxity, and proprioception of this complex joint ***(Ladd et al., 2013).***

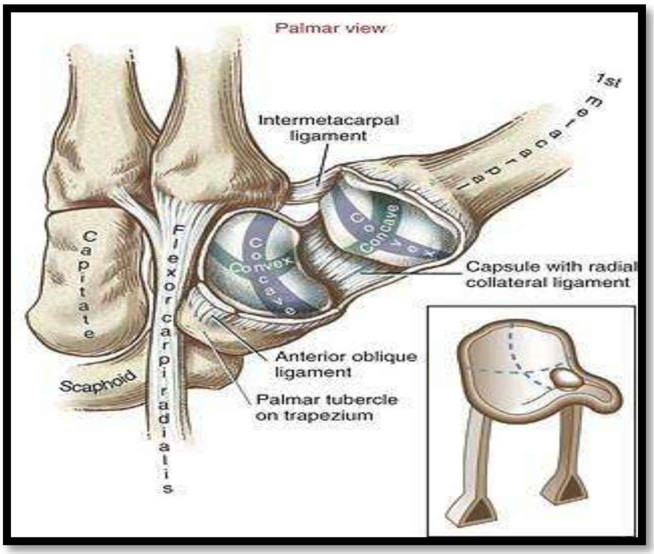

Figure 1: Anatomy of thumb CMC joint ***(Ladd et al., 2013)***.

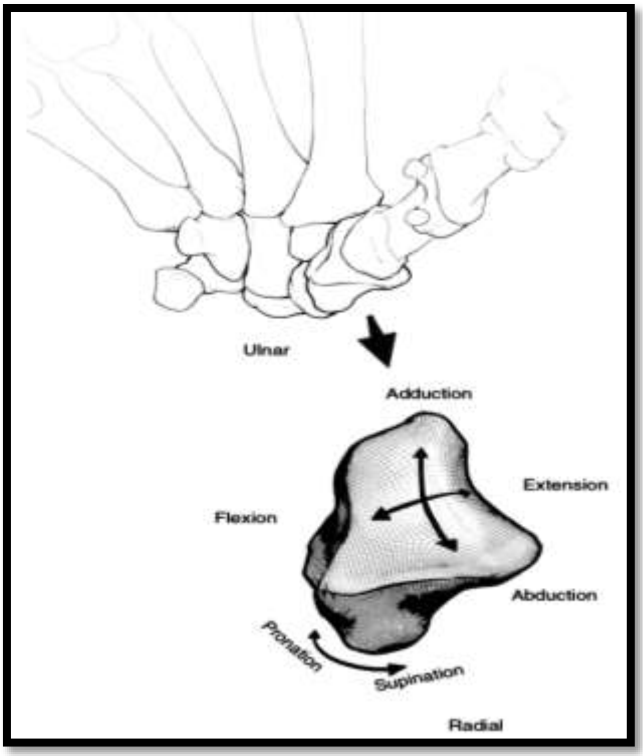

Figure 2: Topography of the distal trapezial joint surface, redrawn from a CT surface rendering of a normal right hand ***(Matullo et al., 2007)***

Capsule and Ligaments

The capsule surrounding the CMC joint of the thumb is relatively large and loose to accommodate a large range of motion. The capsule is reinforced by at least 5 ligaments (table 1) ***(Neumann & Bielefield, 2003***). The primary ligaments at the CMC joint are essential to maintaining static and dynamic stability between the metacarpal and trapezium. These ligaments have 3 functions, these functions are to control the extent and direction of joint motion, to help maintain normal alignment of the joint, and to help control forces produced by activated muscles. Excessive laxity of the ligaments, either through chronic synovitis, inflammation, or repetitive injury, is a primary cause of instability at this joint or can be a precursor to degeneration of the articular cartilage ***(Neumann & Bielefield, 2003)*****.**

Table 1: Ligaments of thumb CMC joint***(Neumann & Bielefield,2003)***

Name	Proximal Attachment	Distal Attachment	Motions That Increase Ligament Tensions
Anterior oblique*	Palmar tubercle on trapezium	Palmar base of thumb metacarpal	Abduction, extension, and opposition
Ulnar collateral	Transverse carpal ligament	Palmar-ulnar base of thumb metacarpal	Abduction, extension, and opposition
Intermetacarpal	Dorsal side of base of second metacarpal	Palmar-ulnar base of thumb metacarpal (with ulnar collateral)	Abduction and opposition
Posterior oblique	Posterior surface of trapezium	Palmar-ulnar base of thumb metacarpal	Abduction and opposition
Radial collateral†	Radial (lateral) surface of trapezium	Dorsal surface of thumb metacarpal	All movements to varying degrees, except extension

* Described as 2 heads: superficial and deep ("beak") fibers.
† Also called dorsal-radial ligament.

Extension, abduction, and opposition (which include varying amounts of flexion, medial rotation, and palmar abduction) elongate most of the thumb's ligaments. The anterior oblique, radial collateral and ulnar collateral ligaments have been described as primary dynamic stabilizers of the thumb, especially during pinch and opposition of the thumb **(Figure 3)** ***(Neumann & Bielefield, 2003)*****.** The anterior oblique ligament plays a particularly important role in 2 functions. These functions are to passively guide the medial axial rotation of the metacarpal during full flexion, and to restrain the extent of radial (lateral) translation of the metacarpal relative to the trapezium. ***Ateshian et al., 1995*** provide evidence that the forces produced by lateral pinch are generally concentrated at the region where cartilage thinning is most often observed in cadavers. This support the idea that stress is a significant precursor to degeneration of the CMC joint.

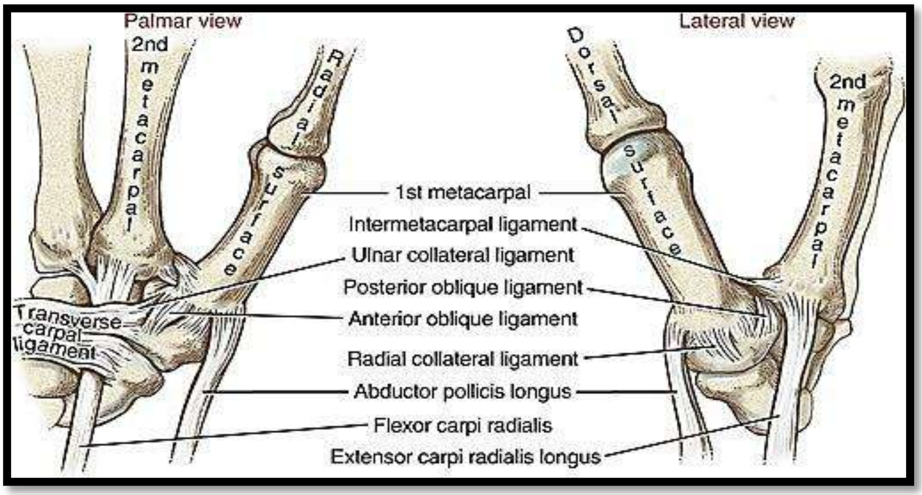

Figure 3: Palmar and lateral views of the ligaments of the carpometacarpal joint of the right thumb. Note the distal attachment of the abductor pollicis longus into the capsule of the carpometacarpal joint of the thumb ***(Neumann & Bielefield, 2003***)

Muscle Function and movement:

Primary actions of muscles that cross the carpometacarpal joint of the thumb.

Flexion:

- Adductor pollicis
- Flexor pollicis longus
- Opponens pollicis
- Flexor pollicis brevis

Extension:

- Extensor pollicis brevis
- Extensor pollicis longus
- Abductor pollicis longus

Abduction:

- Abductor pollicis brevis
- Abductor pollicis longus

Adduction:

- Adductor pollicis
- Extensor pollicis longus
- First dorsal interosseus

Opposition:

- Opponens pollicis
- Flexor pollicis brevis
- Abductor pollicis brevis
- Flexor pollicis longus
- Abductor pollicis longus

Functional anatomy:

Maximal contact area between trapezium and metacarpal bone (53%) is during opposition (abduction, flexion and pronation). Ligaments are taut in this position ***(Neumann & Bielefield, 2003).***

Adductor Pollicis (AP) is a strong thumb adductor in lateral (key) pinch and a significant contributor to thumb OA deformity (adduction contracture). Abductor pollicis longus (APL) serves as an important CMC joint stabilizer (counteracts action of AP) **(Figure 4)** ***(Roush et al., 2005)***.

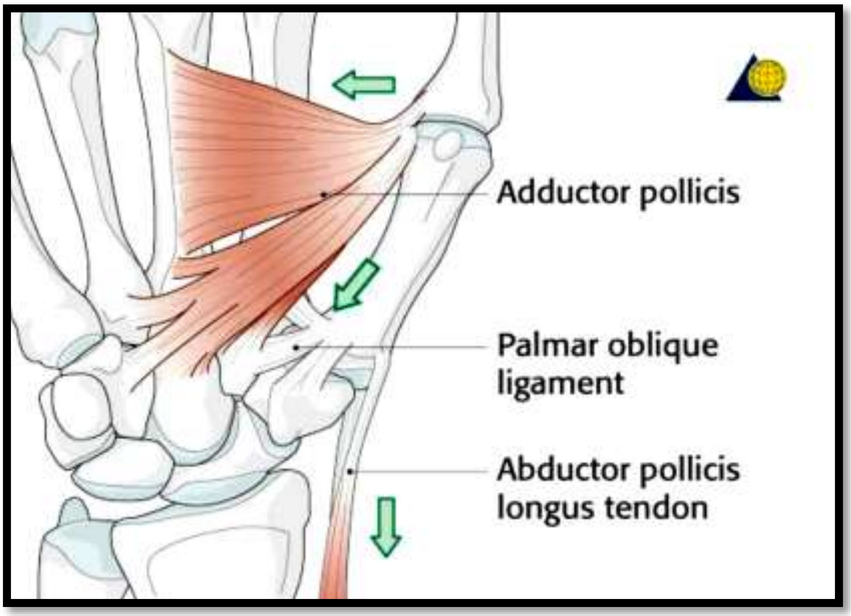

Figure 4: APL muscle counteracts AP to stabilize CMC joint ***(Roush et al., 2005)***

For small grip and pinch we need thumb opposition with screw rotation in which the thumb is in opposition to the tips of the other fingers, the thumb is abducted, flexed and pronated to allow its tip to face toward other fingers. On the other hand, for wider grasp, the thumb needs to be in neutral rotation facing toward the plane of the palm ***(Edmunds, 2011).***

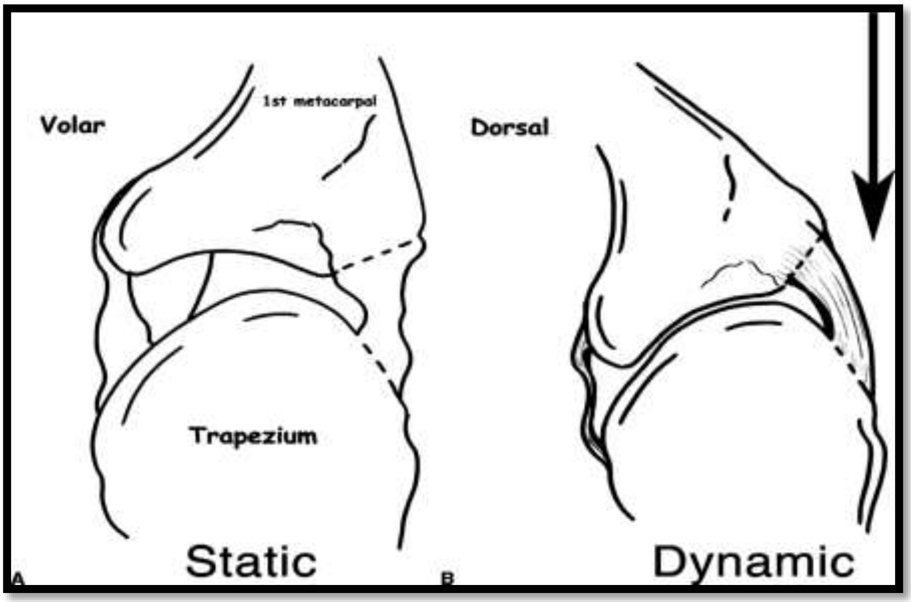

Figure 5: (A): The CMC joint in the static resting position. The volar beak of the thumb metacarpal is Dis-engaged from its recess in the trapezium, the CMC joint space is large, and both the volar beak ligament and the dorsal ligament complex are lax. **(B):** The dynamic CMC position of power pinch or power grip with screw home torque rotation, in which the dorsal ligament complex tightens, the anterior beak ligament becomes even more lax, the CM joint is compressed, and the anterior beak of the thumb metacarpal is compressed into its recess in the trapezium. This forms a dynamic force couple that changes the CMC joint from incongruity and laxity to congruity and rigid stability ***(Edmunds, 2006)***.

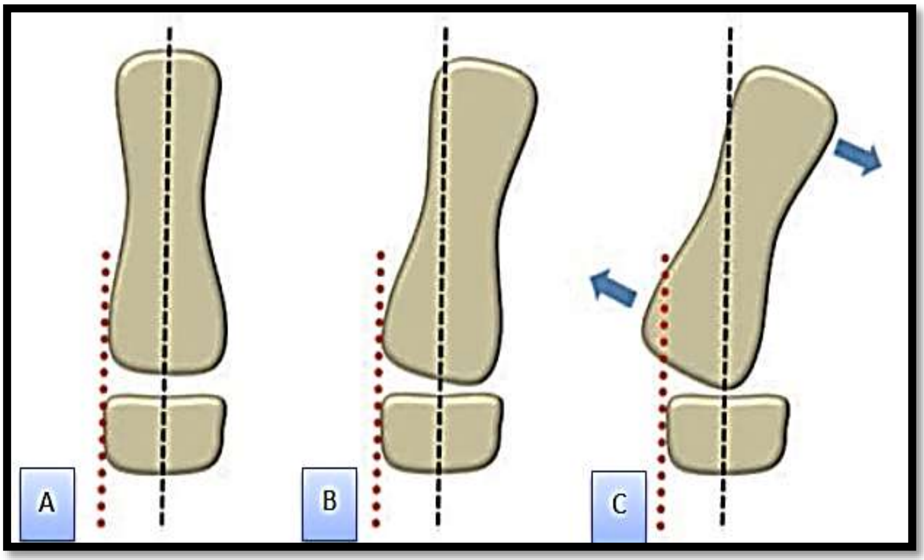

Figure 6: A schematic drawing of a left thumb illustrates the movement of the thumb metacarpal on the trapezium (red dotted line is the dorsum of the thumb). A) Normal thumb CMC joint at rest with the metacarpal and the trapezium in alignment. B) Normal thumb CMC joint flexion; note the bones remain in alignment and C) Thumb CMC joint with osteoarthritis where the first metacarpal base moves out of alignment in the dorsal direction (dorsal translation) while the metacarpal head flexes forward ***(Colditz & Koekebakker , 2010).***

Ideally, the most biomechanically advantageous position to perform the pinch is the arched position (***Pearlman et al., 2004).*** such that there is flexion, in the sagittal plane of both the IP and the MCP joint, while the first metacarpal is in extension on the trapezium. This position is when there is maximum articular contact, ligaments are relaxed. That CMC position is called the neutral position ***(Gibbons & Comerford, 2001).***

Thumb Carpometacarpal osteoarthritis

OA is a major source of disability due to pain and loss of function. It is the most common form of joint disease, and among the top 10 causes of disability worldwide ***(Neogi & Zhang, 2013).***

The carpometacarpal (CMC) joint of the thumb is the second most affected joint by osteoarthritis. Typical symptoms can include pain in the joint, as well as morning stiffness or stiffness due to inactivity. Hand function is therefore often adversely affected in patients with OA in CMC joint ***(Robyn et al., 2017)***. The presence of CMC joint OA of the thumb contributed more to pain and disability than interphalangeal joints (IPJs) OA in a population with symptomatic hand OA ***(Bijsterbosch et al., 2010).*** Most of the cases are idiopathic, and often both hands are affected ***(Bakri & Moran, 2015)***. The resultant loss of thumb function may result in up to 40% to 50% impairment of the upper extremity ***(Luker et al., 2014)***.

Thumb CMC joint OA affects 15% of adults older than 30 years and 66% of women older than 55 years. CMC joint OA is traditionally viewed as a disease endemic in postmenopausal women, which affects up to 36% of postmenopausal women ***(Anne et al., 2015***). Demographic radiographic studies show a 6:1 female-to-male incidence of the CMC joint OA, although this difference decreases with age, with the incidence in women and men at age 75 years of 40% and 25%, respectively. Radiographic thumb CMC OA was reported to affect nearly 21% of the population over 40 years of age ***(Kloppenburg, 2014).***

Osteoarthritis (OA) hand has a predilection for first CMC joint because of different factors, these factors may be anatomical, biomechanical, joint laxity, gender and occupational.

1- Anatomical Factors:

The shallow saddle-shaped joint surfaces provide no intrinsic osseous stability, requiring the ligaments and muscles to assume responsibility for stability to prevent translation during loading. Additionally, the base of the first metacarpal is approximately 34% larger than that of the trapezium which concentrates pressure on the trapezial surface and this increases wear and tear in CMC joint ***(Colditz & Koekebakker, 2010)***.

Three of the extrinsic muscles which influence thumb CMC joint motion (abductor pollicis longus, extensor pollicis brevis and extensor pollicis longus) are relatively inefficient extensors and abductors at the CMC joint. In contrast, three of the four thenar muscles (abdbuctor pollics brevis, flexor pollicis brevis and opponens pollicis) pull the first metacarpal head toward the palm (into flexion), and thus the balance of motion is loaded toward flexion. This muscle force inequality explain**s** the most common direction of deformity of the first metacarpal: flexion and adduction ***(Colditz & Koekebakker, 2010)***.

2- Biomechanical Factors:

The thumb is different from the other digits of the hand in several important ways. It performs up to 50% of total hand function, much of which is due to the biomechanically unique thumb CMC joint. The "saddle" shape of this joint determines that it has relatively little bony stability, which permits a large and complex range of motion. Primary stability is achieved dynamically, by the muscles that cross the joint. In contrast, the hinge joints of the digits feature tightly congruent bony architecture and it is these static constraints that provide primary stability ***(Robyn et al., 2017).***

Biomechanical studies have shown that forces increase exponentially from the tip of the thumb to the CMC joint with grasp and forceful pinch. The joint reactive force at the base of the thumb is 12 times greater than that generated at the tip of the thumb with lateral pinch, and compressive forces of as much as 120 kg may occur at the CMC joint with forceful grasp ***(Ladd et al., 2013)***.

3- *Joint Laxity:*

Joint hypermobility is defined as greater than normal motion at multiple joints. Joint laxity is implying that greater joint mobility leads to abnormal biomechanical stresses on the joint ***(Bird, 2007)***. Studies have suggested that joint laxity affects the thumb CMC joint with radiographic evidence of CMC arthritis in 16% of this population ***(Wolf et al., 2011).***

4- *Gender:*

Women are known to have a smaller trapezium in relation to their metacarpal base as well as a flatter trapezial articular surface. The less congruent CMC joints create smaller contact areas that lead to higher stress for similar daily activities. Women have also been found to have a 20% thinner cartilage layer ***(Halilaj et al., 2014).***

Increased frequency of OA in this joint is also observed in females in the 5th and 6th decades and this has been attributed to increased ligament laxity and flexibility induced by the hormones (estrogen and relaxin) ***(Fotiadis et al., 2010).***

Relaxin is a member of the insulin-like growth factor family that is produced both in pregnant and non-pregnant women and in men. Its mechanism of action is mediated through up-regulation of matrix metalloproteases and suppression of tissue inhibitors of metalloproteases within the extracellular matrix, inducing changes in ligament compliance ***(Jennifer et al., 2014)***.

Researches demonstrated that relaxin binding to the anterior oblique ligament is specific and presumptively reflects the presence of either cellular and/or extracellular matrix receptors. This suggested that the effect of relaxin on the ligaments of the CMC joint may involve attenuation of the ligaments or inhibition of repair, especially during the peak of a woman's reproductive potential ***(Lubahn et al., 2006).***

5- ***Occupational Factors:***

High local stresses that result from repetitive, forceful gripping and pinching motions can slowly degrade cartilage layers. A relationship between CMC OA and specific occupations has been reported such as tasks involving requirements presumed to cause a strain or a high load on the CMC joint such as repetitive thumb use (20 movements per minute and/or thumb flexion– extension at least once per minute), fine or strong pinch actions (tip, lateral, or palmar pinch), gripping/ grasping and pressure on the pad of the thumb. Also, work conditions such as whole body vibration and who used their fingers continuously and rapidly, typists, tailors, dressmakers ***(Zhang & Jordon, 2010)***.

Types of OA according to etiology:

Primary OA:

This is the most commonly diagnosed form of OA and is considered to occur largely due to "wear and tear" over time. Because of this, it is associated with aging. People tend to develop this type of OA starting from the age of 55 or 60 ***(Neogi & Zhang, 2013).***

Secondary OA:

This form of OA results from conditions that induce a change in the microenvironment of the cartilage. Such conditions include significant trauma, repetitive joint over use, congenital joint abnormalities, metabolic defects (eg, Wilson disease), infections, neuropathic or muscular disorders that put abnormal stress on the joint and disorders that alter the normal structure and function of cartilage (eg, Rheumatoid Arthritis, gout). Secondary OA tends to appear in relatively young individuals aged approximately 45 or 50 ***(Neogi & Zhang, 2013).***

Pathogenesis of thumb carpometacarpal osteoarthritis

OA considered as a "degenerative joint disease" would be a misnomer because OA is not simply a process of "wear and tear" but rather a much more complex disease driven by inflammatory mediators within the affected joint ***(Berenbaum, 2013)***.

Articular cartilage main function is to provide a smooth, lubricated surface for articulation and to facilitate the transmission of loads. Throughout life, cartilage is continually remodeled as chondrocytes replace the degraded with newly synthesized components, although it is recognized that this is a slow process in adults ***(Loeser et al., 2016).***

The root cause of OA is not completely understood. However, the biomechanical forces are thought to interact with other environmental, systemic (i.e. biochemical, metabolic) and genetic factors to contribute to the pathogenesis of OA ***(Rahmati et al., 2016)***.

Aging and inflammation are major contributing factors to the development and progression of OA, "Inflammaging" refers to the Chronic, low-grade inflammation in osteoarthritis that contributes to symptoms and disease progression. Networks of diverse innate inflammatory signals, including complement are activated in OA ***(Liu-Bryan &Terkeltaub, 2015).***

The key pathophysiological mechanisms in OA involved pro-inflammatory mediators (interleukins IL-1β, IL-6, IL-8 and tumor necrosis factor α (TNF-α) and pro-catabolic mediators through their signaling pathways and the well-characterized effects of nuclear factor κB (NFκB) and mitogen-activated protein (MAP) kinase signaling responses (***Liu-Bryan & Terkeltaub, 2015).***

The inflammatory mediators that activate transcription factors convert viable chondrocytes to hypertrophic differentiation and promote proinflammatory, and procatabolic responses ***(Mobasheri et al., 2015).*** Moreover, mediators from hypertrophic chondrocytes including vascular endothelial growth factor can promote angiogenesis in joint tissues, including synovium ***(Liu-Bryan &Terkeltaub, 2015***).

Cartilage destruction is the hallmark of the disease, Also synovitis, subchondral bone remodeling (thickening, bone collapse, bone cysts), degeneration of ligaments and hypertrophy of the joint capsule take parts in the pathogenesis of OA ***(Nagai et al., 2015).*** As articular cartilage matrix proteins are fragmented, these fragments feedback and stimulate further matrix destruction ***(Kumahashi et al., 2015)***.

Synovial inflammation plays a critical role in the symptoms and structural progression of OA. Soluble inflammatory mediators, such as cytokines and chemokines, are increased in synovial fluid (SF) in OA and promote synovitis. Recent researches demonstrated that synovitis occurs even in early stages of disease, but the prevalence of synovitis increases with advancing disease stage ***(Wang et al., 2018)***.

The cause of synovial inflammation in OA may be either a result of foreign body reaction of synovial cells to degraded cartilage products inside the joint, or as a primary trigger of OA process. Synovial cells are thought to produce inflammatory mediators, activate chondrocytes, and propagate cartilage breakdown. Synovitis has been shown to correlate with symptom severity and rate of cartilage degeneration ***(Wang et al., 2018)***.

Osteophytes could be considered as physiologic response to mechanical overloading by increasing the articulating joint surface, thus having a supportive function. However, they are mainly found in non–weight-bearing areas. Thus, it is more likely that growth factors play a dominant role in the induction and promotion of osteophyte formation ***(Loeser et al., 2016)***.

As osteoarthritis develops, the capsule of the thumb CMC joint becomes excessively lax as the beak ligament loses its ability to limit the dorsal translation of the metacarpal on the trapezium (movement of the first metacarpal base sliding on the stationary trapezium toward the dorsum). When the thenar muscles contract during pinch, the first metacarpal tilts; i.e. the distal end moves toward the palm and the proximal end shifts dorsally which creates pain ***(Edmunds, 2011).***

Diagnosis of thumb CMC OA

Clinical picture:

The diagnosis of OA of the CMC joint of the thumb is reached by patient history, physical examination, qualitative assessment of the hand as well as radiological findings ***(Berger and Meals, 2015)***.

The patient is typically a 40- to 70-year-old presenting with radial-side hand or thumb pain of insidious onset with a duration ranging from several months to several years.

The typical symptom of these patients is pain exacerbated by common activities, such as handwriting, holding hardbound (i.e., heavier) books, turning doorknobs or keys in locks, doing needle point, and using scissors carrying an object that weighs more than 4.5 kg. Grip strength is diminished in those with symptomatic hand osteoarthritis. Functional limitations vary depending on patient occupation and whether the dominant hand is involved. They may perceive this dysfunction as weakness and loss of dexterity ***(Ladd et al., 2013)***.

By inspection a dorsoradial prominence at thumb metacarpal base may be seen. This may be due to a combination of subluxation, joint inflammation and osteophyte formation. (***Gillis et al., 2011).***

Tenderness is usually well localised over the joint, and this can be reproduced with thumb and finger pressure applied directly over the affected joint. Crepitus evident on examination implies erosion of the articular cartilage Range of motion of thumb CMC joint usually of normal ranges in patients with OA (***Gillis et al., 2011).***

Provocative manoeuvres may be helpful in localizing symptoms to the CMC joint with degenerative changes or synovitis and also confirm the diagnosis (Grind test and lever test) (***Glickel, 2001).*** Grind test is the most commonly referenced diagnostic tool to evaluate and confirm osteoarthritis (it is the most specific test) (Figure 7). The grind test has shown 30% sensitivity and 96.7% specificity ***(Choa et al., 2014)***. Lever test is the most sensitive test (Figure 8) ***(Zina et al., 2016).***

Figure 7: The grind test: The examiner applies axial compression along the plane of the metacarpal bone and rotates the thumb metacarpal base ***(Zina et al., 2016***).

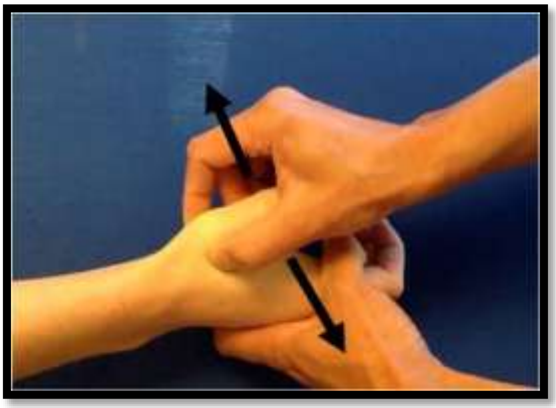

Figure 8: The lever test :The examiner puts his or her thumb and index finger on both sides of the thumb basal joint and levers the first metacarpal joint radially and ulnarly to their endpoints at the basal joint ***(Zina et al., 2016)***.

Several patient-reported outcome measures (PROMs) have been developed for assessing function in patients with rheumatic diseases. The Australian/Canadian OA Hand Index (AUSCAN) and the Functional Index of hand OA (FIHOA) were developed specifically to assess hand function in hand OA ***(Rikke et al., 2010)***.

Some items in FIHOA depend on other factors than a disablity or affection of hand function such as clench your fist and accept a handshake. The handshake could depend on other factors other than a disability. The AUSCAN has two additional scales relating to pain and stiffness that is why it may be preferable ***(Rikke et al., 2010)***.

Grip and pinch strengths have been widely used in clinical practice as an objective index for measuring functionality of the upper limbs. It is very important to measure grip and pinch strength accurately because the measurement can serve as an indicator of the progress of treatment and rehabilitation of the diseased hand ***(Shin et al., 2012)***. Patients with early CMC OA typically have weakness on the affected hand when pinching, grasping, or twisting objects ***(Ladd et al., 2013).***

Pinch positions were defined using the American Society for Hand Therapists guidelines. Tip pinch was defined as holding the sensor on the distal portion of the pads of the thumb and index finger. Palmer (tripod) pinch was defined as holding the sensor on the pad of the thumb opposed by the index and long fingers. Lateral (key) pinch was defined as holding the sensor between the pad of the thumb and the radial aspect of the index finger, located approximately near the proximal interphalangeal joint (Figure 9) ***(Villafane &Valdes, 2014).***

Mean values of grip for individuals with hand CMC OA has been reported to range from 8.63 to 14 kg and key pinch is 5 kg**.** It has also been reported that individuals with hand OA possess only 57%–58% of normal grip strength ***(Kjeken et al., 2005).***

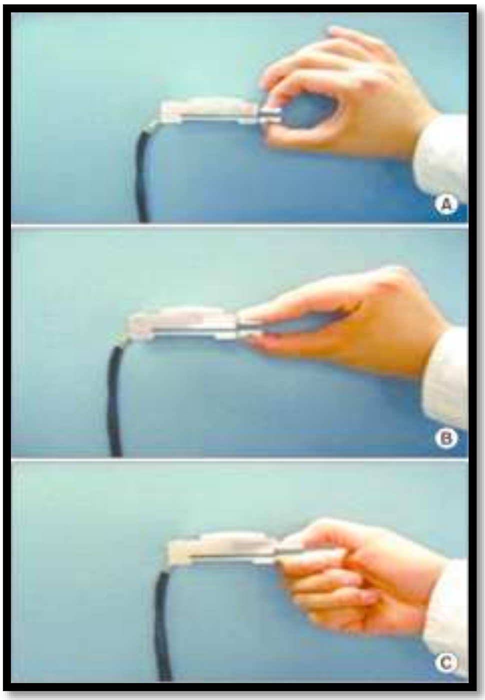

Figure 9: A: Tip pinch, B: palmer pinch & C: lateral pinch ***(Halilaj et al., 2014)*** .

Decreased key pinch had the strongest association with CMC OA, as a 20% loss in strength was associated with approximately a 10% increase in likelihood of diagnosis. Several studies have implied that the key pinch position is associated with translation of the trapezium and instability at the CMC joint and increased mechanical load on the trapezium. This theory supports that the kinematics of the CMC joint during key pinch may be most affected by early weakness and instability ***(Halilaj et al., 2014)***.

Differential Diagnosis:

The differential diagnosis should include other causes of radial-sided wrist pain. The presentation of CMC OA can mimic that of a ganglion, ruptured tendon, carpal fracture, carpal instability, De Quervain's tenosynovitis, trigger thumb, a torn ulnar collateral ligament and tendinitis of the flexor carpi radialis ***(Cook & Lalonde, 2008).***

Findings that suggest an alternative diagnosis include deformity of the back of the wrist, limited or painful movement of the wrist, swelling or hematoma, a positive result on the Finklestein test, locking during flexion, ligamentous laxity and lack of palpable flexor or extensor tendons when assessing range of motion ***(Batra & Kanvinde, 2007).***

Rheumatological diseases such as rheumatoid arthritis and psoriatic arthritis considered also a differential diagnosis to CMC joint OA, Rheumatoid arthritis is associated with prominent, prolonged (>1 hour) morning stiffness, swollen &warm joints. Radiographic findings include bone erosion (eg, periarticular osteopenia or marginal erosions of bone) rather than formation. Laboratory findings that further differentiate rheumatoid arthritis from osteoarthritis including systemic inflammation (elevated erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP] level), positive serologies (rheumatoid factor [RF] or anti–cyclic citrullinated peptide [anti-CCP] antibodies) and elevated white blood cell (WBC) count**.**

Investigations:

1-Plain X-ray:

The most widely used classification system for radiographic staging of CMC OA was first presented by Eaton and Littler which classify it into four stages (stage 1 demonstrated no joint space narrowing, stage 2: mild narrowing while stage 3: marked narrowing in joint space, stage 4 : as stage 3 with scaphotrapezial joint involvement. The Eaton &litter classification is the most common system employed to determine the stage of the disease and assess the severity to decide the plan of treatment ***(Eaton & Littler, 1973)***.

Figure 10: Stages (A) I Thumb CMC OA demonstrates normal joint contours with no evidence of joint space narrowing or sclerosis, (B) II mild joint space narrowing with mild sclerosis and/or subchondral cyst-like changes with osteophytes and/or periarticular debris measuring<2 mm, (C) III joint space narrowing with marked sclerosis and subchondral cyst like changes with osteophytes and/or periarticular debris measuring>2 mm, and (D) IV as III findings with additional joint space narrowing, sclerosis, and subchondral cyst-like changes involving the ST joint ***(Eaton & Littler, 1973***).

Patients with Stage I osteoarthritis are likely to benefit from non-operative interventions, and treatment of those with Stage II to IV osteoarthritis depends on the severity of patient symptoms and their functional demands.

Different surgical strategies done for various stages of osteoarthritis ***(Wajon et al., 2009).***

Clinically, there is often an inconsistent relationship between the severity of symptoms perceived by the patient and the degree of osteoarthritis noted on radiographic imaging ***(VanHeest & Kallemeier, 2008).***

2-Cross-sectional imaging:

While radiography has been the primary imaging modality for assessing thumb CMC joint pathology, cross-sectional imaging, including musculoskeletal ultrasound (MSUS), magnetic resonance (MR) imaging, and computed tomography (CT), may provide additional valuable tridimensional diagnostic information in pre and postoperative evaluation of the thumb CMC joint anatomy and pathology, including OA ***(Kroon et al., 2018).***

US may be used to identify and evaluate both the integrity and thickness of the AOL and other first CMC joint ligaments and to evaluate joint effusion and synovitis ***(Chiavaras, 2010)***. Marginal osteophytes can also be seen on US imaging. Studies found little evidence correlating ultrasound finding with clinical severity (pain & functional impairment) and treatment response to injection therapy in CMC OA. Also there is no association between inflammatory features in ultrasound of CMC OA and the improvement of pain and function in the follow up ***(Ermurat et al., 2018).***

Figure 11: US of thumb CMC OA, the arrow is to osteophyte ***(Ermurat et al., 2018).***

CT and MRI imaging usually done if surgical management is decided. CT imaging has higher reliability and detection rate for scaphotrapezial (ST) joint OA compared with radiography, which may influence treatment selection and surgical planning as surgical treatment selection depends on the presence of pathology in the ST joint ***(Ermurat et al., 2018).***

Figure 12: Eaton stages on CT scan a:stage 1, b: stage 2, c :stage 3 and d : stage 4 ***(Melville et al., 2014)***

MRI imaging is used mainly to visualize the osseous and ligamentous anatomy ***(Hirschmann et al., 2013).*** MRI is of special value to provide information about ligament status for joint-preserving surgical techniques for first CMC osteoarthritis, such as ligament reconstruction. In particular, patients presenting with stage I or II osteoarthritis, according to Eaton and Littler, could benefit from ligament reconstruction when symptomatic clinical instability and MR imaging show that isolated ligament ruptures coincide ***(Hirschmann et al., 2013).*** Also, patients with increased palmar tilt and planned osteotomy of metacarpal bone could possibly benefit more when the ligaments of the CMC are intact. MRI can provide information regarding possible subluxation tendencies prior to prosthetic replacement of the carpometacarpal joint of the thumb ***(Zhang et al., 2013)***.

Figure 13: MRI of thumb CMC joint ***(Roger & Kerr, 2016).***

Treatment of thumb carpometacarpal OA

Treatment of thumb CMC OA:

1- **Conservative treatment.**
2- **Surgical treatment.**

1-Conservative Treatments for Thumb CMC Joint:

The aim of conservative treatment is to restore thumb functionality, including pain relief, stability, mobility, and strength (grip & pinch). So, there is an improvement in all hand functions and performance of activities of daily living (***Villafane et al., 2017).***

The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) acknowledge that Optimal management of CMC joint OA requires multidisciplinary approach include Pharmacologic agents, splinting (orthosis), education and training in ergonomic principles and joint-protection technique instruction, exercises, thermal agents, manual therapy, adaptive equipment devices ***(Bertozzi et al., 2015).***

1-Pharmacologic agents:

Osteoarthritis symptoms, primarily pain, may be helped by certain pharmacologic agents used in the treatment of osteoarthritis include the following:

A-Acetaminophen

Acetaminophen used in patients with mild-to-moderate osteoarthritis symptoms who do not derive sufficient relief from non-pharmacologic measures. Acetaminophen is the drug of choice for patients who have a documented hypersensitivity to aspirin or NSAIDs, who have a history of upper gastrointestinal (GI) tract disease, or who are on anticoagulants. Maximum dose of acetaminophen containing products is not to exceed a cumulative dose of 3.25 g/day ***(Alfredo et al., 2017).***

In patients with renal impairment (creatine clearance ≤30 mL/min) longer dosing intervals and reduced total dose may be warranted and it should be also used with caution with any type of liver disease ***(Atkinson et al., 2014).***

B-Nonsteroidal anti-inflammatory drugs (NSAIDs):

NSAIDs have analgesic, anti-inflammatory effect. They are used to relieve osteoarthritis pain when the clinical response to acetaminophen is unsatisfactory. The mechanism of action is inhibition of cyclooxygenase (COX)-1 and COX-2, resulting in reduced synthesis of prostaglandins and thromboxanes. Other mechanisms may also exist, such as inhibition of leukotriene synthesis, lysosomal enzyme release, lipoxygenase activity, neutrophil aggregation, and various cell-membrane functions ***(Gibofsky et al., 2014).***

NSAIDs can cause stomach upset, cardiovascular problems, bleeding problems, and liver and kidney damage. Topical NSAIDs have fewer side effects ***(Gibofsky, 2014).***

C-Capsaicin

Is one of a topical analgesic of choice in osteoarthritis. Derived from plants of the Solanaceae family, it may render skin and joints insensitive to pain by depleting substance P in peripheral sensory neurons. Capsaicin must be used for at least 2 weeks for the full effects to be appreciated ***(Christiansen, 2015)***.

D-Duloxetine (Cymbalta)

Which is a Potent inhibitor of neuronal serotonin and norepinephrine reuptake. Normally used as an antidepressant, this medication is also approved to treat chronic pain, including osteoarthritis pain in severe cases. Dose is 30 mg/day initially for 1 week to allow for therapy adjustment. The target dosage is 60 mg/day PO; not to exceed 60 mg/day. Avoid use it in patients with renal Impairment (GFR <30 mL/min) and chronic liver disease or liver cirrhosis (***Christiansen, 2015)***.

E-Chondroitin:

Is a specific compound that is considered a type of mucopolysaccharide. These are actually a key component of the various joint structures within the body.

It plays a major role in creating considerable osmotic pressure that expands the matrix and places the collagen network under tension. It provides cartilage with resistance and elasticity allowing it to resist tensile stresses during various loading conditions. The exogenous administration of chondroitin sulphate has been suggested to act against OA by three main mechanisms; anabolic effect by stimulating the production of extracellular matrix of cartilage, suppression of inflammatory mediators and inhibition of cartilage degeneration. Studies have demonstrated that chondroitin play chondroprotective role by counteracting the action of IL-1b (a factor that induces articular inflammation and cartilage degeneration), also it reduce the resorptive activity in subchondral bone ***(Vasiliadis & Tsikopoulos, 2017).***

F- Glucosamine:

Is a key compound that is used within the body to produce new cartilage. It may affect the cytokine-mediated pathways regulating inflammation, cartilage degradation, and immune responses. It appears to have immune-modulatory activity inhibiting the expression and/or activity of catabolic enzymes such as phospholipase A2 and MMPs. Also, it reduces or regulates interleukin-1 (IL-1) levels in synovial fluid and inhibits the actions of catabolic enzymes in the joint ***(Vasiliadis & Tsikopoulos, 2017).***

G- Oral collagen:

Oral collagen can be obtained from a product naturally or processed using enzymes. It has the potential to reduce the progression of OA by inducing an oral tolerance in the arthritic patient. Oral tolerance is a state of immune suppression in response to the oral administration of an antigen, the production of T-cells and cytokines, and suppressed serum antibody responses ***(Woo et al., 2017).***

2-Splinting:

Splinting is the most commonly reported treatment for the thumb CMC OA. The rationale behind the splinting is that it provides external support to the CMC joint avoiding subluxation of the joint and compensatory movements as well as preserving the first joint space. Splinting used to prevent subluxation in those with grades 1 and 2 thumb CMC OA. However, those with more advanced OA (grades 3 and 4) didn't show any effect on preventing subluxation ***(Duong et al., 2017)***.

Figure 14: Thumb spica splint ***(Duong et al., 2017)***.

Patients instructed to wear it during hand use (when the muscles contract and attempt to increase in bulk, the pressure is directed inward to stabilize the first metacarpal bone, maximizing the immobilization effect of the splint and decrease pain to those patients who developed pain during these activities ***(Aebischer et al., 2016).***

Limitation of using splints is that individuals cannot accomplish daily tasks with these splints. Additionally, prolonged use of the splint is not desirable due to the likely disuse atrophy of the thenar muscles. Also it is well known that prolonged immobilization decreases muscle strength, which in turn decreases joint stability which is a contributing factor to the progression of the pathological imbalance at the joint ***(Duong et al., 2017).***

3-Education and training in ergonomic principles and Joint protection principles:

Education and training in ergonomic principles and pacing of activity, formerly included in the recommendations under the term ‘joint protection’, is an important aspect of management, and has been shown to be efficacious ***(Hill et al., 2016).*** The term ‘joint protection’, although still often used, was viewed by the task force as an outdated concept, implying that one should protect the joints and refrain from using them ***(Kloppenburg et al., 2018).***

A. Respect the pain: Stopping the activities before reaching the point of discomfort or pain.
B. Balance Activity: By resting 10 minutes during a difficult activity.
C. Use larger, stronger joints for activities to distribute the weight over non-involved or stronger joints**.**

For example, a patient with thumb CMC joint OA could be taught to avoid tasks that require significant thumb force such as lateral-pinch activities, and trained to perform the task with larger joints. Patients can be provided with adaptive equipment, such as a built-up pencil grip to assist with writing or a wall-mounted jar opener ***(Villafane et al., 2016).***

4-Exercise:

Weakness of thumb musculature leads to an imbalance of forces between the thumb and fingers. This imbalance can cause abnormal wear on the trapezium and metacarpal joints. Exercises to strengthen the thumb muscles can reduce this imbalance and also increase muscle-related stability around the thumb CMC joint and lead to improvement in strength, pain, and hand function. Frequency for active range of motion exercises for thumb CMC joint OA of 10–15 repetitions, 2 times per day.

Doing the following stretching and strengthening exercises twice a day can help in maintaining hand flexibility and stability of the thumb joint ***(Kjeken et al., 2015).***

A-Place and Hold:

This exercise trains the muscles to hold the thumb steady and not allow the middle joint to collapse. Touching the tip of the thumb to the tip of index finger to form a circle ('O' shape). Support the middle joint of your thumb with the opposite hand so that the thumb joint is slightly bent. Pinching the fingertips together lightly and remove the supporting hand while maintaining the circle position. Gradually increase the force of the pinch until it feels as though the circle will collapse and the thumb will lose its bent position.

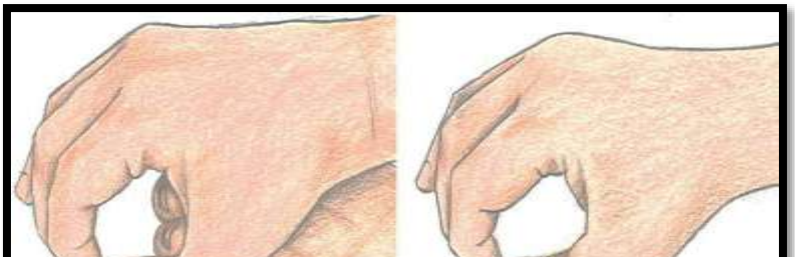

Figure 15: Place and hold exercise ***(Kjeken et al., 2015).***

B-Radial abduction stretch:

Resting the hand on a table, palm down. Spread the thumb away from hand, opening the palm wide. Holding for 5–10 seconds, and then return to the starting position (repeated for a total of 10 stretches).

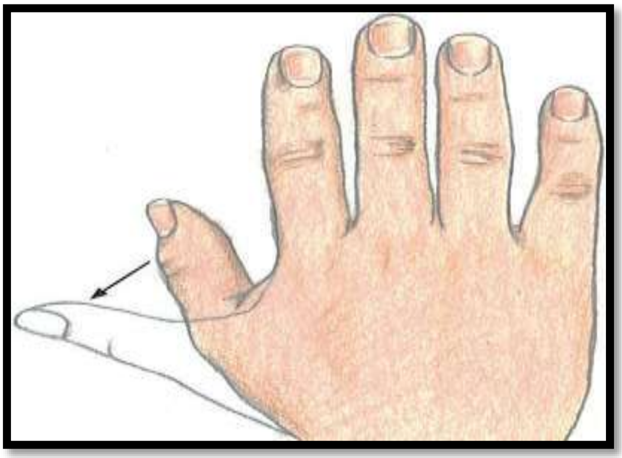

Figure 16: Radial abduction stretch exercise ***(Kjeken et al., 2015).***

C- "C" exercise:

Placing the thumb and fingers in the shape of the letter C, as grasping a tennis ball. Holding this position, tensing the muscles lightly, for 5–10 seconds, and then relax (repeated for 10 times) ***(Kjeken et al., 2015).***

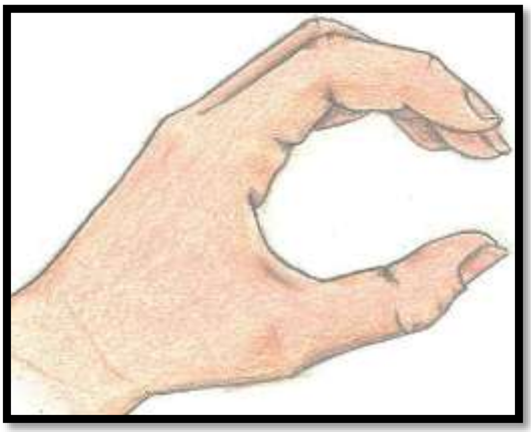

Figure 17: C-Exercise ***(Kjeken et al., 2015).***

5-Thermal physical agent modalities:

Categories of thermal physical agents include superficial thermal agents & deep thermal agents**.** Superficial thermal agents such as hydrotherapy, cryotherapy (cold packs, ice), hot packs, paraffin, water, infrared. Deep thermal agents such as therapeutic ultrasound, short-wave diathermy (***Villafane et al., 2013).***

Although there is only weak-to-moderate evidence to support the use of thermal, some patients may experience pain relief with the application of ice or heat. Some patients with high levels of pain may feel relief with cryotherapy, others prefer paraffin baths and heat wraps that can also provide relief ***((Villafane et al., 2013)***.

6-Manual therapy:

Manual therapy describes a type of clinical physical therapy technique. It uses skilled and sophisticated hands-on movements to diagnose and treat soft tissues and joint structures. It most commonly include manipulation of joints, muscles, and tissues in order to diagnose biomechanical injuries, reduce pain, and promote proper healing (Figure 18) ***(Kjeken et al., 2015).***

Manual therapy effectively addresses the mechanical, biochemical, and psychological qualities of the treatment process. It expected to see better range of motion in stiffer joints and pain relief by improving how brain processes pain signals throught specific muscle movements ***(Otero et al., 2012)***. Manual muscle release to reduce muscle tension, pain, or contracture to improve muscle balance ***(Kjeken et al., 2015).***

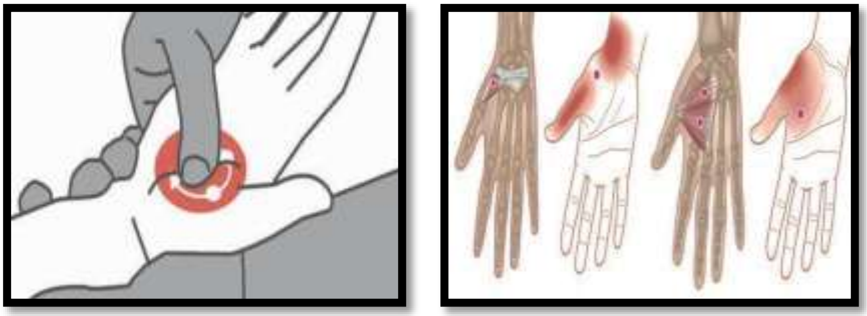

Figure 18: Manual muscle release for APL and OP

Other manual techniques used for thumb pain are transverse friction massage at the joint capsule and the tendon insertions, and joint mobilizations ***(Otero et al., 2012).***

7-Assistive devices:

The use of assistive devices is an important and commonly used strategy to improve patient's self-management. There are a variety of small aids that are available to assist the patients in maintaining independence completing daily activities as shown in Figures from 19 to 24 ***(Kloppenburg et al., 2018).***

Figure 19: Jar twisters : to help opening tight jars.

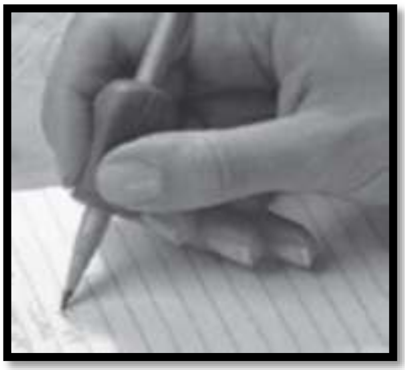

Figure 20: Pen grips: to support griping or writing.

Figure 21: Key turners: if case of difficulty turning key in door.

Figure 22: Wide grip cutlery: If patient find it difficult or painful to hold cutlery.

Figure 23: Tap turners: Attach onto taps to make them easier to turn on and off.

Figure 24: Plug pulls: Assists grip in case of difficulty removing plug.

8- Intra articular injection:

Intra-articular injection is safe treatment modality, which offers drug application in the proximity of damaged intra-articular structures. However, treatment with direct drug injections into the joint has multiple limitations. It should be remembered that intra-articular injections must not be carried out in the presence of uncontrolled coagulopathy, patients who are on anticoagulant therapy, hypersensitivity to the active ingredient or during general or topical infection ***(Szubstarski et al., 2017)***.

A-corticosteroids:

Intra-articular steroid injection (IASI) is an effective, widely used and recommended treatment for individuals with symptomatic osteoarthritis. It has short term pain relief effect lasting up to 3–4 weeks. The local anti-inflammatory effects of corticosteroid injections are hypothesized to decrease inflammation and consequently relieve the symptoms of OA ***(Kloppenburg et al., 2015).***

The EULAR 2007 recommendations advocate the use of intra-articular injection of corticosteroids to alleviate painful flares of OA, especially in thumb-base OA ***(Zhang et al., 2007).*** However, this recommendation was not supported by the 2012 American College of Rheumatology (ACR) recommendations for the management of OA, which recommends not using intra-articular corticosteroids in thumb-base OA ***(Hochberg et al., 2012).*** EULAR recommendation in 2018 could not confirm a beneficial effect of intra-articular glucocorticoids over placebo in patients with thumb base OA ***(Kloppenburg et al., 2018)***

Mechanism of action

Corticosteroids have both anti-inflammatory and immunosuppressive effect, but their mechanism of action is complex. Corticosteroids act directly on nuclear steroid receptors and interrupt the inflammatory and immune cascade at several levels. By this means, they reduce vascular permeability and inhibit accumulation of inflammatory cells, phagocytosis, production of neutrophil superoxide, metalloprotease, and metalloprotease activator, and prevent the synthesis and secretion of several inflammatory mediators such as prostaglandin and leukotrienes ***(Egemen et al., 2014).***

Potential local side effects of corticosteroid injections include infection, subcutaneous atrophy, injury to the joint tissues, particularly with repeated injections, Thinning of joint cartilage, Weakening of the ligaments of the joint through inhibitory effect on collagen synthesis and cross linking of its fibers, Irritation of the nerves caused by the needle during an injection or by the medication and allergic reaction to corticosteroids (***Cole et al., 2016).***

Post steroid injection flare generally occurs in the 24 to 36 hours following injection, and it is thought to be due to crystal-induced synovitis caused by precipitation of preservatives in the injected suspension. Fat atrophy and skin hypopigmentation are more likely at superficial injection site occurring between 6 and 12 weeks after injection, and are in some cases permanent ***(Nichols, 2009).***

Corticosteroids also associated with a range of potentially systemic dangerous side effects, including increased risk of infection, weight gain, gastrointestinal ulcers and bleeding, osteoporosis, elevated blood pressure and blood glucose levels and eye problems, including cataracts and glaucoma ***(Bhagra et al., 2013).***

B- Hyalouronic acid:

Hyaluronic acid (HA) or "hyaluronan", or "sodium hyaluronate preparation" is a polysaccharide with a molecular weight (between 100 kilodaltons (kDa) and 10 megadaltons (MDa). It has been already approved by Food and Drug Administration (FDA) for osteoarthritis (OA) ***(Abate et al., 2014).***

HA is a naturally occurring glycosaminoglycan and a component of synovial fluid (SF) and cartilage matrix. Synovial cells, fibroblasts and chondrocytes synthesize HA and secrete it into the joint. Characterized by its high hydration ratio and high viscoelasticity. HA enhances viscosity and elastic nature of SF. SF with normal HA concentration acts as a viscous lubricant during slow joint movements and as an elastic shock absorber during rapid joint movements ***(Kesmezacar et al., 2014***). Its viscosity is dependent on the length of the polymer fibers (molecular weight, expressed in Daltons). The higher the molecular weight the more time the product takes to be degraded ***(Kaux et al., 2015).***

Various low molecular weight (LMWHA), moderate molecular weight (MMWHA), and high molecular weight (HMWHA) hyaluronic acid injections are now available in the market for viscosupplementation. Low molecular weight: MW < 1MDa, medium molecular weight: 1MDa - 2MDa and High molecular weight: MW > 2MDa ***(Bongkotphet et al., 2009).***

There is conflicting biologic evidence to support use of LMWHA, MMWHA or HMWHA. Based on in-vitro studies, the optimum molecular weight of HA to have a high binding affinity and to stimulate production of endogenous HA is 0.5-4 million Dalton, which supports the use of LMWHA and MMWHA formulations. Conversely, others postulated that HMWHA would restore the rheological properties of synovial fluid by increasing viscoelasticity ***(Shewale et al., 2017).*** The low molecular weight preparations can achieve maximum concentration into the joint and are thought to reduce inflammation, however, they present lower viscoelasticity than native HA. High molecular weight preparations result in a better increase in fluid retention into the joint ***(Migliore et al., 2010***).

So, in small joints such as thumb CMC joint, LMWHA is better than HMWHA as LMWHA acts as anti-inflammatory reducing pain and it has the optimum weight to stimulate endogenous HA and no need to the high viscoelasticity of the HMWHA ***(Shewale et al., 2017).*** That intra-articular hyaluronic acid injections seemed to be the better alternative because of a superior long-lasting effect of at least 6 months. Side effects of HA injection are the side effect of injection itself which are infection, injury to the joint tissues, particularly with repeated injections ***(Fuchs et al., 2006).***

Mechanism of action:

In OA, both the molecular weight and the concentration of HA decrease. The IA injection of HA is thought to restore normal viscoelastic properties of the pathologically altered synovial fluid, which explains the term of the approach: “viscosupplementation”. It is thought that HA restores the lubricating and shock-absorbing effects of SF. Moreover HA also have disease modifying effects, such as reduction of synovial inflammation, protection against cartilage erosion and promotion of intra-articular HA production (***Kesmezacar et al., 2014)***. HA functions through chondroprotective, anti –inflammatory and analgesic mechanisms ***(Axe et al., 2013)***.

1- Chondroprotection effect:

Intra articular hyaluronic acid (IAHA) has been shown to reduce chondrocyte apoptosis, while increasing chondrocyte proliferation (***Brun et al., 2012)***. There are multiple observed effects of IA-HA treatment that produce chondroprotection, many of which are results of HA binding to cluster of differentiation 44 (CD44) receptors. HA binding to CD44 inhibits interleukin (IL- 1β) expression, leading to a decline in matrix metalloproteinase (MMP) -1, 2, 3, 9, and 13 productions. This inhibition of various MMPs impedes catabolic enzyme activity within the joint cartilage ***(Axe et al., 2013)***.

2-Anti-inflammatory effect:

i) Role of HA–CD44 Receptor Binding:

The primary receptor of the HA ligand is the CD44 receptor. The affinity of HA to CD44 receptors is dependent on the molecular size of HA; increased avidity of HA binding to CD44 is correlated with an increase in the size of the polysaccharide chain, as larger HA oligosaccharides are capable of decreasing dissociation through divalent binding. Expression of the CD44 receptor is responsible for the maintenance of cartilage homeostasis, and the principal function of CD44 is to bind and internalize exogenous HA ***(Lesley et al., 2000).*** Through CD44 receptor binding, HMWHA down regulates the expression of IL-8, IL-33, MMPs, proteoglycans and PGE2 and suppresses pro-inflammatory cytokine production mediated by nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) ***(Altman et al., 2018)***.

ii) Role of HA–TLR Receptor Binding:

High molecular weight HA can inhibit TLR-2 signaling, demonstrating the anti-inflammatory ability of HA therapy. Also, HA bind to TLR-4 & TLR-2 and decreased TNF-α, interleukin-1β (IL-1β), interleukin-17 (IL-17), matrix metalloprotease-13 (MMP-13), and inducible nitric oxide synthase (iNOS) levels ***(Altman et al., 2018).***

Role of HA–ICAM Receptor Binding

Lipopolysaccharide (LPS) stimulate production of TNFα, IL-1β, and IL-6. HMWHA suppresses LPS stimulated production of pro-inflammatory cytokines via ICAM-1 through down regulation of NF-κB and I-κB ***(Litwiniuk et al., 2016)***.

3-Analgesic effect:

HA has indirect and direct analgesic activity within the joints. Indirect effect is via the anti-inflammatory properties of HA. Direct effect is by the direct inhibition of nociceptors and the decreased synthesis of bradykinin and substance P. Also, intra-articular HA application causes analgesia by increasing the elastoviscosity of the intercellular matrix of soft tissues around the joint that reduces the force transmitted during joint movements ***(Akgun et al., 2014).***

C-Platelet rich plasma:

Platelet-rich plasma (PRP) is an autologous blood product that contains an increased concentration of platelets and emerged as a safe treatment modality to accelerate healing of musculoskeletal injuries ***(Moraes et al., 2013).*** Platelets contain more than 5000 proteins, of which more than 300 are released upon activation (***Loibl et al., 2016*****).**

PRP prepared by drawing 20 ml of whole blood anti-coagulated with citrate dextrose. Tubes are centrifuged at 1500 rpm for 15 min then the plasma separated from the RBCs and centrifuged again at 3500 rpm for 10 min. The plasma obtained is of high concentration of platelets 5-9 folds greater than the normal found in the whole blood. The top portion of plasma drawn up with the syringe and 1ml was injected directly to the joint ***(Marzocco et al., 2015)***.

PRP varies in the relative concentration of platelets ranging from 2.5 to 5 times as compared to blood. PRP appears to be more effective than autologous blood due to higher concentration of growth factors per unit volume and has been proved in one clinical trial to be better than autologous blood. However preparation of platelet concentrates requires specialized equipment, relatively more expensive and time consuming ***(Jindal et al., 2013).***

Currently, the FDA approval is awaiting, however, such injections are considered exception in use, as they are prepared from patient's own blood. The FDA has no objection in the application of PRP in both medical and surgical management (***Dhurat & Sukesh, 2016).***

<u>Mechanism of action:</u>

The mechanism of action has been attributed to the degranulation of α granules of platelets releasing growth factors such as: Platelet derived growth factor, transforming growth factor β, epithelial growth factor, vascular derived endothelial growth factor, hepatocyte growth factor and insulin like growth factor. These growth factors play a major role in tissue healing and regeneration in areas of degeneration ***(Jindal et al., 2013)***.

PRP injection into joints can modify the biological microenvironment inside the joint. Thereby, PRP affects local and infiltrating cells, mainly synovial cells, endothelial cells, immune cells, and cellular components of cartilage and bone (***Andia & Maffulli, 2013***). Ultimately, it is believed to reduce the inflammatory process and alter the joint homeostasis of anabolism and catabolism in cartilage ***(Scotti et al., 2016)***. It decreases catabolism, improves anabolism and promotes chondral remodelling. Higher amounts of collagen II and prostaglandin (PG) synthesis, increasing chondrocyte proliferation and production of matrix have been documented ***(Pereira et al., 2013)***.

The apoptotic pathway of osteoarthritic chondrocytes is influenced as insulin-like growth factor 1 (IGF-1) in PRP may down regulate the expression of programmed cell death 5 (PDCD5) ***(Yin et al., 2013).***

An overall down modulation of the joint inflammation can explain the well-documented pain reduction. This could be through the regulation of nuclear factor kappa B and cyclooxygenase-2 (COX-2), the principal actors of inflammatory cascade ***(Bendinelli et al., 2010).***

Safety of PRP injection:

It showed not only effectiveness but safety as it was derived from the autologous blood drown at the time of treatment, so no risk of allergy, disease transfer or systemic effect as the PRP was injected locally. PRP is unlike the isolated growth factors, it is derived from the whole blood and acted with its physiologic properties where the balance between the proliferative and inhibitory agents existed. PRP was not mutagenic, no risk of metaplasia or tumor formation ***(Yuan et al., 2013).***

The studies reported that the incidence of patients with side effects of platelet-rich therapy was low, with an average of 2% to 5%. The majority of reported side effects were local tenderness and pain, which lasted for less than 48 hours ***(Filardo, 2010).***

To sum up, studies indicate that PRP is promising for relieving pain, improving knee function and quality of life (***Zhu et al.,2013)***. Very little is known about the implications for PRP treatment of OA in other joints such as CMC OA ***(Gormeli et al., 2015).***

D- Stem cell treatment:

The fluid inside the joint contains mesenchymal stem cells (MSCs) which can differentiate into chondrocytes, but new deposited cartilage is very fragile and can be destroyed by applying a minimal amount of stress on the joint. Additionally there is only a limited quantity of MSCs in the joint available to differentiate and the process of differentiation is slow ***(Gupta et al., 2012)***. Stem cell therapy is still under trial but recently it show promising results in knee OA (***Lamo-Espinosa et al., 2016).***

The aim in using stem cells is to support the self-healing process of the knee joint cartilage which results in relief from OA symptoms. This treatment should be used in conjunction with additional treatment in order to improve patients' functional status and quality of life (***(Gupta et al., 2012***). Along with their immunomodulatory and differentiation potential, MSCs have been shown to express essential cytokines including Transforming Growth Factor beta (TGFβ), Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGF) and an array of bioactive molecules that stimulate local tissue repair. These trophic factors, and the direct cell to cell contact between MSCs and chondrocytes, have been observed to influence chondrogenic differentiation and cartilage matrix formation ***(Windt et al, 2015***).

MSCs are harvested from the patient to be treated thus ensuring that the patient's immune system will not reject the cells ***(Wolfstadt et al., 2014)***.The delivery of MSCs for the treatment of OA could be achieved via either surgical implantation or an intra-articular injection ***(Pers et al., 2015, JO et al., 2014).***

It has been reported significant improvement of symptoms and function in CMC joint OA with MSCs injection ***(Murphy et al., 2017).*** But, Several issues that have to be considered that are likely to make it financially less attractive. Firstly, this treatment is not for affordable by everyone (***Diekman & Guilak, 2013)***. Furthermore it is likely that more than one treatment session would be required, meaning a greater investment of time and money ***(Orth et al., 2014).***

2-Surgical treatment of carpometacarpal osteoarthritis:

While thumb base OA is primarily treated with non-surgical modalities, surgical treatment may be indicated for those whose debilitating symptoms persist (pain, decreased function, instability) despite adequate conservative management. Thumb base OA is one of the most common causes of hand surgery ***(Taccardo et al., 2013).***

Surgical management, however, is associated with a number of complications, including tendon rupture, sensory changes and wound infection ***(Wajon et al., 2015)***. Multiple procedures for thumb CMC osteoarthritis have been described vary with the stage of OA ***(Berger and Meals, 2015)***.

Stage I disease:

- ***Ligament reconstruction***

Stabilization of the CMCJ by isolated reconstruction of the palmar beak ligament (deep anterior oblique ligament) is performed only in stage I disease ***(Wajon et al., 2015)***.

- ***Metacarpal extension osteotomy***

The rationale of this procedure is to compensate for the incompetence of the beak ligament, which increases the volar shear stresses and leads to cartilage breakdown volarly ***(Tropet et al., 2012).***

<u>Stage II and III disease:</u>

- ***Excisional arthroplasty (trapeziectomy)***

Trapeziectomy appears to offer no benefit over tendon interposition or ligament reconstruction.

- ***Trapeziectomy and interpositional arthroplasty***

Although these procedures initially appeared to considerably decrease thumb shortening, it was subsequently noted that, over time, thumb length was lost due to the metacarpal settling into the interpositional material, and that no significant improvement in function was actually obtained (***Tropet et al., 2012).***

- ***Trapeziectomy combined with ligament reconstruction and tendon interposition***

LRTI arthroplasty more consistently improved pinch strength, increased grip strength endurance, and restored thumb web space than did silicone implant arthroplasty.

- ***Partial trapeziectomy***

This would improve stability and thumb strength and lead to less proximal migration of the thumb ray (***Tropet et al., 2012).***

- ***Prosthetic CMCJ arthroplasty***

The aim of the procedure, besides eliminating painful articulating surfaces, is to establish a stable force column during pinching and gripping (***Batra & Kanvinde, 2007)***.

- ***Arthrodesis***

It is indicated for people with stage III and IV OA. It provides stability, strength and pain relief (***Batra& Kanvinde, 2007***).

Stage IV disease:

In the presence of stage IV disease, possible procedures include arthrodesis, trapeziectomy, trapeziectomy with LRTI, interpositional arthroplasties and CMC and ST joint replacements (***Tropet et al., 2012).***.

PATIENTS AND METHODS

This study was conducted on thirty patients with clinical evidence of thumb CMC OA. Patients were collected from outpatient clinic of Physical medicine, Rheumatology and Rehabilitation department, Ain Shams university hospitals.

Inclusion Criteria of our study:

- Age ≥ 40 years old.
- Pain at CMC joint of the thumb.
- Localized tenderness over the thumb CMC joint.
- Decrease pinch and grip strength of affected hand.
- Decrease hand function assessed by AUSCAN score.
- Radiographic evidence of CMC joint OA as defined and graded according to Eaton & Littler classification.

Exclusion criteria of our study:

- Inflammatory arthritides.
- Fibromyalgia.
- Degenerative arthritis of other joints of affected hand and wrist.
- Any other hand condition that is likely to contribute to pain at thumb CMC joint (examples : Scaphoid fracture, Carpal tunnel syndrome, De Quervain tendonitis, tenosynovitis of thumb (trigger finger), joint infection, avascular necrosis of scaphoid, pain

referred from neck and pain following trauma or surgery).

- Intra-articular injection in affected joint in the past year.
- Patients with coagulation disorders or on anticoagulants.

Patients underwent the following:

1- Full medical history taking with particular attention to:

- Age, sex and occupation.
- Duration of the disease.
- Dominant extremity (right or left) and which extremity is affected (dominant or non-dominant)
- History of smoking, medical history, lifestyle history (sports, especially sports involving risks for the thumb and domestic work) and occupational factors. Family history of CMC OA or at least one relative with CMC OA and thumb trauma history.
- History of pain at first CMC joint with tasks such as twisting, open a jar, turning a key in lock, writing, holding a cup, history of weakness when pinching or grasping objects, swelling, morning stiffness lasting less than 30 minutes and stiffness at the joint after period of immobility and history of other joints affection.

2- Full clinical examination with particular attention to:

- General examination and examination of other joints: to exclude rheumatological diseases and to diagnose OA in other joints.
- Local examination:
- Inspection for presence or absence of a dorso-radial prominence of the thumb metacarpal base secondary to subluxation due to ligamentous laxity and the pull of the adductor pollicis longus muscle or osteophyte formation and signs of local inflammation if present e.g swelling and redness.
- Palpation for localized tenderness over the joint, and this was reproduced with thumb and finger pressure applied directly over the affected joint. (Grade1: mild tenderness, grade 2: mild tenderness with grimace, grade 3: severe tenderness with withdrawal, grade 4: severe tenderness & withdrawal from non noxious stimuli (***Cipriano, 2010)***
- ROM:

Active and passive range of motion of the CMC joint were measured using a Goniometer to diagnose stiffness of the joint.

Normal range of motion of thumb:

- Flexion:60-70 degree
- Extension: 0 degree
- Abduction:70-80 degree
- Adduction:0 degree
- CMC joint Flexion: 15 degree
- CMC joint extension:20 degree
- CMC joint abduction:60 degree

- Provocative tests for CMC osteoarthritis of thumb :
- Grind test:

Axial compression was applied along the plane of the thumb carpometacarpal joint and the thumb base was rotated simultaneously. The test is positive if it produces pain in the joint ***(Glickel, 2001)***.

Figure 25: Grind test

- Lever test:

It is performed by grasping the first metacarpal just distal to the basal joint and shucking back and forth in radial and ulnar direction, the test is positive if it produces pain on palpation. The value of lever test is that the maneuver is similar to palpation but with the added manipulation of the CMC joint. The lever test and joint palpation had both high sensitivity and high specificity. The grind test had the lower sensitivity & higher specificity ***(Zina et al., 2016).***

Figure 26: Lever test

3-Clinical assessment scales:

- VAS visual analogue scale for pain assessment at rest:

Patients were asked to rank the pain from 0 to 10 (0 representing no pain and 10 representing the worst pain).

- Australian Canadian Osteoarthritis Hand Index (AUSCAN): AUSCAN score was used for assessment of hand function in patient with hand OA.

- Content: There are 3 subscales: pain, stiffness and function.

- Number of items: There are 15 items divided into 3 subscales: pain (5 items), stiffness (1 item) and function (9 items).

- Response options/scale:

Pain subscale: Patients were asked about each item of pain (at rest and during activites: Gripping, Lifting, Turning & Squeezing) to rank the pain from 0 to 4 (0 for no pain, 1 for mild pain, 2 for moderate pain, 3 for severe pain and 4 for extreme pain).

Stiffness subscale: Patients were asked about stiffness in CMC joint after first wakening in the morning and grade it from 0 to 4 (0 for none up to 4 for extreme stiffness).

Function subscale: Patients were asked about the difficulty in doing each item and grade it from 0 to 4 (0 for no difficulty, 1 for mild, 2 for moderate, 3 for severe and 4 for extreme difficulty).

The sum score of each of the 0–4 item scores within each subscale (pain range 0–20, stiffness 0–4, physical function 0–36). AUSCAN score is used as numerical follow up score before and after interventions ***(Bellamy et al., 2002***).

For the items that may be mainly gender specific to females such as fastening jewellery was replaced it by asking the males about fastening the buckle of the watch. Also wringing out wash clothes was replaced by asking about difficulty in doing other squeezing tasks ***(Bellamy et al., 2002***).

AUSCAN Questionnaire Content:

Pain Subscale

- At rest
- Gripping
- Lifting
- Turning
- Squeezing

Stiffness Subscale

- After first wakening in the morning

Physical Function Subscale

- Turning taps.
- Turning a round doorknob or handle.
- Doing up buttons.
- Fastening jewellery.

- Opening a new jar.
- Carrying a full pot with one hand.
- Peeling vegetables/fruits.
- Picking up large heavy objects.
- Wringing out wash clothes.

4-Grip and lateral pinch strength assessment:

Pain free grip and pinch strength were measured using a digital hand dynamometer (Camry, model: EH101). Participants refrained from taking any analgesic or anti-inflammatory drugs for approximately 24 hours before testing. The participants performed a standardized warm up that consisted of two to three preliminary trials of the test procedure for familiarization with the procedure and instrument used during the procedure. The subjects were given the opportunity to handle the hand dynamometer before measurement recording.

The test was performed in the sitting position with the shoulder of tested arm adducted to the side, the elbow flexed at 90°, and the forearm and wrist were set in neutral position (***Villafane et al., 2013***). Patients were instructed to squeeze the dynamometer as firmly as possible without eliciting pain. Pain was assessed using the verbal analogue scale. If the subject reported pain during testing, the test was re-administered with instruction to stop squeezing before the onset of pain (***Villafane et al., 2013***).

The testing protocol consisted of three pain-free maximal contractions with a 1-min pause between measurements. These three values were averaged and recorded. The measurements were taken in the following order: grip and pinch strength. Grip and pinch strength measurement were expressed in kilograms. In our study we measured lateral pinch. The patients were asked to hold the sensor between the pad of the thumb and the radial aspect of the index finger ***(Villafañe &Valdes, 2014).***

Figure 27: Grip strength

Figure 28: Pinch strength

Table 2: Normal Values of Grip Strength for Males (in kg): ***(Gaikwad et al., 2016)***

AGE	Weak	Normal	Strong
40-44	< 35.5	35.5-55.3	> 55.3
45-49	< 34.7	34.7-54.5	> 54.5
50-54	< 32.9	32.9-50.7	> 50.7
55-59	< 30.7	30.7-48.5	> 48.5
60-64	< 30.2	30.2-48.0	> 48.0

Table 3: Normal Values of Grip Strength for Females (in kg): ***(Gaikwad et al., 2016)***

AGE	Weak	Normal	Strong
40-44	< 18.9	18.9-32.7	> 32.7
45-49	< 18.6	18.6-32.4	> 32.4
50-54	< 18.1	18.1-31.9	> 31.9
55-59	< 17.7	17.7-31.5	> 31.5
60-64	< 17.2	17.2-31.0	> 31.0

Table 4: Normal value for lateral pinch strength in (Kg): ***(Shim et al., 2013)***

AGE	Male		Female	
	Right	Left	Right	Left
40-49	9.8±1.3	9±1	6.5±1.1	6.1±0.9
50-59	8.8± 2	8.7±1.5	6.4±1.2	6±1.3
60-69	8.7±1.3	8.2±1.1	6.6 ±1.1	5.8±0.9

5-Laboratory investigation:

- Complete blood counts (CBC) by using coulter counter.
- Erythrocyte Sedimentation Rate (ESR) by the Westergren method.

6-Radiological assessment:

Plain x ray was done to detect and grade CMC joint OA according to Eaton & Littler classification that describes four stages**:**

Eaton-Littler stage I

Thumb CMC OA demonstrates normal joint contours with no evidence of joint space narrowing or sclerosis; however, there may be mild widening of the joint space secondary to synovitis, effusion, or ligamentous laxity.

Eaton-Littler stage II

Thumb CMC OA demonstrates mild joint space narrowing with mild sclerosis and/or subchondral cyst-like changes with osteophytes and/or periarticular debris measuring$<$2 mm.

Eaton-Littler stage III

Thumb CMC OA shows pronounced joint space narrowing with marked sclerosis and subchondral cyst like changes with osteophytes and/or periarticular debris measuring$>$2 mm.

Eaton-Littler stage IV

Consists of Eaton-Littler stage III findings with additional joint space narrowing, sclerosis, and subchondral cyst-like changes involving the scaphotrapezial (ST) joint ***(Eaton & Little, 1973)***.

Figure 29: Stage 1

Figure 30: Stage 2

Figure 31: Stage 3

Figure 32: Stage 4

7-Treatment schedule:

The patients were randomly divided into two groups:

Group 1: Fifteen patients were injected intra-articularly with Platelet-Rich Plasma (PRP).

Tools used for preparing the PRP for injection:

1. Syringe 20 ml.
2. 70% alcohol swabs for skin disinfection.
3. Gauze or cotton-wool ball to be applied over puncture site.
4. Tourniquet.
5. Anticoagulant as anticoagulant citrate dextrose solution (ACD).
6. Falcon tubes 50 ml.
7. Safety box (puncture-resistant sharps container).

Figure 33: PRP machine used in the study

A PRP device (Centurion Scientific, C2 series) is used for increasing the concentration of platelets in the blood plasma. We take in the patient's whole blood anti-coagulated with citrate dextrose followed by centrifugation to raise the concentration of extracted plasma and to separate the PRP from platelet-poor plasma (PPP).

20 ml of whole blood were drawn from the patients. Tubes are centrifuged at 1500 rpm for 15 min then the plasma separated from the RBCs and centrifuged again at 3500 rpm for 10 min. The plasma obtained is of high concentration of platelets 5-9 folds greater than the normal found in the whole blood. The top portion of plasma were drawn up with the syringe and 1ml was injected directly to the joint ***(Marzocco et al., 2015)***.

Group 2: Fifteen patients were injected intra-articularly with 1 ml hyaluronic acid (hyaluronic acid sodium salt) [Hyalgan manufactured by Fidia Farmaceutici S.P.A- Italy] with a molecular weight (730,000 daltons).

Figure 34: Hyaluronic acid sodium salt (Hylgan)

Figure 35: Hyaluronic acid injection

<u>How to inject thumb CMC joint:</u>

The basal joint is nestled within the anatomic snuffbox at the radial aspect of the wrist. The boundaries of the three-sided snuffbox are easily palpable by placing the thumb in a fully abducted position. It is bounded on the palmar side by the tendons of the abductor pollicis longus (APL) and extensor pollicis brevis (EPB), and dorsally by the tendon of the extensor pollicis longus (EPL). The distal edge of the radial styloid forms the proximal border. The apex of the schematic snuffbox isosceles triangle forms the distal border. The needle was inserted just proximal to the first metacarpal on the extensor surface. Care must be taken to avoid the radial artery and the extensor pollicis tendons. The needle, a 25 gauge, should fall into the joint space.

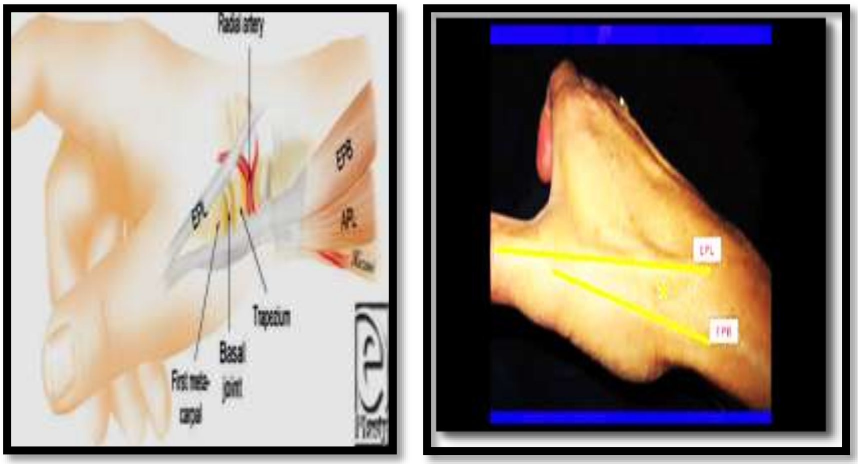

Figure 36: CMC joint injection site ***(Netter and Hansen, 2003)***

After injection, the use of NSAIDs were prohibited. Patients were instructed to limit their hand use for 48 hrs and continue the use of acetaminophen for pain control. Moreover, patients were advised to apply ice on the site of injection for 48 hrs.

8-Follow up assessment:

All patients were assessed again after 4 weeks, and after 12 weeks from the injections by:

- Local examination for tenderness of the affected thumb.
- Visual analog scale (VAS) for pain assessment.
- AUSCAN functional hand index.
- Grip and pinch strength measurement by hand dynamometer.

9- Statistical analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric and median with inter-quartile range (IQR) when their distribution found non parametric. Also qualitative variables were presented as number and percentages.

The comparison between groups regarding qualitative data was done by using ***Chi-square test.***

The comparison between two groups with quantitative data and parametric distribution were done by using ***Independent t-test*** while with non -parametric data were done by using ***Mann-Whitney test***. Also, the comparison between more than two groups with quantitative data and non-parametric distribution were done by using ***Kruskall-Wallis test.***

The comparison between more than two paired groups with quantitative data and parametric distribution were done by using ***Repeated Measures ANOVA test.***

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

P > 0.05: Non significant (NS)
P < 0.05: Significant (S)
P < 0.01: Highly significant (HS)

.

Results

This study was conducted on thirty patients with thumb CMC joint OA. Twenty six patients were females (86.7%), and four were males (13.3%). Their ages ranged from 40 to 70 years (mean: 52.77 ± 8.59). The duration of symptoms ranged from 2 to 12 years (mean: 6.60 ± 2.94). Eighteen patients were housewives (60.0%), 10 patients were manual workers (33.3%) and 2 patients were clerks. Twenty nine of them were right handed and one patient left handed. Dominant extremity affection in 27 patients (90.0%) and non-dominant hand affection in 3 patients (10%) (Table 5).

Table 5: Demographic data of all patients.

		No. = 30
Age	Mean±SD	52.77 ± 8.59
	Range	40 – 70
Sex	Females Males	26 (86.7%) 4 (13.3%)
Manual worker(work-related)	House wife Worker Clerk	18 (60.0%) 10 (33.3%) 2 (6.7%)
Handedness	Right Left	29 (96.7%) 1 (3.3%)
Dominant or Non dominant hand affection	Dominant Non dominant	27 (90.0%) 3 (10.0%)
Duration of symptoms	Mean±SD Range	6.60 ± 2.94 2 – 12

Regarding Eaton and litter classification by plain x ray, four patients were G1, 11 patients were G2, 13 patients were G3 and 2 patients were G4. ESR ranged from 5-20 mean 16.2± 4.31.

Table 6: Results of radiological assessment and ESR in all patients:

		No. = 30
Plain x ray grade	G1	4 (13.3%)
	G2	11 (36.7%)
	G3	13 (43.3%)
	G4	2 (6.7%)
ESR	Mean±SD	16.2 ± 4.31
	Range	5 – 20

Patients were randomly divided into two groups, group I: 15 patients were injected with PRP while group II was injected with hyaluronic acid.

Comparison between both groups:

Comparison between both groups shows that there was no statistically significant difference between both groups regarding age, sex, job distribution, duration of symptoms, handness and dominant hand affection (Table 7, figure 37,38 & 39).

Table 7: Comparison between both groups regarding demographic data of included patients:

		Group I	Group II	Test value	P-value	Sig.
		No. = 15	No. = 15			
Age (years)	Mean±SD	49.93 ± 7.95	55.60 ± 8.50	1.886•	0.070	NS
	Range	40 – 70	40 – 70			
Sex	Females	13 (86.7%)	13 (86.7%)	0.000*	1.000	NS
	Males	2 (13.3%)	2 (13.3%)			
Job distribution	House wife	11(73.3%)	7(46.7%)	3.289*	0.193	NS
	Worker	4(26.7%)	6(40.0%)			
	Clerk	0(0.0%)	2(13.3%)			
Handedness	Right	14 (93.3%)	15 (100.0%)	1.034*	0.309	NS
	Left	1 (6.7%)	0 (0.0%)			
Dominant or Non dominant hand affection	Dominant	15 (100.0%)	12 (80.0%)	3.333*	0.068	NS
	Non dominant	0(0.0%)	3 (20.0%)			
Duration of symptoms (years)	Mean±SD	6.53 ± 2.61	6.67 ± 3.33	0.122•	0.904	NS
	Range	3 – 12	2 – 12			

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant *:Chi-square test

•: Independent t-test *N.S (non-significant)

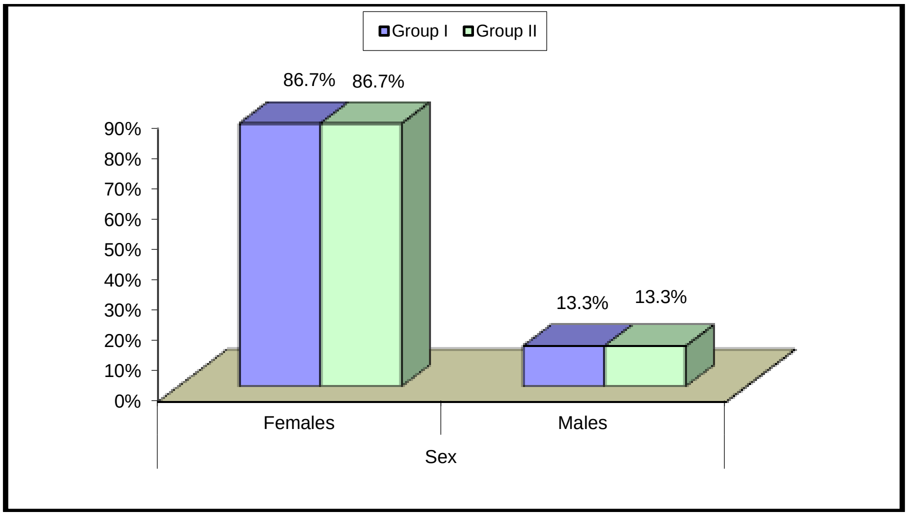

Figure 37: Sex distribution in both studied groups.

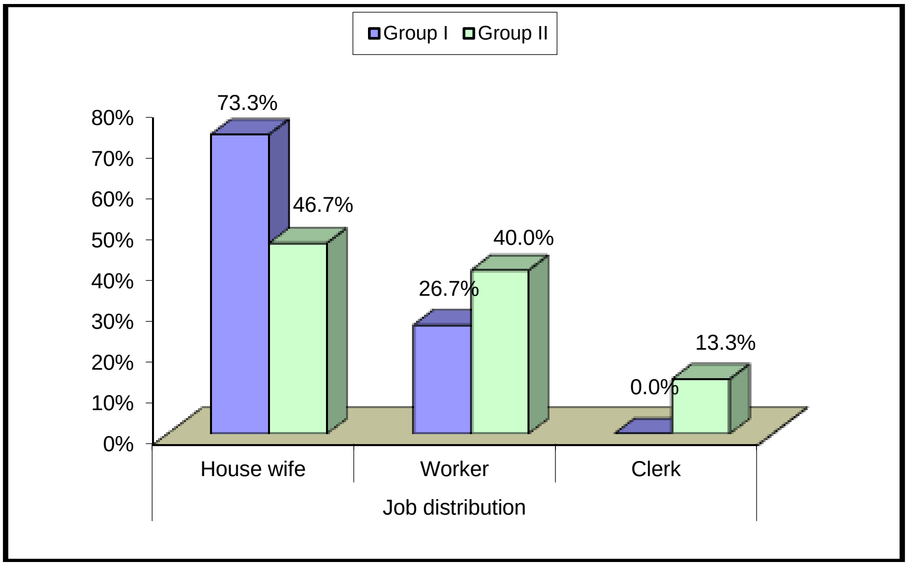

Figure 38: Distribution of type of job in studied groups.

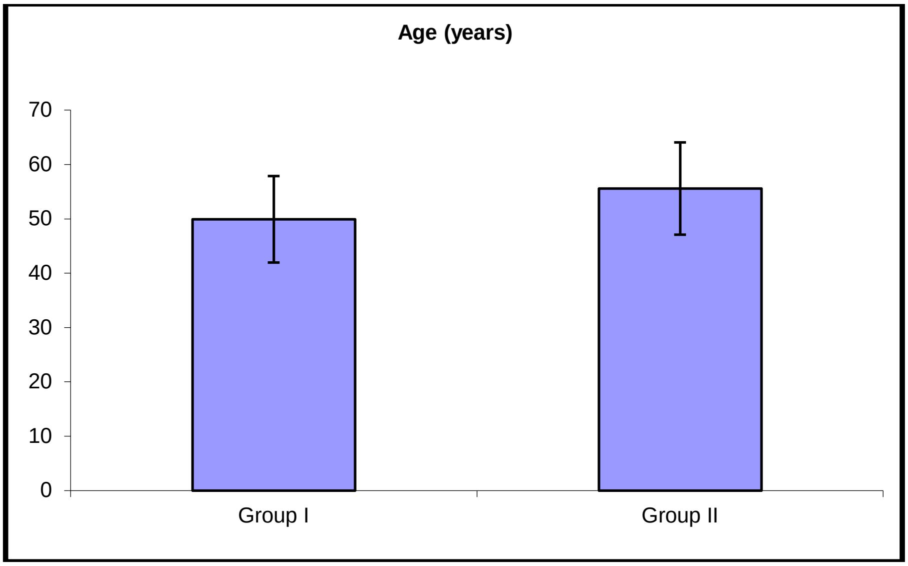

Figure 39: Age distribution in studied groups.

A- <u>Local Examination:</u>

1- On palpation according to tenderness score there was no statistically significant difference between both groups regarding tenderness before injection (Table 8, figure 40).

Table 8: Comparison between both groups regarding tenderness grading before injection:

		Group I		Group II		Test value*	P-value	Sig.
		No.	%	No.	%			
Tenderness grading before injection	G1	5	33.3%	3	20.0%	1.288	0.605	NS
	G2	7	46.7%	10	66.7%			
	G3	3	20.0%	2	13.3%			

P-value>0.05: Non significant; P-value<0.05: Significant;
P-value<0.01: highly significant *:Chi-square test

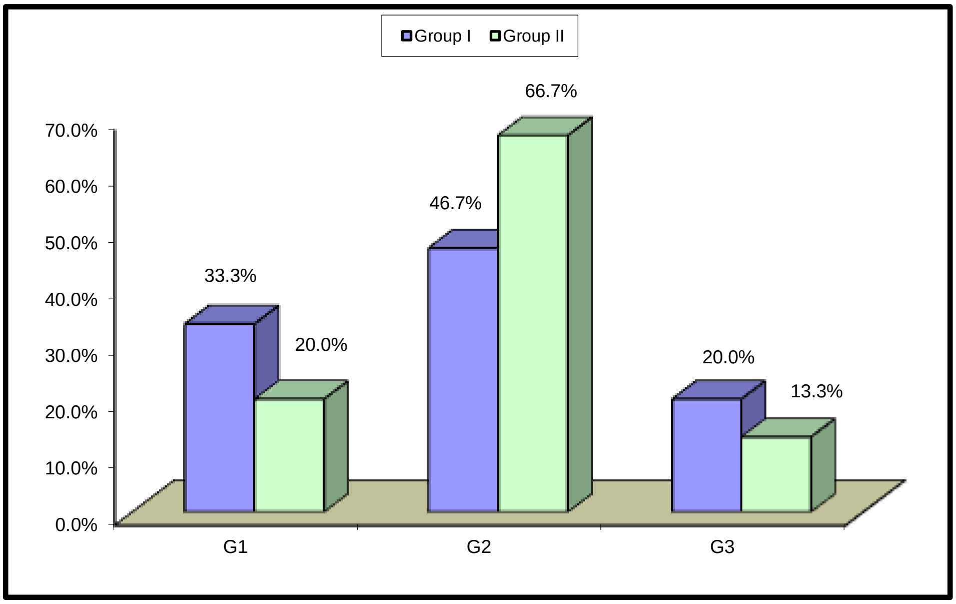

Figure 40: Comparison between the studied groups regarding tenderness grading before injection

2- Provocative tests (Grind test & Lever test):

Grind test was positive in all patients of both groups (100%). In group I, lever test was positive in 7 patients (46.7%) & negative in 8 patients (53.3%). While, in group II lever test was positive in 10 patients (66.7%) & negative in 5 patients (33.3%). Upon comparison there was no statistically significant difference between both groups regarding both provocative tests results (table 9, figure 41).

Table (9): Comparison between both groups regarding results of provocative tests before injection:

		Group I		Group II		Test value*	P-value	Sig.
		No.	%	No.	%			
Grind test	Negative	0	0.0%	0	0.0%	NA	NA	NA
	Positive	15	100.0%	15	100.0%			
Lever test	Negative	8	53.3%	5	33.3%	1.222	0.269	NS
	Positive	7	46.7%	10	66.7%			

P-value>0.05: Non significant; P-value<0.05: Significant;
P-value<0.01: highly significant *:Chi-square test
NA (Not Applicable).

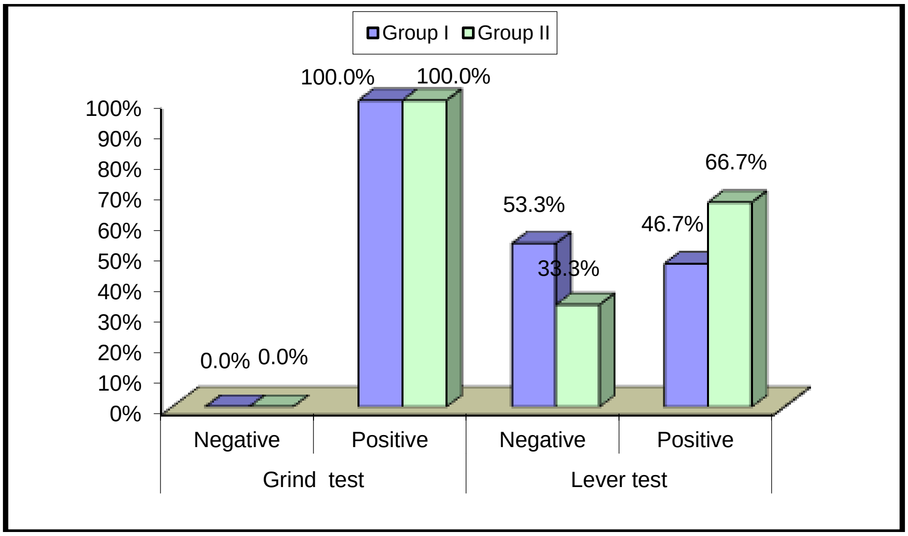

Figure 41: Provocative tests.

3- Range of motion (ROM): Active and passive range of motion of the CMC joint measured using a Goniometer showed full ranges in all patients of both groups.

B- Clinical assessment scales:

1- Australian Canadian Osteoarthritis Hand Index (AUSCAN):

AUSCAN score was used for assessment of hand function in patients with hand OA. There are 3 subscales: pain, stiffness and function.

In group I, pain subscore ranged from 10 to 18 (mean: 11.93 ± 2.69), stiffness subscore (73.3 % of patients were grade 0 & 26.7% of them were grade 1), functional subscore ranged from 18 to 30 (mean: 23.40 ± 2.97) and total score ranged from 28 to 46 (mean 35.27 ± 4.88). In group II, pain subscale ranged from 6 to 20 (mean: 10.27 ± 4.17), stiffness subscore (80% of patients grade 0, 13.3% of them were grade 1 & 6.7% of them grade 2), functional subscore ranged from 18 to 28 (mean: 23.27 ± 3.39), total score ranged from 24 to 48 (mean: 33.53 ± 7.30).

Comparison showed that there was no statistically significant difference between the studied groups regarding pain, stiffness, functional subscore and total score before injection (Table 10).

Table (10): Comparison between both groups regarding findings of AUSCAN score before injection:

		Group I No. = 15	Group II No. = 15	T-value	P-value	Sig.
Pain subscale before injection	Mean±SD	11.93 ± 2.69	10.27 ± 4.17	1.302•	0.203	NS
	Range	10 – 18	6 – 20			
Stiffness subscore before injection	0	11 (73.3%)	12 (80.0%)	1.710*	0.425	NS
	1	4 (26.7%)	2 (13.3%)			
	2	0 (0.0%)	1 (6.7%)			
Functional subscore before injection	Mean±SD	23.40 ± 2.97	23.27 ± 3.39	0.115•	0.910	NS
	Range	18 – 30	18 – 28			
Total score before injection	Mean±SD	35.27 ± 4.88	33.53 ± 7.30	0.765•	0.451	NS
	Range	28 – 46	24 – 48			

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant

*:Chi-square test; •: Independent t-test

2- Pain assessment using VAS:

In group I: VAS before injection ranged from 6 to 9 (mean: 7.53 ± 1.13), In group II: VAS before injection ranged from 5 to 9 (mean: 6.60 ± 1.45). Comparison showed that there was no statistically significant difference between the two studied groups regarding VAS before injection (table 11).

Table (11): Comparison between both groups regarding VAS before injection:

		Group I	Group II	Test value	P-value	Sig.
		No. = 15	**No. = 15**			
VAS before Injection	Mean±SD	7.53 ± 1.13	6.60 ± 1.45	1.966	0.059	NS
	Range	6 – 9	5 – 9			

3-Grip and lateral pinch strength assessment:

In group I: Grip strength measurement before injection ranged from 13 to 19 (mean 16.27 ± 1.53). In group II: Grip strength measurement before injection ranged from 11 to 21 (mean: 15.60 ± 2.95).

In group I: Pinch strength measurement before injection ranged from 2 to 6 (mean: 4.2 ± 1.32), In group II: Pinch strength measurement before injection ranged from 3 to 5 (mean: 3.53 ± 0.64). Comparison showed that there was no statistically significant difference between the studied groups regarding grip and pinch strength before injection (table 12).

Table (12): Comparison between both groups regarding grip and pinch strength assessment before injection:

		group I No. = 15	Group II No. = 15	Test value•	P-value	Sig.
Grip strength before injection	Mean±SD	16.27 ± 1.53	15.60 ± 2.95	0.777	0.444	NS
	Range	13 – 19	11 – 21			
Pinch strength before injection	Mean±SD	4.2 ± 1.32	3.53 ± 0.64	1.760	0.089	NS
	Range	2 – 6	3 – 5			

C- <u>Radiological assessment:</u>

Plain x- ray was done to detect and grade CMC joint OA according to Eaton & Littler classification that describes four stages (G1, 2, 3 & 4):

- **In group I:** Two patients were G1 (13.3%), six patients were G2 (40%), six patients were G3 (40%) and one patient was G4 (6.7%).
- **In group II:** Two patients were G1 (13.3%), five patients were G2 (33.3%), seven patients were G3 (46.7%) and one patient was G4 (6.7%) (figure 42).

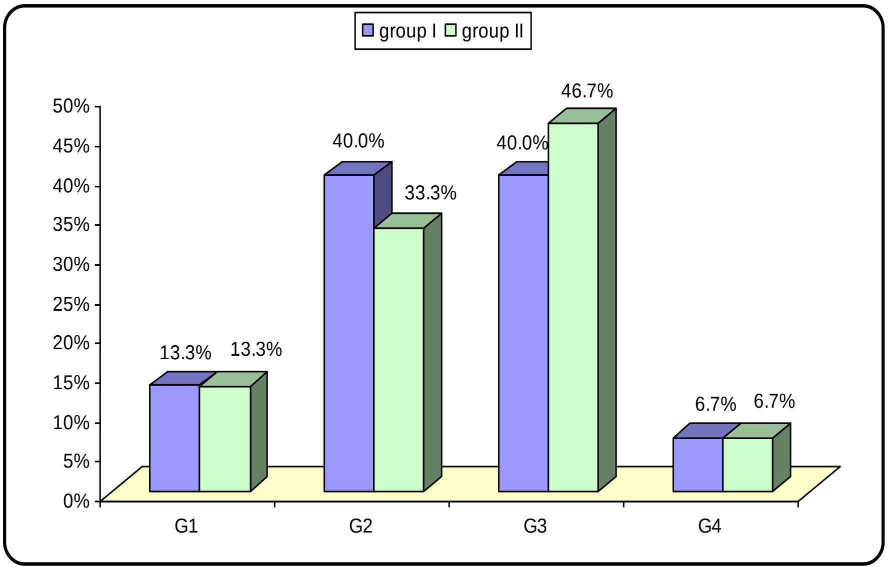

Figure 42: Plain X ray grading in both groups

Comparison showed that there was no statistically significant difference found between both groups regarding plain X- ray grading of CMC joint OA (table 13).

Table (13): Comparison between both groups regarding plain X -ray grading CMC joint OA**:**

		Group I No. = 15	Group 2 No. = 15	Test value	P-value	Sig.
Plain x ray grade	G1	2 (13.3%)	2 (13.3%)	0.624*	0.891	NS
	G2	6 (40.0%)	5 (33.3%)			
	G3	6 (40.0%)	7 (46.7%)			
	G4	1 (6.7%)	1 (6.7%)			

D- <u>Laboratory assessment:</u>

In group 1: ESR ranged from 5 to 20 (mean 15.5 ± 4.98) and 80% of patient had a normal CBC, while 20% had mild anemia. In group 2: ESR range from 10 to 20 (mean 16.53 ± 3.70) and 86.7 % of patients had a normal CBC, while 13.3% of patients had mild anemia. Comparison showed that there was no statistically significant difference found between both groups regarding ESR results (Table 14).

Table (14): Comparison between both groups regarding ESR:

		Group I No. = 15	Group 2 No. = 15	Test value	P-value	Sig
ESR	Mean±SD	15.5 ± 4.98	16.53 ± 3.70	0.085•	0.933	NS
	Range	5 – 20	10 – 20			

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant •: Independent t-test

Previous results clarified that both groups had similar clinical, laboratory and radiological findings before starting treatment.

All patients after assessment received intra-articular injection in CMC joint. Group 1 received PRP injection and group 2 received hyaluronic acid injection. Follow up assessment was done after 4 weeks and 12 weeks of injection using the outcome measures: tenderness grading, AUSCAN score (pain subscore, stiffness, functional subscore and total score), VAS, grip strength and lateral pinch strength assessment.

Follow up in group 1 (PRP injection) (table 15, figure 43):

Regarding tenderness grading, the patients improved after 4 weeks of injection. Ten of them became G0 (no tenderness), 4 patients became G1 and only one was G2. After 12 weeks of injection, the patients re-developed tenderness and 10 of them became G1 and 5 patients G2.

In comparison, there was a highly significant decrease after 4 weeks (P = 0.000). However, there was no significant difference found between tenderness grading after 12 weeks compared to before injection (P =0.171) .There was a highly significant increase in tenderness grading from 4 weeks to 12 weeks follow up (P= 0.002).

Regarding AUSCAN score, there was a highly statistically significant decrease in pain subscale after 4 weeks and 12 weeks follow up (both P=0.000) compared to before injection. No significant difference was found between 4 and 12 weeks follow up (P= 0.331). There was no statistically significant difference in stiffness subscore before injection, after 4 weeks and 12 weeks.

As regard functional subscore and total score there was a statistically highly significant decrease (improvement) after 4 weeks (P = 0.000) and significant decrease after 12 weeks (P=0.018) .However, there was a highly significant increase (deterioration) from 4 to 12 weeks follow up in functional subscore (P=0.000) and total score (P=0.004) .

The patients reported pain with VAS score of 7.53 ± 1.13 before injection , which is highly significantly decreased to 3.20 ± 0.68 at 4 weeks and to 4.33 ± 0.72 at 12 weeks follow up compared to before injection (both P=0.000). There was a highly significant increase in VAS from 4 to 12 weeks follow up (P= 0.000).

There was a highly statistically significant increase in grip strength after 4 & 12 weeks follow up compared to before injection (both P=0.000), while there was a highly significant decrease from 4 to 12 weeks follow up (P=0.000).

There was a highly statistically significant increase in pinch strength after 4 weeks (P=0.000) and a significant increase after 12 weeks follow up compared to before injection (P=0.019). However, there was a highly significant decrease in pinch strength from 4 to 12 weeks follow up (p=0.000).

Table 15: Follow up of group 1 patients after 4 weeks and 12 weeks of injection:

Group I		Before	After 4 weeks	After 12 Weeks	Test value	P -value	P1	P2	P3
		No. = 15	No. = 15	No. = 15					
Tenderness	G0	0 (0.0%)	10 (66.7%)	0 (0.0%)	33.571*	0.000	0.000	0.171	0.002
	G1	5 (33.3%)	4 (26.7%)	10 (66.7%)					
	G2	7 (46.7%)	1 (6.7%)	5 (33.3%)					
	G3	3 (20.0%)	0 (0.0%)	0 (0.0%)					
Pain subscale	Mean±SD	11.93 ± 2.69	6.73 ± 1.67	6.27 ± 1.16	109.878•	0.000	0.000	0.000	0.331
	Range	10 – 18	4 – 10	5 – 8					
Stiffness Subscore	0	11 (73.3%)	14 (93.3%)	15 (100.0%)	5.850*	0.210	0.339	0.099	0.596
	1	4 (26.7%)	0 (0.0%)	0 (0.0%)					
	2	0 (0.0%)	0 (0.0%)	0 (0.0%)					
Functional Subscore	Mean±SD	23.40 ± 2.97	18.47 ± 2.10	21.27 ± 2.28	34.270•	0.000	0.000	0.018	0.000
	Range	18 – 30	16 – 22	18 – 26					
Total score	Mean±SD	35.27 ± 4.88	25.40 ± 3.25	27.53 ± 2.95	104.039•	0.000	0.000	0.000	0.004
	Range	28 – 46	22 – 33	23 – 34					
Grip strength	Mean±SD	16.27 ± 1.53	18.20 ± 1.52	17.20 ± 1.47	149.742•	0.000	0.000	0.000	0.000
	Range	13 – 19	15 – 21	14 – 20					
Pinch strength	Mean±SD	4.2 ± 1.32	5.93 ± 0.80	4.93 ± 0.80	43.622•	0.000	0.000	0.019	0.000
	Range	2 – 6	4 – 7	3 – 6					
VAS	Mean±SD	7.53 ± 1.13	3.20 ± 0.68	4.33 ± 0.72	190.143•	0.000	0.000	0.000	0.000
	Range	6 – 9	2 – 4	3 – 5					

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant *:Chi-square test; •: Repeated Measure ANOVA test

P1: P-value Before Vs After 4 weeks

P2: P-value Before Vs After 12 weeks

P3: P-value After 4 weeks Vs After 12 weeks

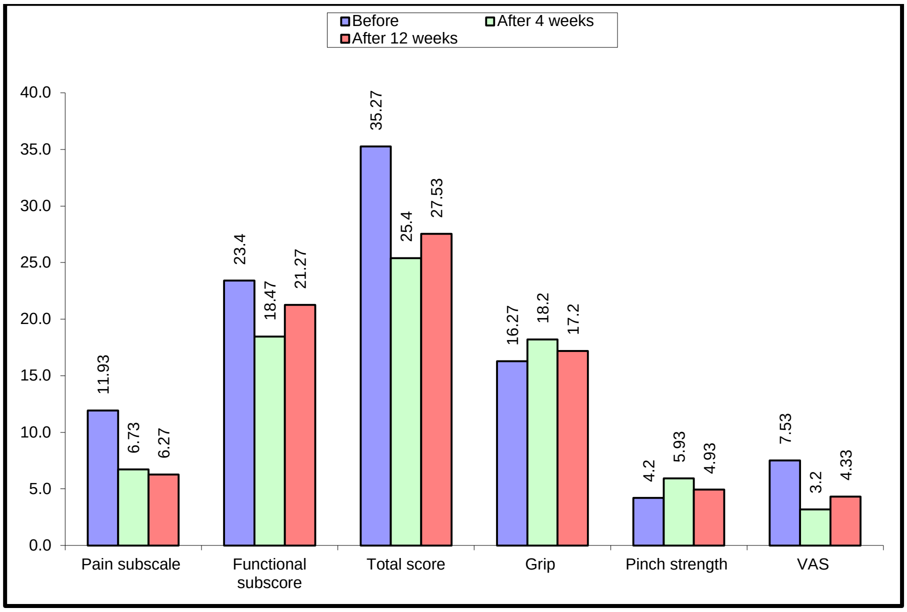

Figure 43: AUSCAN score, VAS, grip and pinch strength assessment before and after PRP injection (group 1)

Follow up in group 2 (hyaluronic acid injection) (table 16, figure 44):

Regarding tenderness grading after 4 weeks of injection, patients improved and 6 of them became G0, 9 patients became G1. After 12 weeks of injection, Patients showed more improvement and 12 of the patients became G0 (no tenderness), 2 were G1 and only one patient G2. Upon comparison, there was a highly statistically significant decrease in tenderness grading after 4 & 12 weeks follow up compared to before injection (P=0.000).

Regarding AUSCAN score, after 4 and 12 weeks follow up, there was no statistically significant difference in stiffness subscore. There was a highly significant decrease (improvement) in pain, functional and total score (P=0.000) after 4 & 12 weeks follow up compared to before injection. Also, there was a highly significant decrease in pain and total score (P=0.000) and significant decrease in functional score from 4 to 12 weeks (P=0.021).

The patients reported pain with VAS score of 6.60± 1.45 before injection , which is highly significantly decreased to 4.00 ± 1.25 at 4 weeks and to 2.47 ± 0.92 at 12 weeks follow up compared to before injection (both P=0.000). Also, there was a highly significant decrease in VAS at 12 weeks compared to at 4 weeks follow up (P= 0.000).

There was a highly statistically significant increase in grip and pinch strength after 4 and 12 weeks compared to before injection (P=0.000). Also, there was a highly significant increase in both from 4 to 12 weeks follow up (P=0.000).

Table 16: Follow up of group 2 patients after 4 weeks and 12 weeks of injection:

Group II		Before	After 4 weeks	After 12 weeks	Test value	P -value	P1	P2	P3
Tenderness	G0	0 (0.0%)	6 (40.0%)	12 (80.0%)	38.688	0.000*	0.000	0.000	0.058
	G1	3 (20.0%)	9 (60.0%)	2 (13.3%)					
	G2	10 (66.7%)	0 (0.0%)	1 (6.7%)					
	G3	2 (13.3%)	0 (0.0%)	0 (0.0%)					
Pain subscale	Mean±SD	10.27 ± 4.17	7.33 ± 3.04	6.07 ± 2.37	63.384	0.000•	0.000	0.000	0.000
	Range	6 – 20	4 – 15	4 – 12					
Stiffness subscore	0	12 (80.0%)	15 (100.0%)	15 (100%)	4.341	0.361*	0.188	0.475	0.596
	1	2 (13.3%)	0 (0.0%)	0 (0.0%)					
	2	1 (6.7%)	0 (0.0%)	0 (0.0%)					
Functional subscore	Mean±SD	23.27 ± 3.39	16.07 ± 2.94	14.33 ± 2.50	126.083	0.000•	0.000	0.000	0.021
	Range	18 – 28	12 – 22	12 – 20					
Total score	Mean±SD	33.53 ± 7.30	23.40 ± 5.70	20.40 ± 4.52	142.947	0.000•	0.000	0.000	0.001
	Range	24 – 48	16 – 37	16 – 32					
Grip strength	Mean±SD	15.60 ± 2.95	23.87 ± 3.89	26.80 ± 4.65	168.474	0.000•	0.000	0.000	0.000
	Range	11 – 21	17 – 30	19 – 33					
Pinch strength	Mean±SD	3.53 ± 0.64	6.20 ± 1.15	7.80 ± 1.21	146.836	0.000•	0.000	0.000	0.000
	Range	3 – 5	5 – 9	6 – 11					
VAS	Mean±SD	6.60 ± 1.45	4.00 ± 1.25	2.47 ± 0.92	219.457	0.000•	0.000	0.000	0.000
	Range	5 – 9	2 – 6	1 – 4					

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant *:Chi-square test; •: Repeated Measure ANOVA test

P1: P-value Before Vs After 4 weeks

P2: P-value Before Vs After 12 weeks

P3: P-value After 4 weeks Vs After 12 weeks

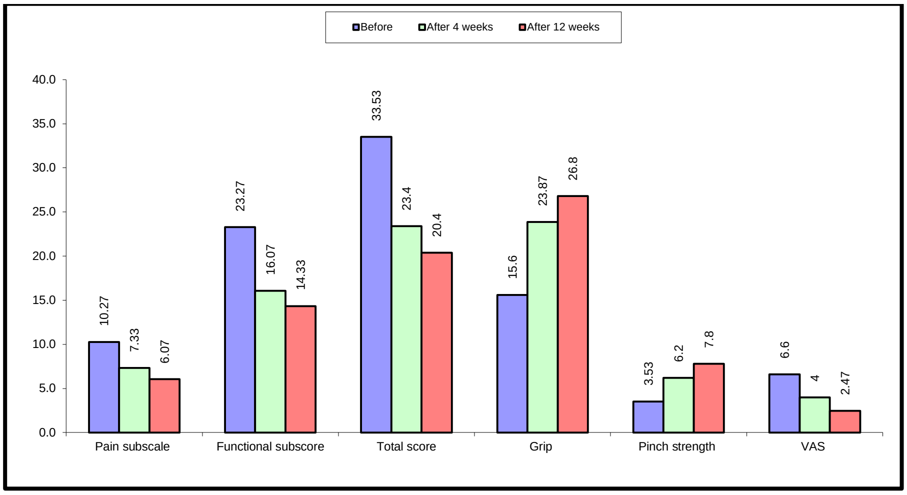

Figure 44: AUSCAN score, VAS, grip and pinch strength assessment before and after HA injection.

Comparison between both groups in follow up assessment:

1- Tenderness grading:

After 4 weeks, both groups showed improvement regarding tenderness grade. Comparison showed that there was no statistically significant difference between them regarding tenderness (P=0.139).

Comparison between both groups after 12 weeks of injection showed that there was highly statistically significant difference between them regarding tenderness grading (P=0.000) (group 2 showed more improvement while group 1 showed deterioration) [table 17, figure 45 & 46].

Table 17: Comparison between both groups regarding tenderness grading after 4 and 12 of injection:

		Group I		Group II		Test value*	P-value	Sig.
		No.	%	No.	%			
Tenderness grade after 4 weeks	G0	10	66.7%	6	40.0%	3.759	0.139	NS
	G1	4	26.7%	9	60.0%			
	G2	1	6.7%	0	0.0%			
	G3	0	0.0%	0	0.0%			
Tenderness grade after 12 weeks	G0	0	0.0%	12	80.0%	21.493	0.000	HS
	G1	10	66.7%	2	13.3%			
	G2	5	33.3%	1	6.7%			
	G3	0	0.0%	0	0.0%			

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant *:Chi-square test

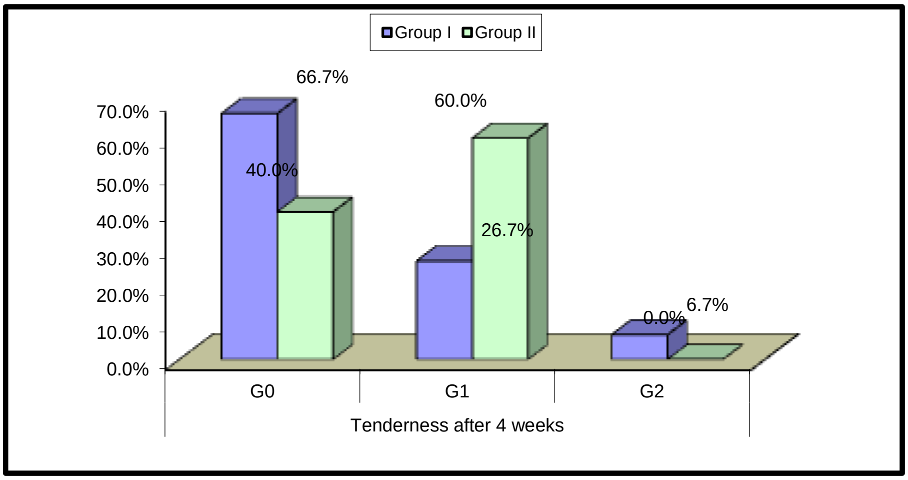

Figure 45: Comparison between both groups regarding tenderness grading after 4 weeks of injection.

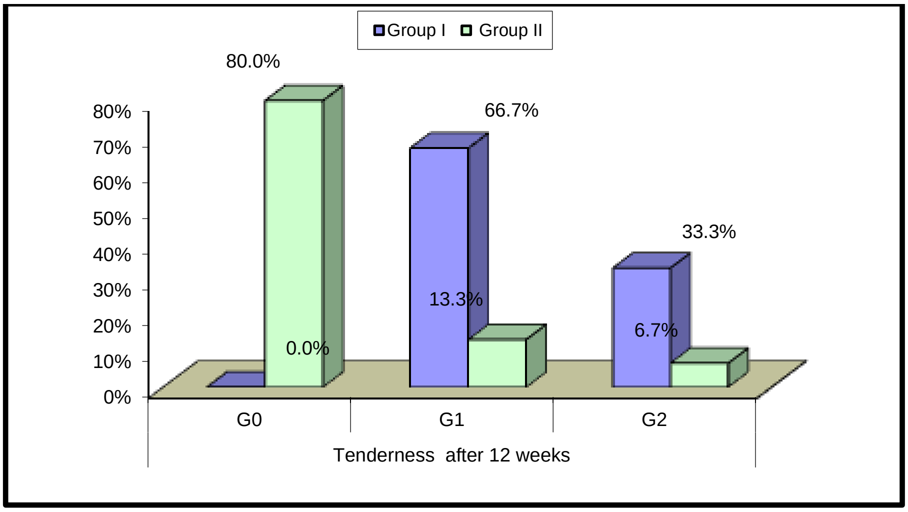

Figure 46: Comparison between both groups regarding tenderness grading after 12 weeks of injection.

2- AUSCAN hand function score:

Upon comparison between both groups regarding pain and stiffness subscore after 4 weeks of injection, there was no statistically significant difference between them. Both groups showed significant improvement. All patients in both groups became grade 0 in stiffness subscore, pain subscale in group I ranged from 4-10 (mean 6.73 ± 1.67) & in group II ranged from 4-15 (mean 7.33 ± 3.04).

In group I, functional subscore ranged from 16 to 22 (mean 18.47 ± 2.10), while in group II the functional subscore ranged from 12 to 22 (mean 16.07 ± 2.94). Total score after 4 weeks in group 1 ranged from 22 to 33 (mean 25.40 ± 3.25) while in group 2, total score after 4 weeks ranged from 16 to 37 (mean 23.40 ± 5.70). There was a significant difference in the functional subscore between the two groups after 4 weeks (P=0.016). Patients treated with hyaluronic acid (group 2) showed more improvement compared with group 1 as reflected by the drop in functional score. However, there was a statistically non-significant difference between both groups in total score (P=0.248) (table 18).

Table (18): Comparison between both groups regarding AUSCAN score after 4 weeks of injection:

		Group I No. = 15	Group II No. = 15	Test value	P-value	Sig.
Pain subscore after 4 weeks	Mean±SD Range	6.73 ± 1.67 4 – 10	7.33 ± 3.04 4 – 15	-0.670•	0.508	NS
Stiffness subscore after 4 weeks	0 1	15 (100%) 0 (0.0%)	15 (100.0%) 0 (0.0%)	1.034*	0.309	NS
Functional subscore after 4 weeks	Mean±SD Range	18.47 ± 2.10 16 – 22	16.07 ± 2.94 12 – 22	2.573•	0.016	S
Total score after 4 weeks	Mean±SD Range	25.40 ± 3.25 22 – 33	23.40 ± 5.70 16 – 37	1.180•	0.248	NS

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant *:Chi-square test; •: Independent t-test

AUSCAN score after 12 weeks of injection.

Both groups showed improvement regarding pain and stiffness subscore. All patients of both groups were grade 0 in stiffness subscore. Pain subscore in group I ranged from 5-8 (mean 6.27 ± 1.16) & in group II ranged from 4-12 (mean 6.07 ± 2.37). Comparison showed that there was no statistically significant difference between both studied groups regarding pain (P=0.293) and stiffness subscore (P=0.309) after 12 weeks.

Regarding functional subscore, In group I ranged from 18 to 26 (mean 21.27 ± 2.28) while in group 2, functional subscore ranged from 12 to 20 (mean 14.33 ± 2.50). Total score in group 1 after 12 weeks ranged from 23 to 34 (mean 27.53 ± 2.95), total score after 12 weeks in group 2 ranged from 16 to 32 (mean 20.40±4.52).

Group 2 patients showed more improvement compared with group 1 reflected as drop in functional and total score. There was highly significant difference between both groups in functional subscore and total score (P=0.000) (table 19, figures 47, 48 & 49).

Table (19): Comparison between both groups regarding AUSCAN score after 12 weeks of injection:

		Group I	Group II	Test value	P -value	Sig.
		No. = 15	No. = 15			
Pain subscore after 12 weeks	Mean±SD Range	6.27 ± 1.16 5 – 8	6.07 ± 2.37 4 – 12	0.293•	0.772	NS
Stiffness subscore after 12 weeks	0 1	15 (100.0%) 0 (0.0%)	15 (100%) 0 (0.0%)	1.034*	0.309	NS
Functional subscore after 12 weeks	Mean±SD Range	21.27 ± 2.28 18 – 26	14.33 ± 2.50 12 – 20	7.937•	0.000	HS
Total score after 12 weeks	Mean±SD Range	27.53 ± 2.95 23 – 34	20.40 ± 4.52 16 – 32	5.122•	0.000	HS

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant *:Chi-square test; •: Independent t-test

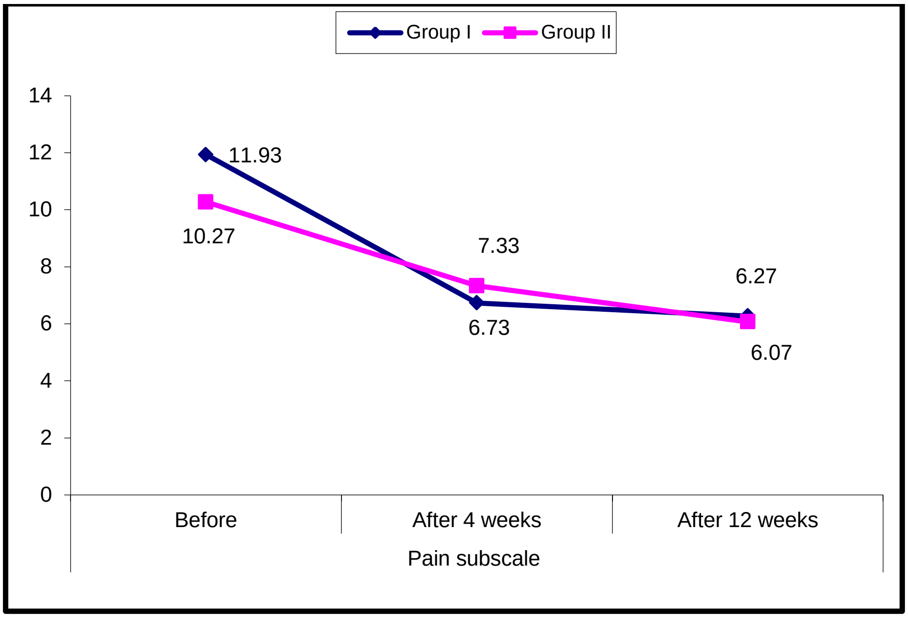

Figure 47: pain subscore in both groups overall study period.

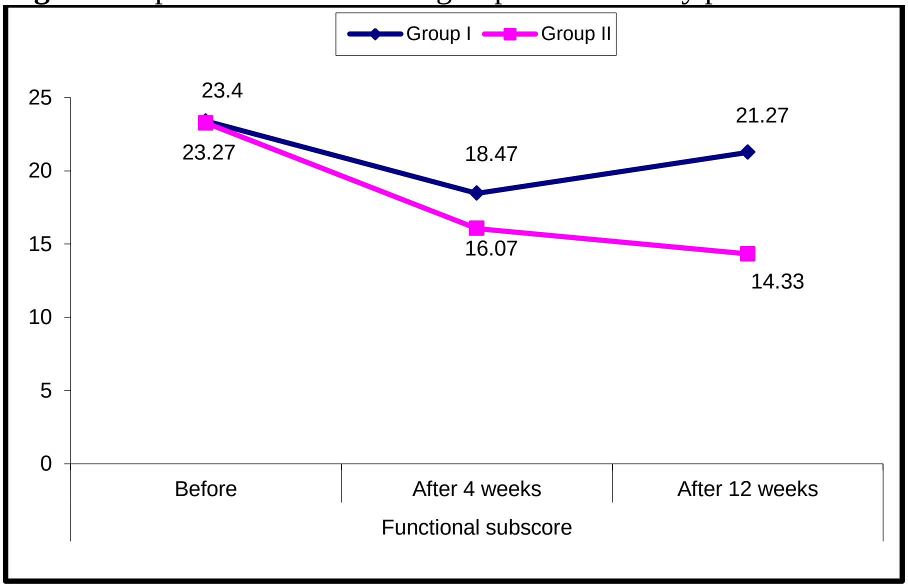

Figure 48: functional subscore in both groups overall study period.

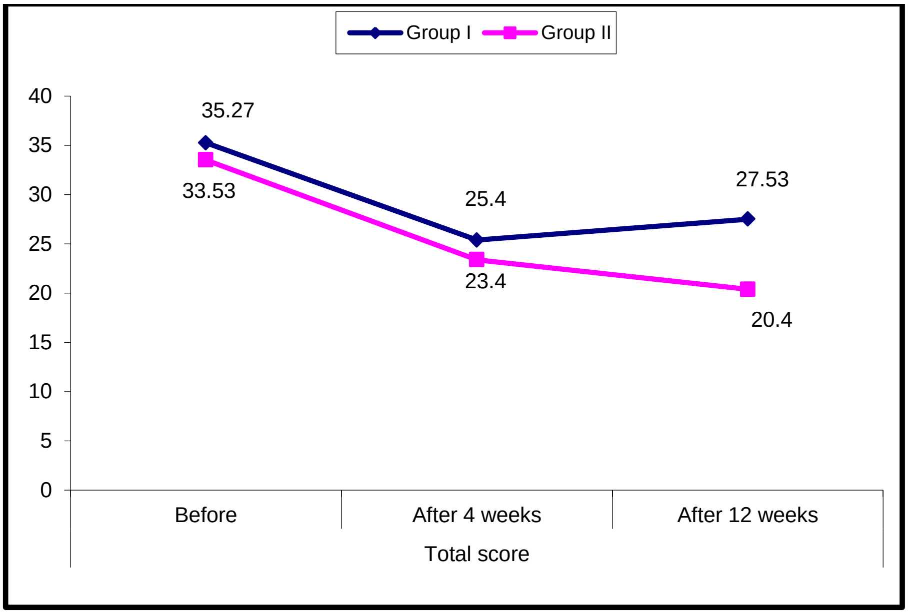

Figure 49: Total score in both groups overall study period.

3- Pain assessment using VAS:

In group I: VAS before injection ranged from 6 to 9 (mean: 7.53 ± 1.13), 4 weeks after injection ranged from 2 to 4(mean 3.20 ± 0.68) and after 12 weeks ranged from 3 to 5 (mean: 4.33 ± 0.72). In group II: VAS before injection ranged from 5 to 9 (mean: 6.60 ± 1.45), 4 weeks after injection ranged from 2 to 6 (mean: 4.00 ± 1.25) and after 12 weeks ranged from 1 to 4 (mean 2.47 ± 0.92).

Comparison showed that there was no statistically significant difference between the two studied groups regarding VAS before injection. After 4 weeks of injection, both groups improved but group 1 showed more improvement compared with group 2. The comparison showed that there was significant difference between them after 4 weeks (P=0.038).

After 12 weeks of injection, group 2 showed more improvement (more decrease in VAS), while group I became worse but still better than before injection. There was highly significant difference between both groups (P=0.000) (table 20, figure 50).

Table 20: Comparison between both groups regarding VAS for pain assessment:

		Group I No. = 15	Group II No. = 15	Test value	P -value	Sig.
VAS before Injection	Mean±SD Range	7.53 ± 1.13 6 – 9	6.60 ± 1.45 5 – 9	1.966	0.059	NS
VAS after 4 weeks	Mean±SD Range	3.20 ± 0.68 2 – 4	4.00 ± 1.25 2 – 6	-2.175	0.038	S
VAS after 12 weeks	Mean±SD Range	4.33 ± 0.72 3 – 5	2.47 ± 0.92 1 – 4	6.195	0.000	HS

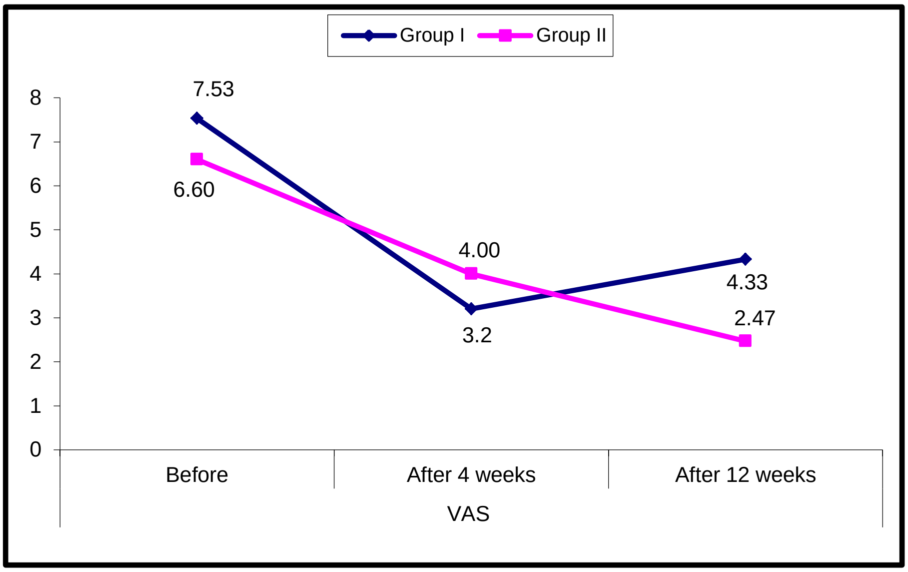

Figure 50: VAS before and after injection in studied groups.

4- Grip strength assessment:

In group I: Grip strength measurement before injection ranged from 13 to 19 (mean 16.27 ± 1.53), 4 weeks after injection ranged from 15 to 21 (mean 18.20 ± 1.52) and after 12 weeks ranged from 14 to 20 (mean 17.20 ± 1.47). In group II: Grip strength measurement before injection ranged from 11 to 21 (mean: 15.60 ± 2.95), 4 weeks after injection ranged from 17 to 30 (mean 23.87 ± 3.89) and after 12 weeks ranged from 19 to 33 (mean 26.80 ± 4.65).

Group II showed more improvement and increase in grip strength after 4 weeks which persist and increased more after 12 weeks. Group 1 show improvement and increase in grip strength (less than group 2) after 4 weeks but after 12 weeks, patients showed decrease in grip strength. Comparison between both groups showed that there was highly statistically significant difference in grip strength after 4 weeks and 12 weeks (table 21, figure 51).

Table 21: Comparison between results of grip strength assessment of both groups over the study duration:

		Group I	Group II	Test value•	P -value	Sig.
		No. = 15	No. = 15			
Grip before Injection	Mean±SD Range	16.27 ± 1.53 13 – 19	15.60 ± 2.95 11 – 21	0.777	0.444	NS
Grip after 4weeks	Mean±SD Range	18.20 ± 1.52 15 – 21	23.87 ± 3.89 17 – 30	-5.256	0.000	HS
Grip after 12 weeks	Mean±SD Range	17.20 ± 1.47 14 – 20	26.80 ± 4.65 19 – 33	-7.626	0.000	HS

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant •: Independent t-test

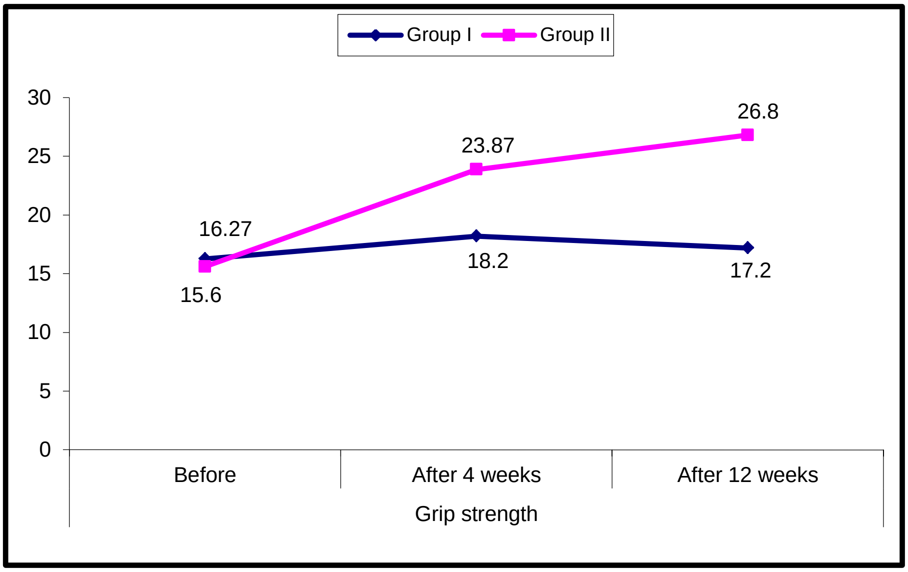

Figure 51: Grip strength before and after injection in both groups.

5- Pinch strength assessment:

In group I: Pinch strength measurement before injection ranged from 2 to 6 (mean: 4.53 ± 1.13), 4 weeks after injection ranged from 4 to 7 (mean 5.93 ± 0.80) and after 12 weeks ranged from 3 to 6 (mean 4.93 ± 0.80). In group II: Pinch strength measurement before injection ranged from 3 to 5 (mean: 3.53 ± 0.64), 4 weeks after injection ranged from 5 to 9 (mean: 6.20 ± 1.15) and after 12 weeks ranged from 6 to 11(mean 7.80 ± 1.21).

Both groups improved after 4 weeks of injection. Comparison showed that there was no statistically significant difference between them regarding pinch strength after 4 weeks (P=0.466). After 12 weeks, there was a highly statistically significant difference between both groups (P=0.000). Group 2 showed more significant improvement (increase in pinch strength) while group 1 showed deterioration (decrease in pinch strength but still better than before injection) (table 22, figure 52).

Table 22: Comparison between results of pinch strength assessment of both groups over the study duration:

		Group I	Group II	Test value•	P-value	Sig.
		No. = 15	No. = 15			
Pinch strength before injection	Mean±SD Range	4.2 ± 1.32 2 – 6	3.53 ± 0.64 3 – 5	1.760	0.089	NS
Pinch strength after 4 weeks	Mean±SD Range	5.93 ± 0.80 4 – 7	6.20 ± 1.15 5 – 9	-0.739	0.466	NS
Pinch strength after 12weeks	Mean±SD Range	4.93 ± 0.80 3 – 6	7.80 ± 1.21 6 – 11	-7.670	0.000	HS

P-value>0.05: Non significant; P-value<0.05: Significant; P-value<0.01: highly significant •: Independent t-test

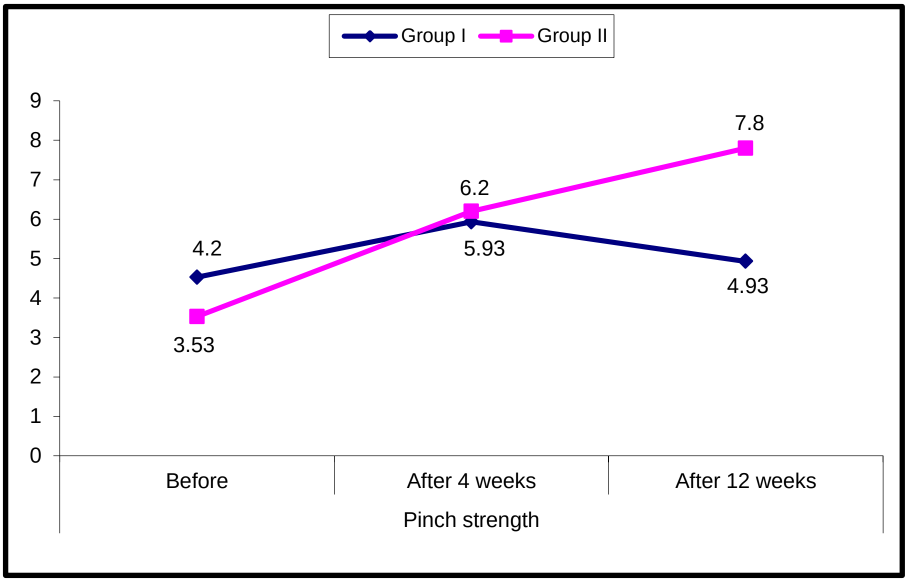

Figure 52: Pinch strength before and after injection in both groups.

Discussion

The carpometacarpal (CMC) joint of the thumb is the second most affected joint by osteoarthritis. Typical symptoms can include pain in the joint, as well as morning stiffness or stiffness due to inactivity. Hand function is therefore often adversely affected in patients with OA in CMC joint ***(Robyn et al., 2017)***.

Several conservative treatment options have been described for the treatment of thumb CMC OA. Local injection treatment could be an attractive treatment modality because of low systemic side effects (***Kloppenburg, 2014).***

The aim of this study is to compare the effectiveness of PRP versus hyaluronic acid injection in osteoarthritis of thumb carpometacarpal joint based on clinical and functional outcome measures.

This prospective study was conducted on thirty patients with clinical evidence of thumb CMC OA. Patients were collected from outpatient clinic of Physical medicine, Rheumatology and Rehabilitation department, Ain Shams university hospitals. Twenty six patients were females (86.7%), and four were males (13.3%). Their ages ranged from 40 to 70 years (mean: 52.77 ± 8.59). Eighteen patients were housewives (60.0%), 10 patients were manual workers (33.3%) and 2 patients were clerks. Twenty nine of them were right handed and one patient left handed.

Dominant extremity affection in 27 patients (90.0%) and non-dominant hand affection in 3 patients (10%)

The patients were randomly divided into two groups. Group 1 was composed of fifteen patients injected intra-articularly with Platelet-Rich Plasma (PRP) and group 2 was composed of fifteen patients injected intra-articularly with hyaluronic acid. Both groups showed no statistically significant difference regarding clinical, laboratory and radiological findings before administration of treatment. All included patients attended their follow up sessions with no drop outs.

Follow up assessment was done after 4 weeks and 12 weeks of injection by tenderness grading, AUSCAN hand function score, VAS for pain assessment, grip & pinch strength assessment.

According to VAS, group 1 patients demonstrated a highly significant pain relief after PRP injection at 4 and 12 weeks follow up compared to before injection (P=0.000). However, the pain increased highly significantly from 4 to 12 weeks follow up (P= 0.000). Also, the patients showed highly significant improvement regarding tenderness (decreased) after 4 weeks (P=0.000), but they reported a highly significant increase in tenderness from 4 to 12 weeks follow up (P=0.002).

Regarding AUSCAN hand function score, there was a highly statistically significant decrease in pain subscale after 4 weeks and 12 weeks follow up (both P=0.000) compared to before injection. As regard functional subscore and total score there was a statistically highly significant improvement after 4 weeks (P = 0.000) and a significant improvement after 12 weeks (P=0.018) .However, there was a highly significant increase (deterioration) from 4 to 12 weeks follow up in functional subscore (P=0.000) and total score (P=0.004).

This agree with the findings of **Loibl et al., 2016** who conducted a study which included a total 10 patients with thumb CMC OA treated with two PRP injections 4 weeks apart under fluoroscopy guidance. He reported that VAS before injection was 6.2 ±1.6 which significantly decreased to 4.0 ± 2.4 at three months follow up and increased again to 5.4 ± 2.2 at six months follow up (both P < 0.05). They also reported that patients with mild to moderate OA especially, experienced a persistent pain relief and patients with more severe stages had pain relief after 3 months, which did not fully retain up to 6 months.

The DASH score remained similar with 32.9±11.9 at baseline and 20.4±14.7 at three-month and 26.8± 18.9 at 6-month follow-up (*P* ≥ 0.24). The Mayo Wrist score significantly improved from 46.5±18.6 to 68.3±18.5 at three month follow-up (*P* = 0.05) and to 67.5 ± 19.0 at six-month follow-up (*P* = 0.05).

The better clinical results observed in patients with early OA could be explained by a better responsiveness to growth factors in less degenerated joints with more vital cells. Therefore, it was hypothesized that PRP injection would yield better outcome in early OA ***(Filardo et al., 2015) (Gormeli et al., 2015)***.

Growth factors could have a crucial role in OA since they influence chemotaxis, differentiation, proliferation and synthetic activity of cartilage. PRP preparations have been used to treat cartilage lesions to regenerate tissue homeostasis and to delay the progression of early knee osteoarthritis ***(Civinini et al., 2013).***

Malahias et al., 2018 Compared PRP versus corticosteroids intra articular injection in CMC OA in (G1-3). Comparison have shown that both treatment modalities significantly improved pain management at 3 months compared with their respective pre-intervention VAS score values (P =0.004 for PRP vs. P = 0.001 for steroid); however, at 12 months this effect was maintained only for the PRP treatment (P = 0.005 vs. P = 0.105, respectively). The exclusion of patients with end stage arthritis and the patients received two ultrasound guided injection could be a contributing factors to this result **(Malahias et al., 2018).**

The improvement of pain and hand function in our study can be explained by an overall down modulation of the joint inflammation. This could be through the regulation of nuclear factor kappa B and cyclooxygenase-2

(COX-2), the principal actors of inflammatory cascade ***(Bendinelli et al., 2010).***

However, this improvement wasn't persistent after 12 weeks may be due to the fact that most of our cases were with moderate to severe OA according to Eaton and Litter classification and they received only single blind injection of PRP.

There is a debate about number of PRP injections. It has been shown that a single PRP injection illustrates inferior results in comparison with more than one injections **(Görmeli et al., 2017)**. In a study done by **Kavadar et al., 2015** recommended at least 2 injections of PRP with 1 week interval. Also, **Gormeli et al., 2015** suggested that multiple PRP injections were more effective in early OA, while **Patel et al., 2013** concluded that a single dose of PRP is as effective as a double dose in knee OA.

There was a highly statistically significant increase in grip and pinch strength after 4 weeks follow up. At 12 weeks, there was a highly significant increase in grip strength (P=0.000) and significant increase in pinch strength (P=0.019) compared to before injection, while there was a highly significant decrease in grip and pinch strength from 4 to 12 weeks follow up (P=0.000).

This improvement in grip and pinch strength is probably due to symptomatic relief of pain after 4 weeks of injection.

This limited PRP effect on hand grip and pinch strength improvement could be because our cases had moderate to severe OA.

Our findings are not in accordance with **Samantha and Marie study, 2017** who compared the efficacy of PRP injection versus corticosteroids in thumb CMC OA. The patients received two intra-articular PRP injection, administrated one week apart under fluoroscopic guidance. They reported that the VAS pain score were significantly lower in the PRP patients at each follow up visits. At 6 months follow up, patients in the PRP group showed a 90% decrease in pain from baseline while the steroid group showed 8 % increase in pain. The PRP group also has significantly better function score (P=0.002) and increased grip & pinch strength at 6 month.

This discrepancy may be due to that these patients received two injection of PRP under fluoroscopic guidance.

Accuracy is a concern with thumb CMCJ injections. U/S is appropriate imaging modality to verify the correct needle positioning and successful joint infiltration. U/S-guided injections had a higher rate of success. Accuracy of thumb CMC injections is 63% ***(Philip et al., 2017)***. In study done by **Pollard et al., 2007** reported a 100% rate of intra-articular accuracy with fluoroscopy-guided injections as compared with 82% in the blind group.

However, **Mandl et al., 2006** reported an accuracy of 100% (no U/S or fluoroscopic guidance) for thumb CMC injections with moderate to severe thumb CMC OA. They concluded that thumb CMC injections could be injected accurately without the need for radiographic guidance. The boundaries of the three-sided snuffbox are easily palpable by placing the thumb in a fully abducted position. It is bounded on the palmar side by the tendons of the abductor pollicis longus (APL) and extensor pollicis brevis (EPB), and dorsally by the tendon of the extensor pollicis longus (EPL). These anatomic landmarks for the CMC joint can facilitate a safe and reliable approach to the percutaneous treatment of CMC joint arthritis ***(Umphrey et al., 2008).***

There is heterogeneity across studies as regard the severity of the OA populations included, the frequency, dose and duration of PRP interventions. In addition, the long term outcomes of this form of therapy has not been established, and the duration of the expected benefit of PRP injections remains unclear, as most of the other studies investigate the persistence of the desirable effects up to 12 months post interventions but only a small number of studies has a follow-up period beyond that ***(Mustafa et al., 2017)***.

Meheux et al., 2016 conducted a systematic review of six randomized, controlled trials, and found that PRP injection for knee OA resulted in significant clinical improvements for up to 12 months post-injection.

In our study, there was no adverse reactions after injection of PRP. As injecting PRP involves using a patient's own platelets, they do not usually experience any adverse reactions to the injections. However, it is possible that patients may have irritation, pain, tissue damage or bleeding related to the injection site ***(Bowman et al., 2018)***.

In our study, group 2 who received a hyaluronic acid injection The patients reported a highly significant pain relief, decrease tenderness and improvement of hand function score after 4 & 12 weeks follow up (both P=0.000). Also, there was a highly significant improvement in pain, tenderness and hand function score from 4 to 12 weeks follow up (P= 0.000).

The improvement of pain and hand function is due to the anti-inflammatory and analgesic effect of HA injection. Intra-articular HA therapy provides therapeutic relief through a number of pathways, including the suppression of pro-inflammatory cytokines and chemokines via inhibitors of the signal transduction pathways from specific cell surface receptors, as well as promotion of the synthesis of anti-inflammatory mediators ***(Altman et al., 2018).***

HA has indirect and direct analgesic activity within the joints. Indirect effect is via the anti-inflammatory properties of HA. Direct effect is by the direct inhibition of nociceptors and the decreased synthesis of bradykinin and substance P. Also, intra-articular HA application causes analgesia by increasing the elastoviscosity of the intercellular matrix of soft tissues around the joint that reduces the force transmitted during joint movements ***(Akgun et al., 2014).*** Anti-inflammatory and analgesic effect of HA injection explain the significant improvement of pain and hand function after 4 weeks which persist and became more improved after 12 weeks of injection.

These results were in agreement with **Ioppolo et al., 2016**. Their patients showed a significant decrease in pain between baseline and the 3rd month and 6th month follow-up visits. This was also in agreement with **Salini et al., 2009** who reported that single injection of HA is effective in treating CMC-OA. The VAS pain score, both at rest and during common daily activities, substantially decreased and the hand function was clearly improved. Their results showed that VAS pain score at rest, was 1.8 ± 1.07, decreased to 0.5 ± 0.68, after treatment (-72.22%). Pain score during activities also decreased from 8.05 ± 0.94 to 4.15 ± 1.42. (48.44%).

Also, **Fuchs and Stahls, 2006** observed a significant improvement of symptoms and function in patients with thumb CMC OA after 3 injections of HA which persisted after 3 and 6 months.

However, **Roux et al., 2007** studied 3 groups in which patients received 1, 2, or 3 hyaluronate injections. They found no statistically significant differences between the groups regarding pain and function. The improvement in pain and hand function was as early as the first month with persistent effects at 3 months as in our study. Morever, single injection of HA has been used by **Salini et al., 2009** which reported that single injection of HA is effective in treating thumb CMC-OA.

Researches by **Stahl et al., 2005 & Fuchs et al., 2006** showed that both hyaluronic acid & steroids injections were effective in relieving pain and improving joint function.

Heyworth et al., 2008 compared steroid, hyaluronate, and placebo injections and found that all patients had decreased pain, which persisted in the hyaluronate group during the entire follow-up period of 26 weeks. The placebo and steroid groups experienced less pain for only 4 weeks.

In a study by **Monfort et al., 2014,** patients in the HA group experienced a functional improvement of greater magnitude than the patients treated with betamethasone group. According to these findings, HA injection seems to be an equivalent and possibly better alternative to corticosteroid injection in the treatment of thumb CMC joint OA, particularly in patients with functional impairment and moderate to severe pain level. Unlike steroids, shown to be effective for reducing acute pain, improvement due to injections of HA was more gradual but more prolonged over time. These results are consistent with the widely accepted idea that corticosteroids could be more effective in reducing inflammation and ameliorating pain in its earliest form, while the regeneration of the viscoelasticity of the synovial fluid achieved by HA could improve the homeostasis of the joint, contributing to more long-lasting improvement of both function and pain.

Major side effects of steroid injections are thinning of joint cartilage, weakening of the ligaments of the joint, fat atrophy and post steroid injection flare. Also, elevation blood pressure and blood glucose levels as systemic side effects (***Cole et al., 2016)***. HA injections are usually safe but it may cause local pain and swelling with frequent injections ***(Bowman et al., 2018)***. For that, HA considered safer & longer acting alternative for corticosteroids.

In our study, there was a highly statistically significant increase in grip and pinch strength after 4 and 12 weeks compared to before injection (P=0.000). From 4 to 12 weeks follow up, patients showed further improvement and more highly significant increase in grip and pinch strength (P=0.000).

The strong effect of HA on grip and pinch strength may be due to lubricating effect of HA and improving viscoelasticity and/or the improvement of the intra-articular environment of the joint ***(Zhang et al., 2018).***

Fuchs and Stahls, 2006 reported that there was significant improvement in grip strength at 6 months. In our study there was significant effect at a shorter follow-up period. We found significant improvement after 1 month and more increase in strength after 3 months of injection and this is similar to the findings of **Salini et al., 2009** study in which hand grip and pinch strength showed an increase of 1.64% and 6.74% respectively after 1 month follow up.

These positive effects that persist for many months after injection cannot be solely attributed to viscous supplementation but also may be mediated by several pathways such as anti-inflammatory and antinociceptive effects, normalization of endogenous HA synthesis, and chondroprotection ***(Bowman et al., 2018)***.

In our study, the comparison between both groups showed that HA has superior longer lasting improvement in tenderness grade, hand function, VAS, grip and pinch strength up to 12 weeks ,while PRP has superior short term effect on VAS pain score after 4 weeks of injection.

Many studies compared PRP and HA for knee OA to determine which was more effective and have not achieved consensus in terms of pain relief and function recovery. In a rabbit model of knee OA, **Liu et al., 2014** reported that PRP is better than HA in promoting the restoration of the cartilage**. Sanchez et al., 2012** showed superior short-term results in alleviating symptoms of mild to moderate OA of the knee for PRP compared to HA in a randomized controlled trial**.** Morever, **Sadabad et al., 2016** concluded that PRP injection for patients has shown that PRP has a greater effectiveness than HA for pain management and articular function.

Some researchers hold promise for PRP of certain specifications for pain management in the early OA as PRP injections reduced pain more effectively than HA injections in OA of the knee at 6 and 12 months of follow-up (***Zhang et al., 2018)***. However, **Filardo et al., 2015** have observed that PRP didn't provide a superior improvement with respect to HA.

The beneficial effects of HA may be attributable to improved lubrication based on the viscoelasticity and/or the improvement of the intra-articular environment by rebuilding the barrier between the synovial membrane and the articular surface ***(Miller & Block, 2013***). HA plays a significant role in anti-inflammatory, anti-apoptotic, anti-angiogenic, and anti-fibrosis. A large number of clinical studies also demonstrated that HA has the effect of relieving joint pain and improving joint function (***Zhang et al., 2018).***

The growth factors secreted from active platelets have a fundamental function to stimulate proliferation and differentiation of chondrocytes, regulate collagenase secretion, and regenerate cartilage. HA acts as a lubricator, while PRP provides many factors to stimulate the synovial membrane and surrounding tissues ***(Zhang et al., 2018***). PRP acts as a vector for large growth factors, which have the function of promoting tissue repair, which is increasingly being used in the treatment of OA ***(Filardo et al., 2015).*** Thereby, PRP could promote the repair of damaged cartilage, while reducing pain and the inflammatory response effect (***Zhang et al., 2018)***.

Combinational treatment using both PRP and HA was performed on patients with early stage primary OA. All patients treated experienced strong functional improvement and substantial gains in pain relief, functionality and quality of life. The authors suggested that combined PRP and HA is safe and potentially effective. Combining PRP and HA could derive benefit from their dissimilar biological mechanisms ***(Kurapati et al., 2018).***

The autologus nature of PRP and low cost are some of the advantages of PRP, While HA has relatively high cost. PRP injections need preparation steps but HA used as prefilled syringes.

Gormeli et al., 2017 compared HA with multiple- or single-dose PRP. There were no differences between HA and single-dose PRP, while multiple-dose PRP was better than both treatments.

In our study, there was no adverse reactions after injection in both groups However**, Filardo et al., 2012** demonstrated that higher post-injection pain was noted in those patients injected with PRP compared to HA.

Summary

The carpometacarpal (CMC) joint of the thumb is the second most affected joint by osteoarthritis. Typical symptoms can include pain in the joint, as well as morning stiffness or stiffness due to inactivity. Hand function is therefore often adversely affected in patients with OA in CMC joint ***(Robyn et al., 2017)***.

The aim of conservative treatment is to restore thumb functionality, including pain relief, stability, mobility, and strength (grip & pinch). So, there is an improvement in all hand functions and performance of activities of daily living (***Villafane et al., 2017).*** Local injection treatment could be an attractive treatment modality because of low systemic side effects (***Kloppenburg, 2014).***

This study was conducted on thirty patients with thumb CMC OA. Diagnosis was based on detailed history taking, full clinical examination and radiological assessment.

The patients were randomly divided into two groups:

Group 1: Fifteen patients were injected intra-articularly with Platelet-Rich Plasma (PRP). Group 2: Fifteen patients were injected intra-articularly with 1 ml hyaluronic acid (hyaluronic acid sodium salt) [Hyalgan]. Patients were assessed before injection and after 4 & 12 weeks follow up by local examination (tenderness grading), VAS for pain assessment, AUSCAN hand functional score,

Grip and pinch strength measurement by hand dynamometer.

In our study, group 1 patients demonstrated a highly significant improvement regarding pain , tenderness, hand function and increase in grip and pinch strength at 4 and 12 weeks follow up compared to before injection. However, that improvement in all parameters decreased from 4 to 12 weeks follow up.

Group 2 who received a hyaluronic acid injection, patients reported a highly significant pain relief, decrease tenderness, improvement of hand function score and increase in grip & pinch strength after 4 & 12 weeks follow up. Also, there was a more highly significant improvement in all parameters from 4 to 12 weeks follow up.

Upon comparison between both groups after 4 weeks of injection, there was a statistically non -significant difference regarding tenderness grading, pinch strength and total hand function score. However, there was a highly statistically significant difference regarding grip strength and significant difference regarding VAS. Group 2 showed more increase in grip strength than group 1, while group 1 showed more pain relief than group 2.

In comparison between both groups after 12 weeks, there was a highly statistically significant difference regarding VAS, tenderness grading, total hand function score, grip and pinch strength. All parameters showed a more highly significant improvement in group 2 after 12 weeks follow up. .

Hyaluronic acid injection offers better therapeutic advantages over a PRP injection especially at longer term follow up (12 weeks).

Conclusions

In our study, we observed clinical improvement in both groups of CMC OA treated either with single dose of HA or PRP at 4 and 12 weeks follow up evaluation. However, HA provide a superior improvement with respect to PRP at 12 weeks follow up.

Intra-articular HA injection showed more and longer efficacy than PRP injection. Single treatment course and follow up period of 12 weeks are associated with improvement of pain, function and strength.

The current study supports the use of a single hyaluronic acid injection as therapy for thumb CMC OA in preference to PRP injection. Hyaluronic acid injection offers better therapeutic advantages over a PRP injection especially in the longer-term follow up (12 weeks), as it is well tolerated with minimal or no side effects. Moreover, it has a superior longer lasting efficacy in improvement of pain, strength and hand function.

Recommendations

After conducting this research we recommended:

- Longer term follow up to be conducted to explore long-term effects of hyaluronic acid and PRP on thumb CMC OA.
- More studies are recommended to test the efficacy of repeated injections of PRP with the optimal time interval.
- Comparative study on the efficacy of both HA and PRP on different stages of thumb CMC OA.
- Comparison between blind versus U.S guided injection of both PRP and HA in thumb CMC joint OA.
- Comparative study on the effect of combined PRP and HA injection versus PRP and/ or HA injection individually.

References

Abate M, Schiavone C, and Salini V (2014): Review Article. The Use of Hyaluronic Acid after Tendon Surgery and in Tendinopathies. BioMed Research International Volume 2014. Muscles Ligaments Tendons J; 5 (4): 264–269.

Aebischer B., Elsig S. and Taeymans J. (2016): Effectiveness of physical and occupational therapy on pain, function and quality of life in patients with trapeziometacarpal osteoarthritis systematic review and meta-analysis. Hand Ther; 21: 5e15.

Akgun I., Egemen A. and Kesmezacar H., (2014): Intraarticular injections (corticosteroid, hyaluronic acid, platelet rich plasma) for the knee osteoarthritis *World J Orthop* July 18; 5(3): 351-361.

Alfredo V., Niccolò L., Monica S., et al. (2017): Regular use of acetaminophen or acetaminophen–codeine combinations and prescription of rescue therapy with non-steroidal anti-inflammatory drugs: a population-based study in primary care, Current Medical Research and Opinion.

Altman R., Manjoo A., Faizan N., et al. (2018): Division of Rheumatology and Immunology, David Geffen School of Medicine, University of

California at Los Angeles, Los Angeles, CA, USA.

Andia and Maffulli, (2013): “Platelet-rich plasma for managing pain and inflammation in osteoarthritis,” *Nature Reviews Rheumatology*, vol. 9, no. 12, pp. 721–730.

Anne S., Paul L., Moshe K., et al. (2015): Conservative Treatment of Thumb Base Osteoarthritis: A Systematic ReviewJ Hand Surg Am.; 40(1): 16-21.

Ateshian G., Ark J., Rosenwasser M., et al. (1995): Contact areas in the thumb carpometacarpal joint. J Orthop Res. 13(3): 450–458.

Atkinson A., Hartley C., Stanescu I., et al. (2014): "Increased Phenylephrine Plasma Levels with Administration of Acetaminophen". New England Journal of Medicine. **370** (12): 1171–1172.

Axe J., Snyder L. and Axe M. (2013): The role of viscosupplementation. Sports Med Arthrosc; 21: 18-2.

Bakri K. and Moran S. (2015): Thumb carpometacarpal arthritis. Plast Reconstr Surg 135: 508–520

Batra S. and Kanvinde R. (2007): Osteoarthritis of the thumb trapeziometacarpal joint. *Current Orthopaedics,* 21(2): 135-144

Bellamy N, Campbell J, Haraoui B, Buchbinder R, Hobby K and Roth JH, (2002): Dimensionality and clinical importance of pain and disability in hand osteoarthritis: development of the Australian/Canadian (AUSCAN) 0 Hand Index. Osteoarthritis Cartil; 10: 855–62.

Bendinelli P., Matteucci E. and Dogliotti G. (2010): Molecular basis of anti-inflammatory action of platelet-rich plasma on human chondrocytes: mechanisms of NF-jB inhibition via HGF. J Cell Physiol 225(3), 757–766. 9–1050.

Berenbaum F., (2013): Osteoarthritis as an inflammatory disease. *Osteoarthritis Cartilage* 2013; 21: 16-21.

Berger A. and Meals R. (2015): Management of osteoarthrosis of the thumb joints. J Hand Surg Am.; 40(4): 843–50.

Bertozzi., Valdes K. and Vanti C., et al. (2015): Investigation of the effect of conservative interventions in thumb carpometacarpal osteoarthritis: systematic review and meta-analysis. Disabil Rehabil; 37(22): 2025-43.

Bhagra A., Syed H., Reed D., et al. (2013): Efficacy of musculoskeletal injections by primary care providers in the office: a retrospective cohort study. *Int J Gen Med*. 6: 237-43.

Bijlsma J., Berenbaum F., and Lafeber F., (2011): “Osteoarthritis: an update with relevance for clinical practice,” The Lancet, vol. 377, no. 9783, pp. 2115–2126.

Bijsterbosch M., Visser W., Kroon T., et al. (2010): Thumb base involvement in symptomatic hand osteoarthritis is associated with more pain and functional disability Ann Rheum Dis, 69: 585–7.

Bird H., (2007): Joint hypermobility. Musculoskeletal Care. 2007; 5(1): 4–19.

Bongkotphet K., Tassanawipas W., Krittiyanunt S., et al. (2009): Comparative efficacy of low- and high- molecular weight intra-articular hyaluronic acids in patients with knee osteoarthritis. J Heal Res; 23: 87–92.

Bowman S., Mohamed E., Mark W., et al., (2018): Recent advances in hyaluronic acid based therapy for osteoarthritis Clin Trans Med 7: 6

Brun P., Zavan B., Vindigni V., et al. (2012): In vitro response of osteoarthritic chondrocytes and fibroblast-like synoviocytes to a 500-730 kDa hyaluronan amide derivative. J Biomed Mater Res B Appl Biomater. 100(8): 2073–81.

Chiavaras M., (2010): Sonography of the anterior oblique ligament of the trapeziometacarpal joint: a study of cadavers and asymptomatic volunteers. AJR Am J Roentgenol.; 195(6): W428–34.

Choa R., Parvizi N. and Giele H. (2014): A prospective case-control study to compare the sensitivity and specificity of the grind and traction-shift (subluxation-relocation) clinical tests in osteoarthritis of the thumb carpometacarpal joint. *J Hand Surg Eur Vol*.; 39(3): 282-285.

Christiansen B., (2015): Management of osteoarthritis with avocado/soybean unsaponifiables. Cartilage.; 6: 30.

Cipriano J. (2010): Photographic Manual of Regional Orthopaedic and Neurological Tests (5th edition).; 81(9): 646-656.

Colditz J. and Koekebakker N. (2010): A New Splint Design for the Thumb CMC Joint, Nea International / Push Braces, 6: 30.

Cole B., Peters K., Hackett L et al. (2016): Ultrasound-Guided Versus Blind Subacromial Corticosteroid Injections for Subacromial Impingement Syndrome: A Randomized, Double-Blind Clinical Trial. *Am J Sports Med* 44 (3): 702-7.

Cook G. and Lalonde D. (2008): Management of thumb carpometacarpal joint arthritis. Plast Reconstr Surg; 121: 1–9.

Dhurat R. and Sukesh M. (2016): Principles and methods of preparation of platelet-rich plasma: A review and author's perspective. *J Cutan Aesthet Surg*.; 7(4): 189-197.

Diekman B. and Guilak F. (2013): Stem cell-based therapies for osteoarthritis: challenges and opportunities. *Curr Opin Rheumatol*; 25: 119-126.

Duong V., Kim L., Leticia A., et al. (2017): Kolling Institute of Medical Research, Institute of Bone and Joint Research. Vol 23, Issue 1.

Eaton R. and Littler J. (1973): Ligament reconstruction for the painful thumb carpometacarpal joint. J Bone Joint Surg Am. 1973; 55: 1655–1666.

Edmunds J., (2006): Traumatic dislocations and instability of the trapeziometacarpal joint of the thumb. Hand Clinics; 22: 365–392.

Edmunds J., (2011): Current concepts of the anatomy of the thumb trapeziometacarpal joint. J Hand Surg; 36A: 170-182.

Egemen A., Hayrettin K. and Isik A. (2014): World J Orthop. Jul 18; 5(3): 351–361.

Ermurat A., Kroon A., Beest V., et al. (2018): In thumb base osteoarthritis structural damage is more strongly associated with pain than synovitis. Osteoarthritis Research Society International. Volume 26, Issue 9, Pages 1196–1202

Fam H., Bryant J. and Kontopoulou M. (2007): Rheological properties of synovial fluids. Biorheol.; 44: 59–74.

Filardo G., Kon A., Martino A., et al. (2012): Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial Musculoskelet Disord, 13, p. 229/

Filardo G., Kon E. and Buda R. (2010): Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. *Knee Surg Sports Traumatol Arthrosc*; 19(4): 528–535.

Filardo G., Kon E. and Pereira R. (2012): "Platelet-rich plasma intra-articular injections for cartilage degeneration and osteoarthritis: Single- versus double-spinning approach," *Knee Surgery, Sports Traumatology, Arthroscopy*, vol. 20, no. 10, pp. 2082–2091.

Filardo G., Kon E., Roffi A., et al. (2015): Platelet-rich plasma: why intra-articular? A systematic review of preclinical studies and clinical evidence on PRP for joint degeneration. *Knee Surg Sports Traumatol Arthrosc*.; 23(9): 2459–2474.

Fotiadis E., Svarnas T., Lyrtzis C., et al. (2010): Isolated thumb carpometacarpal joint dislocation: a case report and review of the literature. J Orthop Surg Res; 5: 16-22.

Fuchs S., Mönikes R., Wohlmeiner A., et al. (2006): Intra-articular hyaluronic acid compared with corticoid injections for the treatment of rhizarthrosis. Osteoarthritis Cartilage.; 14 (1): 82e88.

Fuchs S. and Stahls A. (2006): Intra-articular hyaluronic acid compared with steroids injections for the treatment of CMC OA . Osteoarthritis Cartilage.; 218 (2): 113e173.

Gaikwad N., Sudhir J., Amol R., et al. (2016): Handgrip dynamometry: a surrogate marker of malnutrition to predict the prognosis in alcoholic liver disease Tissue Eng Part A.; 21(19-20): 2536–47.

Gibbons A. and Comerford M. (2001): Strength versus stability: part 1: concepts and terms. Orthop Div Rev; March/April: 21–7.

Gibofsky A., Hochberg M. and Jaros M. et al. (2014): Efficacy and safety of low-dose submicron diclofenac for the treatment of osteoarthritis pain: a 12 week, phase 3 study. *Curr Med Res Opin*. 1-11

Gillis J., Calder K. and Williams J. (2011): Review of thumb carpometacarpal arthritis classification, treatment and outcomes. Can J Plast Surg.; 19(4): 134–8.

Glickel S, (2001): Clinical assessment of the thumb trapeziometacarpal joint. *Hand Clin*.; 17 (2): 185-195.

Gormeli G., Ataoglu C., olak C., et al. (2015): “Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial,” Knee Surgery, Sports Traumatology, Arthroscopy.

Gormeli G., Gormeli C., Ataoglu B., et al. (2017): Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. *Knee Surg Sports Traumatol Arthrosc*.; 25(3): 958–965.

Gupta P., Das A., Chullikana A., et al. (2012): Mesenchymal stem cells for cartilage repair in osteoarthritis. Stem Cell Res Ther*;* **3**: 25.

Halilaj E., Douglas C. , Tarpit K., et al. (2014): Conf Proc IEEE Eng Med Biol Soc.: 4354–4357.

Halilaj E., Rainbow M., Got C., et al. (2014): In vivo kinematics of the thumb carpometacarpal joint during three isometric functional tasks. Clin Orthop Relat Res.; 472: 1114–1122. doi: 10.1007/s11999-013-3063.

Heyworth B., Lee J., Kim P., et al. (2008): Hylan versus corticosteroid versus placebo for treatment of basal joint arthritis: a prospective, randomized, double blinded clinical trial. J Hand Surg Am.; 33(1):40e48.

Hill S., Dziedzic K. and Ong B. (2010): The functional and psychological impact of hand osteoarthritis. Chronic Illn; 6: 101–10.

Hirschmann A., Sutter R., Schweizer A., et al. (2013): The carpometacarpal joint of the thumb: MR appearance in asymptomatic volunteers. Skeletal Radiol; 42: 1105-1112.

Hochberg M., Altman R. & April K. (2012): American College of Rheumatology recommendations for the use of non-pharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip and knee. Arthritis Care Res; 64: 465e474.

Ioppolo F., Fabiana S., Rosaria S., et al., (2016): Comparison Between Extracorporeal Shock Wave Therapy and Intra-articular Hyaluronic Acid Injections in the Treatment of First Carpometacarpal Joint Osteoarthritis , Ann Rehabil Med 2018; 42(1):92-100.

Jennifer M., Danielle L., Scher E., et al. (2014): Clin Orthop Relat Res. 2014 Apr; 472(4): 1130–1137.

Jindal N, Gaury Y, Banshiwal R, Lamoria R, Bachha V. (2013): Comparison of short term results of single injection of autologous blood and steroid injection in tennis elbow: a prospective study. J Orthop Surg Res; 8: 10-15.

Jo, Lee, and Shin. (2014): Intra-articular injection of mesenchymal stem cells for the treatment of osteoarthritis of the knee: a proof-of-concept clinical trial. Stem Cells.; 32(5): 1254-1266.

Kavadar G., Demircioglu D., Celik M., et al. (2015): Effectiveness of platelet-rich plasma in the treatment of moderate knee osteoarthritis: a randomized prospective study, Journal of physical therapy science; 27(12): 3863–3867.

Kesmezacar H., Egemen A. and Akgun I. (2014): Intraarticular injections (corticosteroid, hyaluronic acid, platelet rich plasma) for the knee osteoarthritis *World J Orthop* July 18; 5(3): 351-361.

Kjeken I., Grotle M. and Hagen K. (2015): Development of an evidence-based exercise programme for people with hand osteoarthritis. Scand J Occup Ther; 22: 103–116.

Kjeken M., Christensen B, Mowinckel P, et al. (2005): Activity limitations and participation restrictions in women with hand osteoarthritis: Patients' descriptions and associations between dimensions of functioning. Annals of the Rheumatic Diseases, 64(11), 1633–1638.

Kloppenburg M, (2014): Hand osteoarthritis –non pharmacological pharmacological treatments. Nat Rev Rheumatol; 10: 242–51.

Kloppenburg M., Kroon F., Blanco F., et al. (2018): sAnn Rheum Dis Epub ahead of print: . doi: 10.1136/ annrheumdis-213826.

Kroon A., Ermurat A., Beest V., et al. (2018): In thumb base osteoarthritis structural damage is more strongly associated with pain than synovitis. Osteoarthritis Research Society International. Volume 26, Issue 9, Pages 1196–1202

Kumahashi N., Swärd P. and Larsson S. (2015): Type II collagen C2C epitope in human synovial fluid and serum after knee injury--associations with molecular and structural markers of injury. Osteoarthritis Cartilage; 23: 1506.

Kurapati K., Sanjay T., Madhusudhan R., et al. (2018): Efficacy of Intra-articular Injection of Platelet Rich Plasma and Hyaluronic Acid in Early Knee Osteoarthritis – Case Series. European Journal of Molecular & Clinical Medicine, 5(1): 30–36.

Ladd L., Arnold P., Weiss C., et al. (2013): The Thumb Carpometacarpal Joint: Anatomy, Hormones, and Biomechanics Instr Course Lect.; 62: 165–179.

Lamo E., Mora J. and Blanco M. (2016): Intra-articular injection of two different doses of autologous bone marrow mesenchymal stem cells versus hyaluronic acid in the treatment of knee osteoarthritis: multicenter randomized controlled clinical trial (phase I/II). JTransl Med.; 14(1): 246.

Lesley J., Hascall V., Tammi M., et al. (2000): Hyaluronan binding by cell surface CD44. J Biol Chem.; 275: 26967-75.

Litwiniuk M., Krejner A., Speyrer M., et al. (2016): Hyaluronic acid in inflammation and tissue regeneration. Wounds; 28: 78-88.

Liu B. and Terkeltaub R. (2015): Emerging regulators of the inflammatory process in osteoarthritis. Nat Rev Rheumatol. Jan; 11(1): 35–44.

Loeser R., Collins J. and Diekman B. (2016): Ageing and the pathogenesis of osteoarthritis. Nat Rev Rheumatol; 12: 412.

Loeser R., Goldring S., Scanzello C., et al. (2012): Osteoarthritis: a disease of the joint as an organ. *Arthritis Rheum;* **64**: 1697-1707.

Loibl M., Siegmund L., Lena M., et al. (2016): Leukocyte-Reduced Platelet-Rich Plasma Treatment of Basal Thumb Arthritis BioMed Research International, Article ID 9262909, 6 pages.

Lubahn J., Ivance D. and Konieczko E. (2006): Immunohistochemical detection of relaxin binding to the volar oblique ligament. *J Hand Surg Am.*; 31(1): 80-84.

Luker K., Aguinaldo A., Kenney D., et al. (2014): Functional task kinematics of the thumb carpometacarpal joint. Clin Orthop Relat Res; 472: 1123-9.

Malahias M. , LeonidasR . , Vasileios S., et al. (2018): Platelet-Rich Plasma versus Corticosteroid Intra-Articular Injections for theTreatment of Trapeziometacarpal Arthritis: sagepub 66: 377–88.

Mandl L., Hotchkiss R., Adler R., et al. (2006): Can the carpometacarpal joint be injected accurately in the office setting? Implications for therapy. *J Rheumatol.;* 33:1137-9.

Marshall M., Van der D., Nicholls H., et al. (2009): Radiograhic hand osteoarthritis: Patterns and associations with hand pain and function in acommunity-dwelling samle.Osteoarthritis cartlage.17: 1440-1447.

Marzocco A., McCarthy M., Chowaniec D., et al. (2015): Platelet-Rich Plasma Differs According to Preparation Method and Human Variability; The journal of bone and joint surg; 94- (4).

Matullo K., Ilyas A. and Thoder J. (2007): CMC arthroplasty of the thumb A review. *Hand (N Y);* 2(4): 232-239.

Meheux C., McCulloch P., Lintner D., et al. (2015): Efficacy of intra-articular platelet-rich plasma injections in knee osteoarthritis: a systematic review. *Arthroscopy*,; 32: 495–505.

Melville D., Taljanovic MS., Scalcione L., et al., (2014): Imaging and management of thumb carpometacarpal joint osteoarthritis. Skeletal Radiol.; 44(2):165-77

Miller L. and Block J. (2013): US-approved intra-articular hyaluronic acid injections are safe and effective in patients with knee osteoarthritis: systematic review and meta-analysis of randomized, saline-controlled trials. Clin Med Insights Arthritis Musculoskelet Disord; 6: 57–63.

Monfort J., Delfin R., Nuria S., et al. (2014): Comparative efficacy of intra-articular hyaluronic acid and corticoid injections in osteoarthritis of the first carpometacarpal joint: Results of a 6-month single-masked randomized study. Joint Bone Spine 2, 86–90.

Moraes M., Lenza M., Tamaoki F, et al. (2013): "Platelet-rich therapies for musculoskeletal soft tissue injuries," Cochrane Database of Systematic Reviews, vol. 12, Article ID CD010071.

Murphy P., Christina B., Conor S., et al. (*2017*): Autologous Bone Marrow Stem Cell Use for

Osteoarthritis of the Thumb—First Carpometacarpal Joint; 6: 57–63.

Mustafa A., Mallen C., Murphy A., et al. (2017): The effectiveness and safety of platelet-rich plasma intra-articular injections in the treatment of knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Limerick: Health Research Institute Annual Scientific Meeting.

Nagai K., Matsushita T. and Matsuzaki T. (2015): Depletion of SIRT6 causes cellular senescence, DNA damage, and telomere dysfunction in human chondrocytes. Osteoarthritis Cartilage; 23: 1412.

Neogi T. and **Zhang Y. (2013):** Epidemiology of OA .Rheum Dis Clin North Am.; 39(1): 1–19.

Netter F. and Hansen J.(2003): *Atlas of Human Anatomy*. 3rd ed. Teterboro, NJ: Icon Learning Systems.

Neumann D. and Bielefeld T. (2003): J Orthop Sports Phys Ther; 33: 386–399.

Orth P., Rey A., Venkatesan J. et al. (2014): Current perspectives in stem cell research for knee cartilage repair. Stem Cells Cloning; **7**: 1-17.

Otero M., Favero M., Dragomir C., et al. (2012): chondrocyte cultures as models of cartilage-specific gene regulation. Methods Mol Biol.; 806: 301–36.

Patel S., Dhillon M., Aggarwal S. et al. (2013): Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. Am J Sports Med 41: 356–364.

Pearlman J., Stephanie S. and Valero C. (2004): The fundamentals thumb tip force vectors produced by the muscles of the thumb. J Orthop Res; 22: 306–12

Pereira R., Scaranari M. and Benelli R. (2013): Dual effect of platelet lysate on human articular cartilage: a maintenance of chondrogenic potential and a transient proinflammatory activity followed by an inflammation resolution. Tissue Eng Part A 19(11–12), 1476–1488.

Pers Y., Ruiz N. and Jorgensen. (2015): Mesenchymal stem cells for the management of inflammation in osteoarthritis: state of the art and perspectives. Osteoarthritis

Philip T., Kaylan N., McClary K., et al . (2017): The Accuracy of Common Hand Injections With and Without Ultrasound; sagepub Vol. 12(6) 591-596

Pollard M., Cermak M., Buck W., et al. (2007): Accuracy of injection into the basal joint of the thumb. *Am J Orthop (Belle Mead NJ)*.; 36:204-6.

Psaty B. and Furberg C. (2005): COX-2 inhibitors - lessons in drug safety. N Engl J Med; 352: 1133–5.

Rahmati M., Mobasheri A. and Mozafari M. (2016): Inflammatory mediators in osteoarthritis: A critical review of the state-of-the-art, current prospects, and future challenges. Bone.; 85: 81–90.

Rikke H., Andrew G., Barbara S., et al .(2010): Concurrent evaluation of data quality, reliability and validity of the Australian/Canadian Osteoarthritis Hand Index and the Functional Index for Hand Osteoarthritis. National Resource Centre for Rehabilitation in Rheumatology,8: 10-15.

Robyn T., Susan K., Manja O., et al. (2017): South African Journal of Occupational Therapy.; 47(1): 41-45.

Roush T., Aldridge J., Berger R., et al. (2005): No correlation between trapeziometacarpal arthritis and abductor pollicis longus insertion. Clin Orthop Relat Res.; 434:138–142.

Roux C., Fontas E., Breuil V., et al. (2007): Injection of intra-articular sodium hyaluronidate (Sinovial) into the carpometacarpal joint of the thumb (CMC1) in osteoarthritis. A prospective evaluation of efficacy. Joint Bone Spine; 74(4): 368e372.

Sadabad H., Behzadifar M., Arasteh F., et al. (2016): Efficacy of platelet-rich plasma versus hyaluronic acid for treatment of knee osteoarthritis: a systematic review and meta-analysis. *Electron Physician*.; 8(3): 2115–2122.

Salini A., Deamicis M., Abate L., et al. (2009): Postgraduate School ofOrthopaedics and Traumatology, Department ofHuman Movement Science, University " d'Annunzio" Chieti-Pescara, Chieti; 'Postgraduate School ofPhysical Medicine and Rehabilitation.

Samantha M. and Marie B. (2017): PRP Injections Are an Effective Treatment for Carpometacarpal Joint OA. American academy of orthopedic surgeons 10(1): 26-29

Sanchez M., Fiz N. and Azofra J, (2012): A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. *Arthroscopy*; 28(8): 1070–1078.

Scotti C, A. Gobbi, G. Karnatzikos, (2016): “Cartilage Repair in the Inflamed Joint: considerations for biological augmentation toward tissue regeneration,” *Tissue Engineering Part B: Reviews*, vol. 22, no. 2, pp. 149–159.

Shewale A., Barnes C., Fischbach L., et al. (2017): Comparative effectiveness of low, moderate and high molecular weight hyaluronic acid injections indelaying time to knee surgery, *The Journal of Arthroplasty,* doi: 10.1016/j.arth.2017.04.041.

Shim J., Young R., Kim J., et al.(2013): Normative Measurements of Grip and Pinch Strengths of 21st Century Korean Population Arch Plast Surg.3; 40(1): 52-56.

Stahl S., Karsh I., Ratzon N., et al. (2005): Comparison of intraarticular injection of depot corticosteroid and hyaluronic acid for treatment of degenerative trapeziometacarpal joints. J Clin Rheumatol;11:299-302.

Szubstarski M., Sekuła P., Głodek Ł., et al. (2017): Intra-articular injections – current indications and contraindications. Journal of Education, Health and Sport; 7(8): 907-916. eISSN 2391-8306.

Taccardo G., Rocco D., Parrone G., (2013): Surgical treatment of trapeziometacarpal joint osteoarthritis joints; 1(3):138-144.

Tropet Y., Gallinet D., Lepage D., et al. (2012): Treatment of trapeziometacarpal osteoarthritis by partial trapeziectomy and costal cartilage autograft. A review of 100 cases. Chir Main.; 31: 145–151.

Umphrey G., Brault J., Hurdle M., et al. (2008): Ultrasound-guided intra-articular injection of the trapeziometacarpal joint: description of technique. *Arch Phys Med Rehabil.*; 89:153-6.

VanHeest A. and Kallemeier P. (2008): Thumb carpalmetacarpal arthritis. Jam Acad Orthop Surg.; 16(3): 140–51.

Vasiliadis H. and Tsikopoulos M. (2017): Glucosamine and chondroitin for the treatment of osteoarthritis. World J Orthop 8: 1–11.

Vermeulen G., Slijper H., Feitz R., et al. (2011): Surgical management of primary thumb carpometacarpal osteoarthritis: a systematic review. J Hand Surg Am.; 36 (5): 157e169.

Villafañe J. and **Valdes K. (2014):** Reliability of pinch strength testing in elderly subjects with unilateral thumb carpometacarpal osteoarthritis. J Phys Ther Sci.; 26: 993–995.

Villafañe J., Cleland J. and Fernandez L. (2013): The effectiveness of a manual therapy and exercise protocol in patients with thumb carpometacarpal osteoarthritis: a randomized controlled trial. J Orthop Sports Phys Ther.; 43(4): 204–213.

Villafane J., Valde K., CanteroT., et al. (2016): How do we manage thumb carpometacarpal osteoarthritis? A survey of clinical practice trends for hand therapists in the Spain. Int. J. Clin. Rheumtol. 11, 12e14.

Villafane J., Valdes K., Berjano A., et al. (2017): Clinical update: conservative management of carpometacarpal joint osteoarthritis. J. Rheumatol. 42, 1728e1729.

Wajon A., Carr E., Edmunds I. et al. (2009): Surgery for thumb (trapeziometacarpal joint) osteoarthritis. Cochrane Database Syst

Wajon A., Vinycomb T. and Carr E. (2015): Surgery for thumb(trapeziometacarpal joint) osteoarthritis. Cochrane Database Syst Rev.

Wang X., Hunter D., Jin X., et al. (2018): The importance of synovial inflammation in osteoarthritis: current evidence from imaging assessments and clinical trials. Osteoarthritis Cartilage; 26: 165.

Windt T., Saris D., Cortenbach I. (2015): Direct cell–cell contact with chondrocytes is a key mechanism in multipotent mesenchymal stromal cell-mediated chondrogenesis. Tissue Eng Part A.; 21(19-20): 2536–47.

Wolf J. and Delaronde S. (2012): Current trends in nonoperative and operative treatment of trapeziometacarpal osteoarthritis: a survey of US hand surgeons. J Hand Surg Am.; 37: 77–82.

Wolf J., Schreier S., Tomsick S., et al. (2011): Radiographic laxity of the trapeziometacarpal joint is correlated with generalized joint hypermobility. J Hand Surg Am.; 36(7): 1165–1169.

Wolfstadt J., Cole B., Ogilvie-Harris D., et al. (2014): Current Concepts: The Role of Mesenchymal Stem Cells in the Management of Knee Osteoarthritis. Sports Health: A Multidisciplinary Approach.

Woo T., Lau L., Cheung N., et al. (2017): Efficacy of Oral Collagen in Joint Pain - Osteoarthritis and Rheumatoid Arthritis. J Arthritis 6: 233. doi: 10.4172/2167-7921.1000233.

Yin Z., Yang X., Jiang Y., et al. (2013): Platelet-rich plasma combined with agarose as a bioactive scaffold to enhance cartilage repair: an in vitro study. J Biomater Appl 28(7), 103.

Young, S & Mikola, E (2004), 'Thumb carpometacarpal arthrosis', *Journal of the American Society for Surgery of the Hand,* vol. 4, no.2, pp. 73-93.

Yuan T., Zhang C. and Wang J. (2013): Augmenting tendon and ligament repair with platelet-rich plasma (PRP), Muscles Ligaments Tendons Journal; 3(3): 139–149.

Zhang A., Nortwick V., Hagert E., et al. (2013): Thumb carpometacarpal ligaments inside and out: a comparative study of arthroscopic and gross anatomy from the Robert A. Chase Hand and Upper Limb Center at Stanford University. J Wrist Surg.; 2(1): 55–62.

Zhang W, Doherty M and Leeb BF, (2007): EULAR evidence based recommendations for the management of hand osteoarthritis: Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis; 66: 377–88.

Zhang W., Chen-guang A., Wang H., et al. (2018): Department of Orthopaedics, Tianjin Medical University General Hospital, Tianjin, People’s Republic of China; Cancer & Immunology Research, Children’s Research Institute, Children’s National Medical Center, Washington DC, USA.

Zhang Y. and Jordan J. (2010): Epidemiology of osteoarthritis. Clin Geriatr Med; 26: 355–69.

Zhu Y., Yuan M., Meng H., et al. (2013): Basic science and clinical application of platelet-rich plasma for cartilage defects and osteoarthritis: a review. *Osteoarthritis Cartilage*; **21**: 1627-1637.

Zina M., Andrew Y., Liu K., et al., (2016): Evaluation of Physical Examination Tests for Thumb Basal Joint Osteoarthritis , American Association for Hand Surgery Vol. 11(1) 108-112**.**

الملخص العربي

يعتبر المفصل الرسغى السنعى للإبهام هو ثاني أكثر المفاصل تأثراً بالخشونة. الأعراض النموذجية لخشونة المفصل هى الألم ، وكذلك تصلب في الصباح أو تصلب بسبب عدم النشاط. ومن ثم ، فإن وظيفة اليد تتأثر سلبًا في كثير من الأحيان فى مرضى خشونة المفصل الرسغى السنعى.

الهدف من العلاج التحفظى هو استعادة وظائف الإبهام ، بما في ذلك تخفيف الألم ، ثبات المفصل ، وحركته ، وقوة قبضة وقرصة اليد. لذلك يحدث تحسن في جميع وظائف اليد وأداء أنشطة الحياة اليومية. العلاج بالحقن الموضعى يعتبر طريقة علاج جذابة لعلاج خشونة المفاصل بسبب قلة الآثار الجانبية على الجسم.

أجريت هذه الدراسة على ثلاثين مريضاً بخشونة فى مفصل الرسغى السنعى للابهام تم جمعهم من عيادة الطب الطبيعى، وأمراض الروماتيزم وإعادة التأهيل في مستشفى جامعة عين شمس.

. استند التشخيص إلى أخذ التاريخ المرضى ، الفحص الكامل وعمل الاشعة السينية على المفصل.

تم تقسيم المرضى عشوائيا إلى مجموعتين:

المجموعة ١: تم حقن خمسة عشر مريضا داخل المفصل بالبلازما الغنية بالصفائح الدموية الدموية.

المجموعة ٢ : تم حقن خمسة عشر مريضا داخل المفصل بحمض الهيالورونيك ١ مل (ملح حمض الهيالورونيك الصوديوم).

تم تقييم المرضى قبل الحقن وبعد ٤ و ١٢ أسبوعًا من الحقن عن طريق الفحص الموضعى لمعرفة درجة الالم و قياس درجة الالم بواسطة و استبيان اوسكان لقياس مدي تاثر وظائف اليد و قياس قوة قبضة و قرصة اليد بواسطة الديناموميتر.

في دراستنا ، أظهرت نتائج المجموعة الاولى أن هناك تحسن كبير للغاية فيما يتعلق بالألم و وظائف اليد وزيادة في قوة قبضة وقرصة اليد بعد ٤ و ١٢ أسبوعا متابعة مقارنة بما قبل الحقن. ومع ذلك ، انخفض هذا التحسن بالنسبة للالم ووظائف وقوة اليد فى فترة المتابعة من ٤ إلى ١٢ أسبوعا .

أما المجموعة الثانية التي تم حقنها بحمض الهيالورونيك ، أبلغ المرضى عن تخفيف الألم بشكل كبير ، وتحسن فى وظائف اليد وزيادة في قوة قبضة وقرصة اليد بعد ٤ و ١٢ أسبوعا من الحقن.كما كان هناك تحسن كبير للغاية بالنسبة للالم ووظائف وقوة اليد فى فترة المتابعة من ٤ إلى ١٢ أسبوعا.

عند المقارنة بين المجموعتين بعد ٤ أسابيع من الحقن ، لم يكن هناك اختلاف فيما يتعلق بالالم عند الضغط الموضعى، وقوة القرصة ، واستبيان اوسكان لوظائف اليد . ومع ذلك ، كان هناك فروق ذو دلالة إحصائية فيما يتعلق بقوة قبضة اليد و مقياس الالم .

حيث أظهرت المقارنة أن زيادة قوة قبضة اليد كانت أكثر فى المجموعة الثانية عن المجموعة الأولى و لكن تحسن الألم كان أفضل فى المجموعة الأولى.

بالمقارنة بين المجموعتين بعد ١٢ أسبوعًا ، كان هناك فروق ذو دلالة إحصائية كبيرة فيما يتعلق مقياس الالم واستبيان اوسكان لوظائف اليد و قوة قبضة و قرصة اليد

حيث كان التحسن أكبر فى المجموعة الثانية بعد ١٢ اسبوعا من الحقن.

يوفر حقن حمض الهيالورونيك مزايا علاجية أفضل من حقن البلازما الغنية بالصفائح الدموية خاصة في المتابعة الأطول فى المدى بعد ١٢ أسبوعًا من الحقن.