Acta Scientific Orthopaedics (ISSN: 2581-8635)

Volume 6 Issue 9 September 2023

Research Article

Muscle and Knee Osteoarthritis: "What's New" in 2023

Ray Marks*

Osteoarthritis Research Center, Canada

***Corresponding Author:** Ray Marks, Osteoarthritis Research Center, Canada.

Email: Dr.RayMarks@osteoarthritisresearchcenter.com, rm226@columbia.edu

DOI: 10.31080/ASOR.2023.06.0826

Received: August 11, 2023

Published: August 25, 2023

Abstract

Osteoarthritis, the most common joint disease experienced by many older adults and one that is increasing as societies age remains largely incurable and highly disabling. As such, and in light of the failure of most palliative pharmacologic strategies to date to reverse or mitigate this painful condition, it appears all avenues of potential progress added to those already being explored may yet prove fruitful. Based on emerging and quite promising data outlining a possible link between aspects of osteoarthritis joint damage and muscle deficits, this mini-review elected to examine the most current data in regard to discern whether: 1) Muscle dysfunction continues to be an important potentially modifiable health determinant whose presence might influence the onset and progression of osteoarthritis through direct as well as indirect pathways, and 2) any evidence pointing to its possible detection, categorization, and remediation as being desirable in this regard if indicated. Based on the bulk of available data housed in PUBMED, GOOGLE SCHOLAR, Science Direct, and PubMed Central as of August 15, 2023, it is concluded that a causative, mediating or moderating role for muscle dysfunction in the realm of osteoarthritis cannot be ignored as per data related to its most common form, knee osteoarthritis. Future efforts to advance this line of inquiry that proceed from a multi component muscle specific and whole joint perspective of osteoarthritis disability may prove of immense personal and societal impact and benefit.

Keywords: Aging; Muscle; Knee Osteoarthritis; Pathology; Prevention; Treatment

Abbreviations

MRI: Magnetic Resonance Imaging

Introduction

As documented for more than a century, osteoarthritis, a widespread commonly progressively disabling disease of one or more freely moving joints such as the knee continues to be identified as one of the most serious health care challenges facing many older adults wherever they reside. Possibly emerging in response to alterations in the ability of the human organism to adapt locally and as a biological system in the face of aging, injury, and changes in functional demand these factors and others may converge to cause and perpetuate the resultant erosion and degradation of one or more joints, inducing a chronic incurable painful condition termed osteoarthritis. Moreover, definitive osteoarthritis is very hard to treat as it often only induces pain in its more advanced stages, and is often treated as though only the tissue lining the joint is implicated. Yet, current data show a need to understand osteoarthritis from a whole joint perspective including the cartilage, bone, muscle and joint ligaments that may frequently interact and if untreated or poorly treated may possibly foster the spread of the disease from one affected joint to involve others. Associated with parallel losses of independence, income, physical function, and a reduced life quality, older adults with intractable pain, as well as one or more chronic health conditions [1] may indeed suffer unduly, especially if the disease weakens the knee muscles that foster joint protection and these remain unappreciated, poorly evaluated, or not even evaluated. Alternately, careful attention to the possible presence of muscle dysfunction in cases with confirmed stage specific and comparably localized knee osteoarthritis, and improved treatment applications that embrace a carefully construed follow up of the whole joint and its biomechanical and biochemical features may prove restorative and remedial as well as reparative and clinically effective to a high degree.

In the belief that this idea, now proposed for more than 30 years [2] is a valid one, even though very little progress in preventing this aforementioned cycle of downward spiraling of osteoarthritis induced health events has emerged over time, careful attention

to muscle dysfunction effects on the knee joint do appear worthy of further detailed examination in our view. The knowledge that muscle is extremely mutable and can undergo well defined changes in response to various forms of stress and biophysical forces, as well as governing the distribution of joint load all speak to the potential value of delineating and clarifying the precise role of muscle in the pathogenesis of osteoarthritis.

As such, while far from exhaustive, this mini review elected to examine current evidence that may point to muscle as an important knee osteoarthritis variable worthy of attention in efforts towards mitigating or ameliorating osteoarthritis and/or its severity and rate of progression [3,4], despite the poor adherence to exercise regimes, in favor of joint injections, drugs, and surgery [5].

More specifically, the knee joint, the most common osteoarthritis disease site was specifically studied, and an attempt was made to examine only recent muscle associated data in the context of the pathogenesis of this condition including a possible protective role, given its importance in voluntary muscle contraction, proprioception, and joint stability.

Since osteoarthritis remains the most common form of arthritis and is a disease that affects many older adults highly negatively, this key aim was to build on former work and to offer recommendations for therapeutic purposes. As such, the review specifically examined the degree of support for the idea that the knee muscles and their structure and function are possible factors associated with the biomechanical and biochemical profiles of an older adult diagnosed as having knee osteoarthritis, especially muscle weakness [6].

Predicated on the importance of expanding our understanding of our knowledge of muscle based knee osteoarthritis correlates, it was hoped building on previous work [7], this current mini scoping overview would demonstrate more potential than not exists for uncovering those muscular determinants that may predate or follow knee osteoarthritis and their possible mitigation or remediation. Although not often discussed in the context of efforts to explain the natural history of rapidly progressive knee osteoarthritis development [8] and discounted as playing any salient role by Yoon., *et al*. [9] as far as explaining patella femoral osteoarthritis cartilage damage, we believe as many as four problems not readily explained in knee osteoarthritis discussions, are potentially impacted by preceding or ensuing neuromotor correlates. These include, but are not limited to: 1) the presence or onset of abnormal leg alignment patterns that could be traced to muscle compensatory mechanisms, 2) temporal features of joint responsiveness that alter the ability of bone to absorb impact load, 3) sensory disturbances that may impact joint stability and balance plus movement co-ordination, and 4) deficient joint protective mechanisms and dysfunctional locomotor control, as well as functional capacity due to muscle structural abnormalities, reflex inhibition and inflammation.

Methodology

To obtain up to date information on the general ideas alluded to above, a limited review of currently available documents housed in the PUBMED data base along with GOOGLE SCHOLAR, Science Direct, and PubMed Central published in English largely over the time periods January 1- August 15, 2023 using the key terms *Knee Osteoarthritis, Muscle, Muscle Fatigue, Muscle Force Capacity, Muscle Spindles, and Sarcopenia* was implemented. After scanning the available article listings those that addressed some aspect of the current topic of interest were specifically scrutinized in more depth, and if relevant were selected to be included in this current overview. Those not written in English or those that were not full length reports were excluded. As well, references published before 2023 that revealed tangible support for pursuing this relatively uncharted realm were eligible for inclusion.

Overall, a narrative rather than any systematic approach was adopted in this regard, all forms of muscle dysfunction were deemed acceptable, and salient topical conclusions were highlighted regardless of research approach or whether the osteoarthritis was categorized as being in its early stage or late stage. All forms of muscle assessment were deemed acceptable as well. Readers can refer to an earlier paper for a more in depth report of muscle atrophy as a possibly important osteoarthritis correlate [2]. Ligament injuries at the knee, or post surgical evaluations were not included.

Rationale

Almost 30 years ago, Dieppe [10] a leading osteoarthritis researcher noted osteoarthritis was projected to become one of the most important health care challenges facing future societies. This prediction has been realized for some time, with knee osteoarthritis, the most common and troubling form of this disease remaining associated with varying degrees of knee joint pathology and derangement, including bone and cartilage physiology and structure that continue to cause great suffering among many adults of all ages, especially older adults. While the cause of the condition remains elusive, and no cure exists to counter osteoarthritis at any joint, emergent evidence of a possible important impact in the disease cycle by features of muscle dysfunction such as muscle weakness, and muscle fat mass that are not always addressed or assessed may yet prove insightful and valuable. That is, based on what is known about joint biomechanics and structure, the emergence, perpetuation, and progression of at least some forms of osteoarthritis by one or more muscle impairments appears to have some basis in this regard. This is because muscle impairments may lead to poor

postural stability, gait abnormalities, articular cartilage derangement, sensory disturbances, pain and a possible heightened falls risk as is observed in various knee osteoarthritis cases. Conversely, a further body of evidence shows exercise or interventions designed to improve muscle function at the knee joint often improves function as well as various biochemical attributes of joint cartilage erosion, while reducing pain and disability. However, even though muscle may have a bearing on our ability to mitigate or prevent osteoarthritis of the knee, it is less well documented and discussed in the realm of many current efforts to advance osteoarthritis understandings and especially knee osteoarthritis care, if compared to the multiple reports focusing on articular cartilage.

Since a failure to consider muscle as a possible pathogenic osteoarthritis factor may not only help to explain why this field of endeavor has been poorly understood to date [11] but may prevent the affected adult in multiple adverse ways, even if surgery is indicated, it was felt this topic update was worthy of exploration. It was theorized that an updated understanding of how muscle and joint pathology might be interwoven might prove both insightful and of possible high value in efforts to advancing calls to envisage knee osteoarthritis as a disease of the whole joint, not a singular tissue.

Search Results

General findings

Many works related to knee osteoarthritis currently prevail and that speak to its immense prevalence and public health burden in an aging world. Yet, even though a possible key mediating role for muscle and muscle attributes such as atrophy, weakness, or remodeling in the pathogenic knee osteoarthritis disease cycle has prevailed for some time [12], the association between changes in muscle quantity and quality on the progression of knee dysfunction remain unclear [13]. Yet, one possible insight that could offer hope and a brighter outlook potential is a possible role for excess muscle fat mass of one or more of the knee muscles [13] and calls to examine this issue seem valid in light of the strong osteoarthritis-obesity as well as possible leg malalignment linkages [14].

Unfortunately, despite a plethora of studies that attest to joints such as the knee as being highly problematic from a societal health challenge perspective, very little direct attention is given to any assessment or discussion of the possible impact of associated changes in the surrounding knee muscles that could open the door to an array of treatment alternatives. Many older vulnerable adults or others may thus suffer more unduly than not, when possibly they could be safely treated without recourse to dangerous drugs or costly surgery. Indeed, a systematic review recently conducted showed a high presence of sarcopenia or muscle mass loss among cases with knee osteoarthritis, especially women [15] that might be targeted and improved or prevented from further attrition and possible joint exposure to trauma. In addition, although very poorly researched to date, neuromuscular deficits are evident across different degrees of structural severity among knee osteoarthritis cases including those of muscle strength, voluntary muscle activation, muscle size, balance and force control ability that again are possibly more marked in women with knee joint disease than men [16].

Abnormalities of muscle fiber distribution that may be impacted by or interact with the pathological processes of knee osteoarthritis including possible implications of fiber type grouping that may provide insight into muscle mechanisms that impact knee osteoarthritis remain poorly examined however, despite their possible relevance [11]. For example, in an analysis of seven high-quality and 22 moderate-quality studies including 1146 people with knee osteoarthritis and 1353 age- and sex-matched controls), these focused on quadriceps and hamstring strength deficits and their strength ratios across varying degrees of knee osteoarthritis severity, with less attention to issues of voluntary muscle activation, force control ability, quadriceps cortical or spinal excitability, and muscle size. However, no tissue samples or knee joint innervation attributes, and correlates such as proprioceptive factors [17] were studied or put forth in the analyses. As such, the explored data and research efforts examined, do not truly foster any sense of whether the two distinct muscle fiber types, type I [slow twitch], and type 2 [fast twitch] with different attributes may predict as well as explain functional challenges and knee osteoarthritis progression rates and require targeted, rather than generic treatment directives. Although disputed by Noehren., *et al*. [18] in favor of a more important pathogenic role for muscle extracellular matrix content, a specific loss of one fiber type or another may well place different functional demands on an underlying joint and can possibly induce further pathological changes in muscle fibers whereby their state of atrophy and fibrotic changes if injured, can increase joint vulnerability and eventual derangement magnitude, including a derangement of

- Fiber size where the mean myofiber diameter may be increased or decreased.
- Fiber distribution or predominance
- Fiber architecture and satellite cell activation processes
- Muscle satellite cell density, profibrotic gene expression, and a slow-to-fast fiber type transition that may reduce muscle quality, while impacting bone and cartilage status negatively [18,19].
- Periarticular muscle fat infiltration that can induce excess tibio femoral loading forces concentrations [20].

- Motor deficits associated with decreased neural activation, central nervous system sensitization, decreased quadriceps muscle spindle responsiveness, and increased triceps surae muscle activity [21].

In short, it appears that even though impaired motor function in osteoarthritis while implicating both diverse central as well as peripheral perspectives that control motor activity and reactivity, plus movement and joint protection derangements, a specific and unified focus on muscle and its manifestations is not currently evidenced to any meaningful degree as far as joints such as the knee are concerned. Thus, even though the knee is the most common site of osteoarthritis, rather than helping to elucidate or illustrate if indeed the progressively destructive processes of knee osteoarthritis may involve or implicate one or muscle associated pathways, any tentative relevance for enabling or advancing remediation or mitigation in this respect await more solid verification and further study. In the interim, a need for a salient practice and explanatory model of knee osteoarthritis and how muscle is implicated, if indeed exercise is the generic solution, must await future extensive exploration of all possible multiple muscle associated determinants, not only muscle strength [22-25].

Until then, whether optimal or not, it is likely exercise [in any form] will be advocated for most knee osteoarthritis sufferers even if these are not duly indicated or other non surgical or pharmacologic modalities are more effective [28,29]. The proposed utility of quantitative MRI to assess knee joint attrition extensively in association with muscle that has not been widely reported does appear of high relevance to pursue [30]. In addition, another body of evidence pointing to sarcopenia as a possible correlate of knee osteoarthritis, as well as knee muscle strength and gait patterns [23], grip muscle strength and function [32,33], plus muscle degeneration should be examined [34]. Also warranting attention is the recently observed attribute of quadriceps passive stiffness associated with a higher risk of developing incident knee osteoarthritis at 12 months after assessment [35], as well as its counterpart of passive hip muscle stiffness [36]. An argument in support of hip strength as a knee osteoarthritis determinant has also been put forth and should be duly examined. [37].

Additional observations

While very few studies focus on passive muscle attributes in examining causes and treatments of osteoarthritis, Chen., *et al*. [38] do note though that more and more attention is being paid to the research of muscle mass and knee extensor muscle quality in the context of knee osteoarthritis. In attempting to explore the asymmetric changes of muscle mass, biomechanical property and muscle activation of the knee extensors in patients with knee osteoarthritis, it appeared that muscle asymmetries may prevail that have an impact on functional ability, treatment approaches and rehabilitation efficacy of the disease that could be explored further. Whether any of the observed muscle correlates were of neuropathic or myopathic origin could not be discerned. Wang., *et al*. [39] however conclude gait asymmetry in kinematics and muscle forces do tend to increase the degree of knee osteoarthritis pathology. In addition, one recent report found cases having a knee osteoarthritis diagnosis to demonstrate muscle quality losses as discerned radiographically, while another showed surgery recovery may be impeded if any prevailing muscle impairments are not addressed in a timely targeted manner [20]. In addition, Winkler., *et al*. [20] concluded that perioperative rehabilitation approaches targeting residual muscle quality impairments could help reduce tibiofemoral joint load magnitudes, while improving post surgical knee joint replacement long-term outcomes. On the other hand, Lohnes., *et al*. [40] propose medial and lateral hamstring muscle activation levels may provide utility as a knee osteoarthritis gait biomarker compared to biomechanical outcomes, quadriceps and gastrocnemius activation, when differentiating knee osteoarthritis from asymptomatic cohorts.

Ghazwan., *et al*. [41] note that the presence of a higher than desirable quadriceps and hamstring force generating capacity including any co-contraction of the calf muscles could generate a higher than desirable degree of joint contact forces. Along with any excessive loading this may exacerbate prevailing joint destruction and the adoption of an abnormal gait pattern. It is also possible that poor quadriceps endurance in such cases that induce muscle fatigue can further increase the negative impact of ground reaction forces falling on the knee joint in a dose dependent manner, while increasing possible levels of existing effusion-synovitis [42]. Aging alone may exacerbate the risk of this cycle of adverse events, as may knee strength deficits that impact medial lateral postural stability [42] as well as muscle flexibility [43], endurance capacity, proprioception, balance [44], and the fear of moving and pain [45]. Supporting this idea is the recommendation to possibly unload the diseased joint using an orthotic, while adding muscle vibration approaches to ameliorate abnormal joint biomechanical degeneration impacts [46]. Another idea is to employ laser therapy to advance knee muscle strength gains [47], an approach that does not benefit from concomitant exercise therapy application [48].

Discussion

Despite disagreement over the actual initiating causes of human osteoarthritis, results of several studies advance the theoretical significance of excessive forces applied to a joint by muscle, muscle weakness, fat mass and inhibition. Another body of research supports the fact that muscle can dissipate joint impact and protect a

joint. The primary role of muscles, to move, and control the integrity of the moving joints is therefore of potentially great importance in efforts to understand how degenerative joint changes emerge and how various forms of muscle dysfunction may adversely affect mechanical joint loading and joint biomechanics [41].

However, even if all the data over the past 30 years are aggregated, it is impossible to currently assess whether muscle is a causative or consequential feature of all forms of knee osteoarthritis, or only some, and if so, in what respect. Moreover, even if remediable, what should be done specifically, and in light of the paucity of human studies of early osteoarthritis, and limited explanations for its onset and progression is unclear at best. As those who are concerned with this burgeoning health problem, and desire sound evidence based intervention options, it appears that until more innovative carefully construed insights are tested thoroughly and evaluated, the evidence base for advancing any universal imperative must remain in question. Moreover, whether all knee osteoarthritis patients or those at risk should undertake exercise, must await further study.

At the same time, it is apparent that machine learning strategies designed to hasten knee osteoarthritis diagnoses and prognoses among older adults, and possibly the ability to offer more timely early and targeted recommendations for this disease must await more dedicated global efforts to uncover the precise nature of muscle causes [if any] as well as any muscle consequences in any form of knee osteoarthritis. Attempts to derive predictive models of assessment and practice must also surely await future more careful designed and implemented inclusive and comprehensive research that embraces multiple populations, not only those that predominate in the current data base and derived from the Osteoarthritis Initiative data base, even though insightful [60]. This includes expanding the research towards including healthy disease free individuals, young-middle age adult knee osteoarthritis cases, and bilateral whole joint assessments in unilateral and bilateral knee osteoarthritis cases, especially those in the higher age groups, and muscle tests other than isolated strength measures [60]. The application of advanced MRI, as well as objective functional assessments over fixed periods of time using reliable and sensitive instruments among well defined osteoarthritis subgroups is also highly recommended to overcome multiple current research shortcomings [49].

In the interim, studies under functional conditions such as walking as well as radiographic and biopsy studies suggest that related muscle based investigations of knee osteoarthritis may prove very insightful and helpful to clinicians. As well, interventions that address muscle may not need to only involve exercise [59]. Studies that examine the role of gender in this regard may also help clarify if these observations concerning females are due to sampling concerns, such as oversampling, or over reporting, or actual gender knee osteoarthritis disability differences [56]. The role of intramuscular fat mass and thigh muscle circumference [57], chronic health conditions, efforts to treat the hip not only the knee muscles [50], and nutritional practices that are all promising areas of possible insights should be clarified and carefully delineated as well. Moreover, efforts to include data from those who are homebound, those who have no provider or support systems should be carefully studied as well.

It is also evident that a failure to conduct a detailed differential diagnosis of the condition, plus a sole focus on the knee extensors rather than all the knee muscles [56], plus evaluations that focus predominantly on muscle strength, and omit to examine issues such as muscle fat mass, muscle responsiveness, joint inflammation status, and degree of joint pathology independently and collectively [53-57] may foster suboptimal, spurious, unsafe, or risky treatment recommendations.

Until more data are forthcoming, clinicians may yet help their aging clients even if surgery is indicated by remaining mindful to carefully assess the whole joint of their 'at risk' and definitive knee osteoarthritis clients, including key muscle attributes. This is because a sole focus on the appearance of articular cartilage when compared to the further information obtained when examining parallel muscle attributes may be found to favor efforts to mitigate the disease or even prevent it.

Efforts to study diverse knee osteoarthritis subsets from an early stage of the disease and that draw on best measurement practices and past literature warranting replication may prove highly fruitful in particular. Efforts to uncover possible upstream factors that impact the disease via muscle indirectly, such as diabetic forms of muscle attrition would appear to be highly advantageous as well [51,52]. Even if the data do not yield any meaningful model to emerge, they may still help to support or refute a multitude of current and past data sources that accept that people with knee osteoarthritis will uniformly benefit from various forms of exercise treatment, even if the rationale for this is uncertain at best. In addition, due to a high risk of possible study biases, and low certainty of any available evidence [56], what is needed precisely, and why, is not commonly addressed explicitly. Hence, even if this recommendation is prudent, why one form of treatment is more desirable and not another is hard to discern and is often not articulated in published exercise or muscle based knee osteoarthritis associated studies that may admittedly yield surprisingly comparable results or no results, but are not necessarily powered adequately or readily explained [58].

In sum, even if promising, and based on over two or more decades of discussion and some emergent insightful clinical and animal studies, the clinical and applied significance of muscle in the widely diverse complex osteoarthritis disease cycle and its ramifications must remain in question.

Indeed, due to our inability to identify osteoarthritis in its early or pre arthritic form it remains extremely difficult without some dedicated careful studies to establish whether there is any clear clinical link that may exist in some older populations between muscle and joint attrition, even if this can be shown in animal models to be valid. In addition, no matter what the topic in knee osteoarthritis, many major design flaws and incomplete methodological descriptions, subjective functional assessments, plus unknown measurement properties only provide incomplete estimates at best of those samples that have been studied and met study criteria that often reject older samples and those with multiple health conditions. Yet muscle is often touted as a key intervention target even if surgery is forthcoming and even if no universal agreement supports this approach in the long term, especially if reflex inhibition and inflammation as well as joint instability predominate, and a standard method of measuring possible muscle adaptations relative to bone and knee cartilage architecture remodeling under real world conditions remains to be tested and developed.

Conclusions

Based on the current albeit limited review, and despite flaws in the clinical evidence base, we conclude

- Muscle related correlates in knee osteoarthritis sufferers warrant careful analysis.
- Fostering function and minimizing joint destruction may require efforts to normalize knee muscle force capacity/responsiveness-where indicated but may require a year or more to reap success.
- If muscle rehabilitation is warranted the importance of dedication, adherence, and outcome expectations that are favorable may prove essential to expound upon.
- In addition, to muscle specific exercise approaches, nutrition as well as weight reduction, muscle relaxation and joint unloading may have potential remedial clinical benefits.

Implications

To advance this current line of research and investigative endeavor, pain related gait behavior, posturography or force plate measures, and quantitative MRI muscle and cartilage measures and their individualized assessments, interpretation and thoughtful attention are strongly recommended. As well, efforts to uncover how the sensorimotor system controls joint function and protects joints is strongly indicated as well and using advanced technology to do this may prove exceedingly beneficial.

Moreover, if indicated, exercise needs to be carefully titrated to avoid overuse and fatigue as well as increases in trauma and inflammation, pain and reflex muscle inhibition. Conversely, exercise, while touted as a key generic remedy in multiple papers, may yet do more harm than good if not carefully applied in small steps and in light of the patient's age, goals, ability, health status, health beliefs, and cardiovascular health.

To reduce the disease burden, judicious efforts to evaluate, remediate, prevent, and minimize any observed muscle-based dysfunction wherever this occurs or could occur appears hold great promise.

Acknowledgements

None.

Conflict of Interest

None.

Funding

None.

Bibliography

1. Giorgino Riccardo., *et al*. "Knee osteoarthritis: epidemiology, pathogenesis, and mesenchymal stem cells: what else is new? An update". *International Journal of Molecular Sciences* 24.7 (2023): 6405.

2. Hurley Michael V. "Muscle dysfunction and effective rehabilitation of knee osteoarthritis: what we know and what we need to find out". *Arthritis and Rheumatism* 49.3 (2003): 444-452.

3. Zhang Xini., *et al*. "Relationship between knee muscle strength and fat/muscle mass in elderly women with knee osteoarthritis based on dual-energy x-ray absorptiometry". *International Journal of Environmental Research and Public Health* 17.2 (2020).

4. Øiestad Britt Elin., *et al*. "Knee extensor muscle weakness is a risk factor for the development of knee osteoarthritis: an updated systematic review and meta-analysis including 46 819 men and women". *British Journal of Sports Medicine* 56.6 (2022): 349-355.

5. Srinivasan Vyshnav., *et al*. "Comparison of various modalities in the treatment of early knee osteoarthritis: an unsolved controversy". *Cureus* 15.1 (2023): e33630.

6. Jankaew Amornthep., *et al*. "The effects of low-level laser therapy on muscle strength and functional outcomes in individuals with knee osteoarthritis: a double-blinded randomized controlled trial". *Scientific reports* 13.1 (2023): 165.

7. Marks Ray. "Muscle atrophy and knee osteoarthritis joint status: highlights and their implications [2017-2023]". *Acta Scientific Orthopaedics* 6.5 (2023).

8. Driban Jeffrey B., *et al*. "Risk factors and the natural history of accelerated knee osteoarthritis: a narrative review". *BMC Musculoskeletal Disorders* 21.1 (2020): 332.

9. Yoon Jung-Ro., *et al*. "Quadriceps muscle volume has no effect on patellofemoral cartilage lesions in patients with end-stage knee osteoarthritis". *Knee Surgery and Related Research* 34.1 6 (2022).

10. Dieppe P. "Strategies for the prevention of osteoarthritis". *InternationalJjournal of Tissue Reactions* 15.3 (1993): 93-97.

11. Krishnasamy Priathashini., *et al*. "The role of skeletal muscle in the pathophysiology and management of knee osteoarthritis". *Rheumatology* 57.4S (2018): iv22-iv33.

12. Jarecki Jaromir., *et al*. "Assessment of the impact of physical activity on the musculoskeletal system in early degenerative knee joint lesions in an animal model". *International Journal of Molecular Sciences* 24.4 (2023): 3540.

13. Taniguchi Masashi., *et al*. "A higher intramuscular fat in vastus medialis is associated with functional disabilities and symptoms in early stage of knee osteoarthritis: a case-control study". *Arthritis Research and Therapy* 25.1 (2023) 61.

14. Ma Wenru., *et al*. "Novel ideas for the comprehensive evaluation of varus knee osteoarthritis: radiological measurements of the morphology of the lateral knee joint". *Journal of Orthopaedic Surgery and Research* 18.1 (2023): 196.

15. Pegreffi Francesco., *et al*. "Prevalence of sarcopenia in knee osteoarthritis: a systematic review and meta-analysis". *Journal of Clinical Medicine* 12.4 (2023): 1532.

16. Tayfur Beyza., *et al*. "Neuromuscular joint function in knee osteoarthritis: a systematic review and meta-analysis". *Annals of Physical and Rehabilitation Medicine* 66.2 (2023).

17. Raizah Abdullah., *et al*. "Investigating knee joint proprioception and its impact on limits of stability using dynamic posturography in individuals with bilateral knee osteoarthritis-a cross-sectional study of comparisons and correlations". *Journal of Clinical Medicine* 12.8 (2023): 2764.

18. Noehren B., *et al*. "Alterations in quadriceps muscle cellular and molecular properties in adults with moderate knee osteoarthritis". *Osteoarthritis and Cartilage* 26.10 (2018): 1359-1368.

19. Li Yuanyuan., *et al*. "Gastrocnemius muscle injury is the condition to induce cartilage degeneration of the rabbit tibiofemoral joint: a new perspective". *BioMed Research International* 2022 (2022): 7532434.

20. Winkler Tobias., *et al*. "Periarticular muscle status affects *in vivo* tibio-femoral joint loads after total knee arthroplasty". *Frontiers in Bioengineering and Biotechnology* 11 (2023): 1075357.

21. Mansfield Cody J., *et al*. "The effects of knee osteoarthritis on neural activity during a motor task: a scoping systematic review". *Gait and Posture* 96 (2022): 221-235.

22. Chen Shuai., *et al*. "Osteoarthritis and sarcopenia-related traits: the cross-sectional study from NHANES 2011–2014 and Mendelian randomization study". *Journal of Orthopaedic Surgery and Research* 18.1 (2023): 1-14.

23. Aslan Sefa Gümrük and Hakan Genç. "Sarcopenia in knee osteoarthritis: the association with clinical and sonographic findings, physical function, and nutrition". *Irish Journal of Medical Science* 192.3 (2023): 1231-1239.

24. Dechêne Lola., *et al*. "Characterization of the proteins secreted by equine muscle-derived mesenchymal stem cells exposed to cartilage explants in osteoarthritis model". *Stem Cell Reviews and Reports* 19.2 (2023): 550-567.

25. Christensen Jesse C., *et al*. "Factors associated with trajectories of physical activity over 8 years in knee osteoarthritis". *European Journal of Rheumatology* 10.1 (2023): 1-7.

26. Tzartza Chrysanthi Liliana., *et al*. "Comparative analysis on the effect of sarcopenia in patients with knee osteoarthritis before and after total knee arthroplasty". *Diseases* 11.1 (2023): 36.

27. He Zi-Jun., *et al*. "Pain-related risk factors among radiologic stages of knee osteoarthritis: data from the Osteoarthritis Initiative". *Arthritis Care and Research* 75.6 (2023): 1333-1339.

28. Amiri Pouya., *et al*. "High tibiofemoral contact and muscle forces during gait are associated with radiographic knee OA progression over 3 years". *The Knee* 41 (2023): 245-256.

29. Young James J., *et al*. "Exercise therapy for knee and hip osteoarthritis: is there an ideal prescription?". *Current Treatment Options In Rheumatology* 20 (2023): 1-17.

30. Özüdoğru Anıl and Nihal Gelecek. "Effects of closed and open kinetic chain exercises on pain, muscle strength, function, and quality of life in patients with knee osteoarthritis". *Revista Da Associacao Medica Brasileira (1992)* 69.7 (2023): e20230164.

31. Eck Brendan L., *et al*. "Quantitative MRI for evaluation of musculoskeletal disease: cartilage and muscle composition, joint inflammation, and biomechanics in osteoarthritis". *Investigative Radiology* 58.1 (2023): 60-75.

32. Singla Ravi., *et al*. "The course of knee extensor strength after total knee arthroplasty: a systematic review with meta-analysis and -regression". *Archives of Orthopaedic and Trauma Surgery* 143.8 (2023): 5303-5322.

33. Van Diemen Marcus PJ., *et al*. "Mitochondrial function, grip strength, and activity are related to recovery of mobility after a total knee arthroplasty". *Clinical and Translational Science* 16.2 (2023): 224-235.

34. Taniguchi Masashi., *et al*. "Enhanced echo intensity in vastus medialis is associated with worsening of functional disabilities and symptoms in patients with knee osteoarthritis: a 3 years longitudinal study". *Rheumatology International* 43.5 (2023): 953-960.

35. Li Zongpan., *et al*. "Passive stiffness of the quadriceps predicts the incidence of clinical knee osteoarthritis in twelve months". *European Journal of Physical and Rehabilitation Medicine* 59.1 (2023): 65-74.

36. Preece Stephen J., *et al*. "Individuals with knee osteoarthritis demonstrate increased passive stiffness of the hip flexor muscles". *The Knee* 41 (2023): 302-310.

37. Jolas Elisa., *et al*. "Simulated Increase in monoarticular hip muscle strength reduces the first peak of knee compression forces during walking". *Journal of Biomechanical Engineering* 145.10 (2023).

38. Chen Weijian., *et al*. "Comparison of the asymmetries in muscle mass, biomechanical property and muscle activation asymmetry of quadriceps femoris between patients with unilateral and bilateral knee osteoarthritis". *Frontiers in Physiology* 14 (2023): 1126116.

39. Wang Junqing., *et al*. "Gait asymmetry variation in kinematics, kinetics, and muscle force along with the severity levels of knee osteoarthritis". *Orthopaedic Surgery* 15.5 (2023): 1384-1391.

40. Lohnes Jessica., *et al*. "Do individuals with knee osteoarthritis walk with distinct knee biomechanics and muscle activation characteristics? An investigation of knee osteoarthritis, hip osteoarthritis, and asymptomatic groups". *Gait and Posture* 99 (2023): 14-19.

41. Ghazwan Aseel., *et al*. "Knee osteoarthritis alters peri-articular knee muscle strategies during gait". *PloS One* 17.1 (2022): e0262798.

42. Ucurum Sevtap Gunay., *et al*. "Postural stability and its relation to knee flexor/extensor strength ratio in women with mild to moderate unilateral knee osteoarthritis: a case-control study". *Somatosensory and Motor Research* 5 (2023): 1-8.

43. Nafees Khadija., *et al*. "Dynamic soft tissue mobilization versus proprioceptive neuromuscular facilitation in reducing hamstring muscle tightness in patients with knee osteoarthritis: a randomized control trial". *BMC Musculoskeletal Disorders* 24 (2023): 1447.

44. Choi Wonjae. "Comparison of physical function, proprioception, muscle strength, postural balance, and walking in older women with and without total knee arthroplasty". *Medicine* 102.24 (2023): e33034.

45. Stensdotter Ann-Katrin., *et al*. "Factors associated with self-rated difficulty to descend stairs in persons with knee osteoarthritis". *The Journal of Injury, Function, and Rehabilitation* 15.1 (2023): 9-19.

46. Barati Kourosh., *et al*. "Evaluating the effect of equipping an unloading knee orthosis with local muscle vibrators on clinical parameters, muscular activation level, and medial contact force in patients with medial knee osteoarthritis: a randomized trial". *Prosthetics and Orthotics International* 10 (2023): 1097/PXR.0000000000000243.

47. Jankaew Amornthep., *et al*. "The effects of low-level laser therapy on muscle strength and functional outcomes in individuals with knee osteoarthritis: a double-blinded randomized controlled trial". *Scientific Reports* 13.1 (2023): 165.

48. Malik Shikha., *et al*. "Effect of low-level laser therapy plus exercise therapy on pain, range of motion, muscle strength, and function in knee osteoarthritis - a systematic review and meta-analysis". *Somatosensory and Motor Research* 40.1 (2023): 8-24.

49. Clausen Stine., *et al*. "Do imaging findings modify the effect of non-surgical treatment in patients with knee and hip osteoarthritis? A systematic literature review". *BMJ Open* 13.3 (2023): e065373.

50. Mehwish Bushra., *et al*. "Effect of hip joint mobilisations and strength training on pain, physical function and dynamic balance in patients with Knee Osteoarthritis: a randomized controlled trial". *The Journal of The Pakistan Medical Association* 73.4 (2023): 749-754.

51. Mohajer Bahram., *et al*. "Diabetes-associated thigh muscle degeneration mediates knee osteoarthritis-related outcomes: results from a longitudinal cohort study". *European Radiology* 33.1 (2023): 595-605.

52. Yokoyama Moeka., *et al*. "Exploring the modification factors of exercise therapy on biomechanical load in patients with knee osteoarthritis: a systematic review and meta-analysis". *Clinical Rheumatology* 42.7 (2023): 1737-1752.

53. Spanoudaki Maria., *et al*. "Sarcopenia and sarcopenic obesity and osteoarthritis: a discussion among muscles, fat, bones, and aging". *Life* 13.6 (2023): 1242.

54. Terao Yusuke., *et al*. "The impact of preoperative muscle strength on postoperative walking ability in patients undergoing total knee arthroplasty". *International Journal of Rehabilitation Research* 46.2 (2023): 157-162.

55. Gong Ze., *et al*. "The association between quadriceps strength and synovitis in knee osteoarthritis: an exploratory study from the Osteoarthritis Initiative". *The Journal of Rheumatology* 50.4 (2023): 548-555.

56. Patterson Brooke E., *et al*. "Muscle strength and osteoarthritis of the knee: a systematic review and meta-analysis of longitudinal studies". *Skeletal Radiology* 10 (2022).

57. Mohajer Bahram., *et al*. "Role of thigh muscle changes in knee osteoarthritis outcomes: Osteoarthritis Initiative Data". *Radiology* 305.1 (2022): 169-178.

58. de Zwart Arjan H., *et al*. "High-intensity versus low-intensity resistance training in patients with knee osteoarthritis: a randomized controlled trial". *Clinical Rehabilitation* 36.7 (2022): 952-967.

59. Eymir Musa., *et al*. "Relaxation exercise therapy improves pain, muscle strength, and kinesiophobia following total knee arthroplasty in the short term: a randomized controlled trial". *Knee Surgery, Sports Traumatology, Arthroscopy* 30.8 (2022): 2776-2785.

60. Xu Chunyan., *et al*. "Role of lower limb muscle strength in knee osteoarthritis progression for patients with mild and moderate knee osteoarthritis". *American Journal of Physical Medicine and Rehabilitation* 101.5 (2022): 433-438.

Bibliography