14 Exercise and Osteoarthritis: The Effect of Running with Aging in the Masters-Level Athlete

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Introduction

Participation in long-distance running events has increased across athletes of all ages, sex, and activity levels in recent years. Per the Annual US Marathon Report, a 140 % increase in US Marathon finishers has been observed (224,000 vs. 541,000) with an additional 40 % increase over the last 10 years alone (386,000 vs. 541,000) [1]. Per the same report, 47 % of all finishers were 40 years and older (47 %), which includes all classes of runners, including recreational runners as well as masters athletes. Per the World Association of Masters Athletes, an organization designated by the International Association of Athletics Federations (IAAF), a masters athlete is defined as man or woman of not less than 35 years of age that participates in a wide array of track and field and longer-distance aerobic sports [2]. As the definition of masters athletics infers a level of expertise and veteran status, these runners often demonstrate a high level of fitness with numerous years (and miles) of running and exercise experience. This increase at both the masters and recreational levels is widely supported by physicians of all specialties, as well as multiple federal health organizations, given the association between physical activity and a decreased lifetime risk for developing obesity, hypertension, type 2 diabetes mellitus, and thromboembolic stroke among others [3, 4]. More specifically participating in high-impact sports positively influences bone density scores and overall bone health, decreasing the risk for osteoporosis and fracture [5]. Despite these known health benefits, a persistent dogma and entrenched belief exist in a link between runners and chronic musculoskeletal injuries with the eventual "worn-out knees."

Recent epidemiologic data states that approximately 46 million people in the United States have symptomatic arthritis [6], with recent figures suggesting knee osteoarthritis (OA) affecting 250 million people worldwide [7]. The main studies demonstrate that from 1990 to 2010, OA has been shown to be the fastest increasing health condition, with knee pain limiting activity and impairing quality of life. While the health benefits for aging masters athletes, and all recreational runners, are well documented, there is little evidence to document the relationship between high-mileage runners and the development or worsening of knee OA. Studies have demonstrated knee OA as the most prevalent musculoskeletal disease in the masters athlete and has been well documented as a common complication of sports injury [8]. This chapter will serve to discuss the relationship between masters running and OA in three dimensions. This chapter will highlight:

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1. The currently accepted mechanisms for the development and progression of OA in masters runners and likewise all aging athletes, with presentation of current literature review for associations between running and disease prevalence
2. A proper evaluation and treatment paradigm for an aging runner with OA-associated knee pain and other running maladies
3. The current dogma and recommendations regarding runner activity, cross-training principles, and adequate nutrition associated with prolonged running health

Pathophysiology of Disease, At-Risk Populations, and the Modifiable Lifestyle Factors

In order to discuss the potential effects of long-distance running and high-impact mechanical loading of the articular cartilage in an osteoarthritic knee, the anatomy, mechanisms, and pathophysiology of OA must be addressed. From a mechanical standpoint, the knee joint is a diarthrodial, mobile hinge joint between the distal aspect of the femur, proximal tibia, and patella. This articulation permits flexion and extension as well as rotation to a lesser degree, all of which play a role in various athletic movements. The static and dynamic stabilizers of the joint allow for high amounts of motion throughout the kinetic chain of movement while providing the needed stability during explosive maneuvers associated with running, jumping, and rapid change of direction. These stabilizers include the ligaments (both intracapsular and extracapsular), menisci, muscle tendons that cross the joint, and the joint capsule and retinaculum itself. When in appropriate balance, these stabilizers allow for a relatively even distribution of contact forces throughout the joint surfaces of the femur, tibia, and patella and allow for smooth gliding of the hyaline cartilage-covered articular surfaces during movement. Comprised of chondrocytes, type 2 collagen fibers, negatively charged proteoglycans, and water, hyaline cartilage provides a surface that is resilient to wear, compressible, and sufficiently strong and stiff to tolerate high biomechanical loads and shear stresses during motion at the joint. This all serves to protect the subchondral bone from impact, while also facilitating smooth and energy efficient motion during movement. However, injury to these static and dynamic stabilizers and load-sharing structures can lead to rapid rates of injury and increased predisposition to arthritis. Injury, inflammation, and the degradation of cartilage with resultant pain, effusion, and loss of motion are the hallmark of OA [9].

From a clinical standpoint, the development of OA is broken into two main classifications: primary or secondary OA. Primary OA is initiated and propagated by an imbalance between synthesis and degradation of the articular surface matrix, driven by a complex milieu of pro-inflammatory cytokines [10]. Conversely, a mechanical disruption or direct insult to the joint via trauma can damage the extracellular matrix, causing cartilage fissures and defects that lead to secondary OA [11–13]. Despite this dichotomy, it is generally accepted that OA is a combination of genetic susceptibility and excessive mechanical stress [14–16]. Likewise, the majority of OA observed in aging athletes is a combination of high levels of mechanical stress with an underlying predisposition. As stated by Neogi et al., this predisposition may be genetic, age related, nutritional, or the presence of poor mechanical stability caused by joint malalignment and weak kinetic chain [17]. Aging has been demonstrated as the primary risk factor for OA [18], with common dogma that increased mechanical stresses (via high-impact exercise such as long-distance running) would accelerate this process over time and lead to painful, debilitated joint. This is certainly the case in cohorts of subjects who have sustained a known, traumatic injury to the articular cartilage [19–22]. While it has been shown that moderate, consistent mechanical loading of joints is necessary for maintenance of healthy articular cartilage [23], repetitive abnormal loading of joints is associated with injury and rapid decline of the articular surface [24]. This degradation appears even more rapid in unhealthy, obese individuals due to a combination of mechanical and inflammatory processes, with obesity acting as a major modifiable lifestyle factor in the development and treatment of knee arthritis.

Obesity is a common medical comorbidity in all patient populations. According to a recent study presented in JAMA, 36 % of all American adults are "obese," while 69 % are "overweight" by current BMI standards [25]. As previously discussed, the development and clinical morbidity seen with OA is a combination of mechanical forces and systemic susceptibility, with recent research highlighting obesity as a major modifiable factor. Biomechanical studies have documented that force loads across the knee joint reach levels approximately 4 times the body weight during walking [26] and that obese individuals experience higher vertical ground reaction forces than normal weight individuals [27]. Likewise, studies have also documented that obese individuals have a four- to tenfold higher risk of developing OA than normal weight counterparts [26]. Additional to excessive mechanical force, a component of systemic inflammation induced by the large reserves of adipose tissue is observed in obese individuals [26, 28]. These effects are confirmed by the induction of OA in non-weight-bearing joints, where cartilage destruction is propagated by inflammation rather than mechanical force [29]. Therefore in an event to reduce mechanical stress, as well as the systemic effects of obesity, targeted weight loss and exercise are a mandatory recommendation by clinicians. Weight loss alone has been shown to curtail symptoms of existing knee OA in obese patients [30]. In addition to the health benefits associated with running and mild-moderate cardiovascular exercise, an overall anti-inflammatory and anti-catabolic systemic response has been documented with exercise to aid against joint destruction. A recent review of the literature by Gleeson et al. discusses three possible mechanisms for the anti-inflammatory effect of exercise, each outline in specific review [31]. These include (1) reduction in visceral fat mass, which reduces inflammatory cytokine signaling, (2) increased production of anti-inflammatory cytokines from active skeletal muscle, and (3) decreased expression of toll-like receptors (TLRs) on monocytes and macrophages, exhibiting an overall downregulation of the body's innate immune activity [32–34]. Overall, though mechanisms continue to be elucidated, multiple review and meta-analyses confirm that exercise reduces pain and improves function and that aerobic exercise (compared to strengthening) is superior for long-term functional improvement [35–38].

With all of these findings, persistent theories exist that long-distance, endurance running causes acute, repetitive microtrauma to the cartilage extracellular matrix, and this, combined with normal aging and loss of cartilage resiliency, accelerates the joint toward arthritis. Advanced imaging techniques, when used in the acute setting following rigorous training or marathon distance events, have demonstrated abnormal marrow signals as well as cartilage abnormalities prior to running marathon distance [39], but these lesions were not significantly altered on repeat imaging after completing the marathon. Even in asymptomatic running knees, studies have demonstrated a large amount of knee lesions, especially in runners with higher training levels, suggesting repetitive trauma and the stigmata associated with early arthritic injury [39, 40]. However, often these abnormal findings are alterations in bone marrow edema (BME) signal, with some intrasubstance meniscal lesions, that fluctuate during the season and most of which are asymptomatic in professional distance runners. The authors of this recent study concluded that this fluctuation of BME during the season, not necessarily related to development of clinical complaint, suggests an active remodeling process that does not require acute intervention without further surveillance and monitoring, though future study is certainly warranted [41]. Acute injury to the ligaments, menisci, or kinetic chain musculature has been shown in biomechanical studies to increase the forces on specific regions of the joint surface, accelerating wear and progression to arthritis [42–44]. In this population, timely operative management (discussed later) is important in restoring congruency and effective motion of the articular surface if return to a prior level of activity is the goal. This notion of timely diagnosis and management is further confirmed by risk assessment studies, which document findings that a major risk factor for a running-related injury is injury in the past 12 months [45, 46].

Despite the aforementioned evidence, longitudinal clinical studies have failed to document an increased prevalence of OA in runners [47, 48] nor a significant association between running and OA [49]. On the contrary, aging runners appear to have less pain, better function, and lower rate of death than their non-running, elderly counterparts. A 13-year progressive study following overall health and disability in members of a running club and controls showed a 3.3 times higher rate of death in the control population, with runners boasting decreased disability over that time period [50]. Newer studies searching for mechanisms for the avoidance of OA in runners are examining biomechanical factors, such as the amount of contact pressure divided by strides, such that a decreased stride length or increased frequency of stride reduces the total biomechanical force across the joint [51, 52], though this requires further investigation and will be discussed later in discussion. Due to this breadth of clinical evidence, there is more importance on the musculoskeletal examination and diagnosis than ever before. A new wave of masters-aged, active patients will be presenting with a host of lower extremity orthopedic complaints, and the clinical implications of the expansive research are clear. There are no current associations between running and the development of arthritis, aerobic activity in the presence of existing arthritis is beneficial for pain relief and function, and an articular injury requires immediate medical intervention as continued running will lead to rapid development of post-traumatic arthritis. Therefore a clinician should continue to encourage running activity for its well-known health benefits but must be vigilant in the setting of acute injury and timely intervention.

Evaluation of Masters Athlete with Lower Extremity/Knee Pain Associated with Running

The effective treatment of a masters endurance athlete starts with timely and thorough evaluation. An accurate diagnosis allows for early, focused treatment protocols and provides the athlete the best chance at returning to sport in a timely fashion with preserved pre-injury function. In order to properly assess symptoms about the knee joint, a complete history and physical examination must be performed with the presentation of any new masters athlete with lower extremity symptoms. This should include discussion regarding history of the spine, hip, knee or foot, and ankle pain or past injuries, as all may present with referral pain to the knee or serve as a primary mechanism for deficient knee biomechanics. Inconsistencies observed with perceived mechanism of injury, constellation of symptoms, and response to previous treatment should direct clinicians to alternative diagnoses and work-up for this patient perceived pain about the knee.

Evaluation of the masters runner with lower extremity pain must begin with a thorough patient history. It is also critical for the physician to garner an accurate assessment of the present (and past) activity level of the presenting individual. Whether the patient is a masters-aged athlete attempting to start running or an experienced masters athlete with training goals has large implications on their injury risk, according to recent studies. Videbaek et al. demonstrated in a recent literature review that novice runners face a significantly greater risk of injury per 1000 h (frequency/1000 h) of running, with an average of 17.8 injuries (95 % CI 16.7–19.1) compared to 7.7 (95 % CI 6.9–8.7) for more experienced peers. Even more significant was that of a wide range of reported values from a minimum of 2.5 per 1000 h in long-distance track and field athletes to a maximum of 33.0 per 1000 h in a study of novice runners [53]. This reiterates that all populations can experience a running-related injury, and a focused clinical acumen must be applied to each presenting patient.

Specific information regarding onset of symptoms, accompanying symptoms, time since onset, alleviating or aggravating factors, and any history of traumatic mechanism are critical in directing patient evaluation and eventual treatment. One of the most important pieces of information obtained from the history is localization of pain. This can establish laterality and often locate a specific structure that is injured and acting as an active pain trigger. Failure to localize pain to a specific location may be suggestive of a global inflammatory process, neuropathic condition, or a multifactorial injury to knee joint and surrounding components (the muscle, tendon, ligament, etc.). Subjective patient complaints such as clicking, popping, and mechanical instability (i.e., “knee buckles and gives out”) are suggestive of ligamentous or meniscal pathology, with resulting ineffective static knee stabilization. However, this clicking and popping can be confounded by crepitus. Crepitus, defined as the subjective cracks or pops around and within a synovial joint, present in two basic varieties: (1) painless condition best explained as a synovial fluid phase transformation or (2) painful, common condition that accompanies the osteoarthritic changes of a joint and represents bone on bone collision and grinding. Specific information regarding patient age, history of injury, and/or location of discomfort can help to elucidate between true mechanical instability, healthy crepitus, and osteoarthritic crepitus.

Radiography and advanced imaging modalities are also an effective way to screen for underlying degenerative changes or acute injuries to the articular surface. Plain film study is critical in establishing a reproducible objective comparison of joint health over time and across various symptom presentations. Standing, weight-bearing, anteroposterior radiographs should be a first step in the work-up of any knee pain in a masters runner. In addition, a 45° flexion weight-bearing posteroanterior radiograph may be more sensitive and superior in demonstrating early and subtle joint space narrowing [54]. The presence of osteophytes, flattening of the femoral condyles, sharpening of the tibial spines, chondrocalcinosis, and narrowing of the notch are several radiographic findings suggestive of an arthritic joint, which can be documented over time in the aging masters athlete. In addition, radiographic view of all the joint surfaces from the hip to foot, or the “long cassette view,” can provide valuable information regarding the mechanical and anatomic axes of the lower extremities. Though unilateral articular joint space narrowing, and likewise varus or valgus joint alignment, has been seen as a manifestation of OA and joint pain, this is seen most commonly in chronic meniscal pathology or after a partial/total menisectomy with or without accompanying ligamentous injury [42–44]. Therefore, specific questioning regarding past operative intervention, including obtaining specific operative reports, is critical to ascertain prior to establishing a plan of treatment. Despite these studies regarding post-traumatic narrowing, multiple studies have shown that baseline alignment patterns, either varus or valgus, in the setting of normal, healthy knees do not predispose runners to injury or arthritic changes [55, 56]. However, these imaging studies and an overall assessment of alignment are important and may provide context for lateral or medial-sided knee pain in the masters athlete, especially if a past surgical history exists. Advanced imaging modalities, such as MRI and CT scan, are often indicated for the work-up of soft tissue (cartilage, ligament, meniscus, etc.) injuries about the joint when minimal radiographic findings of OA are noted. Advanced imaging may also be obtained early for preoperative planning, if an operative condition exists. For the purpose of this text, advanced imaging should be reserved for situations where there are mechanical symptoms about the joint and gross instability or after nonoperative regimens have failed and an impending operative plan is developing.

The physical examination, often the last part of the patient visit, will direct the clinician’s decision to pursue specific treatment or advanced imaging modalities. Close side-to-side comparisons should be made between limbs, to evaluate for subtle muscle weakness, effusion, muscle atrophy, or alignment issues as result of chronic injury or past operative intervention. In the event of long-standing unilateral medial or lateral knee joint OA, genu varum (or genu valgum, respectively) may be readily noticeable on exam of lower extremity alignment. This patient may be a candidate for mechanical, off-loading brace technology, the indications for which are collected only on close examination with radiographic support. As mentioned, specific attention should be paid to the specific location of pain over the knee. Focused examination, and knowledge of anatomic landmarks, can differentiate insertional hamstring pain from true medial joint line tenderness. This will prevent an unnecessary and costly imaging work-up and can start the athlete back on the path to recovery and return to sport in a more timely fashion. However, confirmation of joint line tenderness on examination is an important aspect of the exam and important in the early diagnosis of articular surface or meniscal pathology, both of which may need operative intervention and an immediate cessation of activity per treatment recommendations. An arthritic knee will typically present with warmth and swelling on observation and palpation of the joint. Examination of strength and motion will demonstrate weakness, often secondary to pain and/or atrophy of the quadriceps, and restricted range of motion secondary to incomplete flexion and extension in normal activity. However, this loss of motion may be less in active, persevering individuals. In some patients with intermediate to advance OA, significant crepitus and "locking" may be noticeable on testing of knee motion. Though this can mimic a meniscus injury, initial work-up radiographs that demonstrate significant arthritis will preclude the need for MRI and isolate OA as a causative factor for the mechanical symptoms. Though degenerative meniscus tears can accompany OA, the presence of joint space narrowing on 45-degree flexion weight-bearing X-rays removes an indication for advanced MRI imaging [13]. In the running athlete, a thorough examination of patellofemoral mechanics during motion can elucidate a major generator of anterior knee pain while active. Evaluation includes tilt, glide, and palpation for tenderness and can be correlated with patella-specific radiographic tests (i.e., "sunrise" or 45-degree axial Merchant view). With patella testing, comparisons of movement, crepitus, and tenderness to palpation must be associated with contralateral leg testing and can be used in the diagnosis of subtle osteochondral lesions or injury of the patella. Often, these patients will complain of anterior knee pain while going up or down stairs, while the extensor mechanism applies the largest amount of compression of the patella into the femoral notch. Unifying patient history and physical exam is the most important part of the orthopedic examination of the aging runner in the clinic.

Treatment of Masters Athlete: Nonoperative vs. Operative Management

Once thorough evaluation is complete, the clinician must produce a treatment plan that addresses both the functional level and the expectations of the patient. Often, this will present with an initial decision algorithm regarding the need for advanced imaging modalities and the likelihood of operative versus nonoperative treatment. As mentioned, an aging runner that presents with effusion and mechanical symptoms that have minimal findings of OA on plain radiograph would be a good candidate for an MRI. An older athlete, with documented radiographic changes suggestive of progressing OA and history of significant pain with activity despite lifestyle modifications and therapeutics, may not need advanced imaging, rather an early discussion regarding the role of arthroplasty in the active patient. Despite the slow progression and predictable, stepwise progression of OA, aging athletes need personalized care decisions from their healthcare providers in order to preserve activity and level of function into their older years. Recent reviews of diagnosis and treatment recommendations in the aging athlete population document that optimal outcomes are achieved when activity is preserved, with personalized training protocols and medical management of the aging athlete [18, 57]. Therefore in this chapter section, the algorithmic approach to the clinical management of early and advanced OA will be discussed while remembering that all treatment decisions are a balance between level of function, pain, and risk of progressive disease in this population.

In the aging population with knee OA, the paradigm for the management has been symptom management, with the goal of delaying surgery (i.e., arthroplasty) for as long as the patient can tolerate. This approach consists of exercise modification, targeted muscle training, bracing and orthoses, pharmaceuticals, intra-articular corticosteroids, and viscosupplementation. Some newer paradigms include the use of biologically active compounds, such as platelet-rich plasma (PRP), bone marrow aspirate concentrate (BMAC), and mesenchymal stem cells (MSCs), in an effort to stimulate the growth and regeneration of new articular cartilage. Though MSCs and BMAC have shown some anti-inflammatory effect and ability to aid in disease progression in animal models, translation to clinical use is lacking [58]. The current state of biologics advancement will be discussed later in this section.

Initial treatment paradigms for an aging athlete with knee pain, and findings suggestive of early arthritis without anatomic pathology, typically start with physical therapy and a brief stint of rest/activity modification. This should be paired with anti-inflammatory therapy with non-steroidal anti-inflammatory medications (NSAIDs), for a multi-targeted approach of care. At this current time, large review studies have revealed no evidence for a specific NSAID as superior in the management of early OA and therefore recommend that NSAID selection be guided by relative safety, patient preference, and cost [59]. For therapy, multiple large RCTs have demonstrated that muscle-strengthening exercises in addition to low weight-bearing exercise is effective in relieving pain and also restoring kinetic chain balance. Patient cooperation and persistence with scheduled therapy are related to this success, as studies have demonstrated that beneficial effects of therapy can be lost as early as 6 months [36]. In patients that desire to continue running and participate in athletic competitions despite early symptoms of arthritis, knee bracing and orthoses are a common treatment with the main goal of reducing symptoms, not necessarily eliminating symptoms, and therefore improving athletic function. Though there are a large variety of neoprene knee sleeves available for stabilization and relief of minor symptoms, review articles have shown these to be no superior to placebo for the alleviation of pain and symptoms [60]. However, some patients will present to clinic having already tried over-the-counter sleeves and braces, and if these are providing comfort, there is no harm in continuation of this therapy. As mentioned in the evaluation section, the best patient population most suited for bracing therapy is the symptomatic, passively correctable varus or valgus disease of less than 10 degrees [61]. The mechanical goal of these braces is the shift the axis of force transfer through an unaffected region of joint, decreasing symptoms without restricting activity. With this concept, there is evidence from gait analysis that shoe orthoses, specifically lateral wedge orthoses, have been effective in reducing pain and increasing function in patients with isolated medial compartment knee OA [62]. Despite these findings, there is insufficient data for the endorsement or recommendation by the American Association of Orthopaedic Surgeons (AAOS), and this evaluation is presented within the current guideline for non-arthroplasty management of OA [63]. Therefore, in an attempt to achieve return to sport for a presenting aging athlete, a trial of bracing or orthotics when properly indicated may achieve successful results, but expectations must be shaped accordingly given inconclusive literature-based efficacy.

After attempted physical therapy and bracing with concomitant NSAID therapy, the next line of therapy is intra-articular injection therapy, either with viscosupplementation or corticosteroid. Within a healthy joint, hyaluronate is a main component of synovial fluid and articular cartilage [64]. It provides the lubrication and shock-absorbing capacity of the articular fluid and surface. In the pathologic process of OA, the hyaluronate becomes depolymerized from its native structure and cleared at a faster rate which puts the joint at a biomechanical disadvantage by reducing the viscoelasticity of the synovial fluid

[65–67]. Based on these documented changes in an arthritic joint, exogenous intra-articular hyaluronate is available for supplementation aimed at alleviating the symptoms of knee OA. Several meta-analyses have been performed to assess the efficacy of this treatment, but a combination of variable findings, study heterogeneity, and publication bias has led to inconclusive evidence for clinical use. In addition to highlighting this evidence, most recent conclusions published in the *New England Journal of Medicine* document a range of modest effectiveness to minimal effect when compared to placebo [65]. As mentioned previously, inflammation is a major characteristic of the OA joint, leading to prolonged cytokine and innate immune reaction which is implicated in the progressive destruction of articular cartilage. Likewise, intra-articular corticosteroid was identified as a means to dampen the immune reaction, decrease synovial inflammation, and promote relief of OA symptoms. Recent systematic reviews of the clinical efficacy of corticosteroid (triamcinolone) have shown fast-acting but short-lasting clinically significant improvements in pain and function [68]. Past studies comparing corticosteroid to hyaluronic acid injection have concluded that steroid injection produced a rapid maximum benefit (within 2 weeks), while pain reduction and functional improvement were significantly better at the 3- and 6-month follow-up period [69]. A recent publication has documented the promising clinical effect of an extended-release formulation of triamcinolone, which was found to be superior to current standard over a range of 1–12 weeks [70]. More future study is needed to better quantify the clinical effect of longer-lasting, extended-release formulations of these intra-articular pharmaceuticals. As it stands currently, corticosteroid injections are a valuable clinical tool for rapid, short-lasting clinical relief from symptoms associated with early to advanced OA of the knee. However, long-term symptomatic management is dependent upon other treatment modalities, as the effect of intra-articular is only temporary and has not been shown to stop or slow disease progression.

Outside of the widely used corticosteroid and hyaluronate injections, the use of biologically active intra-articular therapies has gained significant momentum in athletic and recreational populations. However, the clinical use of biologic therapy with platelet-rich plasma (PRP) or mesenchymal stem cells (MSCs) has been plagued by significant study heterogeneity and variable results across studies, making conclusions and clinical advancement difficult. Aside from high cost of therapy, the standardization of therapy across research studies is lacking, with specific information regarding ideal platelet concentration in PRP and ideal dosing schedule, and long-term safety data have not been well characterized [71]. However, recent meta-analyses state that intra-articular PRP shows improvement in patient outcomes at 6 months that are maintained for up to a year. From the studies, these improvements were noted as clinically relevant development for decreased pain and increased function compared to control therapy [72]. There is a need for more prospective studies with multicenter collaboration to advance the role of biologic therapies for articular cartilage injury and early arthritis into the active, aging population. In an attempt to evaluate the main injectable therapies for early OA, the most recent randomized control trial comparing intra-articular PRP injections to viscosupplementation (hyaluronic acid injections) showed that PRP did not provide a superior clinical improvement when compared to hyaluronic acid therapy [73]. In regard to intra-articular MSCs for the treatment of early OA, animal studies have shown significant progress in restoring articular cartilage, with improvement in both histologic and radiographic studies when compared to controls [74]. When compared to surgical interventions, such as autologous chondrocyte implantation (ACI) or microfracture, intra-articular MSCs have shown similar efficacy. However, additional review shows that no human studies have compared intra-articular MSCs to non-MSC techniques in the absence of surgery [75]. Future prospective, multicenter studies comparing PRP, MSCs, and other intra-articular injectable therapies for the symptomatic relief of

OA are needed for biologics to emerge as a viable therapy for relief with quick return to sport and activity.

In the treatment of the aging, masters-level athlete, surgical intervention is often warranted when nonoperative management of symptoms no longer reduces pain or restores function. However, there are instances where a presentation of suspected arthritic knee pain has an acute surgical indication. For example, acute or symptomatic meniscal lesions, osteochondral defects, loose bodies, and ligamentous injuries, appropriately confirmed with MRI testing, are several pathologies that indicate an operative management paradigm. These are the variety of injuries that are most prevalent in athletic, sport-participating populations and have the highest documented rate of progress to post-traumatic arthritis [19, 76]. It is these types of intra-articular injury that disrupt the stability of articulation and the distribution of contact forces, serving to propagate cell death, inflammation, and a cyclic pattern of cartilage destruction. Therefore, it is critical that ligament and meniscal repair surgeries, with the goal of restoring normal anatomic biomechanics, be performed in a prophylactic manner to prevent repetitive trauma and early onset arthritic processes. In the event that meniscal and ligamentous stability is intact in an early or advanced OA knee, other surgical options remain for the preservation of function and activity level. These include arthroscopy, high tibial osteotomy, and arthroplasty. Each of these procedures has specific indications and must first begin with a discussion between athlete and clinician to clarify expectations for postoperative outcome and return to sport. Arthroscopic intervention is a common but controversial technique for an osteoarthritic knee. Studies have shown that approximately 50–75 % of patients have an initial benefit post debridement. However, this same study documents that 15 % of patients experience progression to total knee arthroplasty (TKA) within 1 year of arthroscopic debridement [77]. Other studies that support arthroscopy argue that the degree of disease (mild vs. severe) is an independent predictor of outcome and that there is much clinical benefit to be obtained when patients are properly selected, while others (i.e., end-stage OA or mechanical alignment) are contraindicated from the procedure [78, 79]. However, other recent studies report unfavorably upon arthroscopic debridement of the early osteoarthritic joint, stating that this "clean-out procedure" has not been shown to have any beneficial effect or prevention of disease progression and that it provides no additional benefit to an otherwise optimized patient [80, 81]. Though not shown to be beneficial in slowing the progression of disease, the aforementioned studies that suggest benefit in mild, early arthritis knees will continue to keep the option of arthroscopic knee surgery available for competitive yet aging athletes as they strive to preserve their competitive function. However, the risks of surgical intervention and future need for arthroplasty must be discussed with patients prior to this treatment. Along the same lines in preserving athletic function, high tibial osteotomy (HTO) is a popular operative procedure for the patient with isolated, unicompartmental disease. As the surgical counterpart of mechanical braces, the goal of these procedures is to shift the mechanical axis of the knee to an area that is not affected by degenerative changes (i.e., remove the arthritic area from the zone of weight bearing). The significant benefit of this procedure is that while the weight-bearing zone is ideally located to a healthy area of articular cartilage, there is no modification of activity level needed once healed from the initial operation. It is most commonly implicated in treatment of unicompartment varus or valgus OA and is emerging as a technique used in conjunction with biologic cartilage restoration procedures [61]. It will not be effective in global arthritic degeneration and therefore must be reserved for the ideal active patient. Multiple studies suggest positive results, with one such study stating good to excellent function in 77 % at 17 years [82], while another reports survivorship of 98 % and 90 % at 10- and 15-year follow-up, respectively, for HTO [83]. A recent review summarizes the risk factors that contribute to the deterioration of an osteotomy procedure, citing time (i.e., continued wear and tear), increasing age, and obesity as factors shown by the literature to decrease the long-term effectiveness of this procedure [61]. However, if an osteotomy procedure can provide 10–15 years of high functional ability (i.e., continued ability to run) prior to mandatory arthroplasty procedure, among the running population, it would be difficult not to call this a great success. After osteotomy, unicondylar knee arthroplasty (UKA) and total knee arthroplasty (TKA) are typically a last resort option for runners despite their effectiveness in relieving pain and symptoms of OA, mainly due to the propensity for wearing out of polyethylene spaces and loosening of components in high-demand individuals. However, due to advances in design and increased durability of polyethylene, documented survivorship rates continue to increase. A study performed by Pennington et al. focused on UKA in the younger (<60) high-demand active patients and demonstrated an HSS score of excellent in 93 % of patients and good in 7 % [84]. Multiple studies in younger patients document high survival rates and low revision rates; however, the activity level is not well documented [85, 86]. Although it has been consistently shown that TKA is highly regarded and superior for the relief of symptoms, studies without documentation of activity level provide little benefit for the active, running population who may require TKA. Therefore, as the amount of arthroplasty performed in the future decades increases, more focused studies are needed to elucidate how aggressive runners can be in attempting return to sport after arthroplasty procedure. In conclusion to these operative options, it is clear that clinicians must present the risks of significant activity loss in a population of athletes focused upon return to sport. Surgical options for OA should be reserved until all nonoperative treatment paradigms have been attempted. Though runners can continue high levels of activity with osteotomy, and in most cases a UKA, important discussions regarding the expectations of return to preoperative function levels are needed to achieve satisfactory patient-reported outcomes.

Conclusion (Summary of Evaluation and Treatment, "Barefoot" Running, Role of Diet, and Cross-Training for Healthy Running)

The development of OA of the knee is a multifactorial issue. Clinicians must be able to understand and discuss a wide array of approaches to manage this disease in an active, aging population. Genetic susceptibility, aging, and past injury to the articular surface are well-defined risk factors, which accompany biomechanical principles in our ability to predict the development of joint pathology. Focused evaluation of all aging runners that present with knee complaints and any range of documented OA is needed to provide optimal treatment recommendations. Modifiable lifestyle factors, including diet, level of activity, and weight, have been shown to be effective in the modification of arthritis symptoms and the maintenance of function. The use of neoprene sleeves, off-loader braces, and supportive footwear has been shown in certain studies to be equal to or better than placebo in the relief of symptoms. The strongest conclusion that can be drawn is that there are specific circumstances (i.e., isolated medial unicompartmental OA) where unloader braces will be of best utility and other times where a brace may facilitate confidence if only to start activity and movement of the afflicted joint. The use of biologic compounds has enormous potential for the preservation of joint physiology and slowing of OA progression, but more study is needed before this potential can be realized and applied in clinical setting. Viscosupplementation and corticosteroid injections have their role in management to provide periods of symptom-free activity, but are not effective in slowing or preventing disease progression. Surgical intervention can be effective in a selected population of patients but is accompanied by serious risk of decreased function and inability to return to previous level of activity. Specifically, more data will need to be collected in order to recommend arthroplasty procedures to runners who continue to strive for high-demand activity as wear-out rates and aseptic loosening have been directly linked to activity levels. There is no supported increase risk in the development of OA in the knees of healthy aging runners, but clinicians should not recommend running as a primary mode of exercise in severe, advance knee osteoarthritis. For this patient population, alternative lower-impact modalities (biking, swimming, low contact weight training) should be recommended.

A recent Cochrane review by Yeung et al. [60] evaluated a broad set of interventions, including specific exercises, modification of training schedules, orthotics, and specific footwear and socks intended to prevent or reduce the incidence of running-related overuse injuries. Of the reviewed studies, 19/25 involved service personnel, while only three focused on general population athletes. Though this likely does not address the masters athlete or recreational runner, the findings concluded that the clinical evidence for most interventions is weak, with few prospective, low-bias studies [60]. Based on previous discussion within this chapter, this type of review is not surprising as it is difficult to evaluate the subjective effectiveness in such a high-demand, heterogeneous population of athletes. This lack of evidence will not stop athletes from pursuing their craft, and therefore clinicians must be accepting of a multi-tooled approach to this multifactorial disease. The emergence of "medically based running analysis" and designated sports performance centers are focused on tailoring training plans and injury prevention techniques to the individual runner [87]. In order to work in concert with these emerging concepts, clinicians must familiarize themselves with the newest trends in running. Given the high percentage of all-aged individuals that use running as aerobic exercise and the high proportion who suffer running-related injury, the running community is frequented by trends and new technologies that promise faster recovery and pain-free running. An example of this would be the minimalist, or barefoot, running movement that has spread rapidly across the running and fitness community. With less structure, less arch support, and lower heel drop (distance in height between heel and forefoot) profiles and softer, more forgiving fabrics, running shoes have sought to create a "barefoot" sensation that forces the foot, ankle, and knee to absorb shock in a natural, biomechanically favorable way. Though shoe companies are quick to state that progression to these shoes must be scheduled and gradual, so as to not overload the knee, midfoot, and heel-cord structures, there are minimal longitudinal studies to document the effect of this barefoot phenomenon. A recent study, seeking to evaluate the biomechanical and runner adaptations to the barefoot or minimalist running shoe, documented some of the first literature regarding the topic. This study by Perkins et al. found moderate evidence to state that barefoot apparel results in overall less maximum vertical ground reaction forces, less extension moment and power absorption at the knee, less ground contact time, shorter stride length, and increased stride frequency among other variables [88]. Coupled with findings from other recent research in *The American Journal of Sports Medicine*, shorter stride length and increased stride frequency may decrease or at least not increase propensity for running injuries. However, the same study stated that one stride length does not appear to be clearly superior and that different foot strike styles may predispose runners to injury [89]. Not surprisingly, it can be concluded that the need for future well-designed RCTs testing the biomechanical effect of shoes, stride length, and running cadence is important to delineate recommendations and find a regimen to suit runners of all sizes and ability levels.

Regardless of the age or experience level of the masters-aged runners that present, time must be spent in the clinical visit discussing the importance of balanced diet and role of strength and resistance exercise in running at optimal health. Full dietary recommendations for athletic performance are available through multiple government resources, such as the US Anti-Doping Agency (www.usada.org/resources/nutrition). Optimal dietary and hydration methods, in addition to balanced training and recovery, are global principles that can be reinforced by clinicians for all athletes. Even though running requires a combination of flexibility and strength, runners can achieve improved form and function by employing a full-body fitness regimen. The following recommendations are derived directly from the

US Department of HHS and should be a rubric for a clinical exercise protocol. Adults should participate in a balance of strength and training exercises in addition to >150 min/week of moderate-intensity or >75 min/week of vigorous-intensity aerobic activity. Strength training should be incorporated approximately 2–4 day/week, for approximately 30 min per session. In order to allow for adequate recovery and to avoid injury, 48 h of rest are recommended in between strength sessions. This type of routine can achieve an increase of approximately 2–3 times in strength in a period of only 4 months and can help improve the dynamics of the kinetic chain, making a faster and more efficient runner. In the event of an injury, prior to presentation in a medical clinic, first aid principles that include rest, ice, and anti-inflammatories should always be reiterated by clinicians to their practicing athletes. And lastly, athletes must have a sense of appropriate level of exertion based on their current level of fitness. Overtraining and inability to perform a mixture of strength and cardio exercises increase the risk of an injury, which will only set an athlete back in terms of performing at optimum function.

Overall, prolonged healthy running in the aging athlete is dependent upon a balance of injury-free running, intermittent cross-training, and the practice of healthy dietary principles. Practice of these concepts will increase the ability of an aging runner to participate at a high level of function. In order to promote injury-free running, clinicians must employ prompt diagnosis and accurate management aimed at relieving symptoms and preserving articular function. Prompt referral to a surgical specialist is needed when an intra-articular injury exists, as these are the most likely cause of post-traumatic OA and a premature decline in running function. Clinicians should encourage continued participation in running for the known health benefits and to preserve function in the presence of early OA of the knee. Health professionals should always address the goal of staying active and healthy and may explore other recommended activity options in patients with severe OA for whom high-impact running is no longer recommended.

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