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Advances in the pathogenesis of traumatic temporomandibular joint ankylosis

Mi Na[1], Yao Zhitao[1, *]

[1]School of Stomatology, Xinjiang Medical University, Urumqi, China
[*]Corresponding author

Abstract: *Temporomandibular joint (TMJ) is a synovial joint composed of condyle, articular disc, temporal fossa and other structures. TMJ is prone to joint diseases due to its frequent activities and bite force. Temporomandibular joint ankylosis (TMJA) is a serious joint disease, which can lead to fibrous adhesion or bone adhesion within the joint, affect mandibular movement and cause facial deformity. Previous studies have shown that trauma, infection, systemic diseases and other causes can cause TMJA, among which trauma factors account for about 90%. The pathogenesis of traumatic TMJA is complex, treatment is difficult and there is a certain recurrence rate. However, the pathogenesis of traumatic TMJA has not been truly revealed, and animal model studies vary. In this article, the related factors and pathogenesis of traumatic TMJA were discussed.*

Keywords: *Traumatic temporomandibular joint ankylosis, Incidence related factors, pathogenesis*

1. Introduction

Temporomandibular joint (TMJ) is a synovial joint composed of condyle, articular disc and glenoid fossa of temporal bone. TMJ is prone to joint diseases due to frequent movement and bite force. temporomandibular joint ankylosis (TMJA) refers to the disease caused by fibrous or bony adhesion of one or both temporomandibular joints, which leads to decreased joint mobility and limited mouth opening. Previous studies have shown that trauma, infection, systemic diseases and other causes can lead to TMJA, of which trauma accounts for about 90%. Traumatic TMJA is a serious temporomandibular joint disease, characterized by joint cavity occlusion, secondary intraarticular and periarticular bone abnormalities, intact joint cavity, condylar fracture caused by external forces, with or without joint capsule tears.[1] Ankylosis can lead to progressive limitation of mouth opening, which in turn can lead to speech and eating disorders, facial deformities, airway obstruction, and even psychological disorders. [2]It brings great pain to the patient and seriously reduces the quality of life of the patient. The pathogenesis of traumatic TMJA is complex, the treatment is difficult, and there is a certain recurrence rate. However, the mechanism of traumatic TMJA has not been truly revealed, and the animal models are different. This article reviews the related factors and pathogenesis of traumatic TMJA.

2. Related factors of traumatic temporomandibular joint ankylosis

2.1. Traumatic temporomandibular joint ankylosis and condylar fracture types

Condylar fracture is the main cause of traumatic temporomandibular joint ankylosis, accounting for about 69%-74% in China mainland.[3] In contrast, earlier experiments reported that only 0.4% of condylar fractures will progress to ankylosis. It can be seen that not any kind of condylar fracture will lead to ankylosis, and the formation of ankylosis may be related to the fracture type. Condylar fractures are due to anatomical and biomechanical particularities, Temporomandibular Joint Reconstruction in the Growing Child. Oral condyle is prone to fracture when the mandible is injured and accompanied by disc and fossa injuries.[4] Classification of condylar fractures: According to the fracture location (fracture occurrence level), it can be divided into high fracture (condylar head or intracapsular fracture), middle fracture (condylar neck fracture), low fracture (condylar neck or base fractur and high fracture (condylar head or intracapsular fracture). [5]Sagittal and comminuted condylar fractures are most likely to cause ankylosis.[6]

Ankylosis of TMJ often occurs in children, and coincidentally, sagittal fracture of the condyle is the

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most common fracture type in children. Thoren et al.[7] found that 58% of condylar fractures in patients younger than 6 years old were sagittal condylar fractures. Meng et al.[8] compared the skeletal morphology of TMJ in adults and children and found that children were more prone to sagittal fracture of condyle than adults under the action of external force: Compared with children, adults have a larger inclination Angle of the condyle longitudinal axis and a smaller ratio of the minimum cross-sectional area of the condyle neck to the maximum cross-sectional area of the condyle. According to the mechanical principle, when the TMJ is subjected to injury-induced external force from the mandibular ramus, adults are prone to condylar neck fracture, resulting in stress interruption, while children are prone to sagittal condylar fracture. Clinically, not all sagittal fractures of the condyle necessarily develop ankylosis. Duan et al. [9]found in a clinical study that ankylosis would not occur if the condyle or ramus were not displaced and there were intact or partial articular discs on it, even if a sagittal fracture of the condyle occurred in the mandible. In a study of 206 cases of TMJ ankylosis, Sarma et al. [10] found that 93% of the joints were laterally ankylosed, and the condyle was displaced inward but not embedded in the ankylosed mass. No sagittal fracture of the condyle was found in the series of cases they studied. Therefore, sagittal fracture of the condyle plays an important role in ankylosis, but is not a necessary factor. TMJ ankylosis is more likely to occur in patients with high horizontal condylar fracture, internal displacement of the condyle and upward displacement of the ramus. When condylar fracture combined with mental or mandibular fractures, the widening of the mandibular arch will cause the lateral column of the condyle or the residual end of the ramus to shift upward and make close contact with the zygomatic arch/glenoid fossa, thus increasing the possibility of ankylosis.

2.2. Traumatic temporomandibular joint ankylosis and disc defect or displacement

The articular disc is an important and special component of the TMJ, many experimental and clinical studies have found that the absence, breakage, or displacement of articular discs are an intact articular disc is an important prerequisite for traumatic TMJ.It can prevent the occurrence of traumatic TMJ. There have been studies in which one side of the rat cage was excised postdiscal findings: Severe degenerative changes in joints, partial fibrous TMJ ankylosis was found in the joints.Animal experiments have confirmed that the articular disc can prevent the formation of ankylosis[11]. The articular disc is an important part of the TMJ, which is the natural barrier to prevent joint ankylosis. When the articular disc is injured or displaced, it is easy to cause joint ankylosis, and when condylar fracture is accompanied by articular disc injury, it is more likely to occur. [12]It has been found that removal of the fibrous layer on the joint surface by partial disc resection may lead to traumatic TMJ ankylosis. In addition, it has been shown that removal of the condylar fibrous layer is more critical than removal of the fossa fibrous layer for traumatic TMJ ankylosis, although bony ankylosis appears to be typical and not severe. [13]However, some animal experiments have found disc injury, perforation, displacement or even tear, but the results did not indicate traumatic TMJ ankylosis. Disc injury alone does not lead to TMJ ankylosis, and it should be combined with other factors to lead to TMJ ankylosis.[14] Therefore, disc defect or displacement is an important factor in the occurrence of traumatic TMJ ankylosis, but it is not the only factor.

2.3. Traumatic temporomandibular joint ankylosis and limitation of mandibular movement

Miyamoto et al. found that limiting mandibular movement on the basis of destroying the surface of condyle and glenoid fossa and removing the articular disc, found that mandibular movement restriction can promote the occurrence of ankylosis, but once ankylosis is established, it will develop at the same rate regardless of the presence or absence of braking. [15]The study showed that more than 80 patients with condylar fracture were fixed in the passive opening position with open jaw splint for 3 to 6 months. The results showed that not only no ankylosis occurred, but also the morphology and function of the temporomandibular joint recovered well. Therefore, limiting the movement of the mandible with an opening pad or an occlusal splint at the initial stage of condylar fracture can maximally block the stretching effect of the lateral pterygium muscle on the condyle, and then prevent the occurrence of traumatic TMJ ankylosis. It is suggested that the limitation of mandibular movement plays an important role in the occurrence of traumatic TMJ ankylosis.[16]

2.4. Traumatic temporomandibular joint ankylosis and lateral pterygoid muscle

The principle of distraction osteogenesis is to apply appropriate and continuous traction at the broken end of the fracture or both ends of the osteotomy line, so as to achieve bone regeneration in the fracture gap. Anatomically, the lower head of the lateral pterygoid muscle is usually attached to the

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pterygoid fossa medial to the condyle, and when the condyle undergoes a sagittal fracture, the pulling action of the lateral pterygoid muscle pulls the sagittal fracture fragment anteromedial. Previous studies have shown that distraction osteogenesis of lateral pterygoid muscle (LMP) during the process of sagittal condylar fracture healing is an important cause of traumatic TMJ ankylosis.[17] Meng et al. proposed that sagittal or comminuted fracture of the condyle may cause medial and downward displacement of the condyle due to stretching of the lateral pterygoid muscle, thus providing evidence that the stretching effect of the lateral pterygoid muscle on the condylar fracture may be one of the causes of traumatic TMJ ankylosis. [18]In addition, it was found that blocking the lateral pterygoid muscle during traumatic TMJ ankylosis model could prevent TMJ ankylosis. Distraction osteogenesis of lateral pterygoid muscle may be related to horizontal osteogenesis, but it does not seem to be related to condylar vertical osteogenesis and temporal bone thickening.[19]

2.5. Genetic susceptibility

The incidence of TMJ ankylosis is different in different regions of the world, especially in developing countries, which is higher than that in developed countries. Arakeri et al. [20] believe that this may be caused by factors such as large population and poor medical conditions in developing countries, and they also believe that it may be related to ethnic genetic differences. Hall [21]believes that the occurrence of TMJ rigidity may also be related to the genetic biological behavior of a specific population. Gu et al. [22]conditionally inactivated Shox gene on neural crestderived cells in the mouse skull, resulting in abnormal development of condyle and glenoid fossa. Although the articular disc was formed, it fused with the articular surface to form ankylosis. Porto et al. [23] used mouse stem cells and bone transplantation to study the occurrence of induced ankylosis, and proved that stem cells played a role in inducing fibrous ankylosis, but did not cause skeletal ankylosis. All these studies suggest that there may be an organism susceptibility to TMJ rigidity. It can be seen from the above analysis that no single traumatic factor will inevitably lead to TMJ ankylosis. Traumatic TMJ ankylosis may be the result of a comprehensive effect of various traumatic factors. Sagittal fracture of the condyle is more likely to develop TMJ ankylosis on the basis of joint disc injury or displacement and inappropriate restriction of mandibular movement.

3. Pathogenesis of traumatic TMJ

3.1. Cytological study of traumatic TMJA

3.1.1. Mesenchymal stem cells (MSCs) and bone formation.

Mesenchymal stem cells (MSCs) are a group of adult stem cells with self-renewal ability, multi-directional differentiation potential and immunomodulatory properties.[24][25] De Bari et al.[26] first reported that human synovial mesenchymal stem cells could be isolated from adult synovial tissue. The synovial membrane of TMJ is mainly located in the inner lining of the joint capsule, which has a special position and accurate positioning. [27]Previous studies have found that synovial mesenchymal stem cells have the advantage of osteogenesis in cartilage formation in rabbit model. [28]Synovial mesenchymal stem cells have the ability of osteogenesis in vitro. Under normal conditions, synovial stem cells do not have osteogenic effects, but under pathological conditions, such as the synovial fluid of patients with osteoarthrosis, calcium pyrophosphate mineralized particles are found in the joint synovial fluid, and osteophytes are formed at the joint edge. The expression of transforming growth factor (TGF) in the joint region of LPM functional group was higher than that of LPM severed group during the repair process of TMJ injury. A variety of factors such as interleukin-1a, bone morphogenetic protein 7(BMP7), cartilage oligomeric matrix protein, calcitonin receptor were differentially expressed. These factors may be derived from the directional migration and osteogenic differentiation of TMJ synovial mesenchymal stem cells induced by trauma.[29] In conclusion, the TMJ synovial mesenchymal stem cells could migrate to the fracture sites after condylar fracture due to pathological changes in the local microenvironment. After condylar fracture, trauma induces the migration of synovial mesenchymal stem cells to the fracture surface and induces excessive osteogenesis.

3.1.2. Osteoclasts and macrophages

Osteoclasts are the key cells for bone resorption and bone remodeling during fracture healing. Cathepsin K is a key factor secreted by osteoclasts. Previous findings have suggested that osteoclast deficiency may be an important factor in hypertrophy and high-density callus formation. [30]However,

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hypertrophy and high-density bone mass are typical imaging and histological features of TMJA. Studies have shown that the number of osteoclasts is decreased, especially in the late stage of TMJA bone mass formation, and the ability of osteoclast differentiation is weakened. This suggests that osteoclast deficiency may contribute to bone mass formation in TMJA patients.

Macrophages, the precursor cells of osteoclasts, are present in the inflammatory phase of fracture healing in humans and animals, and they play a key role in initiating the fracture repair process. [31]Macrophages clear pathogenic microorganisms, cell debris, and necrotic tissue, and induce high expression of inflammatory factors after injury, such as interleukin 1 (IL-1), interleukin 6 (IL- 6), and interleukin 1 (IL-1). IL-6) and tumor necrosis factor-α (TNF-α). [32]Studies have shown that depletion of macrophages from the time of injury or reduction of macrophage-associated inflammatory factors may affect fracture healing. [33]In the study of TMJA, Zhao et al.[34] found that the number of macrophages was large in the early stage of the TMJA animal model of New Zealand rabbits. Interestingly, once the number of macrophages was inhibited during the operation of the TMJA animal model, the degree of bone stiffness could be reduced, and the expression of cartilage-related genes was also reduced. The above studies indicate that macrophages play an important role in initiating the process of fracture healing and TMJA, and are closely related to bone formation.

3.1.3. Chondrocytes and autophagy

Human cartilage is mainly divided into primary and secondary cartilage. Primary cartilage forms with individual development and is mainly controlled by genetic factors, including long bone cartilage and costal cartilage. Secondary cartilage has a delayed development time, the cells are derived from the periosteum that has already formed bone, and has no characteristics such as secondary ossification centers[35],such as mandibular condylar cartilage. The cartilage structure was divided into three layers. The surface layer was a static layer, containing fibroblasts and cartilage precursor cells.[36] The middle layer was the proliferative layer, which was composed of chondrocytes in the proliferative phase. [37]At the very bottom is the hypertrophic chondrocyte layer, and the enlarged chondrocytes gather in this layer. autophagy is a process by which cells degrade intracellular components to produce energy and small molecules for reuse by cells. Autophagy plays an important role in cell tolerance to harsh environmental stimuli (hypoxia, starvation, pathogens, etc.), removal of misfolded proteins and damaged senescent organelles, and maintenance of intracellular homeostasis. Previous studies have revealed the changes of chondrocyte autophagy level, condylar excessive osteogenesis, and condylar enlargement deformity in animal models of traumatic temporomandibular joint ankylosis. Chondrocytes are in a special hypoxic environment, and hypoxia inducible factor (HIF) mediates the adaptation of chondrocytes to this hypoxic environment. HIF1 enhances the autophagy activity of chondrocytes under hypoxia by phosphorylating AMPK and inhibiting mTOR signaling.[38] Inhibition of HIF1α degradation can promote mitophagy and reduce the apoptosis and senescence of chondrocytes under hypoxic conditions. In contrast to HIF1α, HIF2α can inhibit the level of autophagy in chondrocytes and promote the degradation of extracellular matrix in chondrocytes.[39]

3.2. Molecular biology study of traumatic TMJA

Molecular biological studies have suggested that traumatic TMJA space tissue has persistent excessive osteogenic capacity. Hu et al. [40]proposed that traumatic bony ankylosis of TMJ is abnormal osteogenesis after condylar fracture, which leads to enlarged condylar volume and irregular shape, and further damages the articular disc and fossa during mandibular movement, leading to joint ankylosis.[41] Angiogenesis is closely related to osteogenesis. In the progression of traumatic TMJA, angiogenesis may be involved in bone formation after condylar fracture. Angiogenesis can promote fracture healing, while insufficient angiogenesis can lead to atrophic nonunion. [42]In the study of traumatic TMJA, osteogenic and angiogenic cytokines, such as bone morphogenetic protein 4 (BMP-4), bone morphogenetic protein 7 (BMP-7), and bone morphogenetic protein 7 (BMP-7), were found to be involved in the pathogenesis of traumatic TMJA. BMP-7) and angiopoietin-2 (Ang-2) were down-regulated. Yan et al.[43] and Zhang et al. [44]analyzed TMJA animal specimens and found decreased expression of Wnt5a, β-catenin, lymphocyte enhancer factor, RUNX2 (runt-related transcription factor 2), etc. Pilmane et al. [45]found that increased expression of transforming growth factor-β1 (TGF-β1) and MSX2 in TMJA samples led to persistent bone formation. Liang et al.[46] found that the expression of angiogenesis-related genes for hypoxia-inducible factor 1-alpha, vascular endothelial growth factor, angiopoietin 1, cysteine-rich angiogenesis-inducing factor 61, and matrix metalloproteinases was higher in patients with osteoankylosis than in patients with fibrous ankylosis. These results suggest that increased angiogenesis in TMJA bone mass may be an important factor in the continuous supply of blood, nutrients, and osteocytes. Some studies have suggested that autophagy is

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closely related to traumatic temporomandibular joint ankylosis. PI3K/AKT signaling pathway can promote the proliferation of chondrocytes and inhibit autophagy. Activated AKT can regulate chondrocyte survival, autophagy and apoptosis through phosphorylation of a variety of related downstream target molecules such as Bad, NF-κB, mTOR and Caspase-3, and mediate the process of cartilage tissue injury. Inhibition of PI3K/AKT signaling pathway activity impairs proteoglycan synthesis and reduces the survival rate of chondrocytes. In addition, inhibition of AKT activation is an important mechanism of IL-β-induced autophagy in chondrocytes. AKT inhibitor can obviously block the effect of certain drugs (such as ginsenoside, shikonin, etc.) on autophagy in chondrocytes.

4. Summary and Prospect

Since the 20th century, the etiology and pathogenesis of traumatic temporomandibular joint ankylosis have been greatly revealed due to the progress of science. The existing studies speculate that traumatic temporomandibular joint ankylosis is caused by abnormal biological structure and related complex microenvironment (including but not limited to SMSc, osteoclasts, macrophages, etc.), but still cannot provide effective help for the clinical treatment of traumatic temporomandibular joint ankylosis. Therefore, the molecular mechanism and biological characteristics of traumatic temporomandibular joint ankylosis still need to be further explored.To explore the pathogenesis of TMJA and prevent the occurrence of TMJA is to solve this problem.The fundamental pathway of disease. At present, there are many animal studies on traumatic TMJA at home and abroad, but different animal studies use different modeling methods, and most studies only form fibrous rigidity in the TMJ. Animal studies of skeletal ankylosis mostly use open complex injuries of condyle, articular disc, and glenoid fossa. However, open injuries in animal models are not exactly the same as closed injuries of TMJ in clinical patients, and animal models also have certain limitations.

In conclusion, the research on traumatic TMJA is still focused on the establishment of standardized and highly reproducible animal models that can better simulate the TMJ traumatic microenvironment of clinical patients. Although previous studies have preliminarily revealed the pathogenesis of traumatic TMJA, the exploration in this area is still at an early stage. In the future, the microscopic mechanism of traumatic TMJA will be further explored from the aspects of cytology, molecular biology and gene level.

References

[1] Yuan Xihang, Lu Changsheng. Treatment progress of temporomandibular joint ankylosis [J]. Chinese Medical Cosmetics, 2018,8(03):80-87
[2] Prechel U, Ottl P, Ahlers OM, et al. The treatment of temporomandibular joint dislocation. Dtsch Arztebl Int 2018; 115: 59-64.
[3] Xiao E, Zhao Lu, Zhang Yi. Etiology and treatment of traumatic temporomandibular joint ankylosis [J]. Chinese Journal of Applied Stomatology, 2017, 10(03):146-152.
[4] Resnick CM. Temporomandibular Joint Reconstruction in the Growing Child. Oral Maxillofac Surg Clin North Am. 2018 Feb; 30(1):109-121.
[5] Gu Jiana, Jiao Boqiang, Li Zhiyong. Research progress on the etiology of anterior disc displacement of temporomandibular joint [J]. Stomatology, 2012, 42(10):942-945.
[6] Xia L, Zhang Y, An J, et al. Evaluating the remodeling of condyles reconstructed by transport distraction osteogenesis in the treatment of temporomandibular joint ankylosis. J Craniomaxillofac Surg. 2020 May;48(5):494-500.
[7] Ning Y,Wang X,Lammi MJ,et al. Changes in the NF- κB signaling pathway in juvenile and adult patients with Kashin-Beck disease[J]. Exp Cell Res, 2019, 379(2):140-149.
[8] Meng F, Liu Y, Hu K, et al. A comparative study of the skeletal morphology of the temporo-mandibular joint of children and adults [J]. J Postgrad Med, 2008, 54(3):191-194
[9] Duan DH, Zhang Y. A clinical investigation on disc displacement in sagittal fracture of the mandibular condyle and its association with TMJ ankylosis development [J]. Int J Oral Maxillofac Surg, 2011, 40(2):134-138.
[10] Sarma UC, Dave PK. Temporomandibular joint ankylosis: An Indian experience [J]. Oral Surg Oral Med Oral Pathol, 1991, 72(6):660-664.
[11] Guo Jun, Fei Wei, LI Qing-hua. An animal study on the outcome mechanism of traumatic temporomandibular joint ankylosis [J]. International J Stomatology, 2019, 46(01):12-19.

ISSN 2616-5791 Vol.5, Issue 3: 42-48, DOI: 10.25236/AJMHS.2024.050308

[12] Jiang Xin, HU Kaijin. Prevention of traumatic temporomandibular joint ankylosis [J]. Chin J Practical Stomatology, 2013, 6(03):132-135.
[13] Deng TG, Liu CK, Wu LG, et al. Association between maximum mouth opening and area of bony fusion in simulated temporomandibular joint bony ankylosis[J]. Int J Oral Maxillofac Surg, 2020, 49(3): 369-376.
[14] Yan Y, Zhang Y, Sun Z, et al. The relationship between mouth opening and computerized tomographic features of posttraumatic bony ankylosis of the temporomandibular joint[J]. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2011, 111(3): 354-361.
[15] Yang Cheng, SUN Moyi, Yang Yaowu et al. Treatment of condylar fracture in children with open plate fixation. J Practical Stomatology, 2003; 19(6):620-632
[16] Zavodovskaya R, Vapniarsky N, Garcia T, et al. Intra - and extra - articular features of temporomandibular joint ankylosis in the cat (felis catus)[J]. J Comp Pathol, 2020, 175: 39-48. doi: 10.1016/j.jc-pa. 2019.12.006.
[17] Deng Tiange, Liu Ping, Liu Changkui et al. Pathological role of lateral pterygoid muscle in traumatic temporomandibular joint ankylosis [J]. Stomatology Research,2021,37(05):442-447.
[18] Fan-Wen Meng et al. A new hypothesis of mechanisms of traumatic ankylosis of temporomandibular joint[J]. Medical Hypotheses,2009,73(1):92-93.
[19] Mei Jie, Jiang Yangmei, Li Yunfeng et al. Treatment of temporomandibular joint ankylosis and its secondary deformities in children [J]. Stomatology Research,2018,34(03):274-277.
[20] Arakeri G, Kusanale A, Zaki GA, et al. Pathogenesis of post-traumatic ankylosis of the temporomandibular joint: A critical review[J]. Br J Oral Maxillofac Surg, 2012, 50(1):8-12.
[21] Hall MB. Condylar fractures: Surgical management [J]. J Oral Maxillofac Surg, 1994, 52(11): 1189-1192.
[22] Gu S, Wei N, Yu L, et al. Shox2-defi ciency leads to dysplasia and ankylosis of the temporomandibular joint in mice[J]. Mech Dev, 2008, 125(8):729-742.
[23] Dong L,Su N,Miao KS,et al. PI3K/Akt and caspase path-ways mediate oxidative stress-induced chondrocyte apoptosis[J]. Cell Stress Chaperones, 2019, 24(1):195-202.
[24] Liu Ziwei, Shi Quan, Wang Situo et al. Advances in the application of mesenchymal stem cell-derived exosomes in dentistry [J]. Chin J Gerontology, 2012,20(03):174-178.
[25] Yan YB, Zhang Y, Gan YH, et al. Surgical induction of TMJ bony ankylosis in growing sheep and the role of injury severity of the glenoid fossa on the development of bony ankylosis. J Craniomaxillofac Surg. 2013 Sep; 41(6):476-486.
[26] Ma D, Zhang S, Pang C, et al. The Application of intraoperative computed tomography in surgical management of temporomandibular joint ankylosis[J]. J Oral Maxillofac Surg, 2021, 79(1): 90.e1-90.el.
[27] Myrto Bami et al. Superiority of synovial membrane mesenchymal stem cells in chondrogenesis, osteogenesis, myogenesis and tenogenesis in a rabbit model[J]. Injury,2020,51:2855-2865
[28] Zheng Weiwei, Yang Min, WU Cheng et al. Experimental study on osteogenic properties of synovial mesenchymal stem cells in vitro and in vivo [J]. Chinese Journal of Reparative and Reconstructive Surgery, 2016, 30(01):102-109.
[29] Jiang Xin, Li Jinchao, DOU Chunbo et al. The role of synovial mesenchymal stem cells in traumatic temporomandibular joint ankylosis [J]. J Clin Stomatology,2021,37(11):651-654.
[30] He LH, Liu M, He Y, et al. TRPV1 deletion impaired fracture healing and inhibited osteoclast and osteoblast differentiation. Sci Rep. 2017 Feb 22;7:42385.
[31] Muire PJ, Mangum LH, Wenke JC. Time Course of Immune Response and Immunomodulation During Normal and Delayed Healing of Musculoskeletal Wounds. Front Immunol. 2020 Jun 4;11:1056.
[32] Wang X, Chen X, Lu L, et al. Alcoholism and Osteoimmunology. Curr Med Chem. 2021; 28(9):1815-1828.
[33] Xia L, Zhang Y, An J, et al. Evaluating the remodeling of condyles reconstructed by transport distraction osteogenesis in the treatment of temporomandibular joint ankylosis[J]. J Craniomaxillofac Surg, 2020, 48(5): 494-500.
[34] Zhao L, Xiao E, He L,et al. Reducing macrophage numbers alleviates temporomandibular joint ankylosis. Cell Tissue Res. 2020 Mar; 379(3):521-536.
[35] Shi Mei-xia, GAO Jing, XU Yan-hua. Research progress on gene regulation of growth and remodeling of mandibular condylar cartilage [J]. Medicine Review,2018,24(06):1052-1056+1061.
[36]] Xu Wei, Liu Da, Wang Wei et al. Research status of autophagy in the pathogenesis and treatment of osteoarthritis [J]. Chin J Orthopedics, 2021, 30(10):902-905+910.
[37] Xia L, An J, He Y, et al. Association between the clinical features of and types of temporomandibular joint ankylosis based on a modified classification system. Sci Rep. 2019 Jul 19;

ISSN 2616-5791 Vol.5, Issue 3: 42-48, DOI: 10.25236/AJMHS.2024.050308

9(1): 10493.
[38] Hu SL, Zhang CW, Ni LB, et al. Stabilization of HIF-1α alleviates osteoarthritis via enhancing mitophagy [J]. Cell Death Dis, 2020, 11 (6): 481.
[39] Duan R, Xie H, Liu ZZ. The role of autophagy in osteoarthritis [J].Front Cell Dev Biol, 2020, 8: 608388.
[40] Hu Kai-jin, Ma Zhen, WANG Yiming, et al. New progress in the pathogenesis of traumatic temporomandibular joint ankylosis [J]. Prevention and Treatment of Stomatology, 2021, 29(12): 793-800.
[41] Liang SX, Wang HL, Zhang PP, et al. Differential regulation of blood vessel formation between traumatic temporomandibular joint fibrous ankylosis and bony ankylosis in a sheep model. J Craniomaxillofac Surg. 2019 Nov;47(11):1739-1751.
[42] Vincent AG, Ducic Y, Kellman R. Fractures of the mandibular condyle[J]. Facial Plast Surg, 2019, 35(6): 623-626.
[43] Wang L,Gai P, Xu R, et al. Shikonin protects chondrocytes from interleukin-1beta-induced apoptosis by regulating PI3K/Akt signaling pathway[J]. Int J Clin Exp Pathol, 2015, 8(1):298-308
[44] Zhang J, Sun X, Jia S, et al. The role of lateral pterygoid muscle in the traumatic temporomandibular joint ankylosis: A gene chip based analysis. Mol Med Rep. 2019 May; 19(5):4297-4305.
[45] Pilmane Mara, Skagers Andrejs. Growth factors, genes, bone proteins and apoptosis in the temporomandibular joint (TMJ) of children with ankylosis and during disease recurrence.[J]. Stomatologija, 2011, 13(3): 96-101.
[46] Duan D, Li J, Xiao E, et al. Histopathological features of hypertrophic bone mass of temporomandibular joint ankylosis (TMJA): An explanation of pathogenesis of TMJA. J Craniomaxillofac Surg. 2015 Jul; 43(6):926-933.