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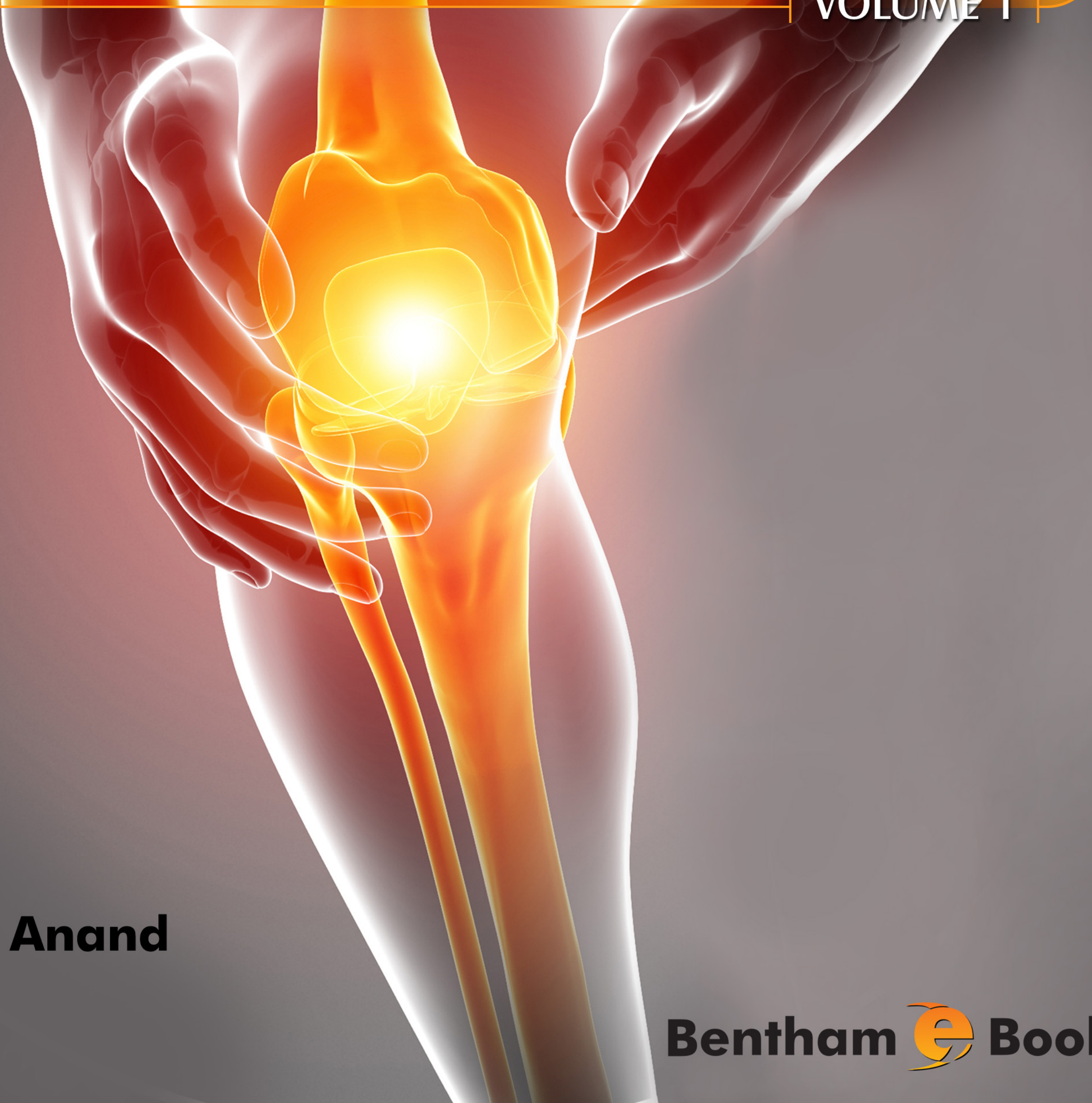
FRONTIERS IN ARTHRITIS

MANAGEMENT OF OSTEOARTHRITIS A HOLISTIC VIEW

VOLUME 1



Editor:
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Frontiers in Arthritis

(Volume 1)

Management of Osteoarthritis - A Holistic View

Edited by

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Frontiers in Arthritis

Management of Arthritis-A Holistic View

Volume # 1

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FOREWORD

Osteoarthritis is known enigma for Orthopedic Surgeons and it continues to be amongst the most important cause of chronic pain and disability. It is estimated that around 6 billion dollars/year are spent alone on management of this epidemic.

The purpose of this monograph is to offer the reader treatment options available for the management of osteoarthritis of knee and hip. If one reviews the current spectrum of literature available to, it becomes clear that there is a large body of literature in which the patient has to sort through with varying degree of scientific evidence, making anyone embarking on this Journey a difficult and conducing one. This Monograph provides an in depth analysis of the Pathology, Role of Nutrition and Exercise in treatment of arthritis there by offering a unique perspective to the Reader.

The book also provides insights into Role of injectables such as Platelet rich plasma and Viscosupplementation and elaborates on the Role of Amniofix- stem cells from the Amnion and Chorion in the treatment of Osteoarthritis. Finally, the book presents a number of surgical options for the reader that have had an established place for decades in the field of surgical arthritis such as Osteotomy, Arthroscopy and Replacement surgery.

Dr. Ashish Anand, MD has done a commendable Job in editing the manuscript. This book is a good read for Medical students, residents in training and the busy practitioner.

Khaled J. Saleh
President Orthopaedic Education
Southern Illinois University School of Medicine in Springfield,
Illinois, USA

PREFACE

The book contains eight chapters with initial ones focusing on pathology behind osteoarthritis, Role of Nutrition in management of Osteoarthritis and Role of exercise in Management of Osteoarthritis. All of them point and educate the reader/clinician on their important role in pathogenesis as well as prevention of osteoarthritis. The Reader is encouraged to incorporate Nutrition and Exercise management in his Clinical practice.

The next chapter tells us about the Role of Viscosupplementation and Platelet Rich Plasma(PRP) in management of osteoarthritis and what the current clinical evidence is for the above two modalities.

Chapter 5 is an interesting chapter on Amniofix, which is relatively unheard of. Amniofix is an allograft tissue obtained from a Human baby and contains growth factors which have the potential for treating osteoarthritis pain when everything has failed and the patient is not interested in surgery. It may even possibly reverse the early damaging changes to the Cartilage. As time goes by, I am sure one will hear a lot about this "Novel" approach.

The second last section deals with surgical aspects of treatment of arthritis of knee in which the book dwells on the role of Arthroscopy with Cartilage Surgery, role of Osteotomy around the knee, and Current Concepts in Total Knee Replacement.

The last section deals with surgical management of arthritis of Hip-namely Role of Arthroscopy with Cartilage Surgery as well as Current Concepts in Total hip replacement.

It is my sincere hope that this book will stimulate the minds of the busy clinicians to read more about the subject and possibly also add some new tools to their armamentarium to give their patients the best possible treatment.

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ACKNOWLEDGEMENTS

I always used to wonder what does work of an editor involve? All my questions were answered as I worked diligently during the preparation of this monograph. It gave me sleepless nights so that I could stick to the schedule given to me by the publishers. Interacting with the various authors and then editing their work was an excellent learning experience. I would like to thank all the authors who spent there valuable time in preparing the manuscripts and sticking to my schedule. All of us enjoyed writing this book and we sincerely hope that the reader gets the same pleasure and adds something more to his knowledge while reading this book.

I am indebted to my parents for instilling the values of hard work, perseverance and commitment as all these qualities served me in good stead during the preparation of this manuscript. I would like to thank my wife Varsha for constantly nudging me to go above and beyond. Finally, I would like to thank my two lovely daughters Advikaa and Vahita for helping me out with computer glitches and sparing me valuable time without which this book would not have seen light of the day.

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DEDICATION

Dedicated to my brother, Rishi Anand.

CHAPTER 1

Pathology of Osteoarthritis

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Abstract: The pathology of osteoarthritis is extremely complex and multifactorial. Recent technological advances have allowed the identification of specific genes and genetic alterations which have helped to elucidate some intricacies involved in the molecular basis of disease development and progression. Known factors and key recent discoveries in pathogenesis, plus typical gross and histologic pathologic findings are described in this chapter.

Keywords: Degenerative joint disease, Gene, Genetic, Gross, Histology, Microscopic, Molecular, Morphology, Osteoarthritis, Pathology.

INTRODUCTION

Osteoarthritis (OA), also known as degenerative joint disease, is characterized by the progressive degradation of articular cartilage causing loss of function as a shock absorber [1]. The term OA was introduced by Archibald E. Garrod, an English physician in the 1890s [2]. The characteristic features of OA include initial softening, splitting, and fragmentation of articular cartilage followed by sclerosis of the bone underlying the articular surface cartilage (subchondral bone), bone cysts, and bony outgrowths at the joint margins (osteophytes) [3].

ETIOLOGY/PATHOGENESIS

OA is a multifactorial disease with a complex pathogenesis involving both environmental and genetic factors. The molecular basis of disease development

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and progression encompasses chondrocyte injury, repair, and ultimately, death. Chondrocyte injury elicits an inflammatory response and lymphocyte production of pro-inflammatory mediators, including TNF and IL-B. OA chondrocytes produce IL-1, inducing the expression of MMPs, and other catabolic enzymes. Pro-inflammatory mediators and catabolic enzymes subsequently lead to cartilage destruction [6]. In most cases, OA results from aging and an unknown underlying cause. In a minority of cases, OA develops in young patients with a predisposing condition, such as a previous joint injury, congenital deformity, or systemic disease. Environmental factors include aging and biomechanical stress related to physical characteristics like body weight and joint stability. Genetic factors include both intrinsic genes and altered gene expression *via* epigenetic modifications. Family and epidemiological studies show that OA is associated with multiple genes and has a heritability component. Genome wide association studies identified specific genes associated with the development and progression of OA [4, 5]. Genome wide methylation studies suggest that DNA methylation plays a significant role regulating the inflammation in cartilage through epigenetic modifications and together with cytokines, growth factors and changes in matrix composition, are involved in the development of OA. One in particular reports hypomethylation leading to increased transcription of pro-inflammatory factors including TFF, IL-1 and IL-6. Furthermore, epigenetic regulation involving microRNAs play a role in skeletal development and chondrogenesis [7, 8].

GROSS PATHOLOGY

The osteoarthritic articulating joint commonly displays cartilaginous outgrowths or osteophytes and loss of normal roundness. In the early stages of OA, hyaline cartilage on the articular surface is soft and granular. With disease progression, the articular cartilage sloughs off and is partially or completely lacking over weight bearing areas and remnants are usually present at the periphery. The underlying bone will have a polished, smooth appearance or eburnation in areas where it is in direct contact with another bone (Fig. **1**). The bony surface may have regenerative cartilage clusters where repair is taking place. Characteristic features seen on cross section include subchondral bone with a sclerotic appearance, subcortical cysts and wedge shaped necrosis (Fig. **2**). Subcortical cysts form when synovial fluid enters the subchondral bone space through small fractures on the bone surface. Multiple loose bodies may be present within the joint space [9 - 12].

Fig. (1). Femoral head with osteoarthritis. The articular surface is eburnated and there are remnants of cartilage around the periphery *(Image courtesy of Reggie Thomasson, MD)*.

MICROSCOPIC PATHOLOGY

Injury and repair related changes are seen histologically within bone and cartilage tissue. As the superficial layers of cartilage and collagen degrade, vertical and horizontal fibrillation become apparent with subsequent matrix cracking. Cartilage repair or regeneration occurs both intrinsically and extrinsically. Intrinsic repair exists within the original articular hyaline cartilage as islands composed of chondrocyte clones within the matrix. Extrinsic repair presents as a highly cellular fibrocartilage with coarse and disorganized collagen overlying remnants of articular hyaline cartilage and at the joint margin (Fig. **3**).

Subchondral bone denuded of surface cartilage shows osteoblast proliferation and associated new bone formation, corresponding with areas of sclerosis seen grossly

CHAPTER 2

Exercise in the Prevention and Treatment of Osteoarthritis

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Abstract: Exercise can reduce the risk for osteoarthritis by aiding in the prevention of obesity, joint instability, and muscle weakness. It can also serve as an effective treatment by helping patients manage weight, improve muscular strength, decrease joint stiffness, improve range of motion, increase functionality, and reduce the risk for falls. Before starting an exercise program, patients should obtain a physician's consent and complete a thorough fitness assessment with an exercise specialist. The exercise program should be progressive, beginning with low-to-moderate intensity exercises followed by gradual increases in intensity. Low impact aerobic training and isometric or isotonic strength training are recommended modes of exercise for effective management of osteoarthritis symptoms. Yoga and tai chi provide low impact exercises and are considered effective therapy options for osteoarthritis symptom management. In addition, water-based exercise programs may improve adherence to an exercise program and be equally effective as land-based exercise for improving gait, functionality and pain. Since exercise adherence is the primary predictor of long-term outcomes in osteoarthritic patients, strategies to improve exercise adherence should be implemented.

Keywords: Aerobic, Exercise, Exercise adherence, Exercise prescription, Fall risk, Flexibility, Functionality, Isometric, Isotonic, Joint pain, Joint stiffness, Older adult, Osteoarthritis, Prevention, Strength, Tai chi, Treatment, Water exercise, Weight management, Yoga.

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INTRODUCTION

Obesity, physical injury, joint instability, and muscle weakness are modifiable extrinsic risk factors associated with the development and progression of osteoarthritis. Obesity is a risk factor for several cardiovascular and metabolic diseases that plague more than one-third of U.S. adults and approximately 17% of American youth [1]. Gradual weight gain that leads to obesity can result from a combination of genetics, sedentary activity, and poor nutrition. Despite physical activity, aging adults reach their peak strength between the second and third decades in life. After 50 years of age, muscular strength declines at a rate of 12-15% per decade with even greater losses after 65 years [2]. Muscular power, the ability to generate force and velocity, is suggested to decline with greater magnitude and exceed losses in strength with age [3].

A lack of physical activity can accelerate declines in muscular performance and contribute to excessive weight gain. Higher body weight is associated with increased joint pain in older adults, and it has been estimated that the risk for developing osteoarthritis increases by 36% for every 5 kg increase in body weight [4]. Excess weight places additional load on the joint, which can lead to increased inflammation and structural changes in the joint and articular cartilage [5]. In addition to excess weight, a loss in both muscle mass and muscular strength, two important factors for joint movement, stability, and protection, are associated with joint degeneration and increased risk for osteoarthritis. These losses may be due to factors such as age-related sarcopenia, muscle-wasting diseases, and physical inactivity. Furthermore, obesity may contribute to these changes as intramuscular adipose tissue has been linked to losses in muscular strength and functional ability in older adults [6]. Both obesity and muscular weakness can affect movement and gait kinematics, which can cause the load-bearing portion of the joint to be shifted to areas that are not normally accustomed to the excess loading, resulting in cartilage degeneration and the progression of osteoarthritis [7]. The knees and the hips are the two most common joints affected by osteoarthritis as they are the joints which bear the greatest weight.

Comparatively, those who are physically active and participate in high impact sports are also at risk for osteoarthritis, as physical trauma can increase the disease's incidence [8]. Not only does damage to the joint affect the cartilage, but injury may lead to muscle weakness from disuse and weight gain from inactivity. Incorporating a safe and comprehensive exercise program into an individual's daily routine can help induce weight loss, prevent obesity, maintain muscular strength, and reduce injury, thus attenuating the development and symptoms of osteoarthritis.

Exercise Recommendations

The American College of Sports Medicine (ACSM), the largest sports medicine and exercise science organization in the world, has several position stands formulated from evidence of heavily scrutinized scientific literature. These position stands provide guidelines for appropriate physical activity intervention strategies for weight loss, weight regain, and health benefits. To avoid significant weight gain, ACSM recommends that adults engage in a minimum of 150 minutes per week of moderate intensity physical activity [9]. Overweight and obese adults can use the same recommendation to induce moderate weight loss; however, there is most likely a dose response relationship for exercise and weight reduction [9]. To achieve greater weight loss and prevent weight regain, ACSM recommends approximately 200 to 250 minutes of moderate intensity physical activity, which is equivalent to expending approximately 2,000 kcal, per week [9].

ACSM has also provided guidelines for physical activity for healthy older adults. These recommendations were developed based on evidence of the benefits of aerobic exercise and resistance training on health and functional capacity. For endurance, older adults should engage in moderate-intensity aerobic exercise accumulating at least 30 minutes of exercise time per day in bouts of at least 10 minutes to total 150-300 minutes per week. If working at a vigorous intensity, older adults should accumulate 20-30 minutes per day or more to total 75-150 minutes per week [10]. To determine the level of physical exertion, a 0 to 10 point scale is used where a score of 10 equals maximal physical exertion. Moderate intensity is a 5 to 6 and vigorous intensity is 7 to 8. Aerobic exercise modalities that do not exacerbate symptoms of orthopedic stress such as walking, cycling, and aquatics are recommended [10].

CHAPTER 3

Nutritional Impacts on Joint Health

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Abstract: Osteoarthritis is a common cause of musculoskeletal disability among the elderly. This can place burdens on society as this becomes more problematic for health care professionals to treat. For years, the management of osteoarthritic symptoms has been limited through the use of non-steroidal. Anti-inflammatory drugs (NSAID) for relief of pain and other debilitating symptoms. Since NSAIDs can cause other adverse side effects, nutritional supplements are being promoted as aids for preventing and reducing symptoms that relate to osteoarthritis without the development of adverse side effects. This chapter reviews the background of osteoarthritis as a degenerative joint disease while also looking at animal studies and human clinical trials that evaluate the effects of various nutritional supplements on joint health.

Keywords: Boron, Chondroitin sulfate, Curcumin, Dietary supplements, Dimethyl sulfoxide, Functional foods, Glucosamine sulfate, Inflammation, Joints, Magnesium, Nutrients, Omega-3, Osteoarthritis, Resveratrol, Soy, Vitamin E.

INTRODUCTION

Osteoarthritis (OA), known as degenerative arthritis, is the most common form of joint disease and is characterized by erosion of articular cartilage, thickening of subchondral bone and osteophyte formation [1]. Articular cartilage is a highly

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specialized connective tissue consisting of water, collagen and proteoglycan. The conformation of these components creates a stiff fiber-reinforced water gel with friction and shock-absorbing capacity. Joints that can be most affected by OA are of the knee, hips, hands, and spine. Symptoms of OA include but are not limited to localized pain that is worsened with activity and relieved by rest, stiffness and decreased range of motion [2, 3]. With advanced OA, weight bearing joints may give out and joints will develop bony enlargements. These bony knobs (nodes) will enlarge the finger joints creating a gnarled appearance. These nodes can take years to appear. OA will gradually worsen over time yet no cure is available. Cartilage degeneration is due to failure in the elastic restraint because of alterations in the structure of collagen. Degenerative conditions are also accompanied by local inflammatory components that may accelerate the joint destruction. The proteoglycan content in OA is gradually depleted, leading to an increase in water content and a loss of compressibility and shock absorption.

OA can be caused from previous joint injury, abnormal joint development, genetics, muscle weakness, joint instability and repetitive microtrauma. Two major risk factors for OA are increasing age, with most patients affected being 45 years and older, and increasing obesity [1]. However, staying active and maintaining a healthy weight through proper diet may help slow progression of the disease and help improve pain and joint function [4]. Conventional treatments, commonly prescribed pharmaceuticals, are available to those suffering from OA; however, adverse side effects are often associated with prescription medications. Non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics can often relieve symptoms of OA but can cause peptic ulcers, hepatic or renal failure. While failing to prevent or delay the progression of the disease, NSAIDs may accelerate joint destruction when used as a long-term pain relief [3, 5]. The need to develop safer and more effective ways for treating OA is still needed. Other alternative approaches for therapeutic treatment are through natural, herbal, physical manipulation, holistic and nutritional techniques. Many substances that occur naturally within the body, may pose as a valuable treatment method for managing OA, as well as some functional foods, as these methods may present long-term pain relief as well as keeping the structural damage of the cartilage to a minimum. In most cases, a nutritional compound has only limited effects on its biological target and pertinent differences are reached over time through a buildup effect, in which case the benefits will add up day after day. In theory, chronic diseases like OA should benefit from nutrition, more so than acute diseases. The appeal of using nutrition coincides with ailment prevention. Long-term pharmacological interventions for OA are frequently associated with adverse side effects. Nutraceuticals, a term coined from 'nutrition' and 'pharmaceutical' and defined as a food or part of a food that provides *medicinal* or health benefits to prevent or treat a disease, and functional foods could provide an advantageous alternative because, by laws, they have to be devoid of adverse effects [6].

ROLE OF NATURAL SUPPLEMENTS FOR PREVENTION AND TREATMENT OF OSTEOARTHRITIS

Nutritional Supplements have been developed for individuals with OA and have become popular because these supplements can provide the natural components that are able to inhibit or enhance the biological mediators that are able to preserve the structure of the joint [7]. Nutraceuticals are functional ingredients that are sold as powders, pills, and other medicinal forms that are not generally associated with food.

Glucosamine Sulfate and Chondroitin Sulfate

Glucosamine Sulfate is found both in the human body, produced from glucose, as well as found in nature among shellfish, and commonly used to treat arthritis. Articular cartilage contains a group of large protein molecules called proteoglycans. These are the proteins that give cartilage its strength and flexibility [3]. Glucosamine is an important precursor in the biosynthesis of many connective tissue macromolecules such as hyaluronic acid, glycosaminoglycan's (GAGs), glycolipids, and glycoproteins.

Glucosamine and Chondroitin are among the most popular OA supplements. Gaby suggests that glucosamine supplements may be an effective treatment for OA [3]. Articular pain, joint tenderness, swelling, and range of motion greatly improved in clinical trial groups that received glucosamine treatment compared to the counterpart group that only received a placebo [8]. This suggests that glucosamine supplements may slow the progression of the disease unlike current

CHAPTER 4

The Role of Viscosupplementation and Platelet Rich Plasma in the Management of Osteoarthritis of Knee and Hip

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Abstract: Osteoarthritis (OA) affects millions of people worldwide. However, there is no consensus on the treatment of OA. Treatments aim to reduce pain and help joint function. But they only improve symptoms in the medium term. Nowadays, we have diverse intra-articular treatments, which aim to get better results. Viscosupplementation and Platelet rich plasma are based on the physiologic relevance of hyaluronic acid in synovial joints, and the effect of platelets in the intra-articular homeostasis respectively. HA is used with good results in young patients with Knee OA grade I-II.

Additionally, there is enough evidence to consider the PRP as a valid and effective treatment to reduce pain and to improve the quality of life of patients with knee OA.

Keywords: Hip osteoarthritis, Hyaluronic acid, Knee osteoarthritis, Platelet rich plasma, Viscosupplementation and growth factors.

INTRODUCTION

The aims of medical treatment of osteoarthritis (OA) are the control of symptoms and to modify the natural history of the disease. Despite different pharmacological treatments that are currently available, they only improve symptoms in the short- and medium term, Hence we have not yet succeeded in modifying OA. All treat-

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ments have limitations such as the adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs: gastrointestinal, hepatotoxicity and nephrotoxicity) or the loss of efficiency over time.

Nowadays, we have diverse intra-articular treatments; among them, viscosupplementation and Platelet rich plasma, are based on the physiologic relevance of hyaluronic acid in synovial joints and on the effect of platelets in the intra-articular homeostasis respectively.

Action Mechanism of Viscosupplementation

Hyaluronic Acid (HA), also called hyaluronan, is a non-sulfated glycosaminoglycan polysaccharide. HA structure is a polymer chain of disaccharides of different lengths, composed of D-glucuronic acid and D-N-acetylglucosamine [1, 2]. The molecular weight of HA ranges between 5000 and 20 million Da. In the human body the average molecular weight is around 4 million Da. It is soluble in water as a sodium salt. It was discovered in the vitreous humor of bovine eye in 1934.

The HA is part of the connective tissue (which is a major component of the extracellular matrix) and the synovial fluid. It is widely distributed in the human body, being the skin and the cartilage tissues rich in hyaluronic acid, where it plays an important role in the healing processes of wounds and skin injuries [3 - 5].

Synoviocytes are the ones responsible for the synthesis and secretion of HA in the synovial fluid. Between the properties described for HA we can find increasing viscoelasticity, and anti-inflammatory, anabolic, analgesic and chondroprotector effects.

- ***Physical Properties***: Hyaluronic acid has viscoelastic properties, which allows the synovial fluid to absorb the impact during movement, whilst it lubricates the joint at rest or in slow movements. However, direct evaluation of kinetics of HA is difficult [5].
- ***Anti-inflammatory Effect***: It has an effect on the function of phagocytes, adhesion and stimulation of mitosis. Its administration leads to a decrease of

inflammatory mediators such as Interleukin 1β (IL-1β) and matrix metalloproteinases (MMPs) [6, 7].

- ***Analgesic Effect***: An analgesic effect, by inhibiting nociceptors trough substance P, has been observed [3, 8].
- ***HA Production***: The application of HA also seems to stimulate the endogenous production of HA by synoviocytes [9, 10]. In OA, a reduction in the concentration and density of HA occurs due to a molecule of smaller size that, causes an alteration in the elastic properties and a decrease, in the synovial fluid, hampering cartilage nutrition.

It is for this reason that a theoretical intra-articular administration would contribute to the restoration of the properties of the synovial fluid, and protect the arthritic joint from further deterioration. In the long term, the reestablishment of joint mobility due to pain relief is thought to trigger a sequence of events, which restores the trans-synovial flow, and subsequently the metabolic and rheological homeostasis of the joint.

There are different commercial compounds such as Hyalgan®, Synvisc®, Durolane®, Euflexxa®. A variety of products have been developed depending on the viscosity and frequency of injections needed [1]. Multiple injections are required, 3 to 5 spaced in 1 to 2 weeks. Although there are new compounds with high-molecular weight HA in a single injection.

The adverse effects (AEs) described in the literature can be classified into local and systemic, and according to literature the rate ranges between 2 and 10% [10, 11]. The most common AEs are local ones, being these erythema, swelling and pain that doesn´t exceed more than two days. The greater problem described at this level is the post injection reactive arthritis, typical of the high molecular weight of HA, and characterized by pain, swelling and flushing which appears in the 1.5-7.2% of patients. This reactive arthritis improves with rest, cold and administration of acetaminophen in the first 48-72 hours. In some cases, patients have leukocytosis in the joint fluid, similar to a septic arthritis, although the cultures are sterile. A 1% of cases of septic arthritis have been described. The main systemic adverse effects are hypertension episodes (4%), fatigue (1%), phlebitis and arrhythmias [12].

CHAPTER 5

Use of Human Amnion/Chorion Allografts in the Treatment of Osteoarthritis

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Abstract: Currently, there is no cure for osteoarthritis (OA). Preliminary treatments focus on symptomatic relief. Initially, patients receive cortisone shots, followed by viscosupplementation in a few weeks. Platelet rich plasma injections are also an option. Surgical options include debridement of joints, osteotomy, arthroscopy, or fusion of the bones. Laboratory studies using rats support the use of amniotic membrane (AM) and chorion membrane (CM) in the regeneration and repair of soft tissues. The potential for CM and AM to moderate osteoarthritis has not been explored in length as yet; however, indirect evidence suggests that they may have advantageous effects on cartilages.

Keywords: Amnion, Arthritis, Chorion, DHACM, Growth factors, Knee, Mesenchymal cells, Placenta, regenerative, Osteoarthritis.

INTRODUCTION

For practitioners treating orthopedic diseases, osteoarthritis (OA) is a frequently encountered pathology. OA is a degenerative joint disease in which the articular cartilage deteriorates, resulting in bone-on-bone contact [1], and it is considered the most common disease of the joints that is associated with high costs [2]. OA

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develops through mineralization of the extracellular matrix (ECM), surface erosion, depletion of proteoglycans (PG), lesion formation, and hypertrophic differentiation of chondrocytes [3]. The loss of articular surface causes joint stiffness and swelling, and as the disease progresses, further sequelae can occur, including bone spur formation around the joint [1]. Ligaments and tendons supporting the joint may also become stiff or weakened secondary to inflammation [1].

Like many disease processes, OA has a pattern of presentation and risk factors. OA has no gender predilection in patients younger than 55 years of age, but is more common in women patients over the age of 55 [1]. There tends to be a familial link, and there is increased prevalence in people who perform repetitive weight-bearing activities [1]. Fractures or trauma to the joint earlier in life can predispose an individual to OA later [1]. Medical conditions that have been associated with OA include hemophilia, which results in bleeding in the joints, decreased or disrupted blood supply to the joints, leading to avascular necrosis, and auto-immune disorders [1].

Symptoms of OA typically begin to manifest during middle age. Almost everyone experiences some degree of symptomatology by age 70 [2]. The most common presenting symptom is pain, especially when the patient is in weight-bearing positions. Patients can sometimes have an audible or palpable grinding and crepitus during specific movement [4]. Stiffness in the morning and after prolonged sedentary activity is common and typically lasts for 30 minutes [4]. This decrease in the range of motion improves upon continued movement; however, over time, there is permanent loss in the degrees of motion. Clinically, the joint can present as swollen and tender, with limited and sometimes severe pain in the range of motion due to bone spurs, pain, or inflammation. A plain radiograph reveals the characteristic “loss of joint space” along with bone wearing or spur formation along the joint line [4].

There is currently no cure for OA [5]. Articular cartilage heals poorly due to its limited capacity for self-repair [6]. Preliminary treatments for OA focus on symptomatic relief. This includes lifestyle changes, such as avoiding repetitive motions, exercising, weight loss, use of assistive devices, and pain management with non-steroidal anti-inflammatory drugs (NSAIDs), pain cream, heat or cold [5]. Physical therapy has the capability to improve range of motion and strengthen supporting joint musculature, but the results vary. Off-loading braces can help by allowing redirection of force transmitted through the joint, decreasing the overall load placed on the joint. However, the off-loading braces can be associated with increased joint damage, pain, and stiffness. Clinical trials have also tested a variety of disease modifying OA drugs (DMOADs), none of which have shown a definitive therapeutic benefit as yet [3]. To find a list of DMOADs currently under clinical trials and their results thus far, the reader is directed to go through the FDA website.

If the conservative methods listed in the previous paragraph fail, injections or surgery are options. Initially, patients receive a series of cortisone shots, followed by viscosupplementation [2]. Platelet rich plasma (PRP) injections are also an option. PRP injections are created by centrifuging the patient's blood and injecting it into the joint space to promote growth factors, cytokines, and adhesive proteins [7]. PRP injections provide additional growth factors, such as transforming growth factor beta (TGF-B1), platelet derived growth factor (PDGF), insulin-like growth factor (IGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and hepatocyte growth factor (HGF) [7]. In addition, PRP injections also contain the cytokine tissue inhibitor of metalloproteinase-4 (TIMP-4), along with the adhesive proteins fibronectin, fibrinogen, vitronectin, thrombospondin-1, and laminin [7]. PRP injections and their therapeutic benefits are discussed in greater detail in a subsequent chapter. Currently accepted surgical options include debridement of the joints *via* arthroscopic surgery, osteotomy to relieve stress on the bone, arthroscopy, or fusion of the bones [1].

In recent years, several studies using rat models support the use of amniotic membranes and chorion in the regeneration and repair of soft tissues. These findings have led to an interest in their use in OA. The potential for chorion and amnion to moderate osteoarthritis has not been explored in length as yet; however, indirect evidence suggests that they may have advantageous effects on cartilage [3]. In this regard, we will discuss two modalities and their therapeutic potential in the treatment of OA: the use of human amniotic membrane cells (HAMCs) and

CHAPTER 6

Role of Cartilage Regeneration in the Management of Early Knee Arthritis: Current Concepts

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Abstract: In this chapter, we discuss review cartilage restoration surgery in the setting of early knee osteoarthritis (OA). We introduce an algorithmic approach to determining treatment and discuss procedures including microfracture, autologous matrix-induced chondrogenesis (AMIC®), osteochondral autograft transfer (OATS), osteochondral allografting (OCA), autologous chondrocyte implantation (ACI)/matrix-assisted chondrocyte implantation (MACI), and stem cell therapy. These techniques have particular advantages and disadvantages. The authors share their approach and outline the protocol for postoperative rehabilitation.

Keywords: ACI, AMIC, Cartilage, MACI, Microfracture, OATS, OCA, Osteoarthritis, Rehabilitation, Stem cell therapy.

INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease characterized by the breakdown and ultimate loss of articular cartilage [1, 2]. It is extremely common, with an estimated prevalence of 27 million in the United States [3]. The knee is commonly involved, and symptoms of knee osteoarthritis include pain and swelling and often lead to functional loss and disability [4]. One of the pathways to OA includes focal cartilage breakdown or defect [5]. Focal defects have been found in 7% of patients under the age of 40 at the time of arthroscopy and 9% of patients under

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the age of 50 [6]. Often these cartilage defects are associated with other pathology, including meniscus tears and knee instability [6].

The initial management of early knee OA includes weight loss, activity modification, physical therapy, bracing, oral analgesics, and intra-articular injections (corticosteroid or hyaluronic acid). These treatments are designed to decrease symptoms and delay total knee arthroplasty (TKA) until a point is reached at which the benefit of such a procedure outweighs the risk [4, 7].

In recent years, much attention has been paid to joint-preserving techniques. If one could reverse or slow early arthritic cartilage loss, tremendous benefit could be provided to many people living with early OA. The purpose of this chapter is to review cartilage restoration surgery in the setting of early knee OA.

An algorithmic approach will be presented followed by a brief discussion about the following cartilage restoration procedures: microfracture, autologous matrix-induced chondrogenesis (AMIC®), osteochondral autograft transfer (OATS), osteochondral allografting (OCA), autologous chondrocyte implantation (ACI)/matrix-assisted chondrocyte implantation (MACI), and stem cell therapy. Techniques will be described along with advantages and disadvantages of each. The authors approach will be outlined along with their postoperative rehabilitation protocol.

ALGORITHM

In many ways, the approach to focal early osteoarthritic cartilage defects is similar to the algorithmic approach to traumatic cartilage defects (Fig. **1**) [8]. This algorithm is contingent on both patient-specific and lesion-specific factors in deciding between palliative, reparative, and restorative approaches [8 - 12]. Patient age, expectations, and activity level significantly influence treatment decisions. Patient sex and body mass index (BMI) are other factors that may influence outcomes [12].

Younger patients are likely to have better results after cartilage restoration surgery than older patients, especially after microfracture [13, 14]. Defect size, defect location, involvement of the subchondral bone, and presence of an intact peripheral rim *versus* diffuse changes are lesion-specific factors that the surgeon needs to assess before offering cartilage surgery to any patient.

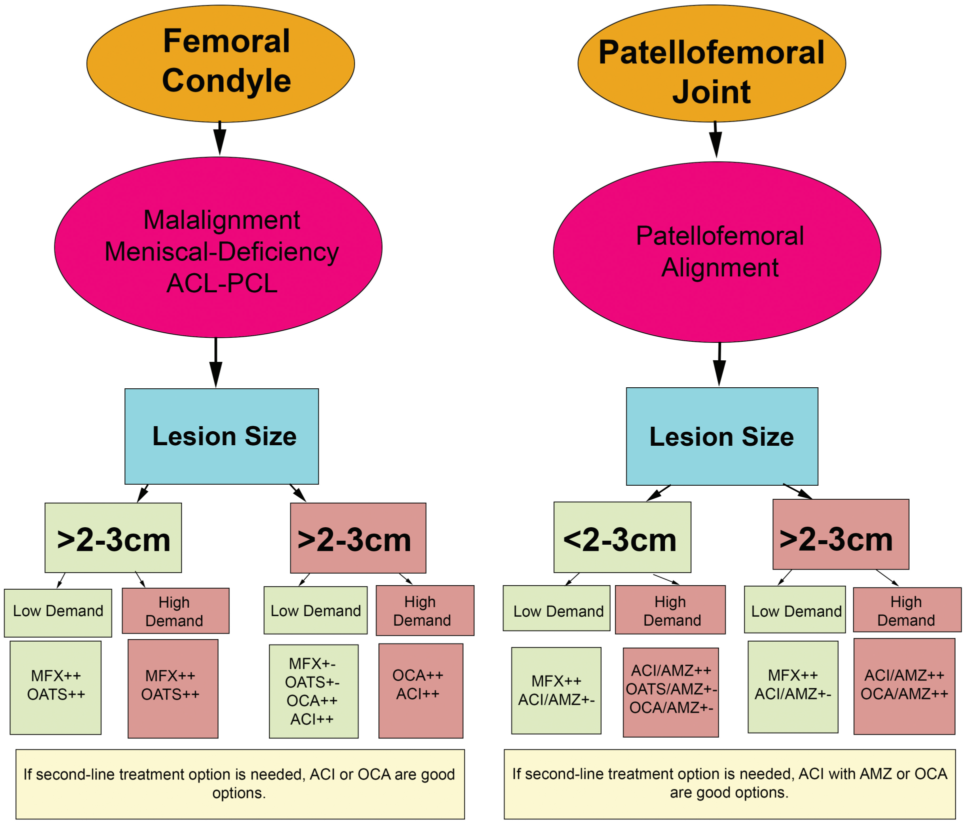

Fig. (1). Treatment algorithm for focal chondral lesions. Before treatment, it is important to assess the presence of correctable lesions. Surgical treatment should be considered for trochlear and patellar lesions only after use of rehabilitation programs has failed. The treatment decision is guided by the size and location of the defect, the patient's demands, and whether it is first- or second-line treatment. ACL = anterior cruciate ligament, PCL = posterior cruciate ligament, MFX = microfracture, OATS = osteochondral autograft transplantation, ACI = autologous chondrocyte implantation, OCA = osteochondral allograft, AMZ = anteromedialization, ++ = best treatment option, and +− = possible option depending on patient's characteristics. Reprinted with permission from Cole BJ, Pascual-Garrido C, Grumet RC. Surgical management of articular cartilage defects in the knee. J Bone Joint Surg Am. 2009 Jul;91(7):1778-90.

Isolated factors, such as patient age, should be considered but should not arbitrarily influence treatment decisions. For example, one could argue that a

CHAPTER 7

Opening Wedge Osteotomies of the Proximal Tibia and Distal Femur

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Abstract: The use of osteotomy is a method to restore knee alignment and is based on the transfer of weight-bearing forces from the area affected by arthrosis to a healthy region of the knee. This force redistribution is the distinctive aspect of osteotomy when compared to other treatment methods. In the last decades, since the introduction and success of knee arthroplasty, the predominance of osteotomy has gradually declined. Nowadays, the actual necessity of osteotomy, beside as a prophylactic operation, is still debated. However, osteotomy remains a valuable technique, in agreement with precise patient indications.

Keywords: Biomechanics, Lateral opening wedge, Medial opening wedge, Osteotomy, Osteotomy contraindications, Patient selection, Postoperative axis, Postoperative rehabilitation, Preoperative axis, Radiographic evaluation, Surgical procedure.

INTRODUCTION

Knee osteotomy is a surgical procedure that may be recommended when arthritis damage is observed in confined to one area of the knee joint. The procedure consists of removing or adding a wedge of bone to the proximal tibia or lower femur to help shift your body weight off the damaged portion of your knee joint

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(Fig. **1**). Knee osteotomy is performed on people who may be considered too young for a total knee replacement.

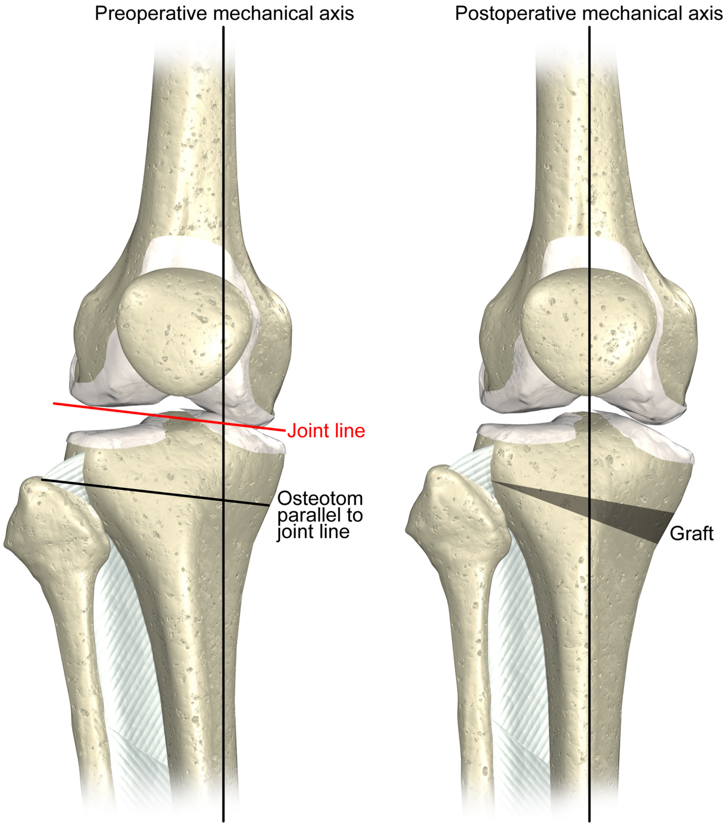

Fig. (1). Preoperative mechanical axis and postoperative mechanical axis (Medial opening wedge proximal tibial osteotomy).

Because prosthetic knees may wear out over time, an osteotomy procedure can enable younger, active osteoarthritis patients to continue using the healthy portion of their knee. The procedure can delay the need for a total knee replacement for up to ten years. In the last decades, since the introduction and success of knee arthroplasty, the predominance of osteotomy has gradually declined. Nowadays, the actual necessity of osteotomy, beside as a prophylactic operation, is still debated. Osteotomy is an efficient surgical technique if used with precise patient indications. Osteotomy can present many complications and adequate patient selection is mandatory to minimize major complications.

BIOMECHANICAL CONSIDERATION

During normal walking, a TKR is subjected to different joint loading conditions due to a number of highly demanding activities. *Load stress concentration, due to load transmission between the tibial and the femoral components, may have critical effects during daily living of the knee.* A simplification of these waveforms, derived from fluoroscopic analyses is showed in Fig. (**2**).

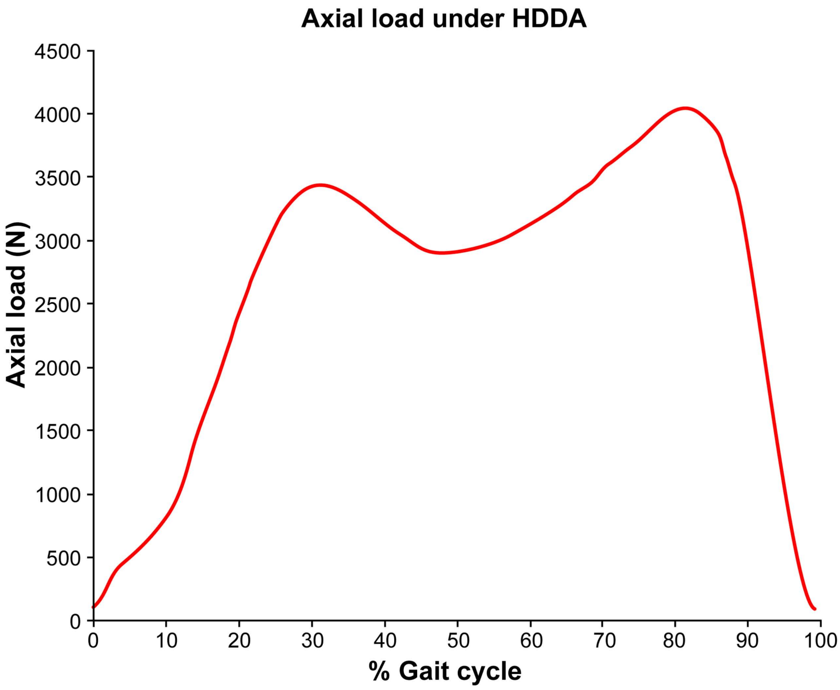

Fig. (2). A simplification of the axial load derived from fluoroscopic analyses.

The first peak is caused by the large quadriceps tension that is necessary to arrest the descent of the body mass, when the weight transfers from the leg that is pushing off from the ground, to the leg that is accepting the load shortly after the heel strikes the ground. This force curve includes a second peak, when the knee and hip are extended, the heel is raised from the floor and the forefoot is pushing off, propelling the body forwards [1]. Osteoarthrosis commonly arises when biological resistance is not able to bear mechanical stressing and excessive pressure on articular surface [2]. This loss of force balance causes, as a start, a

CHAPTER 8

Total Knee Replacement in Arthritis - Current Concepts

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Abstract: Total knee replacement is one of the most successful and cost-effective interventions in the modern medicine for the treatment of pain caused by advanced arthritis of the knee. Great advances have been made in the last five decades in the mechanical properties and the design of the knee implants, surgical techniques and prevention of complications. Both cruciate-retaining and sacrificing designs are widely used with the proponents of both the designs. More constrained designs are used in complex primary and in revision cases. Pain affecting the activities of daily living in an elderly person suffering from severe osteoarthritis is the commonest indication for a primary total knee arthroplasty followed by rheumatoid arthritis. Current or recent infection is an absolute contraindication for a knee replacement. Most commonly the procedure is performed through a midline longitudinal incision and a medial parapatellar arthrotomy. Recent advances include computer aided navigation (has shown to improve the component positioning), gender specific knee (better choice of component sizes) and patient specific instrumentation (to improve the accuracy of bone resection). Long term results and cost effectiveness of these techniques remain unproven. Infection (1-3%) is the most common and serious complication followed by thromboembolism, instability, and neurovascular injury.

Keywords: Knee implants, Osteoarthritis, Primary knee replacement, Revision knee arthroplasty, Rheumatoid arthritis, Surgical treatment of arthritis, Total knee arthroplasty, Total knee designs, Total knee replacement.

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INTRODUCTION

Total knee arthroplasty is one of the most successful and cost-effective interventions for the treatment of severe arthritis (Fig. **1**) of the knee [1]. Number of procedures performed each year have been increased tremendously in the last decade and it has been projected to increase further in the coming years [2, 3]. Many studies have documented over 95% of survival of these components, over 15 years of follow-up [4 - 6].

Fig. (1). Severe osteoarthritis of the knee.

COMPONENT DESIGN AND HISTORICAL PERSPECTIVE

Interposition of metallic components in the knee to relieve pain began with the work of Campbell (distal femoral metallic mould) [7], Macintosh (tibia mould) [8], and McKeever (tibial tray with a keel) [9]. This was followed by the development of hinged designs like Walldius hinge [10] and Guepar hinge [11]. Total condylar prosthesis designed by Insall and others in 1973 ushered the modern era of total knee arthroplasty [12]. This design improved many previous prostheses in terms of stability and survivorship. In this design both the cruciate ligaments were sacrificed. Stability was attained by the congruity of the articular surfaces.

Antero-posterior translation of the components were resisted by the anterior and posterior lips of the tibial component and the median eminence. Double dish design of the tibial polyethylene component provided stability in extension and coronal plane stability in flexion. Femoral component was made from cobalt chrome alloy whereas all poly tibial component was later changed to metal back. Patellar polyethylene dome had single peg for fixation. To prevent the posterior dislocation reported in the total condylar design, the Insall-Burstein posterior cruciate-substituting or posterior-stabilized design was developed in 1978 by adding a central cam mechanism to the articular surface geometry of the total condylar prosthesis [13].

Another milestone was the development of kinematic knee prosthesis which was evolved from duo patellar prosthesis where PCL retention was possible [14]. Originally medial and lateral tibial components were separate, but later on these components were joined to make a single tibial component. This design was widely used in 1980s. Patellar complications were significantly high in 1980*s* and 1990s [15]. Most of the current designs are derivatives of the Insall-Burstein and kinematic designs. Newer designs incorporate greater areas of patello-femoral contact through a larger range of motion and asymmetrical anterior flanges designed to resist patellar subluxation.

COMPONENT DESIGN AND CHOICE OF IMPLANTS

Choice of components of a modern total knee arthroplasty depends on the available bone stock, integrity of the cruciate ligaments and collateral ligaments. Increasing degree of constraint is incorporated in the various designs to compensate for the deficiencies in these structures.

Cruciate Retaining Knee (CR)

Cruciate retaining knee designs incorporate the least amount of constraint among the various designs of the total knee components (Fig. **2**). This design allows retaining the posterior cruciate ligament. Theoretical advantages include, better roll back and more natural gait especially while climbing the stairs, bone preservation and less strain on the metal-bone interface [16, 17]. However these claims are difficult to establish in the clinical studies. Reported disadvantages

CHAPTER 9

Role of Cartilage Surgery and Hip Arthroscopy in the Management of Early Hip Arthritis: Current Concepts

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Abstract: The main aim of cartilage surgery and hip arthroscopy in the management of early hip arthritis is to avoid conversion to total hip arthroplasty, and the earlier the treatment, the greater is the possibility to achieve this purpose. Several techniques have been proposed, such as microfracture, simple debridement, and autologous chondrocyte implantation-matrix assisted autologous chondrocyte implantation (ACI-MACI) for arthroscopic approach and open ACI-MACI and mosaicplasty for open surgery. Arthroscopic debridement associated with microfracture, depending on the patient's condition, represents the best choice for the treatment of early stages osteoarthritis (OA) of the hip joint, especially where an associated chondral defect has to be fixed. The cause of OA must be promptly individuated and the cartilage surgery must always be associated (except for degenerative OA) with procedures aimed to fix any other structural defect in order to avoid further degeneration and to improve the outcome of the surgery.

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Keywords: Articular cartilage repair, Autologous chondrocyte implantation, Cartilage surgery, Debridement, Hip arthroscopy, Hip chondral lesion, Hip osteoarthritis, Microfracture, Mosaicplasty, Open hip surgery, Osteochondral allograft transplantation.

CHONDRAL DISEASE OF THE HIP JOINT, LESIONS AND CLASSIFICATIONS

The pelvis, and the hip region in particular, are some of the most relevant weight-bearing surfaces of the body, and this is one of the reasons for progressive overload of the hip cartilage in adults as well as in younger subjects involved in athletics, jumping sports, or other high demanding physical activities [1]. The overload of the joint is a common feature of the disease for both elderly and young people, but while the former are more likely to be affected by a degenerative disease, the latter usually have an underlying mechanical cause that provides pathological shearing of the cartilage or altered articular structures that leads to instability, femoral-acetabular impingement (either cam or pincer impingement), and focal cartilage overload. The main causes of hip pathology in the young adult are developmental dysplasia, Perthes disease [1], collagen deficiency syndromes (Marfan's disease, ochronosis) and coxa valga, while trauma, labral tears, autoimmune disorders, osteonecrosis and Paget's disease are more commonly diagnosed in the elderly [1]. A specific kind of chondral injury which may lead to further development of arthritis is the so called "lateral impact injury" [2] (lateral trauma on the greater trochanter), which results in chondral defects of the labrum and/or of the femoral head. The site of the first cartilage insult is termed as "Watershed zone" [3] and if this site is near the labrochondral junction, it is more likely that the surrounding cartilage develop*s* arthritis because of destabilization. The cause of osteoarthritis (OA) or of the cartilage defect must be assessed clearly and addressed before selecting the patient for surgery, in order to treat the defect in its totality and not aiming to relieve the symptoms only. Tönnis classification is utilized to assess the OA degree in plain radiographs, while surgically, the Outerbridge classification is commonly used to define the grade of hip chondral disease in direct arthroscopic view. Grade I has been described as softening and swelling of the cartilage, Grades II and III involve proper lesions and fragmentation of the tissue, and Grade IV refers to subchondral bone exposure. The following tables (Tables **1** and **2**) summarize these classifications for the hip joint.

Table 1. The Tönnis classification.

Grade	Description
0	No osteoarthritis.
1	Increased sclerosis, slight narrowing of the joint space, no or slight loss of head sphericity.
2	Small cysts, moderate narrowing of the joint space, moderate loss of head sphericity.
3	Large cysts, severe narrowing or obliteration of the joint space, severe deformity of the head.

Table 2. The Outerbridge classification.

<table>
<tr><th>Grade</th><th>Size</th><th>Description</th></tr>
<tr><td>I</td><td></td><td>Softening/swelling</td></tr>
<tr><td>II</td><td>≤1.3 cm (1/2 inch)</td><td rowspan="2">Fragmentation/fissuring</td></tr>
<tr><td>III</td><td>>1.3 cm (1/2 inch)</td></tr>
<tr><td>IV</td><td></td><td>Erosion/subchondral bone exposure</td></tr>
</table>

Talking about early OA, one should take into consideration Grades 1-2 of the Tönnis classification or I-II of the Outerbridge classification. The main aim in arthroscopic or open treatment of early hip chondral defects is to avoid the conversion to total hip arthroplasty (THA), and the earlier the surgery, the greater is the possibility of success in this regard. Before arthroscopic evaluation, the first view in imaging (mainly radiography and MRI) using Tönnis classification may be a potential predictor of success of the surgery, since it has been reported that the narrowing extent (<2mm) strongly predicts the conversion to THA. Moreover, the early detection of cam or pincer impingement can lead to a prompt treatment of these defects, through debridement of the spurs, in order to stop further progression of OA.

MORPHOLOGICAL FINDINGS IN EARLY ARTHRITIS

Early arthritis usually affects the surface cartilage of the femoral head and the acetabular labrum; sometimes the acetabular fossa can also be involved. Technically speaking, a labral tear is not a proper form of arthritis, although it

CHAPTER 10

Total Hip Arthroplasty-evolution and Current Concepts

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Abstract: Total hip arthroplasty (THA) has been designated as the Operation of the century. The past 3-4 decades have seen tremendous improvement in the patient outcomes, products and technology that has enabled all these changes to improve the quality of life of our patients with problems of the hip joint. We have reviewed the surgical approaches to the hip joint, the bearing surfaces, implant selection and their problems and complications in this chapter. We have also stated our approach and philosophy to have good outcome of THA.

Keywords: Approaches to the hip, Bearing surfaces, Cemented arthroplasty, Deep vein thrombosis, Dislocation of the hip, Total Hip Arthroplasty, Un-cemented arthroplasty, Wear.

INTRODUCTION

Total hip arthroplasty has a rich history of innovation and some have rightly called it the "Operation of the century". The earliest total hip replacement goes back to 1891 where Professor Themistocles Gluck presented the use of ivory to replace femoral head for post tubercular arthritis. Along the way there were attempts by Smith-Peterson with his "mold arthroplasty" using glass in 1925 and then went onto Stainless steel as a material of choice in his later generation prosthesis. Meanwhile, the true revolution in joint replacement is attributed to Sir John Charnley, who worked at the Manchester Royal Infirmary and developed the

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principle of "Low Friction Arthroplasty" in the early 1960's and thus heralded the revolution in joint replacement surgery.

Surgical Approaches to Total Hip Arthroplasty (THA)

There are many surgical approaches which have been described for performing THA. The approach is primarily determined by surgical training, perceived advantage and disadvantage of each approach and surgeon familiarity with each approach. Broadly, surgical approaches in THA can be divided as posterior, lateral and anterior approaches. In posterior approach the abductor mechanism of the hip is not violated and posterior capsule is divided and arthroplasty performed. The primary criticism of this approach is the higher incidence of dislocation in comparison to other approaches. Lateral or antero-lateral approach in some way or other violates the abductor mechanism and thus has the disadvantage of potentially disturbing the main motor of the hip joint and could lead to long term issues if there is no healing of the abductor mechanism. Direct anterior approach is a true inter-nervous approach with minimal disruption to the hip musculature and thus leading to a better early recovery than other approaches. Having said that a well performed THA by any approach will generally result in a good clinical outcome; the idea should be to tailor the approach to a given clinical situation.

Posterior Approach

This is the most commonly used approach for performing THA. The advantages of this approach is, it is the most commonly used and taught approach. The basic premise of this approach is that the Gluteus Maximus is split and the hip joint approached just posterior to the Gluteus medius tendon (Fig. **1**). The other advantage is that there is no disruption of in the abductor mechanism of the hip joint while the disadvantage is a higher dislocation rate in comparison to the lateral, anterolateral or the anterior approach.

The lateral approach to total hip arthroplasty has numerous modifications which go by eponymous names as described by its authors. But, it suffices to mention that all these approaches in some form or another involve damage to the abductor mechanism of the hip joint. The most widely used approach is the Hardinge approach, where the Gluteus medius and the Vastus lateralis are taken in a single lazy J incision and an anterior dislocation of the hip performed. This approach can be performed either with the patient supine or in the lateral position. The disadvantage of this approach is that if dissection extends 5 cm proximal to the tip of the trochanter it could end up damaging the Superior gluteal nerve and leading to a limp clinically.

Fig. (1). The approach is just posterior to the gluteus medius tendon.

Direct anterior approach to THA *has off late taken* the fancy of arthroplasty surgeons. This approach has been described long time ago, where the patient is positioned supine and approached by an inter-nervous plane involving the femoral and Superior gluteal nerve. The plane is developed between the TFL and the Sartorius superficially and Gluteus medius and Rectus femoris in the deeper plane (Fig. **2**). The advantage of this approach is early mobilization, earlier restoration of gait kinematics and lesser dislocation rates. The disadvantages of this approach is *the* difficulty *to* access femoral canal, which *needs* special equipment like offset broaches, reamers and some surgeons use a specialized table for this approach.

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The book is a well-conceived, lucidly written, concise and comprehensive review of osteoarthritis of the hip and knee to provide the pertinent evidence based information to the readers. It covers the pathological basis, role of nutritional supplements, physical therapy to prevent and treat osteoarthritis as well as medical treatment, strategies to induce cartilage regeneration and treatment of advanced arthritis. I can vouch for the fact that this book fills the vacuum in the current available text books to provide a holistic view on osteoarthritis. I congratulate the editor and the authors for their work and wish them success.

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