Treating Cartilage Injuries in Young Patients

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Abstract: Young people tend to suffer from cartilage injuries caused by extraneous trauma. There are many treatments for cartilage injuries. This article recommends treatments for different cartilage injuries targeted towards young patients. For young patients with mild or asymptomatic symptoms without cartilage displacement, this article recommends mandatory conservative treatment for young patients. Depending on the recovery condition of conservative treatment, the surgeon can subsequently plan for surgical treatment. Depending on lesion size, this article recommends the following operations. For lesions less than 1 cm2, arthroscopic debridement is recommended. For lesions between 1 and 4 cm2, MACI is recommended. For lesions larger than 4 cm2, OCA is recommended as a priority. If OCA is not feasible, OAT can be considered.

Keywords: Cartilage Injury; Arthroscopic Debridement; MACI; OCA; OAT.

1. Introduction

Cartilage tissues have a limited capacity for self-regeneration (Körner et al., 2021a). This tissue has a few blood vessels, nerves, and lymphatic tissues (Zhou et al., 2021). Slight injuries do not cause dysfunction of cartilage tissues, causing a delay in the diagnosis of slight and acute injuries (Badekas et al., 2013). Cartilage injuries are likely to develop arthritis if a patient does not receive adequate treatment, whether caused by endogenous or exogenous factors (Eichman et al., 2021; Occhetta et al., 2016). Thus, cartilage damages frequently cause joint pain and loss of mobility (Mardones et al., 2020). Young and active patients are more prone to develop potential cartilage damage related to a traumatic injury than older people (Daud et al., 2021; Körner et al., 2021b). For example, 50% of patients develop cartilage defects after an acute ankle sprain (Savage-Elliott et al., 2014). Because inflammatory factors lead to necrosis and apoptosis of chondrocytes after an acute injury (Barakat et al., 2019), their symptoms will deteriorate if patients are not appropriately treated (Cinats et al., 2021). There are many treatment options for cartilage injuries, including conservative and surgical treatments (Dong et al., 2021). Each treatment has its advantages and disadvantages (Versier & Dubrana, 2011). Doctors should balance risks and outcomes when planning treatments for their patients to help them recover better. For young patients, treatments need to consider several factors, such as the recovery of motor function, the success rate of treatment, and long-term treatment outcomes. It is vital to choose practical and suitable treatments to restore motor function for patients. This article will focus on the following two questions to advise patients regarding their treatment:

What is the recommended treatment? What are the current findings of this treatment?

What are the advantages and disadvantages of each treatment? Why is this treatment more suitable for young patients than other treatments?

This article will advise treatment options for young patients in different conditions to help them recover their motor function. This article will explain the reasons for treatment design based on answers to the above questions.

2. Treatment suggestions

This article suggests that young patients select different treatment options depending on their conditions. The detailed treatment protocol is as follows:

Firstly, doctors need to obtain information on patients' situations, such as surgical history and patients' age. These factors affect doctors' decisions on how to treat patients. Doctors should advise children to start with conservative treatment (Reilingh et al., 2014). For obese patients, doctors should advise patients to lose weight, both in conservative treatment and post-operative rehabilitation training (Lopa et al., 2019).

Secondly, doctors should evaluate patients' symptoms. For example, whether there is swelling in joints or patients suffer from pain on movement (Prakash & Learmonth, 2002). After patients get a magnetic resonance imaging (MRI) scan, doctors can determine if there is cartilage displacement in affected areas and the narrowed joint cavity (Thompson & Roukis, 2020). After evaluating patients, conservative treatment is recommended for asymptomatic patients without displacement; patients with symptoms and displacement are recommended for arthroscopy (López-Alcorocho et al., 2021). MRI is suitable for screening soft tissues around joints pre-operatively as a non-invasive test (De Schepper et al., 2000). However, MRI cannot identify lesion size and location (Magnussen et al., 2008). Thus, symptomatic patients with cartilage displacement should proceed with arthroscopy to help surgeons decide on a suitable surgical approach.

Lesion size is determined in arthroscopy. Depending on lesion size, patients are recommended for arthroscopic debridement, matrix-assisted autologous chondrocyte transplantation (MACT), osteochondral allograft (OCA), or osteochondral autograft transplantation (OAT).

After conservative or surgical treatment, patients will be provided rehabilitation training with education treatment to help them restore their daily physical activities. The treatment protocol is shown in Figure 1.

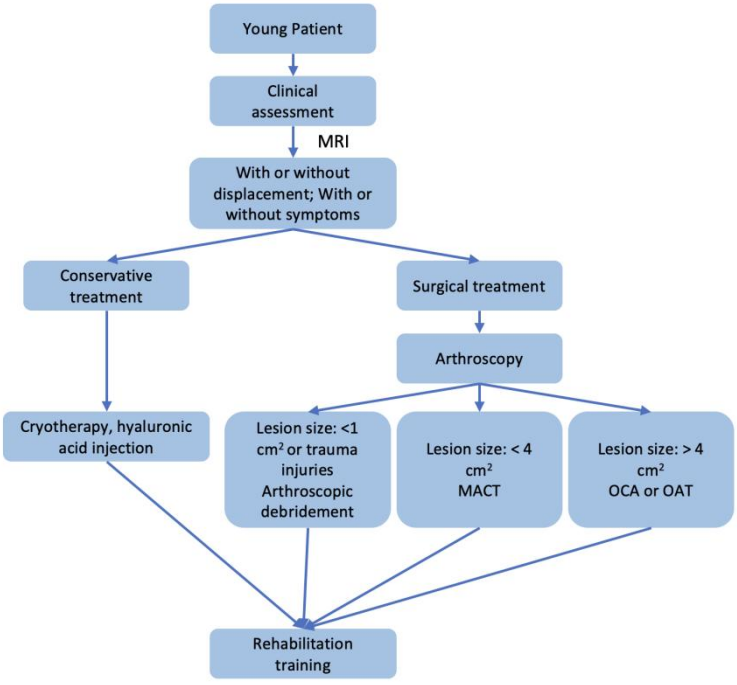

Figure 1 Treatment suggestions for young patients

3. Explanation of treatment options

Patients and doctors should decide the most cost-effective and safest treatment option for their conditions. Whether conservative or surgical treatments, no one treatment option is suitable for all conditions of cartilage defects (Magnussen et al., 2008). Young patients have higher post-operative motor recovery and recovery time requirements than older patients (Di Martino, Silva, et al., 2021). Therefore, doctors should consider young patients' requirements and balance the risks and benefits of treatment when selecting a treatment approach.

3.1 Conservative treatment

Conservative treatment is effective in the short term for patients with mild or acute symptoms. For patients with cartilage defects, conservative treatments include oral non-steroidal anti-inflammatory drugs (NSAID), hyaluronic acid injections, cryotherapy, immobilization, and non-weight bearing. Conservative treatments aim to help cartilage tissues self-recover by reducing oedema surrounding injured joints (Thompson & Roukis, 2020). Although cartilage tissues have a limited ability to self-repair, the recovery rate of conservative treatment is impressive at 45% (Zhang et al., 2022). Conservative treatments provide good results for more stable diseases (Körner et al., 2021b). Conservative treatments usually require 3-9 months for recovery (Eichman et al., 2021). Patients should be treated with cryotherapy at the initial phase of an injury, followed by hyaluronic acid intra-articular injections and oral medications depending on patients' inflammatory status to satisfy young patients' daily activity requirements.

Cryotherapy can effectively help patients with acute injuries to relieve pain, reduce inflammation and improve joint mobility. Cryotherapy is a treatment that uses a topical cold environment such as ice or ice massage to lower tissue temperature and help patients relieve pain, stiffness and joint mobility (Dantas et al., 2019). Cryotherapy is commonly used in patients with acute cartilage trauma and some post-operative swelling (Lieberthal et al., 2015). Low temperature reduces periarticular vasoconstriction and vascular permeability, reducing tissue fluid leakage and joint swelling (Fayyad et al., 2020). Furthermore, low temperature reduces the excitability of periarticular nerves, which reduces pain in patients (Dong et al., 2021). When cartilage is injured, the expression of catabolic genes will increase in vivo, and pro-inflammatory cytokines will promote the breakdown and shedding of chondrocytes (Alexander et al., 2013). Cryotherapy reduces high inflammatory responses and oxidative stress in vivo (Puntel et al., 2013). Riegger et al. (2018) found that hypothermia increased chondrocyte survival after a trauma, and cryotherapy inhibited MMP release and type II collagen breakdown. This study showed that a long-term (7 days) low-temperature environment inhibited MMP gene expression ($P=0.0273$) more than medium-term (24 hours) intervention ($P=0.0371$). Thus, long-term cryotherapy prevents further degradation of chondrocytes. Besides cryotherapy, some physiotherapies also effectively reduce oedema and inflammatory responses (Dong et al., 2021). This article recommends cryotherapy for young patients rather than traditional physiotherapy treatment because most physiotherapies require special equipment and are more expensive. Cryotherapy is more straightforward and more cost-effective. Young patients can be treated more conveniently depending on their schedules.

Hyaluronic acid intra-articular injections are safe and effective in reducing pain and improving joint movement. Abnormal structures cause a release of inflammatory factors after cartilage injuries (Buckwalter, 2012). Thus, acute treatment for cartilage injury aims to inhibit cytokine-induced inflammatory responses (Anderson et al., 2011). Intra-articular injections keep a high concentration of drugs in an articular cavity of damaged cartilage (Bonasia et al., 2005). Thus, intra-articular injections can more rapidly inhibit inflammatory responses than oral NSAIDs. Barakat et al. (2019) studied that patients significantly improved motor function and joint pain after three months of hyaluronic acid injections. But 10% of patients' symptoms got worse. This study had limited participants. And the control group in this trial was without a joint cavity injection rather than a placebo injection. Therefore, the results of this study were subjectively biased. However, the

results of this study provided evidence for the role of hyaluronic acid in the acute phase of inflammation. Studies of joint cavity injections involve hyaluronic acid, mesenchymal stem cells (MSCs), and exosome cell injections. And all three drugs showed significant improvement in joint function and pain management in patients (Centeno et al., 2015; Xia et al., 2021). Each drug has its advantages and disadvantages (Table 1). In recent studies, exosomes showed great advantages and potential (Wu et al., 2019). However, the effects of exosomes on gene expression after injection in vivo still need further investigation (Valadi et al., 2007). Thus, hyaluronic acid injection is very suitable as a treatment for young patients in the acute phase of injury.

	Advantages	Disadvantages
Hyaluronic acid	Safe; effective; cost-effective	Short-term outcomes
MSCs	Promote the regeneration of chondrocytes; Precise number of injected cells	Potential induction of osteoma growth
Exosomes	Reproducible; sustainable; low toxicity than MSCs	Expensive; Uncontrolled gene translation; lack of targeting

Table 1 Advantages and disadvantages of three drugs

This article recommends mandatory conservative treatment for children and adolescents before surgery, as children's chondrocytes have a higher regenerative potential than adults (Salzmann et al., 2018). Patients can start with conservative treatment for six to eight months and decide whether surgery is needed depending on their recovery (Thompson & Roukis, 2020). Every operation has the risk of complications (Harris et al., 2010; Versier & Dubrana, 2011). Therefore, surgical treatment should be carefully chosen for children. The combination of conservative treatment and exercise therapy can be more effective in restoring motor function (Lopa et al., 2019). Thus, young patients should get different rehabilitation training levels to help them to restore joint function, similar to post-surgical rehabilitation training.

3.2 Surgical treatment

Surgery is an effective treatment for patients who have failed conservative treatment or those with severe symptoms, such as free bodies and loose cartilage in patients' joint cavities (Eichman et al., 2021; Zhang et al., 2022). The surgical approaches include arthroscopic debridement, arthroscopic microfracture, MACT, OCA, OAT. According to the international cartilage regeneration & joint preservation society (ICRS), cartilage injuries are classified into four levels according to the defect depth and four levels according to the lesion's continuity. There are various criteria for evaluating cartilage injury, but success rates for different operations depend on lesion size (Chu et al., 2020). There is no single surgical approach suitable for all types of cartilage injury, and there is no gold standard for surgical approaches (Mardones et al., 2020). Different operations have different advantages and disadvantages (Table 2). This article recommends different surgical approaches depending on lesion size. For young patients, the factors to consider are the recovery rate of movement, recovery time, the difficulty of operation, and surgery costs. Based on these factors, this article recommends arthroscopic debridement, MACT, OCA, and OAT for young patients depending on lesion size.

	Advantages	Disadvantages
Arthroscopic debridement	Good Short-term and moderate-term outcomes.	Limited treatment effects
Arthroscopic microfractures	Few pre-operative plans, few surgical types of equipment	The regenerating bone is fibrocartilage. Overgrowth of bone may occur

MACT (the third generation of ACI)	Good clinical outcomes; Precise number of transplanted cells	Two operations are required; expensive
OCA	Only one operation is required; Less fibrocartilage regeneration	Limited Donors; expensive
OAT	Only one operation is required	Expensive; Fibrocartilage regeneration still present

Table 2 Advantages and disadvantages of different surgical approaches

3.2.1 Trauma injuries and lesion size less than 1 cm2

Arthroscopic debridement should be offered for patients with less than 1 cm2 lesion or some acute symptomatic patients. Arthroscopic operations are minimally invasive and high safe (Cohen et al., 2000). Arthroscopic debridement involves debridement of damaged cartilage and removal of free bodies to help improve the function of the damaged joint with minimal tissue damage (Weinstein et al., 2000). Arthroscopic surgeries are characterized by smaller incisions, simpler operations, short operating time, and minor bleeding than other types of surgery (Dong et al., 2021). Although the risk of postoperative complications is low and patients recover quickly after arthroscopic debridement, the overall recovery rate for this operation is not very good (Dervin et al., 2003). For patients with severe symptoms, arthroscopic debridement can buffer a formal operation (Gu et al., 2018), which means that debridement can only partially alleviate symptoms in patients with severe symptoms but cannot replace the final treatment operation. For patients with milder symptoms, arthroscopic debridement can significantly improve their symptoms (Aaron et al., 2006). However, arthroscopic debridement can be adequate to decrease young patients' pain and improve their joint range of motion (Cohen et al., 2000). Rahusen et al. (2006) found that fifteen patients with exfoliated cartilage had a highly significant improvement of elbow function ($p<0.001$) and a highly significant reduction in pain levels ($p<0.001$) after arthroscopic debridement. 80% of patients were recovered within five years, and no patients had postoperative complications. Although this study had a limited number of patients, the recovery ratio was similar to other studies where patients with mild disease were recovered (Aaron et al., 2006; Weinstein et al., 2000). Thus, arthroscopic debridement is well-suited to treating young patients with mild disease.

For patients with minor cartilage injuries, microfracture surgery is a treatment operation with a high recovery rate in the short term. Microfracture is an operation to repair damaged cartilage tissue by causing new damage to the damaged cartilage tissue, destroying subchondral bone tissue, and inducing the proliferation of pluripotent stem cells from the bone marrow to differentiate into fibrocartilage (Magnussen et al., 2008). Microfracture is similar to arthroscopic debridement in advantages. Both operations are suitable for small scale cartilage injuries (Zhou et al., 2021). Also, microfracture is simple, inexpensive, and has an excellent short-term recovery effect (Kon et al., 2021). However, the biggest problem with this operation is that it can cause an overgrowth of subchondral bone and the growth of fibrocartilage (Ibarra et al., 2021). Fibrocartilage is less durable than hyaline cartilage for intra-articular wear (Harris et al., 2010). The instability of fibrocartilage causes patients to deteriorate after two years of surgery (Lolli et al., 2019). Patients who performed microfracture showed decreased motor performance at a 5-year follow-up (Harris et al., 2010). And a failed microfracture operation affect the success of subsequent cartilage revision operations. Lamplot et al. (2018) found that patients who had a history of failed microfracture operation had a lower success rate with ACI operation than patients having their first ACI operation. Thus, this article does not recommend microfracture surgery for young patients. Patients with cartilage defects between 1 and 4 cm2 should be treated with a MACT operation, which offers a high recovery rate.

3.2.2 Lesion size less than 4 cm2

For cartilage defects in 1 to 4 cm2, this article recommends that young patients have a MACI operation. For cartilage repair operations, new cartilage formation requires sufficient chondrocytes, scaffolds to support chondrocyte growth, and adequate mechanical performance of newly implanted cartilage or scaffolds to maintain cartilage function (Shetty et al., 2018). MACI is a third-generation ACI operation (Ibarra et al., 2021), which is a 3-step operation (Versier & Dubrana, 2011):

Firstly, chondrocytes are taken from a non-weight-bearing region at arthroscopic debridement.

Secondly, chondrocytes are transferred on a bio-scaffold after expansion in culture in vitro.

Finally, the bio-scaffold is implanted in the damaged cartilage area.

A sufficient cell density is vital in cartilage repair surgery (Liu et al., 2021), and MACI provides patients with a precise number of cells, making this operation have a high recovery rate for young patients who have not been treated with other cartilage operations (Hamblin et al., 2010). Andriolo et al. (2021) found that 29 patients who completed a MACI operation had a high implant survival rate (87%) over 12 years following the operation. The four failed patients all occurred in the early stages after their operation. Furthermore, 60% of these patients had recovered their pre-injury level of exercise. However, patients who recovered from this surgery are not suitable for high-intensity exercise (Niethammer et al., 2021).

This operation has some drawbacks due to its procedures. First, it is a two-step operation. It is challenging to operate arthroscopically in the second operation and is primarily an open operation (Wang et al., 2017). Secondly, the whole operation is complex and requires a long recovery time (12 months) (Edwards et al., 2013). These factors make the whole operation more costly. One study combined a cell-free bio-scaffold with microfracture surgery to avoid secondary surgery, transplanting the scaffold directly onto defective cartilage tissues (Drobnič et al., 2021). However, the recovery rate for this operation is not high (59%). An innovative technique (Chimutengwende-Gordon et al., 2021) involves extracting stem cells from the bone marrow, culturing them in vitro, transferring them to a bio-scaffold and transplanting them into the body. This approach has significant advantages as it is a one-step operation. However, this study only involved three patients, and there are no mid-term or long-term clinical results to support the recovery rate of this approach, which needs further validation. Considering the long-term recovery outcomes of the MACI operation, this article argues that it is well-suited as a treatment option for young patients with cartilage defects of 1-4 cm2.

3.2.3 Lesion size over 4 cm2

For patients with cartilage defects larger than 4 cm2, only OCA and OAT operations have good outcomes. If a patient has an opportunity to receive an OCA operation, it is recommended as a priority. The OAT operation is an alternative if OCA is not available. The OCA surgery involves placing a fresh and frozen osteochondral allograft in the location of cartilage defects (Versier & Dubrana, 2011), fixed with bioresorbable screws (Eichman et al., 2021). This cartilage repair technique has high cellular viability and no production of fibrocartilage (Bisicchia et al., 2014). A fresh allograft cartilage graft does not cause complications (Merritt et al., 2021), but this approach has a high risk of immunogenicity (Chu et al., 2020). Although fresh and frozen allograft cartilage is less immunogenic, cryogenic temperatures reduce chondrocyte viability (Lattermann & Romine, 2009). Currently, allograft cartilage grafts present an excellent survival rate (Abolghasemian et al., 2019). Daud et al. (2021) found that 38.1% of 244 patients had good grafts survival on average 11 years after surgery, and 43.7% of patients had a 20-year lifespan of their grafts during a long-term follow-up. For patients aged less than 50 years, 80% of patients had good survival with their grafts. Although allograft surgery is ideal for young patients, its availability is limited in most countries for reasons such as the lack or mismatch of grafts (Di Martino, Perdisa, et al., 2021). Therefore, if an OCA operation is unavailable, an OAT operation can be an alternative option.

The OAT operation involves filling defective areas with autologous cartilage derived from non-weight-bearing areas (Baltzer et al., 2016). The advantage of this technique is that it uses mature hyaline cartilage for filling and treats defective cartilage areas very well (Richter et al., 2016). The risk of postoperative complications after OAT operation is not high (Andrade et al., 2016). Patients with OAT surgery recovered more quickly than other surgeries (Krych et al., 2017). However, this operation affects patients' recovery because multiple cartilage plugs are implanted, which lead to potential fibrocartilage production around these plugs (Bisicchia et al., 2014). However, OAT operation is still the best option when OCA is unavailable.

4. Rehabilitation training

Rehabilitation and educational therapy for patients following conservative and surgical treatment are necessary. Patients are educated on postoperative prognostic information, combined with exercise therapy, which effectively manages their pain (Crossley et al., 2015). Pain reduced as training time increased, and a clinically significant improvement needed at least eight weeks to happen (Skou et al., 2017). Postoperative rehabilitation is divided into 3 phases. The first phase is graft protection; the second phase is functional recovery; the third phase is movement recovery. The first rehabilitation phase can be skipped for conservative treatment, and exercise training can be conducted in Phases 2 and 3. The duration and intensity of training should be adjusted to fit patients' conditions. Avoid patients suffering secondary injuries to their cartilage by increasing intensities of exercise.

5. Conclusion

There are many treatment options for cartilage injuries, and this article presents different treatment options for cartilage injuries in young patients. This article recommends conservative and surgical treatments depending on the lesion size of cartilage damage areas to help patients recover. After conservative and surgical treatments, patients should combine exercise therapy and educational therapy to regain mobility of damaged joints more effectively. Cryotherapy and hyaluronic acid injections are recommended for acute or asymptomatic patients without displacement. These two methods are safe and effective to help young patients reduce inflammatory responses in areas of damaged cartilage and reduce the death of chondrocytes to facilitate rapid recovery in young patients. Surgical treatments are divided into three classes depending on lesion size. This article recommends the arthroscopic debridement procedure for patients with lesions smaller than 1 cm^2. In contrast, patients are not advised to have micro-fracture surgery. Microfracture surgery only brings a short-term recovery. Most patients will deteriorate within two years and affect success rates of subsequent cartilage repair surgery. The MACI operation is recommended for patients with lesions between 1 and 4 cm^2. This operation has a high recovery rate and few complications for young patients. And it has shown good outcomes in short-term and medium-term follow-ups. For patients with a lesion size above 4 cm^2, this article recommends that patients give priority to OCA. However, this operation is not always available to all patients due to low graft trapping and donor mismatch. For young patients, the treatment outcomes of this operation can be sustained for ten to twenty years. When OCA surgery is not available, patients may consider OAT surgery. Although this operation can lead to the production of fibrocartilage caused by cartilage plugs, this operation also has a good recovery rate. Thus, it is suitable as an alternative treatment option to OCA surgery.

Patients and doctors can choose different treatment options depending on patients' requirements. This article recommends these treatment methods by comparing the results of existing clinical treatments for young patients. Although there is a subjective bias in selecting treatment methods, these treatments showed good clinical results. For most patients, these treatments can help them to regain their mobility.

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