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Platelet Rich Plasma In Treatment Of Temporomandibular Joint Disorders

A Project Submitted to the College of Dentistry, University of Baghdad, Department of Oral Diagnosis /Oral Medicine Clinic in Partial Fulfillment of the Requirement for B.D.S.

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Dedication

To god almighty, who graced my life with opportunities, my source of inspiration and strength, the one who never give up on nobody.

To my parents, my mentors, for encouraging me and rising me believing that everything is possible.

To my brothers and sister, without whom none of this would be possible. To my friends who I shared this journey and memories with.

Acknowledgment

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Abstract

Temporomandibular Disorders (TMD) are a class of degenerative musculoskeletal conditions associated with morphological and functional deformities. TMD are accompanied by malpositioning of the TMJ disc termed ‘internal derangement’, or dysfunction of the associated musculature. Signs and symptoms of TMD include painful joint movement, deviation or limitation in the mandibular movements, and TMJ sounds. Prevalence of TMD differs from study to study due to the multifactorial nature of the disorder with no specific etiological cause. The complexity and unique nature of each TMD case, makes the diagnosis specific and tailored to each patient and accompanied by various diagnostic modalities. There is no unified strategy for the management of this disease, but most cases of TMD respond well to simple treatment with anti-inflammatory medications, soft diet and occlusal therapy, without the need for surgical intervention. Prognosis is good and symptoms usually remit with simple care. This research is reviewing the etiology, classification, diagnosis, epidemiology, and treatment of TMD.

PRP is a biological product defined as a portion of the plasma fraction of autologous blood with a platelet concentration above the baseline (before centrifugation).

The ubiquitous nature of the mechanism of action of PRP suggests that, in theory, it can be applied to multiple pathologies to aid the body’s natural healing processes.

After the procedure there will be some pain, mild swelling or redness, of the skin following injection of the platelet rich plasma - PRP. Bruising is also a possibility as the needle is used to place the PRP into the skin. This may take a week or so to resolve.

Different definitions of this outcome were reported by authors, for example mandibular opening, mandibular motion, mouth voluntary opening and maximum mouth opening, minimal interincisal opening, range motion.

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List of Abbreviations

TMD	Temporomandibular Disorders
TMJ	Temporomandibular Joint
PRP	Platelet Rich Plasma
DDWR	Disc Displacement with Reduction
DDWoR	Disc Displacement without Reduction
RDC/TMD	Research Diagnostic Criteria for Temporomandibular Disorders

DC/TMD	Diagnostic Criteria for Temporomandibular Disorders
NSAID	Non-Steroidal Anti-Inflammatory Drugs
RA	Rheumatoid arthritis
BoNT	Botulinum Toxin
LLLT	Low- level Laser Therapy
TENS	Transcutaneous Electrical Nerve Stimulation
MRI	Magnetic Resonance Imaging
CBCT	Cone Beam Computed Tomography
GFs	Growth Factors
PPP	platelet-poor plasma
PDGF	platelet-derived growth factor
VEGF	vascular endothelial growth factor
TGF-β	transforming growth factor-β superfamily
FGF	fibroblast growth factor
IGF	insulin-like growth factor
MSCs	mesenchymal stem cells
PDCD5	programmed cell death 5
MMPs	matrix metalloproteinases
IL-1β	interleukin-1β
OA	osteoarthritis

CMS	Coleman modified score
RCT	randomized controlled trial
L-PRP	leukocyte-rich PRP
P-PRP	pure PRP
ACl	anterior cruciate ligament
LPCGF	Liquid Phase Concentrated Growth Factor
VAS	visual analogue scale

Introduction

Temporomandibular joint and muscle disorders, commonly called "TMD" are a group of conditions that cause pain and dysfunction in the jaw joint and the muscles that control jaw movement. We don't know for certain how many people have TMJ disorders, but some estimates suggest that over 10 million Americans are affected. The condition appears to be more common in women than men.

For most people, pain in the area of the jaw joint or muscles does not signal a serious problem. Generally, discomfort from these conditions is occasional and temporary, often occurring in cycles. The pain eventually goes away with little or no treatment. Some people, however, develop significant, long-term symptoms , it's important to avoid, when possible, procedures that can cause permanent changes in your bite or jaw (1).

TMDs are classified to articular disorders and masticatory muscle disorders, articular disorders include the articular surface, intra-articular disk, or articulating bones, while masticatory muscle disorders are problems within the muscles surrounding the TMJ (2).

Common symptoms include jaw pain or dysfunction, earache, headache, and facial pain. The etiology of TMD is multifactorial and includes biologic, environmental, social, emotional, and cognitive triggers. Diagnosis is most often based on history and physical examination. Diagnostic imaging may be beneficial when malocclusion or intra-articular abnormalities are suspected. Most patients improve with a combination of noninvasive therapies, including patient education, self-care, cognitive behavior therapy, pharmacotherapy, physical therapy, and occlusal devices. Nonsteroidal anti-inflammatory drugs and muscle relaxants are recommended initially, and benzodiazepines or antidepressants may be added for chronic cases(3).

In general, TMD is believed to affect anywhere between 5 and 15% of adults in the population (4,5), yet TMD related symptoms have been reported to be present in up to 50% of adults (6). Interestingly, there is evidence that the prevalence of TMD appears to be on the rise in recent years (7,8). A recent systematic review and meta-analysis in 2021 concluded that the prevalence of TMD was 31% for adults and 11% for children and adolescence (9). The fact that TMD encompasses a broad assortment of clinical diseases is partially responsible for the wide range of prevalence rate estimates among studies, as the classification of different types of TMD, the distinction between disease and non-disease, as well as whether to include those with inactive disease as having TMD, may all be subject to

the partialities of the assessing clinical researchers. In addition, studies that are questionnaire-based might over-estimate the prevalence of TMD.

Platelet Rich Plasma (PRP) has recently been considered as an orthobiological adjuvant treatment. It also restores intra-articular hyaluronic acid, increases glycosaminoglycan chondrocyte synthesis, balances joint angiogenesis, and provides a scaffold for stem cells migration. Basic scientific studies have indicated that PRP stimulates cell proliferation and the production of cartilage matrix by chondrocytes and bone marrow-derived mesenchymal stromal cells and increases the production of hyaluronic acid by synoviocytes.(10)

Chapter One
Review of Literature

1.1 Temporomandibular Joint

1.1.1 Definition

The Temporomandibular Joint (TMJ), also known as the craniomandibular joint/articulation. It is the articulation between the squamous part of the temporal bone and the head of the mandibular condyle. It consists of a mandibular or glenoid fossa, an articular eminence or tubercle, a condyle, a separating disk, a joint fibrous capsule and an extracapsular check ligaments (11).

The temporomandibular joint is critical for normal mouth function, and thus plays a role in chewing, swallowing, speaking, oral health and nutrition (12).

It is distinguished from most of the joints by following points :

* The TMJ differs from other synovial joints by the presence of teeth, which can offer anterior stabilization during surface articulation.

* The articular surface of the mandibular fossa is composed of fibrocartilage, not hyaline cartilage, and is nonarticular because of the presence of the posterior band of the temporomandibular disk (13).

* It has bilateral articulation with cranium, so both the joints must function together (14).

* It is classified as a ginglymoarthrodial joint. It has the features of a hinging movement characteristic of a ginglymus joint, as well as a sliding movement characteristic of an arthrodial joint (15).

1.1.2 Anatomy of the Temporomandibular joint

1.1.2.1 The Primary Components of the TMJ

- Condyle of the Mandible.
- Squamous Portion of the Temporal Bone.
- Articular Disc (contained within the TMJ).
- Ligaments (serve as boundaries) (16).

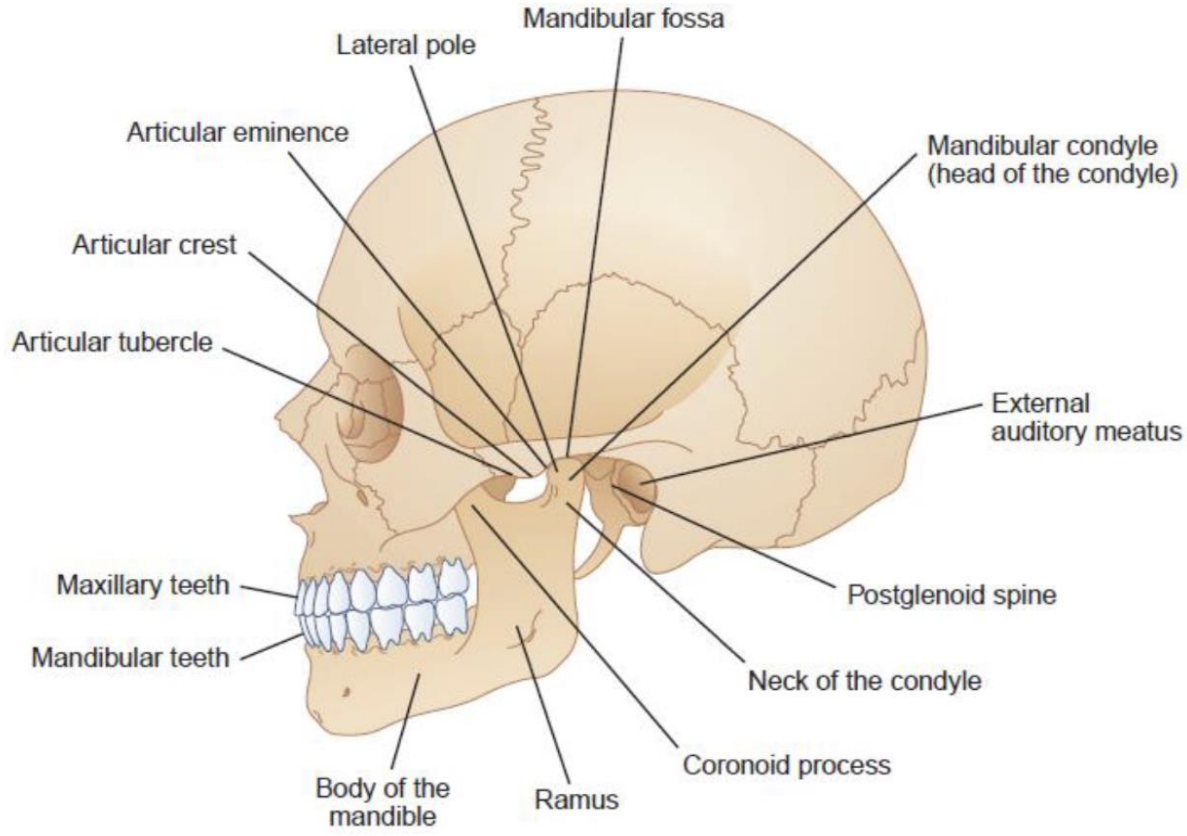

Figure (1-1) Lateral View of the Skeletal Anatomy (13).

The Condyle

Is the portion of the mandible that articulates with the cranium around which movement occurs. From the anterior view it has medial and lateral projections, called poles. The medial pole is generally more prominent than the lateral one. From above, a line drawn through the centers of the poles of the condyle will usually extend medially and posteriorly toward the anterior border of the foramen magnum (17). It is 15 to 20 mm side to side and 8 to 10 mm from front to back (18).

The adult condyle varies considerably in form from that found in the young child. In the former, the neck is thin and elongated and is readily fractured. Although an apparent weakness, this feature gives some protection to the delicate roof of glenoid fossa (19).

The most prevalent bony changes of the condyle are, for example, the flattening, the erosion, the sclerosis, the presence of osteophytes, and the resorption (20).

Squamous Portion of the Temporal Bone

The temporal bone forms the roof of the TMJ, the concave mandibular fossa marks the posterior border, and the convex articular eminence forms the anterior boundary (13). The glenoid fossa is wider in its mediolateral portion, compared to the anteroposterior area (21). The posterior roof of the mandibular fossa is quite thin, indicating that this area of the

temporal bone is not designed to sustain heavy forces. The articular eminence, however, consists of thick dense bone and is more likely to tolerate such forces (17).

Articular Disc

It is a firm yet flexible biconcave fibrocartilage structure consisting of dense bundles of collagenous fibers, which allows it to conform to the incongruence of the TMJ. This fibrocartilaginous surface provides greater pliability during translation and increased tensile strength for prolonged pressure and friction (13).

Because of its position between the condyle and the temporal bones, the disk divides the joint into an upper and a lower compartment. The lower compartment serves as the socket in which the condyle rotates, whereas the upper compartment allows the socket to slide up and down the eminence (22).

It has a biconcave shape, with the thinnest portion near its center. The posterior border is thicker than the anterior border, and the medial border is thicker than the lateral border. These thicker borders aid in keeping the disc in place atop the round condylar head. The articular disc is also held in place by additional soft tissues attached circumferentially (23).

It is avascular and aneural in its central part but is vascular and innervated in the peripheral areas, where load-bearing is minimal. The main load-bearing areas are located on the lateral aspect, This is an area of potential perforation (16).

Rees has divided the disc into four zones, which he has named the anterior band, intermediate zone, posterior band, and bilaminar zone (24). The anterior extension of the disc is attached to fibrous capsule superiorly and inferiorly and through that to temporal bone and the mandibular neck respectively. In between it gives insertion to lateral pterygoid muscle where the fibrous capsule is lacking and synovial membrane is supported only by loose areolar tissue (19). Posteriorly, the disc attaches superiorly to the temporal bone and inferiorly to the posterior condyle (the posterior attachments are frequently called the bilaminar zone). Laterally and medially, the disc attachments blend into the joint capsule near its attachment to the condylar head (25).

The bilaminar region consists of two layers of fibers separated by loose connective tissue. The upper layer or temporal lamina is composed of elastin and is attached to the postglenoid process, medially extended ridge, which is the true posterior boundary of the joint. It prevents slipping of the disk while yawning. The inferior layer of the fibers or inferior lamina curve

down behind the condyle to fuse with the capsule and back of the condylar neck at the lowest limit of the joint space. It prevents excessive rotation of the disk over the condyle (18). Some investigators think that the bilaminar zone has an active role in limiting retrusion of the mandible; Others think it has only a passive role (24). The lateral pterygoid, fibers from the temporalis, the zygomaticomandibularis muscle, and the masseter were observed to attach to the disc (26).

Ligaments

The Capsular Ligament is a thin, inelastic, fibrous connective tissue envelope, oriented vertically, that attaches to the margins of the articular surfaces. The capsular ligament does not restrain condylar movements.

The Lateral Temporomandibularl Ligament is the main ligament of the joint, lateral to the capsule but not easily separated from it by dissection. Its fibers pass obliquely from bone lateral to the articular tubercle in a posterior and inferior direction and insert in a narrower area below and behind the lateral pole of the condyle. In earlier literature, this ligament was identified as an oblique band from the condylar neck to the anterosuperior region on the eminence and as a horizontal band from the lateral condylar pole to an anterior attachment of the eminence. A recent study was unable to confirm a distinct structure separate from the capsule (27). This ligament limits the movement of the mandible in a posterior direction and thus protects the external auditory meatus (28).

The Collateral (Discal) Ligaments attach the medial and lateral borders of the articular disc to the poles of the condyle. The medial discal ligament attaches the medial edge of the disc to the medial pole of the condyle. The lateral discal ligament attaches the lateral edge of the disc to the lateral pole of the condyle. The discal ligaments are true ligaments, composed of collagenous connective tissue fibers, therefore they do not stretch. They function to restrict movement of the disc away from the condyle. These ligaments are responsible for the hinging movement of the TMJ. The discal ligaments have a vascular supply and are innervated, their innervation provides information regarding joint position and movement, strain on these ligaments produces pain (17).

Sphenomandibular Ligament is found on the medial side of the joint and courses from the spine of the sphenoid to the lingula of the mandible. It is thin and functions as the primary passive support of the mandible (29).

Stylomandibular Ligament passes from the styloid process of the temporal bone to the posterior margin and angle of the mandible (30).

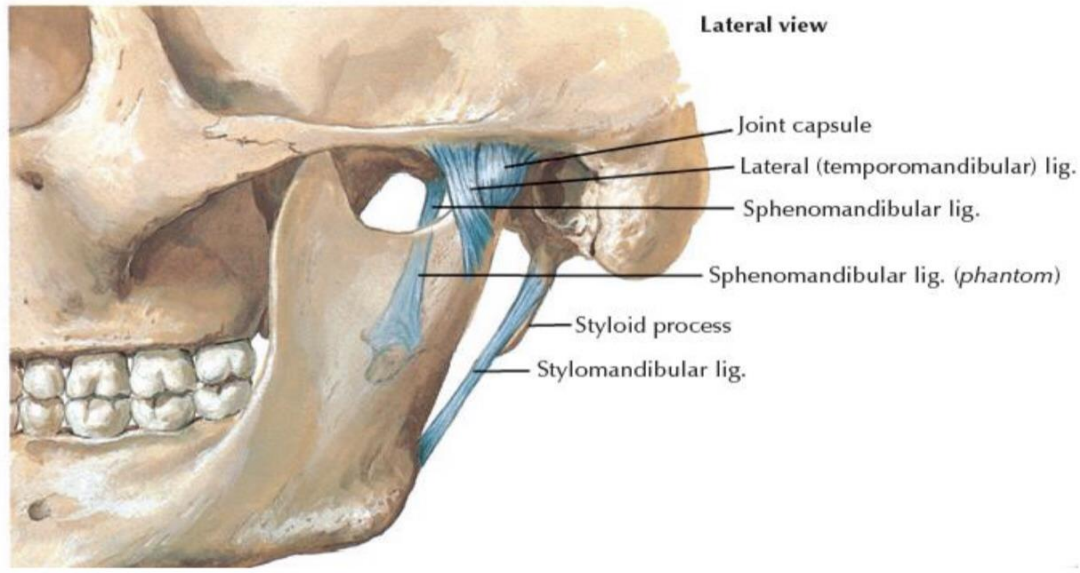

Figure (1-2) Ligaments of the Temporomandibular Joint (16).

Joint Capsule

The anterior capsule attached superiorly to the anterior slope of the articular eminence and inferiorly to the anterior articular rim of the condyle. Laterally, the lateral discal ligament and capsule are not separate entities, but rather they both attach at the condylar pole level. Marguelles-Bonnet et al. (31) reported a similar finding (32).

The posterior segment of the joint capsule is made up of the so called “bilaminar zone” of the articular disc. The upper internal portion of the posterior segment of the capsule was reinforced by the discomalleolar ligament (33).

The articular capsule is largely divided into two parts, an outer fibrous layer and inner synovial membrane. The synovial membrane, which is involved in the production, secretion and resorption of synovial fluids, consists of the synovial lining layer, and the connective sublining layer(34). It contains specialized cell types with phagocytic and immunologic capacity, and produces the synovial fluid that provides the nutritional and metabolic

requirements to the avascular tissues of the mandibular condylar and articular eminence fibrocartilage as well as to the disc. It also serves as a joint lubricant (35).

1.1.2.2 Muscles Associated with Mandibular Movement and Function

1.1.2.2.1 Muscles of Mastication

- Masseter Muscle.
- Temporalis Muscle.
- Medial Pterygoid Muscle.
- Lateral Pterygoid Muscle.

Masseter Muscle

It is a broad, thick, flat rectangular muscle (almost quadrilateral) on each side of the face, anterior to the parotid salivary gland. It has two heads that differ in depth, Superficial and deep.

The superficial head originates from the zygomatic process of the maxilla, and from the anterior two thirds of the inferior border of the zygomatic arch. The deep head originates from the posterior one third and the entire medial surface of the zygomatic arch. Both these heads then pass inferiorly to insert on different parts of the external surface of the mandible, The superficial head on the lateral surface of the angle, and the deep head on the ramus superior to the angle (36).

Numerous reports state that the posterior part of the deep layer of the masseter attaches to the lateral part of the disc (26). Anteriorly, the deep portion is covered by the superior portion of the masseter, while posteriorly; the parotid gland covers the deep portion. The masseter is primarily responsible for the elevation of the mandible and some protraction of the mandible. It receives its motor innervation from the mandibular division of the trigeminal nerve. The blood supply is primarily from the masseteric artery, a branch of the internal maxillary artery(37).

Temporalis Muscle

The temporalis muscle is a fan-shaped muscle with anterior fibers that have a vertical orientation, mid fibers have an oblique orientation, and posterior fibers have a more of a horizontal orientation.

The origin of the temporalis muscle spans from the temporal fossa to the inferior temporal line of the lateral skull. The temporalis muscle fibers converge inferiorly forming a tendon that exits the temporal fossa, passing underneath the zygomatic arch and inserting on the coronoid process of the mandible.

The function of the anterior and mid fibers of the temporalis muscle is to elevate the mandible. The posterior fibers of the temporalis muscle function to retract the mandible (38). Akita et al.(39) reported that the midmedial muscle bundle of the temporalis run into the articular disc. This muscle bundle originated from the medial surface of the temporalis as a part of the temporalis, it ran inferiorly and posteriorly to condylar process. The fact that the insertion of the muscle bundle of the temporalis is on the condylar process is a very important factor for jaw movement (40).

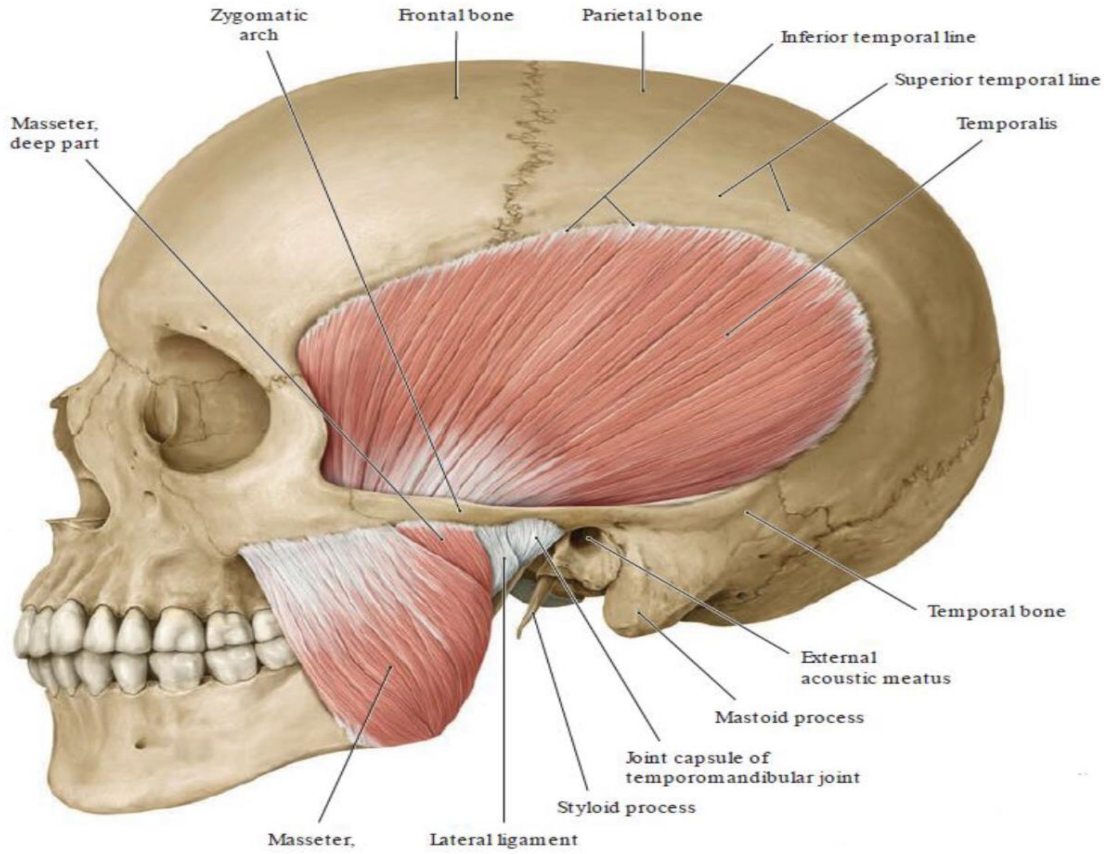

Figure (1-3) Temporalis and Masseter Muscles (41).

Mdial Pterygoid Muscle

It is quadrangular in shape and has deep and superficial heads, The deep head is attached above to the medial surface of the lateral plate of the pterygoid process and the associated surface of the pyramidal process of the palatine bone, and descends obliquely downward,

medial to the sphenomandibular ligament, to attach to the roughened medial surface of the ramus of the mandible near the angle of the mandible. The superficial head originates from the tuberosity of the maxilla and adjacent pyramidal process of the palatine bone and joins with the deep head to insert on the mandible (30).

It has a triple function, First, bilateral contraction of the muscle with lateral pterygoid muscle results in protrusion of the mandible, This action results as the muscle fibers are aligned anteroposteriorly. Second, unilateral contraction of the medial pterygoid muscle with lateral pterygoid muscle ipsilaterally results in lateral movement of the mandible towards the opposite side. This action occurs due to the mediolateral direction of the muscle fibers. Third, the muscle functions with masseter and temporalis muscles to elevate the mandible (42). During vertical jaw movements, lateral pterygoid muscle act as a primary muscle that generates horizontal forces. However, the medial pterygoid muscle may also play a role in controlling horizontal jaw positions (43). The medial pterygoid muscle is innervated by the medial pterygoid nerve, which is a branch of the main trunk of the mandibular branch of cranial nerve V (trigeminal nerve) (44). The medial pterygoid muscle was supplied by the following 5 branches of the external carotid artery:

1-the pterygoid artery of the maxillary artery

2- a direct muscular branch of the facial artery

3-the ascending palatine artery

4-an anterior muscular branch of the facial artery

5-a previously undescribed muscular branch that directly arose from the external carotid artery (45).

Lateral Pterygoid Muscle

It is a short, thick muscle which conventionally is described to consist of two parts or heads. The superior (upper) head and the inferior (lower) head. The superior head arises from the infratemporal surface and infratemporal crest of the greater wing of the sphenoid bone. The inferior head arises from the lateral surface of the lateral pterygoid plate. From the two origins, the fibres converge, and pass backwards and laterally, to be inserted into a depression on the front of the neck of the mandible and into the articular capsule and disc of the TMJ (46).

The lateral pterygoid muscle has a typical penniform structure comparable to that of the masseter and medial pterygoid muscle (47). It receives blood supply from the pterygoid

branch of the second part of the maxillary artery and receives innervation from the mandibular branch of the trigeminal nerve (48).

It is considered to be related to the movement of the articular disc and to play a unique and complex role in the temporomandibular joint (49). The inferior head is said to be active during jaw opening, jaw protrusion, and contralateral jaw movements. The superior head during jaw closing, jaw retrusion, and ipsilateral jaw movements (50). It is thought to play an important role in the aetiology of temporomandibular disorders (TMD) it becomes hyperactive, or thought to be a lack of co-ordination between the upper and lower heads of the muscle, or thought to be a disturbance to the normal postulated role for the muscle in the control or stabilization of the temporomandibular joint (51).

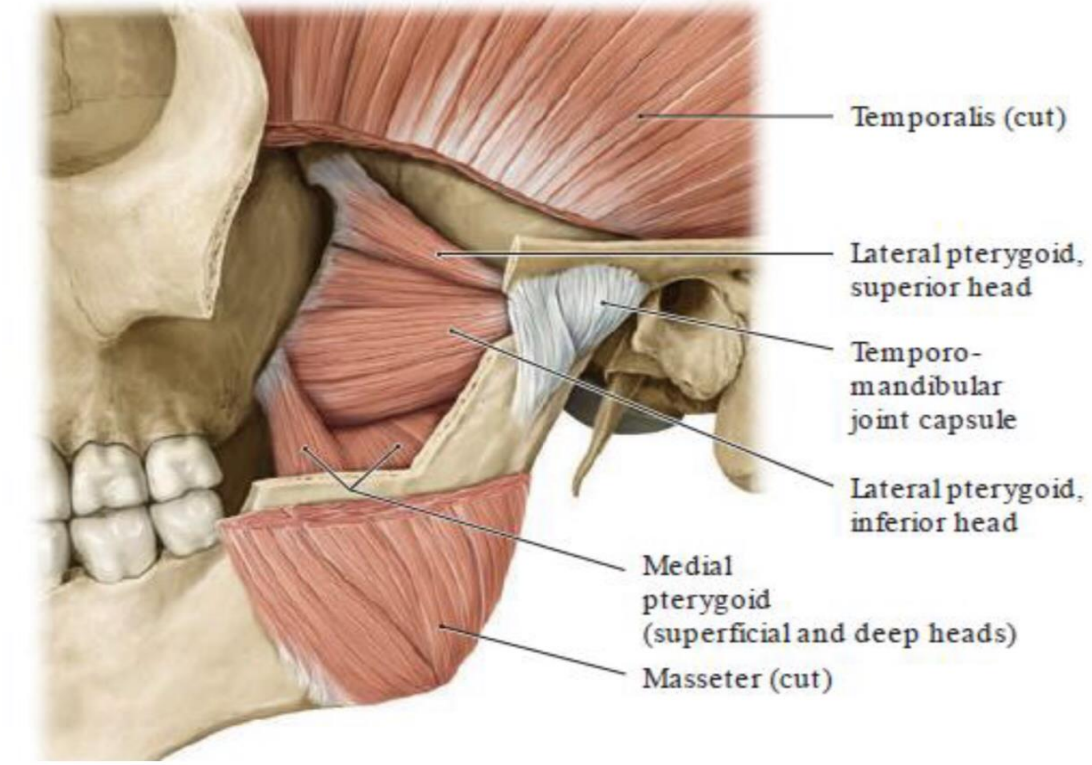

Figure (1-4) Medial and Lateral Pterygoid Muscles (41).

1.1.2.2.2 Accessory to Masticatory Muscles

Digastric Muscle

There is a pair of digastric muscles in the neck, and each digastric muscle has the anterior belly and the posterior belly. The anterior belly is attached to the digastric fossa on the base of the mandible close to the midline and runs toward the hyoid bone. The posterior belly is attached to the notch of the mastoid process of the temporal bone and also runs toward the

hyoid bone. The two bellies meet as the intermediate tendon, which penetrates the stylohyoid muscle and also passes through the fibrous loop which is attached to the body and greater cornu of the hyoid bone (52). The mylohyoid nerve innervates the anterior belly and the facial nerve innervates the posterior belly. Acting in pairs, the digastric muscles act either depresses the mandible or elevate the hyoid bone. The posterior bellies are especially active during swallowing and chewing (53).

Mylohyoid Muscle

It is a flat and triangular muscle that originates from the mandible near the molars and inserts on the hyoid bone. The mylohyoid mainly functions to elevate the hyoid bone, elevate the oral cavity, and depress the mandible. The source of motor innervation is via the mylohyoid nerve (54).

Geniohyoid Muscle

It is a narrow muscle superior to the medial part of each mylohyoid muscle. Arises from the inferior mental spine of the mandible and passes backward and downward to insert on the body of the hyoid bone. It is innervated by a branch from the anterior ramus of C1 carried along the hypoglossal nerve. It has two functions depending on which bone is fixed, fixation of the mandible elevates and pulls the hyoid bone forward, fixation of the hyoid bone pulls the mandible downward and inward (30).

Buccinator Muscle

It is a bilateral square-shaped muscle constituting the mobile as well as the adaptable cheek area. It has both motor and sensory innervations. Sensory innervation is by the long buccal nerve, motor innervation is via the temporal and cervical divisions of the facial nerve(55). It has three origins, the outer surfaces of the alveolar processes of the maxilla and mandible, and the pterygomandibular raphe. The inferior fibers of the buccinator that were attached to the deep tendon of the temporalis could assist in coordination of the movements of the mandibular region and the mouth angle in the timing and strength of contraction of the muscles during mastication, facial expression, and speech (56).

1.1.2.3 Vascularization of the Temporomandibular Joint

The predominant vessels are the superficial temporal artery posteriorly, the middle meningeal artery anteriorly, and the internal maxillary artery inferiorly. Other important arteries are the deep auricular, anterior tympanic, and ascending pharyngeal arteries. The condyle receives its vascular supply through its marrow spaces by way of the inferior alveolar artery and also its vascular supply by way of "feeder vessels" that enter directly into the condylar head both anteriorly and posteriorly from the larger vessels (17).

1.1.2.4 Innervation of the Temporomandibular Joint

TMJ is innervated by the same nerve that provides motor and sensory innervation to the muscles that control it, which is the trigeminal nerve. Most innervation is provided by the auriculotemporal nerve as it leaves the mandibular nerve behind the joint and ascends laterally and superiorly to wrap around the posterior region of the joint (57). Cranial nerves VII, IX, X and XI and cervical nerves 2 and 3 also contribute (58).

1.1.3 Biomechanics

The TMJ is an extremely complex joint the fact that there are two TMJs connected to the same bone (the mandible) further complicates the function of the entire masticatory system. Although each joint can simultaneously carry out a different function, neither can act without influencing the other.

The disc and its attachment to the condyle are called the condyle–disc complex, this is the joint system responsible for rotational movement in the TMJ (Rotation), it takes place in the inferior joint space. The second system is made up of the condyle–disc complex functioning against the surface of the mandibular fossa, this movement occurs when the mandible is moved forward (translation), it occurs in the superior joint space (17). Movement is guided by the shape of the bones, muscles, ligaments, and occlusion of the teeth (59). Mandibular motions include depression, elevation, protrusion, retrusion, and lateral deviation. Main functions are chewing, talking, and swallowing which are achieved by the action of muscles and constrained by ligaments and the TMJ contacting surfaces.

Mandibular elevation and moth closing are achieved by the masseter, temporalis, and medial pterygoid muscles. Mandibular depression and mouth opening are achieved by the lateral pterygoid and digastric muscles. Protrusion or anterior movement of the chin is achieved by the masseter, medial pterygoid, and lateral pterygoid muscles while acting together

bilaterally. Retrusion or posterior movement of the chin is achieved by the posterior fibers of the temporalis, the digastric, and suprahyoid muscles while acting bilaterally. Lateral deviation is achieved by the lateral and medial pterygoid muscles which deviate the mandible to the opposite side and the temporalis muscle which deviate the mandible to the same side depending on which muscle fibers activate (60).

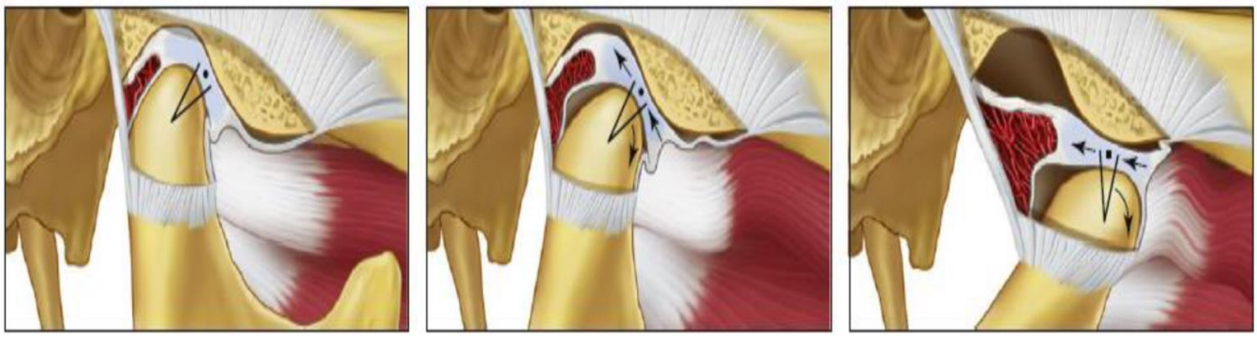

Figure (1-5) Normal Movement of the Condyle and Disc during Mouth Opening (17).

1.2 Temporomandibular Joint Disorders (TMDs)

Temporomandibular joint disorders (TMDs) encompass a group of musculoskeletal and neuromuscular conditions that involve the temporomandibular joints (TMJs), the masticatory muscles and all associated tissues (61). The most frequent presenting feature is pain, usually localized to the muscles of mastication, the preauricular region, or the TMJ. The pain is often worsened or triggered by chewing or talking, and may be associated with limited or asymmetric jaw movements as well as joint noise (clicking) with jaw excursion or locking on opening the mouth (62).

1.2.1 Etiology

The etiology of temporomandibular joint disorders (TMDs) is multidimensional. Biomechanical, neuromuscular, biopsychosocial, and neurobiological factors may contribute to the disorder (63 , 64). Factors that increase the risk of temporomandibular disorders are called “Predisposing factors” and those causing the onset are called “Initiating factors” and factors that interfere with healing or enhance the progression are called “Perpetuating factors”. The contributing factors may include occlusal abnormalities, orthodontic treatment, bruxism and orthopedic instability, macrotrauma and microtrauma, factors like poor health and nutrition, joint laxity, exogenous estrogen, and psychosocial factors. Initiating factors are

related primarily to trauma or adverse loading of the masticatory system. Predisposing factors are pathophysiologic, psychological or structural processes that alter the masticatory system, while the perpetuating factors may include behavioral factors, social factors, emotional factors, and cognitive factors (65).

Some of the contributing factors are the following :

Parafuntional Habits Statistically significant association was found between parafunctional habits such as nail biting, grinding, biting of lips, biting of objects and mouth breathing and TMDs (66).

Emotional Distress TMD-pain seems to have a strong association to emotional, behavior and somatic functioning. With higher frequencies of anxiety, depression, somatic problems, aggressive behavior and thought problems than children and adolescents without TMD-pain (67).

Acute Trauma from Blows or Impacts trauma to the head and cervical region is relatively common as an initiating factor in the etiology of temporomandibular joint disorders and patients with a history of trauma have more pronounced symptoms than TMD patients without previous trauma (68).

Trauma from Hyperextension e.g. Intubation procedures, third molar extraction, and lengthy dental appointments. In fact, any lengthy wide opening of the mouth has the potential of elongating the disc ligaments (69).

Comorbidity of other Rheumatic or Musculoskeletal Disorders (70).

Poor General Health and Unhealthy Lifestyle (71).

Age associated with bone loss, osteoarthritis, low condylar bone quality, and decreased remodeling capacity of TMJ fibrocartilage (72).

Functional Overloading and Increased Joint Friction presence of reactive oxidative radical species in synovial fluid due to mechanical stress can damage the articular tissues of the TMJ (73).

Hormonal Influence related to female reproductive hormones, especially estrogen (74). Despite the historic views, the current available evidence suggests that the influence of the occlusion on the onset and development of TMDs is low. Occlusal factors may be the result rather than the cause of the disease (75). Occlusal correction does not reliably improve the symptoms or signs of TMJ disorders (76,77).

1.2.2 Epidemiology

Epidemiological studies of TMD are important for amassing knowledge of symptomatic complexes and therapeutic approaches that might help to establish prevention and control programs (78). The prevalence of symptoms is variable, and almost always TMD is diagnosed by associating signs and symptoms. A large number of epidemiological studies have been conducted on the epidemiology of TMDs on patient and nonpatient populations. Studies have revealed that around 60%–75% of the subjects will manifest one TMD sign and 35% TMD symptom, and TMD signs are present in 50%–75% of the population at some moment in life, whereas an estimated 35% exhibit mild symptoms (79).

It has been well established, by means of epidemiological studies in which signs and symptoms of TMDs are common in adults of all ages. Reports have shown that signs and symptoms of temporomandibular disorder (TMD) increase with age (80). However, other studies have shown a decrease in symptoms with increasing age (81). Over a 20-year period, investigations on TMD have revealed predominately mild signs and symptoms already present in childhood. An increase in symptoms occurs until young adulthood, after which they level out (82).

A systematic review including only studies adopting the Research Diagnostic Criteria for TMDs (RDC/TMD) reported a prevalence of up to 13% for masticatory muscle pain, up to 16% for disc derangement disorders, and up to 9% for TMJ pain disorders in the general population (83 , 84). While the prevalence of the different diagnoses in TMDs within patient populations varied widely, the results of a meta-analysis showed a prevalence of 45%, 41%, and 30% for muscle disorders, disc derangement disorders, and joint pain disorders, respectively (85). Studies show that TMDs are primarily a condition of young and middle-aged

adults, rather than of children or the elderly, and are approximately twice more common in women than in men (86 ,87 , 88). Only 3.6% to 7% of individuals with TMDs

are estimated to require treatment, and the annual incidence rate is estimated to be 2% (89,90).

Cigarette smoking has been associated with increased risk of TMDs in young adults, and higher levels of pain, psychosocial distress, and sleep disturbances are reported in TMD patients (91 ,92).

Prevalence of temporomandibular joint disorder in the population of residents of the Specialties Hospital was 66%; it could be correlated to the first two years of residency when subjects are subjected to greater stress and general anxiety (93).

Between 65% and 85% of people in the United States experience one or more symptoms of TMD during their lives, but the symptoms are self-limiting for most individuals and resolve without professional intervention (27).

Among university students many epidemiological studies have been published showing the prevalence of TMDs by using different diagnostic criteria such as Fonseca anamnestic index (94), Helkimo index (95), and The research diagnostic criteria for temporomandibular disorders (RDC/TMD) (96). Prevalence of TMD has been reported among university students in Riyadh, Saudi Arabia (46.8%) (97). Another study in north Saudi university students showed that prevalence of TMD was (94.7%) (98). Whilst, a low rate of TMD (25.4%) among students at Gulf Medical University Ajman, UAE (99). Additionally, the prevalence of TMD in Indian university students was (45.16%) and showed women slightly higher than men (36.58% and 31.48% respectively) (100). A higher prevalence of TMD among the university students in Brazil was 57.7% and showed the women higher prevalence than men (68.7% and 48.2%) (101), Yemeni university students (41.07) % (102). Others epidemiological studies estimated the prevalence of TMDs in various communities including: Southern Portugal (25.2 %) (103), Caucasian population (23.78% in male and 25.32 in female) (104), and Syrian (28%) (105). A higher prevalence rate of TMDs has been documented among university Students in Sudan and Jordan (77.8% and 68.6 % respectively) (106 ,107).

1.2.3 Signs and Symptoms of Temporomandibular Disorders

The primary signs and symptoms associated with TMD originate from the masticatory structures and, therefore, are associated with jaw function (108). TMD signs and symptoms include pain, limited or asymmetric mandibular motion, and TMJ sounds, ear pain and

stuffiness, tinnitus, dizziness, neck pain, and headache. The most common symptom reported by patients with temporomandibular disorders is unilateral facial pain.

The pain may radiate into the ears, to the temporal and periorbital regions, to the angle of the mandible, and frequently to the posterior neck. The pain is usually reported as a dull, constant ache that is worse at certain times of the day. There can be bouts of more severe, sharp pain typically triggered by movements of the mandible. The pain may be present daily or intermittently, but many patients have pain-free intervals.

Patients frequently describe “locking” of the jaw, either in the closed-mouth position, with inability to open (most common), or in the open-mouth position, with inability to close the jaw. These symptoms are often worse in the morning, particularly in patients who clench or grind their teeth during sleep (109).

The main signs and symptoms of the articular TMD are pain in the joint area, limited and/or altered mandibular movement, and TMJ sounds such as clicking, popping, or crepitus (110). Crepitus is rough, sandy, diffuse noise or vibration produced by the rubbing together of irregular bone or cartilage surface, While Clicking is distinct snapping or popping sound emanating from the TMJ during joint movement or with joint Compression (75). TMD symptoms are more prevalent in women than men due to hormonal influence and sex hormones especially, elevated levels of Estrogen (111).

1.2.4 Classification

TMJ disorders are separated into two main categories based on the anatomic origin of the problem, articular disorders and masticatory muscle disorders. Articular disorders include the articular surface, intra-articular disk, or articulating bones. Masticatory muscle disorders are problems within the muscles surrounding the TMJ (2).

Most masticatory muscle disorders present as myofascial pain focused to the muscles of mastication, fibromyalgia, muscle strain, and myopathies. It is theorized to arise from clenching, bruxism, or other parafunctional habits.

Articular disorders can be divided into inflammatory and noninflammatory arthropathies. Inflammatory articular disorders include rheumatologic processes such as RA, seronegative spondylopathies such as ankylosing spondylitis, psoriatic arthritis, gout, and infectious arthritis. Noninflammatory articular disk disorders include osteoarthritis, joint damage from prior trauma or surgery, or other cartilage or bone disorders (112).

The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) and their updated version, Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) are the current reference to standardize TMD diagnoses and classification for clinical research purposes. The protocol of (RDC/TMD) includes a dual axis evaluation, providing diagnoses based on both the physical data and the psychosocial data. The Axis I protocol is based on guidelines for oral history taking and clinical assessment, while the Axis II protocol encompasses an evaluation of several psychological factors (e.g., the level of pain- related impairment, depression, and somatization) that are considered key factors for TMD onset, clinical manifestation, and treatment outcome (113).

1.2.4.1 Masticatory Muscle Disorders

1-Myofascial Pain Disorder

It is the most common of all temporomandibular disorders, the vast majority of patients present with facial pain, limitation of jaw motion, muscle tenderness and stiffness, along with any number of associated symptoms in the head, face, and neck region. Imaging studies of the TMJ usually show no evidence of anatomic pathology. Patients with myofascial pain disorder generally respond to the simple, noninvasive treatments (109).

2-Myospasm

It is a toxic muscular contraction created by CNS, also known as trismus, it is an acute disorder and sudden and involuntary contraction of muscles characterized by acute pain, Persistent contraction of muscle, Hyperactivity of EMG, Pain at rest, decrease in activity, and tenderness to palpation (114).

3-Myositis

It is inflammation of a muscle due to local causes such as infection or injury. Pain is usually acute and in a localized area with localized tenderness over the entire region of the muscle. The inflammation can occur also in the tendinous attachment of the muscle “tendonitis or tendomyositis”.

Clinical presentation characterized by Increased pain with mandibular activity with alteration in function due to inflammation or pain, Swelling, tissue reddening and an increase in temperature over the entire muscle can be noticed (115).

1.2.4.2 Articular Disorders

1.2.4.2.1 Disc Displacement

It is an anatomical problem arising when the articular disc moves from its original position, either anteriorly or posteriorly within the joint space (116). The most frequent type of disc displacement described in the publication is the anterior disc displacement. Lateral and medial disc displacement can also occur, with few reported cases regarding Posterior disc displacement (117).

If the displaced disc returns to its normal position when the mouth is opened, accompanied by a popping sound, it is referred to as disc displacement with reduction. If the displaced disc does not return to the normal position and acts as an obstacle during attempted mouth opening, the joint appears as locked. This is referred to as disc displacement without reduction (118).

Pathological mechanical loads are one of the principal causes of disc displacement. The superior head of lateral pterygoid muscle which attaches to the medial aspect of the articular disc thought to play a role in disc displacement (119).

A- Anterior Disc Displacement with Reduction

It is one of the most common intra-articular disorders of the temporomandibular joint. Clinically, DDWR is related to TMJ noise. The movement of the disc onto and off may result in a clicking, snapping, and/or popping sound known as opening and closing click.

It is usually asymptomatic and requires no treatment, since the TMJ structures adapt very well and painlessly to different disc positions, the main disc adaptive physiological process is the retrodiscal fibrosis (120). DDWR corresponds to 41% of TMD clinical diagnoses (121). Although the main characteristics of DDWR are the joint clicking, it should not be considered as a pathognomonic, since it may result from other conditions, such as hypermobility, shape alterations, disc adhesions, imprisonments or perforations, and even a chronic disc displacement without reduction (122).

B- Anterior Disc Displacement without Reduction

It is a specific temporomandibular disorder (TMD) that can cause TMJ pain and limited mouth opening (painful locking), sometimes called a “closed lock”. DDwoR can be acute or chronic depending on the duration of locking. Its incidence among TMD patients is estimated at 2% to 8% (123).

The main symptoms are pain and decreased range of mouth opening, the disc is displaced anteriorly, blocking mechanically translating movement of the condyle resulting in restricted

mouth opening. In addition the bilaminar zone becomes overloaded by direct contact with the condyle, which is the main reason of pain in the TMJ. Although it is self-limiting and significant improvement of clinical symptoms is observed in 75% of patients in a 2.5 year follow-up, it may lead to osteoarthrosis (124).

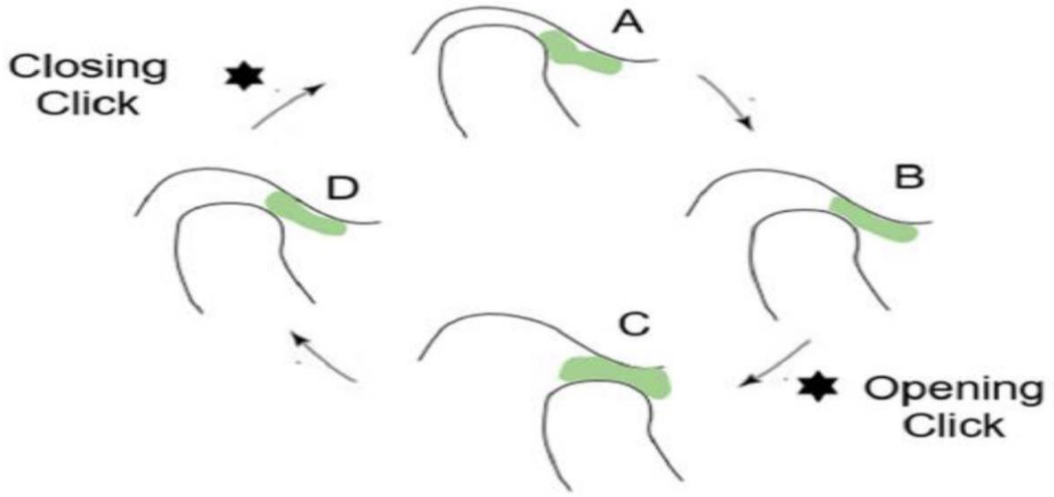

Figure (1-6) Disc Displacement with Reduction (DDWR). A: Closed mouth, the articular disc is displaced; B: Mouth opening, followed by an opening click; C: Open mouth, the articular disc is reduced. D: Mouth closing, followed by a closing click (120).

1.2.4.2.2 Inflammatory Joint Disorders

Inflammatory joint disorders are a group of disorders in which various tissues that make up the joint structure become inflamed. Any or all of the joint structures may be involved synovitis, capsulitis, retrodiscitis, and the arthritis. There are also a few systemic inflammatory disorders that can affect the TM joint structures.

Unlike disc derangement disorders, in which pain is often momentary and associated with joint movement, inflammatory disorders are characterized by a constant dull, aching pain that is accentuated by joint movement (17).

A- Synovitis and Capsulitis

Synovitis is inflammation of the synovial tissues that line the joint. Pain is characterized by constant intracapsular pain that is enhanced by joint movement caused by any irritating condition within the joint. It may result in unusual function or trauma. Synovitis and Capsulitis are nearly impossible to separate Clinically (17).

Excessive mechanical stress leads to cartilage degradation, decreased lubrication, synovial inflammation and release of inflammatory mediators and cytokines. These biochemical changes in the tissues can lead to synovitis (125).

While Capsulitis is inflammation of the capsular ligament that may manifest with swelling and continuous pain localized to the joint. Movements that stretch the capsular ligament cause pain with resultant limitation of such movement (126).

B- Retrodiscitis

It is caused due to trauma or due to progressive disc displacement and dislocation. The patient complains of pain, which increases with clenching, limited jaw movement, swelling of retrodiscal tissues, and acute malocclusion are associated with the disease (127).

C- Arthritis

Pain originating in the joint with clinical characteristics of inflammation or infection over the affected joint that is edema, erythema, and/or increased temperature. Associated symptoms can include dental occlusal changes. It involve Osteoarthritis, Osteoarthrosis, Systemic Arthritis like Rheumatoid arthritis (127).

1- Osteoarthritis

It is a common disease that can cause severe pain and dysfunction in any joint, including the temporomandibular joint. Pathology is characterized by progressive cartilage degradation, subchondral bone remodeling, and chronic inflammation in the synovial tissue.

Radiographic features of the condyle and articular eminence, including erosive resorption, sclerosis, attrition, osteophyte formation, and cyst-like change (128).

A strong association with disc displacements, in particular, disc displacements without reduction and osteoarthritis (129).

Osteoarthritis has a complex and multifactorial etiology; risk factors include age, genetics, trauma and disturbances of joint or muscle. It occurs with greater frequency as age increases. The most common clinical signs and symptoms include pain, restriction in joint function, and joint sounds. Pain is usually dull aching and may have occasional sharp component on movement. It may be associated with joint stiffness, limitation in mouth opening, increasing sensitivity to cold and damp and may be relieved with rest, and NSAIDs. Patients usually have morning stiffness for more than 30 min, joint crepitus, joint sounds and absence of joint warmth (130).

2- Osteoarthrosis

It is a progressive degenerative disease, gradually affecting cartilage, synovial membrane and bone structures. It develops because of imbalance between reparative and degenerative processes of the joint. Clinically manifests with joint noises, pain and restricted mouth opening. In later stages, it results in severe damage of TMJ structures and development of ankylosis and the height of the condylar process may be shortened. It is a multifactorial disease; the occurrence is associated with TMJ overloading (131).

3- Rheumatoid arthritis

It is an autoimmune disease that causes chronic inflammation in joint tissues; it is usually seen in other joints prior to temporomandibular joint involvement. The common clinical findings in RA of the TMJ are tenderness, pain, clicking, crepitation, stiffness, and limitation in jaw movements.

Joint space becomes obliterated due to loss of condylar height and with destruction, erosion, sclerosis, and flattening of the articular surface of the condyle and eminence (132). TMJ involvement is seen in 50% of RA patients (133).

In later phases of the disease, ankylosis is more likely to occur. TMJ involvement is usually bilateral. Degenerative changes are seen as Macrophages, granulocytes, and plasma cells infiltrate the synovial tissues and the synovium can becomes thicker and called “pannus” resulting from the invasion of the bone, cartilage, and tendons by inflammatory synovial tissue mass that grows towards the joint space and forms protruding folds, this creates pain by disrupting joint functions and causing soft tissue to stretch (134).

1.2.4.2.3 Hypermobility

It refers to hypertranslation of the mandibular condyle anterior and superior to the articular eminence during mouth opening. TMJ hypermobility could be classified according to its reduction as subluxation or dislocation. TMJ subluxation is a condition where the condyle translates anterior to its normal range and the patient exhibits a momentary inability to close the mouth from a maximally open position (temporary locking sensation) reduced spontaneously or with self- manipulation. TMJ dislocation (luxation) occurs when the condyle moves outside the glenoid fossa, locking anteriorly to the articular eminence, where it cannot be self-reduced. This locking action is maintained by spasms of masticatory muscles(135).

It is either bilateral or unilateral, acute, and chronic protracted or chronic recurrent. It occurs due to either imbalance in the neuromuscular function or structural deficit. Age and changes in the dentition also play a role with long dental treatments like third molar extractions or root canal treatments.

The most common clinical symptom is the inability to close the mouth “open lock,” difficulty in speech, drooling of saliva, and lip incompetency. In acute dislocation, pain in the preauricular region, but chronic recurrent dislocation is rarely associated with it. Usually bilateral and at times unilateral dislocation may lead to deviation of the chin to the contralateral side. Palpation over the preauricular region may suggest emptiness in the joint space (136).

1.2.4.2.4 Ankylosis

It is fibrous or bony fusion between the condyle and fossa. The main clinical features of TMJ ankylosis are progressive limitation of mouth opening, facial deformity, and obstructive sleep apnea syndrome (OSAS). It usually develops before the age of 10 years, but could develop at any age.

There are four types of TMJ ankylosis starting with Type I non-bony ankylosis of the Joint, Type II lateral bony ankylosis, Type III complete bony ankylosis with radiolucent line, and Type IV extensive bony ankylosis without any radiolucent line (137). The etiologies include trauma, arthritis, infection, previous TMJ surgery, congenital, and idiopathic (138).

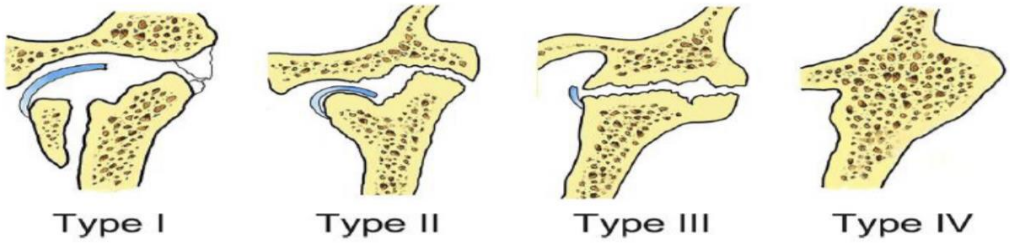

Figure (1-7) The Four Types of Temporomandibular Joint Ankylosis (137).

1.2.5 Diagnosis of Temporomandibular Joint Disorders

Different clinical approaches have been established for TMD diagnosis, but the Research Diagnostic Criteria for TMD (RDC/TMD) and the updated version Diagnostic Criteria for TMD (DC/TMD) are most commonly used. The symptoms of TMD are often associated with pain in the TMJ or muscles of mastication which may radiate to distant structures, clicking, popping, or crepitus of the temporomandibular joint, altered mandibular movements,

headache limited to the temporal region, and otalgia or tinnitus, or both in the absence of aural disease (139).

The diagnosis of TMD is based largely on history taking and physical examination, assisted with Imaging:

1.2.5.1 History

The patient should be asked about the presence of TMJ pain, noises that occur during chewing or yawning, a history of trauma, and ear pain. Questions about the involvement of other joints in the body are also important because this finding can be indicative of osteoarthritis or rheumatoid arthritis, so taking thorough medical history, dental history and personal history (140).

1.2.5.2 Physical Examination

The examination is focused on abnormal mandibular movement, decreased range of motion, tenderness of masticatory muscles, pain with dynamic loading, signs of bruxism, and neck or shoulder muscle tenderness, clicking, crepitus, or locking of the TMJ. A single click during opening of the mouth may be associated with an anterior disk displacement and second click during closure of the mouth results in recapture of the displaced disk, this condition is referred to as Disk Displacement with Reduction. When disk displacement progresses and the patient is unable to fully open the mouth, this condition is referred to as closed lock associated with Disc Displacement without reduction.

Crepitus is related to articular surface disruption, which often occurs in patients with osteoarthritis. Reproducible tenderness to palpation of the TMJ is suggestive of intraarticular derangement.

Deviation of the mandible toward the affected side during mouth opening may indicate Anterior Disk Displacement (141).

Assessment of parafunctional habits by the examination of tooth wear, multiple fracture of enamel and restorations, and soft-tissue changes like lip or cheek chewing, a hyperplastic occlusal line, and scalloped tongue borders (27).

1.2.5.3 Imaging

TMJ imaging methods are used to assess the integrity of its components and their functional association to confirm the extent or progression of an existing disease and to assess an already established treatment. They are essential for assessment in cases of trauma, occlusal alterations and sudden limitation of mouth opening, presence of joint noises, systemic joint diseases, infection and failure of conservative treatments (142).

1- Panoramic Radiography

It can reveal advanced bone alterations in the condyle, such as asymmetries, erosions, osteophytes, fractures, changes in size and shape, degenerative and inflammatory processes, growth alterations, maxillary tumors, metastases, and ankylosis. However, it does not provide functional information on condylar excursion. Also, only gross alterations in the articular tubercle morphology can be seen because of the superimposition of images of the skull base and the zygomatic arch.

This technique is useful as a screening tool, as it allows the initial diagnosis and assessment of TMJ alterations that are not so subtle. It is also indicated when the patient has reduced mouth opening and the differential diagnosis of fracture is considered (142).

2- Plain Radiography

Consists of transcranial projection of TMJs at different angulations to avoid the superposition of the temporal bone and the opposite TMJ, lateral oblique transcranial projections, anterior-posterior projections, submental-vertex projection, transpharyngeal view. Plain radiography is useful in depicting degenerative joint disease in advanced stages, condylar fracture and dislocation (143).

3- Magnetic Resonance Imaging (MRI)

It allows detailed evaluation of TMJ anatomy because of its inherent tissue contrast and high resolution using surface coils. It enables visualizing soft tissues such as disc, ligaments, muscles, and retrodiscal tissue. MRI also allows assessment of joint biomechanics through imaging patients in the closed and open jaw positions.

MRI is the standard imaging choice for evaluating the TMJ for internal derangement. It can show joint effusion, osteoarthritis, abnormal disc morphology (144).

4- Arthrography

It is an invasive technique for diagnosing temporomandibular joint (TMJ) soft tissue derangements when magnetic resonance imaging (MRI) is not an option. It shows the disc and associated adherences or perforations. It is obtained by injecting radiopaque contrast medium into one or both joint spaces and viewed under fluoroscopic guide (145).

5- Computed Tomography

It plays an important role in the diagnosis of anomalies and pathological conditions of the TMJ, providing a complete visualization of joint region for more accurate diagnosis and it is superior to the conventional imaging exam for TMJ (146).

It shows Internal disc derangement, Erosive arthritis, Idiopathic condylar resorption, Osteoarthritis, Ankylosis, Condylar fractures, Synovial chondromatosis, Osteochondroma, Condylar hyperplasia, and Fibrous dysplasia (147).

6- Cone Beam Computed Tomography (CBCT)

It is increasingly being used as an imaging modality in the assessment of the TMJ, and has been reported to provide superior reliability and greater accuracy than panoramic projections in the detection of condylar cortical erosions. Moreover, it offers a low-dose alternative to conventional CT imaging for visualization of the osseous structures (148).

7- Ultrasonography

It is a cost-effective and noninvasive imaging modality commonly employed for imaging the abdominal region and extremities. It shows soft tissues such as disc, muscles, and ligaments when MRI is not an option (149).

1.2.6 Treatment of Temporomandibular Joint Disorders

Treatment strategies for TMDs are as diverse as the patients that present with it. Each patient is treated in a different way depending on the distinctiveness of the problems. A treatment is aimed towards symptomatic relief and not cures, since most of the conditions that affect the temporomandibular system are irremediable.

One should utilize first conservative and non-surgical treatment, and if this failed, irreversible treatment such as surgery should be offered but only in extreme conditions (150).

The treatment of TMD can be divided into two main groups. The first is the non-surgical therapy and it includes treatments such as counselling, physiotherapy, pharmacotherapy, and occlusal splint therapy. The other is the surgical therapy and it ranges from temporomandibular joint arthrocentesis and arthroscopy to the more complex open joint surgical procedures, referred to as arthrotomy (151).

1.2.6.1 Non-Surgical Management

1- Counseling and Physiotherapy

Represented as Homecare practices measures and may include avoidance of excess chewing, parafunctional habits, change to a soft consistency diet, limited talking, and avoidance of wide yawning, use of physical therapy such as local application of ice for acute pain or heat for low-grade chronic pain, muscle massage, hot showers, saunas, transcutaneous electrical stimulation, ultrasound, and steam baths.

Passive or active jaw exercises have been recommended for joint clicking, restricted opening, irregular mandibular movement, lack of muscle coordination, and recurrent anterior dislocation of the condyle (152).

2- Pharmacotherapy

Pharmacological intervention has been used for many years, and the most effective pharmacological agents for the treatment of TMD include analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, corticosteroids, anxiolytics, muscle relaxants, antidepressants, anticonvulsants and benzodiazepines (153).

Drug therapy as part of TMD management should follow the general principles of analgesic therapy and be used on a fixed dose schedule rather than as needed for pain (154).

3- Occlusal Splint

It is a removable appliance, usually fabricated of resin and most often designed to cover all of the occlusal and incisal surfaces of the teeth in the upper or lower jaw. Occlusal splint therapy is most commonly used clinical approach because of its ease of use, low cost, and broad indications. Splint therapy effectively reduces pain levels in TMD patients, and reduces the frequency of pain inpatients with TMJ clicking (155).

There are alternative treatment modalities for temporomandibular joint disorder and involve Acupuncture, Low- level Laser Therapy, Transcutaneous Electrical Nerve Stimulation, Therapeutic Ultrasound, and Botulinum toxin. but there is insufficient evidence to draw any conclusions about their effectiveness in the literature (156).

A- Acupuncture

Acupuncture may stimulate the production of endorphins, serotonin, and acetylcholine within the central nervous system, or it may relieve pain by acting as a noxious stimulus.

Acupuncture uses bodies own mechanism to reduce pain. When needles are inserted as per the location of pain, it leads to the release of endogenous opioids (endorphins, enkephalins) which floods the afferent interneurons thereby blocking the noxious stimuli (156).

B- Botulinum Toxin (BoNT)

It is a150-Kilodalton exotoxin produced from clostridium botulinum, whose action is mediated through the cleavage of docking proteins that are responsible for membrane fusion of pre-synaptic vesicles.

BoNT is used for pain relief in numerous conditions including tension headaches, migraine headaches, post-herpetic neuralgia and myofacial TMD. BoNT injection has therefore

become an attractive choice as adjuvant therapy in patients with myofacial TMD who do not achieve a complete response with conservative management and pharmacotherapy (157).

C- Low- level Laser Therapy (LLLT)

Also known as low- intensity laser therapy (LILT) is a noninvasive, reversible therapy without any known side effects. LLLT uses electromagnetic radiation, which is having a single wavelength (red or infrared) be used as treatment for several pathologies such as wound healing, pain conditions, and inflammatory situations.

LLLT is used for pain management in chronic joint disorders including osteoarthritis of the knee, cervical spine, lumbar spine, and TMJ disorders. LILT has little evidence for its effectiveness in the management of TMDs and it has been widely used in the treatment of musculoskeletal disorders (158).

D- Transcutaneous Electrical Nerve Stimulation (TENS)

It is a well- known physical therapy useful for the relief of pain by use of controlled, low voltage electrical pulses applied to the nervous system. It is safe, noninvasive, inexpensive, and an effective method of providing analgesia, with reduced potential adverse reactions related to other methods (159).

E- Therapeutic Ultrasound

It is a noninvasive therapeutic method which includes vibrations above 16,000 vibrations or 16 Hz. It is known to accelerate healing, decrease joint stiffness, alleviate pain, increase the extendibility of collagen fibers, and reduce muscle spasm (159).

1.2.6.2 Surgical Management

The indications for performing TMJ surgery are as follows:

1. The patient has severe TMJ pain and mandibular dysfunction.
2. The cause of the pain and or mandibular dysfunction is attributable to a diagnosis consistent with a significant intraarticular pathologic condition (synovitis, osteoarthritis, adhesions) leading to disc displacement.
3. A full course of nonsurgical therapy has failed to improve the patient's symptoms.

The surgical options that are available to treat the more common TMJ disorders are arthrocentesis, arthroscopy, and open joint surgery when indicated (148).

1- Arthrocentesis

It is a minimally invasive procedure completed under local anaesthesia refers to lavage of the upper joint space, hydraulic pressure and manipulation to release adhesions or the 'anchored

disc phenomenon' and improve motion. The treatment decreased pain, increased maximal incisal opening, and at follow-up it showed prolonged relief of symptoms.
The microscopic tissue debris resulting from the breakdown of the articular surfaces and the pain mediators such as the enzymes and prostaglandins can be washed out, and normal lubricating properties of synovial membrane can also be stimulated. It is used for treatment of acute closed lock, chronic closed lock, chronic anterior displaced disc with reduction, and degenerative joint disease (160).

2- Arthroscopy

It is minimally invasive surgery performed under general anaesthesia. The superior joint space is lavaged, intracapsular adhesions lysis, and intracapsular betamethasone is injected. The upper compartment of the TMJ is examined with a telescope and irrigated with lactated Ringer's solution and any fibrous adhesions are released in a semiblind fashion using a blunt trocar (161).

3- Condylotomy

It is an osteotomy completed in a manner identical to the vertical ramus osteotomy without wire or screw fixation is placed, and the patient is placed into intermaxillary fixation.
The theory behind this operation is that muscles attached to the proximal segment will passively reposition the condyle, resulting in a more favorable relationship between the condyle, the disk, and the fossa. It is advocated primarily for treatment of disk displacement with or without reduction, degenerative joint disease, and subluxation or dislocation have also been suggested as possible indications (162).

4- Condylar Shave and Arthroplasty

It consists of removing several millimeters of the articular surface with Recontouring (11).

5- Condylectomy

It is the excision of the condyle. This procedure had mixed results and multiple complications, particularly an open bite, malocclusion and deviation of the mandible on opening (11).

6- Eminectomy

It is reduction in the height of the articular eminence by exposing it surgically through a preauricular incision and reducing it with a bur. If this barrier is removed then the condyle will not get locked and will travel freely to and fro and the subluxation or dislocation will not take place (163).

1.3 Platelet Rich Plasma (PRP)

1.3.1 Definition

PRP is a biological product defined as a portion of the plasma fraction of autologous blood with a platelet concentration above the baseline (before centrifugation) (164). As such, PRP contains not only a high level of plate- lets but also the full complement of clotting factors, the latter typically remaining at their normal, physiologic levels (165). It is enriched by a range of growth factors (GFs) , chemokines, cytokines, and other plasma proteins (166).
The PRP is obtained from the blood of patients before centrifugation. After centrifugation and according to their different density gradients, the separation of blood components (red blood cells, PRP, and platelet-poor plasma (PPP) follows.
In PRP, besides the higher concentration of platelets, other parameters need to be taken into account, such as the presence or absence of leucocytes and activation. This will define the type of PRP used in different pathologies.

1.3.2 Mechanism of action

Platelets are anucleated cytoplasmic fragments of megakaryocytes that differentiate down the myeloid cell line- age (167). They contain α-granules, often thought of as the storage units of platelets (168) which studies suggest contain an abundance of growth factors . These are believed to influence inflammation, angiogenesis, stem cell migration and cell proliferation (169). Platelets are well known to be the initiators of the healing process; however, not all tissues have a rich blood supply, for example tendons, ligaments and cartilage. This results in relatively low levels of GFs being available to these tissues to enact effective healing. Application of PRP to these, and other, areas can therefore introduce supra-physiological levels of GFs to theoretically stimulate resolution of chronic pathological processes.
Commercial ELISA (Vector Laboratories, Burlingame, CA; Quantikine Immunoassay, R&D Systems, Minneapolis, Minnesota) and Luminex kits (Luminex Corporation, Austin, Texas) were used to accurately quantify GFs in software based statistical analysis in the following section.
Once recruited to an area of injury, platelet adhesion is facilitated through adhesive glycoproteins secreted by α-granules (170) including vitronectin, fibronectin, thrombospondin and von Willebrand factor (171 , 172). Once the clot is formed the platelets are activated (173)allowing the release of the GFs from α-granules to stimulate healing.

There are myriad GFs contained within α-granules, of which the complex interchange amongst them is hypothesized to be of additional benefit to the healing process beyond simply introducing a higher concentration of platelets at hypovascular sites (167).
Growth factors enact their functions primarily via ligand binding to associated extracellular cell surface receptors, which signal intracellular cytoplasmic proteins to attach to phosphorylated tyrosine. This is followed by multiple phosphorylation and activation steps of protein kinases within the cytoplasm, finally leading to translocation of a phosphorylated kinase to the cell nucleus. This phosphorylates transcription factors enabling gene transcription and ultimately the execution of the encoded function (174 ,175).
Growth factors contained within α-granules thought to be crucial to the efficacy of PRP include platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), the transforming growth factor-β superfamily (TGF-β), fibroblast growth factor (FGF) and insulin-like growth factor (IGF). PDGF is able to initiate callus formation via chemotaxis and mitogenesis of fibroblasts and chondrocytes (176 ,177) along with chemo- taxis of mesenchymal stem cells (MSCs) (178). The promotion of endothelial cell proliferation by PDGF also has an important role in angiogenesis (179). VEGF is involved in neovascularization through its strong endothelial chemokine and mitogenic properties (180). TGF-β is well established as a promoter of chondrogenesis (181), but has also been shown to: stimulate osteogenic MSC differentiation (182) and undifferentiated mesenchymal cell proliferation; regulate the mitogenic effects of other GFs; and inhibit macrophage and lymphocyte proliferation (183) The FGF family is involved in multiple biological processes including osteoblastogenesis (182,184), growth and differentiation of chondrocytes and MSCs (183). IGF regulates the proliferation and maturation of chondrocytes (185,186) and IGF-1 may down-regulate expression of programmed cell death 5 (PDCD5), thereby inhibiting apoptosis of osteoarthritic chondrocytes (187).
In addition to GF release following platelet activation, Xie et al (188)demonstrated that PRP also forms a fibrin gel, which acts as a conductive bioscaffold to allow incorporation of migrating cells for tendon healing. Entrapment of GFs within a fibrin matrix (189, 190) may hold the key to con- trolled release of GFs at the intended site of action. How- ever, it is important to note that cellular response to GFs is limited by number of target receptors available on cell surfaces, therefore high platelet concentrations and subsequent GF release may not be of benefit (170). This may explain why PRP preparations with GFs over six times the physiological concentration may have an inhibitory effect (191).

This leads on to an important point, that while there are many GFs that have been shown to have beneficial effects on cartilage, tendons, bone and other tissues, there are other components that can have negative effects such as pro-inflammatory cytokines, matrix metalloproteinases (MMPs) and interleukin-1β (IL-1β). For example, Browning et al (192) demonstrated an increase in MMP-1 and MMP-3 in osteoarthritis (OA) synoviocytes incubated with PRP. Thereby suggesting PRP application to joints may lead to accelerated cartilage breakdown due to a pro- inflammatory response. Most in vitro studies support PRP use in cartilage tissue because of the ability to increase chondrocyte proliferation and production of matrix molecules whilst not affecting chondrogenic phenotype (193). However, the importance of platelet-derived GF dosage has also been highlighted through the different results they can produce (194).

Perhaps the biggest area of controversy surrounding PRP is the concentration of cellular components, particularly leucocytes. There has been debate around whether leucocytes are adverse because of cytokines causing inflammation and subsequent weaker fibrotic tissue and/ or proteases and reactive oxygen species they release (193) or beneficial as a result of cytokines that can prevent infection and improve healing (195). This is something we will explore in the following section.

1.3.3 Applications and Indications

The ubiquitous nature of the mechanism of action of PRP suggests that, in theory, it can be applied to multiple pathologies to aid the body's natural healing processes.

1-Tendinopathies

The majority of research into PRP treatment for tendinopathy centres on lateral epicondylitis, where PRP has been shown through systematic review (196) to have a better, albeit delayed, therapeutic effect compared to corticosteroid injection for up to two years post injection coleman modified score53 (CMS 53). Three of the five randomized controlled trial (RCTs)analysed used leukocyte-rich PRP (L-PRP), the others did not document the type of PRP used. On further analysis, the RCTs that showed the most significant improvements compared to corticosteroid, were those documenting L-PRP was used.

Systematic review and meta-analyses of studies assess- ing PRP efficacy in Achilles tendinopathy (197)showed that PRP conferred no clinical benefit when compared to saline

placebo or an eccentric loading program (CMS 65). Two of the studies used L-PRP, the other did not document the type of PRP used.

A systematic review and meta-analysis of two RCTs assessing L-PRP efficacy for patellar tendinosis (198) suggested that PRP was statistically better than dry needling or extra-corporeal shockwave therapy at six months post treat- ment (CMS 66).

There have been two RCTs assessing PRP versus saline injection (199) and dry needling (200) respectively in the treatment of rotator cuff disease (tendinopathy or partial tears). Rha et al (200) found that PRP provided more symptomatic relief and functional improvement (based on greater reduction in shoulder pain and disability index) at six weeks to six months post injection than dry needling (CMS 66). The type of PRP was not documented. Whereas, Kesikburun et al (199) found no difference between L-PRP and saline injections at any follow-up point up to a year post injection (CMS 71).

The combined evidence for PRP efficacy in tendinopathies shows that in the studies where PRP has shown statistical improvement to control measures, it is L-PRP that has been used.

2-Cartilage pathology

Laver et al (201) reviewed all studies that assessed PRP for the treatment of degenerative cartilage pathology. A total of 29 studies were included, nine prospective RCTs, four prospective comparative studies, 14 case series, and two retrospective comparative studies. Of the nine RCTs, all reported improved symptoms with PRP groups at the final 12-month follow up, seven of which were significantly superior results. Generally, all studies appear to show overall positive results and clinical benefit from PRP, irrespective of methodological variation. Interestingly, there was a trend towards improved outcomes in either patients of younger age or early OA changes. Only one study followed up patients beyond 12 months (to two years). In this study, while there was symptomatic improvement at 12 months follow up; there was significant decrease in functional scores at two years, albeit still higher than the baseline level (CMS 61). Twenty studies used pure PRP (P-PRP), seven studies used L-PRP and two studies did not document PRP leukocyte content. Of the nine RCTs report- ing improved outcomes, eight used P-PRP, while one used L-PRP. Whilst not directly investigated, these findings suggest P-PRP is more suitable to intra-articular pathology. Further review and meta-analysis by Chang et al (202) reinforced the findings of Laver et al (201). Specifically that less severe OA benefits more from PRP, and PRP is likely to be superior to hyaluronic acid for functional outcomes and have longer duration of action (up to a year).

A case series by Ko et al (203) (level 4) has even shown L-PRP can significantly reduce chronic low back pain in patients with sacroiliac joint (SIJ) instability when injected under ultrasound guidance into the SIJ, lasting up to four years (CMS 59).

3-Acute muscle injuries

A systematic review and meta-analysis of six RCTs assess- ing the effectiveness of PRP in reducing return to sport times, demonstrated that when taking into account all six studies, the return to sport time was significantly shorter (by 7.17 days) in the PRP group (CMS 67) (204). However, when only the double-blinded studies or studies including only hamstring injury were included in the analysis, no significant difference was noted. In addition, re-injury rates were similar between PRP and controls across studies. There were no significant differences regarding pain, muscle strength, flexibility, muscle function or healing (on ultrasound scan or magnetic resonance imaging) (204). Two studies used P-PRP, two used L-PRP, and two did not document PRP type. These findings suggest that when return to play as early as possible is the primary motivation (such as for professional sport) it can be worth using PRP. However, the results are varied and the type of PRP best suited is unknown.

4-Surgical augmentation

Multiple studies have looked at the use of PRP as an aug- mentation for surgery to expedite healing and recovery time. The majority of studies assessing this are focussed on rotator cuff repair and anterior cruciate ligament (ACL) surgery. Cohn et al (205) reviewed five RCTs assessing the effect of PRP versus no treatment in conjunction with rota- tor cuff repair. Only two of the studies showed any benefit. Randelli et al (206) demonstrated less pain in the early post- operative period and increased strength of external rota- tion at three months post-operatively in the L-PRP group (CMS 76). Interestingly, subgroup analysis of grade 1 and 2 tears showed greater strength of external rotation from 3 to 24 months post-operatively, suggesting milder tears may benefit more from L-PRP. Jo et al (207) looked at PRP efficacy in large rotator cuff tears and found that re-rupture was 20% lower in the PRP + surgery group compared with surgery alone, as well as the overall shoulder function being significantly better (CMS 73). However, the type of PRP used was not described. The other RCTs showed no significant differences in peri-operative morbidity, clinical outcomes of structural integrity between PRP + surgery and surgery alone. Two of the studies used P-PRP while the other did not specify the PRP classification. Overall, these results show L-PRP may be of benefit in rotator cuff repair. A 20% reduction in large tear re-rupture is certainly worth

the addition of PRP. However, the type was not documented. Interestingly, of the three RCTs showing no benefit with these tendon injuries, two used P-PRP and the other was unspecified. A systematic review of nine RCTs and two cohort studies assessing PRP use in ACL surgery (208) (level 3) showed there is evidence that adding PRP to the graft or tunnels could be beneficial in expediting graft maturity (CMS 60). Seven studies used L-PRP, two used P-PRP and two did not document PRP type. Similarly to muscle injuries, where early return to play is a crucial, these finding suggest the addition of PRP during ACL reconstruction may be of benefit. However, the type of PRP is again unclear.

1.3.4 Preparation techniques

There are two techniques to prepare PRP: (209)

• **Open technique:** Exposure of the product to the working environment with contact to different materials like pipettes or product-collection tubes. Product contamination during microbiological handling must be guaranteed.

• **Closed technique:** Commercial devices with CE marking involving centrifugation is used and thus environmental exposure to product is not there (recommended).

1.3.5 Complications and Side Effects of PRP.

After the procedure there will be some pain, mild swelling or redness, of the skin following injection of the platelet rich plasma - PRP. Bruising is also a possibility as the needle is used to place the PRP into the skin. This may take a week or so to resolve. There can be side effects. Here are the most common: (210)

1-Pain in the Injured Area: Some people who've undergone PRP therapy complain about an acute ache or soreness in the spot of the injection. Sometimes this pain is even felt deep inside the area, whether in the muscle or bone.

2-Infection: As with any injection-based treatment, infection is a slight possibility regardless of thorough sterilization procedures.While a tremendous amount of precaution is taken when injecting a patient with a PRP serum-intense sterilization procedures are, in fact, followed closely for each treatment-sometimes an infection can break out in the injured area.

3-No Improvement in Injured Area: While this is not necessarily a side-effect, we still need to mention that not all athletes respond to a PRP injection. (Of course, this particular

type of sports medicine is undergoing more studies so we can understand exactly why. Sometimes the original pain and soreness of the injury remains (it may even get worse), even after an extended rest period after the PRP therapy.

4-Allergic Reaction: Some patients' body will reject their own serum and react negatively to the treatment. This is rare, but it does happen. Again, more studies need to be done to understand why.

5-Blood Clot: Normally, a blood clot forms when there is damage to the lining of a blood vessel, like with a cut. Because a PRP injection uses a needle (guided by a sonogram) there is a chance that a artery or vein could be damaged. If that happens a blood clot occurs and is treated like any normal clot.

6-Skin Discoloration: Sometimes the color around the skin of a PRP injection will appear bruised. This could be normal, based upon your history of bruising.

1.3.6 Platelet Rich Plasma In Treatment Of Temporomandibular Joint Disorders

In four studies (Hegab et al., Kiliç et al., 2015 and 2016 and Lin et al.) out of 10 osteoarthritis was the only affect tested; however in one work (211) (Giacomello et al.), authors evaluated also anterior disc displacement without reduction. Fernandez-Ferro evaluated both osteoarthritis an disc displacement with or without reduction (212). Hanci et al. recruited a sample suffering from disc displacement with reduction (213), Pihut and al. evaluated a sample affected by general temporomandibular disfunctions (214), and Yang et al. and Al-Delayme et al. evaluated non-reducing disc displacement samples (215 ,216).
One study out of 10 compared PRP injections to arthrocentesis (213) (Hanci et al.), two studies out of 10 compared PRP injections to HA injections (217 ,212) (Hegab et al., Frenandez-Ferro et al.). Three studies tested different doses of PRP injections without a control group (Giacomello et al., Pihut et al., Al-Delayme et al.,) and Yang et al. tested LPCGF (Liquid Phase Concentrated Growth Factor) injection combined with centric relation occlusal splint without comparison (215, 211,214 ,216). In both studies of Kiliç et al. (2015, 2016) PRP and arthrocentesis and PRP injection was compared with arthrocentesis alone

(2015) and with HA arthocentesis (218,219). In Lin et al. PRP arthrocentesis was compared with PRP injection (220).

1.3.6.1 Outcome of Pain Improvement

Pain was measured by VAS (visual analogue scale) in all works evaluated. Statistically significant results in terms of pain improvement were highlighted in all works examined, except in Lin et al.(220).

Intra-group and inter-groups differences were noticed in all works where a control group was involved. In those studies where control groups were not present, statistical differences were noted between the baseline and the end of follow-up in the study group.

In Lin's work, arthrocentesis plus PRP was compared to PRP injection in osteoarthritis and the two groups did not show statistically significant differences in TMJ arthralgia (220).

Results of VAS scores from all studies were found to be similar in values, except in Fernandez-Ferro et al. where a slighter improvement was noticed, probably due to the larger sample tested (212).

Pain seems to improve when PRP is used, both by injections combined with arthrocentesis. Furthermore, PRP injections were found to be more effective than HA injections (Hegab et al., Fernandez-Ferro et al.) (217 ,212).

1.3.6.2 Outcome of Joint Sound

In two studies joint sound was not evaluated (Giacomello et al. and Fernandez-Ferro et al.) (211 ,212). In three studies the joint sound was evaluated using VAS scale (Kiliç et al. 2015, 2016 and Al-Delayme) (215,218 ,219), in three other studies it was calculated on joints affected by sound or crepitus (Hanci et al., Hegab et al., Yang et al.) (213 ,217, 216), and in another two number of patients reporting sound was scored (Pihut et al., Lin et al.) (214 ,220).

In all of the works analysed joint sound was found to improve during follow up. In Hegab et al. and in Pihut et al. results were not statistically significant, nevertheless an improvement was noticed (217 ,214). In particular, Hegab et al. reported improvements of joint sound when treated with PRP injection compared to HA injection at 1 month of follow-up, however this improvement became equal at 12 months follow-up (217).

In both studies carried out by Kiliç et al. statistically significant inter-groups resulting in decreasing of joint sound were reported (218 ,219). Hanci et al. showed also statistical

differences between two compared groups, as well as in Yang et al. and in Al-Delayme where statistical differences in outcome were reported comparing baseline to end of follow-up (215 , 213, 216).

In Lin et al. at 1 month and at 12 months statistically significant improvement of joint crepitus sound was detected in patients treated by arthrocentesis and PRP. However, authors reported no statistical differences until 12 months between two groups (arthrocentesis and PRP compared to PRP injections) demonstrating a similar improvement of joint crepitus sound in both groups (220).

1.3.6.3 Mandibular Motion Outcome

Different definitions of this outcome were reported by authors, for example mandibular opening, mandibular motion, mouth voluntary opening and maximum mouth opening, minimal interincisal opening, range motion. We generally assumed all of these as mandibular motion.

In all studies, except Yang et al., mandibular motion was considered and tested at baseline and at the end of follow-up; furthermore, comparison between groups was carried out where a control group was present (216).

In Giacomello et al. (2 PRP Injections) differences in mandibular opening between pre-injection and post-injection were statistically significant (211).

Hanci et al. (PRP injection vs. arthrocentesis) investigated minimal interincisal opening founding no statistically significant differences between study and control group (213).

Pihut et al. (PRP injection) reported a decrease of mandibular motion but the results are not clearly explained (214).

Results in mandibular voluntary opening in Hegab et al. (PRP injections vs. HA injections) were found to be statistically different between two groups (217). In Kiliç et al. (2015) (PRP arthrocentesis vs. arthrocentesis) results in maximum mandibular opening were not statistically different in two groups whereas in the work of 2016 (PRP arthrocentesis vs. HA arthrocentesis) statistical differences were noticed between study and control group (218,219). Fernandez- Ferro et al. (PRP injection vs. HA injection) did not find differences with statistical relevance between the two groups in testing mouth opening before intervention and at the end of follow-up (212).

In Al-Delayme et al. (PRP injections), statistical differences between baseline and end of follow-up were noticed (215).

Lin et al. (PRP arthrocentesis vs. PRP injections) showed a statistical significant improvement in both groups after interventions (range motion higher than 6 mm), however no differences were noticed in terms of mouth-assisted opening (220).
Yang et al. did not evaluate range motion outcome (216).

Conclusion

- The Temporomandibular Joint (TMJ), also known as the craniomandibular joint/articulation. It is the articulation between the squamous part of the temporal bone and the head of the mandibular condyle. It consists of a mandibular or glenoid fossa, an articular eminence or tubercle, a condyle, a separating disk, a joint fibrous capsule and an extracapsular check ligaments.
- The Primary Components of the TMJ are Condyle of the Mandible , Squamous Portion of the Temporal Bone , Articular Disc and Ligaments .
- Ligaments of the Temporomandibular Joint are The Capsular Ligament , The Lateral Temporomandibularl Ligament , The Collateral (Discal) Ligaments , Sphenomandibular Ligament and Stylomandibular Ligament .
- Muscles of Mastication of TMJ are Masseter Muscle , Temporalis Muscle , Medial Pterygoid Muscle and Lateral Pterygoid Muscle.
- The predominant vessels of TMJ are the superficial temporal artery posteriorly, the middle meningeal artery anteriorly, and the internal maxillary artery inferiorly.
- TMJ is innervated by the same nerve that provides motor and sensory innervation to the muscles that control it, which is the trigeminal nerve.
- Temporomandibular joint disorders (TMDs) encompass a group of musculoskeletal and neuromuscular conditions that involve the temporomandibular joints (TMJs), the masticatory muscles and all associated tissues.
- The etiology of temporomandibular joint disorders (TMDs) is multidimensional. Biomechanical, neuromuscular, biopsychosocial, and neurobiological factors may contribute to the disorder .
- The prevalence of symptoms is variable, and almost always TMD is diagnosed by associating signs and symptoms. A large number of epidemiological studies have been conducted on the epidemiology of TMDs on patient and nonpatient populations.
- TMD signs and symptoms include pain, limited or asymmetric mandibular motion, and TMJ sounds, ear pain and stuffiness, tinnitus, dizziness, neck pain, and headache. The most common symptom reported by patients with temporomandibular disorders is unilateral facial pain.
- TMJ disorders are separated into two main categories based on the anatomic origin of the problem, articular disorders and masticatory muscle disorders.

- Different clinical approaches have been established for TMD diagnosis, but the Research Diagnostic Criteria for TMD (RDC/TMD) and the updated version Diagnostic Criteria for TMD (DC/TMD) are most commonly used.
- The patient should be asked about the presence of TMJ pain, noises that occur during chewing or yawning, a history of trauma, and ear pain.
- The examination is focused on abnormal mandibular movement, decreased range of motion, tenderness of masticatory muscles, pain with dynamic loading, signs of bruxism, and neck or shoulder muscle tenderness, clicking, crepitus, or locking of the TMJ.
- TMJ imaging methods are used to assess the integrity of its components and their functional association to confirm the extent or progression of an existing disease and to assess an already established treatment.
- Treatment strategies for TMDs are as diverse as the patients that present with it. Each patient is treated in a different way depending on the distinctiveness of the problems. A treatment is aimed towards symptomatic relief and not cures, since most of the conditions that affect the temporomandibular system are irremediable.
- PRP is a biological product defined as a portion of the plasma fraction of autologous blood with a platelet concentration above the baseline (before centrifugation).
- The ubiquitous nature of the mechanism of action of PRP suggests that, in theory, it can be applied to multiple pathologies to aid the body's natural healing processes.
- After the procedure there will be some pain, mild swelling or redness, of the skin following injection of the platelet rich plasma - PRP. Bruising is also a possibility as the needle is used to place the PRP into the skin. This may take a week or so to resolve.
- Different definitions of this outcome were reported by authors, for example mandibular opening, mandibular motion, mouth voluntary opening and maximum mouth opening, minimal interincisal opening, range motion.

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