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mechanics

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Review

Osteoarthritis year in review 2021: mechanics

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SUMMARY

Osteoarthritis (OA) has a complex, heterogeneous and only partly understood etiology. There is a definite role of joint cartilage pathomechanics in originating and progressing of the disease. Although it is still not identified precisely enough to design or select targeted treatments, the progress of this year's research demonstrates that this goal became much closer. On multiple scales - tissue, joint and whole body - an increasing number of studies were done, with impressive results. (1) Technology based instrument innovations, especially when combined with machine learning models, have broadened the applicability of biomechanics. (2) Combinations with imaging make biomechanics much more precise & personalized. (3) The combination of Musculoskeletal & Finite Element Models yield valid personalized cartilage loads. (4) Mechanical outcomes are becoming increasingly meaningful to inform and evaluate treatments, including predictive power from biomechanical models. Since most recent advancements in the field of biomechanics in OA are at the level of a proof op principle, future research should not only continue on this successful path of innovation, but also aim to develop clinical workflows that would facilitate including precision biomechanics in large scale studies. Eventually this will yield clinical tools for decision making and a rationale for new therapies in OA.

Introduction

Osteoarthritis (OA) is a serious and complex condition that has long been recognized as a whole organ disease, or collection of diseases[1,2]. Despite many potential OA phenotypes[2,3], a key overarching etiological factor in OA-related structural damage and symptoms relates to mechanics[3,4]. Not surprisingly, the concept of mechanics is often operationalized – and thus investigated and understood – differently among various fields of research[5]. On account of work done in this field to date, this annual presentation often focuses on joint-level, primarily knee, biomechanics. However, through growing interdisciplinary collaborations and novel research methods, new evidence regarding mechanical characteristics in OA reflects a bridging across multiple perspectives, and an expansion towards linking multiple biological scales, from the molecular level through to the level of the 'whole person'[5].

For this Year in Review, we conducted a narrative review of evidence published in the past year to highlight key new findings relating to mechanics and OA.

Methods

We performed a literature search using Pubmed. We searched for peer-reviewed publications published between April 1, 2020 and April 1, 2021. Our search terms were based on key words ("osteoarthritis") AND ("biomechanics" OR "mechanics" OR "gait"), including related keywords and MeSH terms (Box 1). Our initial search yielded 958 titles, from which we selected 398 publications of interest. Several themes emerged, and from those we narrowed our focus to emerging evidence within four key topics: (i) joint-level biomechanics; (ii) computational modeling and methodology; (iii) wearable technology; and (iv) use of mechanics as outcomes in clinical research. Fig. 1 presents a graphical summary of data acquisition methods and modeling modalities that have been highlighted in this review.

Results

Joint-level biomechanics, knee OA

As in previous years, the knee was the most studied joint, and different data acquisition methods and modelling modalities were

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Box 1. Pubmed search terms

((“biomechanical phenomena”[MeSH Terms] OR (“biomechanical”[tiab] AND “phenomena”[tiab]) OR “biomechanical phenomena”[tiab] OR “biomechanic”[tiab] OR “biomechanics”[tiab] OR “biomechanical”[tiab] OR “biomechanically”[tiab]) OR (“mechanical”[tiab] OR “mechanically”[tiab] OR “mechanicals”[tiab] OR “mechanics”[MeSH Terms] OR “mechanics“[tiab] OR “mechanic”[tiab]) OR (“gait”[MeSH Terms] OR “gait”[tiab])) AND (“osteoarthritis”[MeSH Terms] OR “osteoarthritis”[tiab] OR “osteoarthritides”[tiab]) AND (2020/04/01:2021/04/01[Date - Publication])

used (Fig. 1). In this section we highlight insights gained primarily from joint-level biomechanical studies using motion capture and imaging, which were most prominent this year. Knee OA studies using other methodologies are highlighted in other sections.

This year, several studies focussed on differentiating biomechanics in different stages of knee OA. For example, using fluoroscopy, more severe knee OA ($n = 39$) was associated with increased tibial external rotation and posterior translation during squatting[6], During gait initiation, individuals with moderate and severe knee OA ($n = 48$) demonstrated reduced centre of pressure displacements and slower, longer lasting anticipatory postural adjustments[7]. Individuals with knee OA and joint instability ($n = 20$) responded to gait perturbations with higher knee flexion angles and greater muscle co-contractions compared to stable OA knees and controls[8]. These studies suggest that biomechanics may differ across stages of OA.

New evidence, including relatively large observational studies, demonstrated the clinical importance of kinetic changes in knee OA. A study of muscle activation patterns in individuals with knee OA ($n = 54$) demonstrated that higher hamstrings activation, greater lateral co-contraction, and prolonged quadriceps and hamstrings stance activation was associated with undergoing total knee arthroplasty 5–8 years later, suggesting higher and more sustained knee loading in these individuals[9]. Sustained knee loading was also suggested by the Multicenter Osteoarthritis Study (MOST) ($n = 1576$), showing less dynamic and more sustained vertical ground reaction force (vGRF) patterns in individuals with knee OA compared to controls, adjusting for gait speed[10]. Another large observational study of individuals with medial knee OA ($n = 691$) showed a lower cadence was associated with higher knee loading per step, controlling for gait speed[11]. The results suggest that increasing cadence from 100 to 120 steps/min could lead to a 25% decrease in knee adduction moment (KAM) angular impulse. Gait retraining focused on cadence may thus represent a novel intervention to improve mechanical loading in knee OA, which might mitigate symptoms or slow disease progression.

Aiming at the prediction of more detailed biomechanical measures, novel methodologies were presented. To easily estimate knee contact forces, one study acquired *in vivo* force measures in instrumented knee implants, then used machine learning to predict medial tibiofemoral peak contact forces from gait speed, peak KAM and peak vertical knee reaction force[12]. When predicting peak medial contact force in knee OA participants, this model explained 35% of the variance in reduced medial tibial cartilage volume over 2.5 years[12]. This study demonstrates that higher loads predict future cartilage damage, but also that machine learning may facilitate less invasive and more accurate methods for acquiring biomechanical measures that relate to cartilage degeneration.

Caution is indicated when interpreting biomechanical measures. Ismailidis *et al.*[13] report differences in sagittal plane kinematics mainly resulted from reduced walking speed in knee OA, indicating this should be controlled for. However, despite correcting for gait speed, differences in kinematics and kinetics often persist in individuals with OA[10,11]. External factors should also be considered, as inter-laboratory results differ in kinematics, kinetics and muscle activity patterns in individuals with knee OA, potentially limiting generalizability among studies[14].

Joint-level biomechanics, anterior cruciate ligament (ACL) studies

Given the elevated risk for developing OA following traumatic knee injury, anterior cruciate ligament (ACL) studies continue to serve a prominent role in knee OA research. Below we highlight several studies linking altered biomechanics with both structural and symptomatic findings, which may explain the elevated risk for developing post-traumatic knee OA.

In individuals with ACL-deficient knees up to 1 year post-injury, magnetic resonance imaging (MRI) was acquired before and after 20 min of walking (double echo steady state) to measure changes in load-related compressive strain[15]. Cartilage strain was higher in the medial intercondylar notch and tibial plateau regions in the ACL-deficient compared to the contralateral knee (6 vs 2 %). This suggests that ACL injury may result in either a change in mechanical loading pattern or an increased susceptibility to cartilage loading. Evidence for the former was found in a study of individuals up to

Graphical summary of the OA Year in Review, Mechanics: Aim is to quantify or understand cartilage load (in the middle) in the context of OA as a target, recognizing different levels of precision. Data acquisition methods (blue outlines): (A) wearables, (B) motion capture, and (C) imaging; Modeling modalities (green outlines): (D) deep learning networks, (E) musculoskeletal models, and (F) finite element models.

2 years following ACL reconstruction[16]. Compared to contralateral knees, reconstructed knees demonstrated 1–2 mm greater anterior tibial translation; further, increased translation was associated with longer T1ρ and T2 relaxation times[16]. In another study in ACL-deficient knees, lower KAM angular impulse was related to longer T2 relaxation times in the medial tibiofemoral compartment and shorter times in the lateral compartment[17]. Three months after ACL reconstruction, inter-limb differences in peak KAM and peak knee flexion moments were related to deep layer tibiofemoral joint T2 relaxation times[18]. Two years after reconstruction, increased knee flexion and external rotation angles at heel strike were related to patellofemoral deep cartilage matrix disruption, as assessed by ultra short echo time T2* MRI[19]. Collectively, these studies suggest altered loading is associated with early cartilage changes following ACL injury.

In addition to the association between altered biomechanics and early structural changes, researchers also found a prospective link between biomechanics and symptoms[20]. Two years after ACL reconstruction, two distinct patterns of gait were seen: approximately half of the sample ($n = 13$) showed reduced early stance peak vGRF during gait compared to the contralateral side, and the other half ($n = 15$) showed increased peak vGRF. Despite no mean differences in vGRF compared to the contralateral side, higher vGRF at 2 years was associated with worse patient-reported outcome scores 10 years after reconstruction. This study suggests that following ACL injuries, as in individuals with knee OA, simple biomechanical measures may predict long-term outcomes.

Joint-level biomechanics, other joints

Despite the usual focus on knee OA research as in previous years, we acknowledge the work done this year to elucidate the role of biomechanics in other joints affected by OA. For example, 42 individuals with hip OA demonstrated altered kinematics during stair climbing compared to 30 controls[21]. However, another study showed that among 55 individuals with hip OA, variability in hip joint kinematics during gait was not explained by pain severity or radiographic OA severity[22], calling into question what factors might be driving hip OA–related changes in kinematics.

More distally, 52 individuals with isolated ankle OA showed altered ankle kinematics and kinetics during walking compared to 25 controls, however there were no changes in distal foot biomechanics, suggesting there was no distal compensation for mechanical ankle dysfunction[23]. A systematic review of midfoot OA revealed that, compared to controls, individuals had more foot protonation, more first ray mobility, less subtalar and first metatarsophalangeal joint range of motion, longer central metatarsals, and during gait they had increased peak plantar pressures, pressure time integrals and contact times in the heel and midfoot[24]. .

Biomechanics may also play a role in OA of non-weightbearing joints. In glenohumeral OA, resting scapula position did not differ from controls, however during shoulder flexion with internal rotation, scapula anterior tilt was greater, possibly as an adaptation to limited glenohumeral motion[25]. To more accurately measure finger, hand and wrist forces, wearable sensors[26] and multi-scale computational models[27] were developed this year, enabling future studies to understand the role of mechanics in hand OA and the effects of joint protection strategies.

Computational modelling

For several years, *in silico* modelling has been employed to study biomechanics with the potential to inform clinical decision making[28]. Models at different scales have been developed, from whole body to joint, tissue and cell levels. Based on input from acquired data, mostly motion capture and imaging, modelling can provide tissue scale biomechanical measures to quantify cartilage load (Fig. 1). Types of models include musculoskeletal, discrete element and finite element models.

Musculoskeletal models enable researchers to determine joint contact forces. Within the past year, several papers employed musculoskeletal models to answer clinical questions[29–38], with a focus on joint contact forces in individuals at risk for OA. In individuals with transtibial amputations, increased contact forces at the hip[33] and knee[30] joints were reported. In individuals with developmental dysplasia of the hip, an altered contribution of muscles to hip contact forces was reported[34] as well as changes in hip contact forces resulting from rehabilitation exercises[31]. After total hip arthroplasty, small but significantly increased lateral knee loading in the contralateral leg was reported[36].

A major limitation of computational modelling studies is small sample sizes. Only three modelling studies in this review included more than 20 participants[29,35,38]. Starkey *et al.*[35] used data from a randomized clinical trial (RCT) to determine the effect of physical exercise on knee contact forces. They included 41 patients following partial medial meniscectomy, and included participant-specific information using electromyography (EMG). Although exercise did not affect knee contact forces, the large within-patient variability suggested that individual changes are important to consider. Wellsandt *et al.*[29] also estimated knee contact forces using an EMG-driven workflow in individuals 5 years after ACL injury treated either surgically ($n = 40$) or non-surgically ($n = 17$). Individuals treated non-surgically had increased medial compartment contact forces compared to the surgical group, despite no differences in radiographic tibiofemoral OA prevalence. Sritharan *et al.*[38] compared patellofemoral joint contact forces between injured and non-injured limbs in 55 participants following ACL reconstruction. Despite no difference in lower limb kinematics, patellofemoral joint contact forces were lower in ACL-reconstructed limbs.

The use of finite element models in OA research was less common than musculoskeletal models this past year[39–42]. Virtual surgeries were used to simulate post-surgical outcomes in two studies[40–42]. Sano *et al.*[42] studied cartilage stress distribution following virtual surgery for anterior shoulder instability. A concentration of stress was found in the humeral head cartilage, which authors speculated could lead to glenohumeral OA. Pan *et al.*[41] studied the effect of proximal fibular osteotomies in individuals with mild knee OA and varus deformity. Under the assumptions of an equal vertical load pre- and post-surgery, these osteotomies shifted stress concentration in the knee towards the lateral compartment, thereby reducing medial compartment stress, suggesting that proximal fibular osteotomy may alter knee load distributions.

Besides publications that apply *in silico* models for clinically relevant questions, there is ongoing development and validation of these computational models at different scales, i.e., musculoskeletal[43,44], discrete element[45], and finite element[46–53] models. Naghibi *et al.*[51] validated models in a clinical study investigating the effect of positional changes of a medial meniscus prosthesis. They validated calculated contact pressures from finite element models by comparing to cadaveric experiments under axial loading. Using the validated model, during gait an anatomically positioned meniscal prosthesis could improve pressure distribution in the knee joint, but it did not fully restore the distribution seen in intact knee joints.

While these models involve a single scale, multi-scale *in silico* modelling couples multiple biological scales. Multi-scale modelling is a promising tool for better understanding OA[28,54–56]. In the past year, few studies were published that link joint and tissue scales in relation to the OA development[27,57–60]. Two studies aimed to validate a multi-scale workflow by comparing predicted changes in loss of proteoglycan fixed charged density[59] or collagen degeneration and proteoglycan depletion[57] to follow-up MRI T1ρ and T2 relaxation times. Gustafson *et al.*[58] combined biplane fluoroscopy with discrete element models to estimate changes in patellofemoral joint stress. Eskelinen *et al.*[61] presented a novel mechanobiological framework using biochemically and biomechanically-driven mechanisms to predict cartilage degradation[61]. The model was able to predict matrix losses occurring near the free surfaces especially near the lesion, while no losses were predicted away from the lesion, and results were validated by experimental data. Multi-scale modelling is also relevant in non-weight bearing joints. Changes in finger muscle co-contraction ratios altered contact pressure distributions among finger joints, which could promote OA development[27].

The importance of considering multiple scales is also highlighted by Putignano *et al.*[62]. They present a novel numerical multi-scale lubrication theory to explain a motion-induced cartilage rehydration mechanism and showed the sliding-induced fluid recovery, also within the loaded contact area. They concluded that this rehydration is activated by hydrodynamic pressure originating from sliding.

Multi-scale *in silico* models are a very promising tool for assessing cartilage structure and function, as the models appear to yield valid estimates of cartilage loads. However, in order to introduce *in silico* models as a clinical tool, they should be personalized for each patient (e.g., based on imaging), as similarly stated for musculoskeletal models[63]. Moreover, combining this with wearables or deep learning networks will enable the efficient handling of larger sample sizes ((Fig. 1).

Wearables

The use of wearable sensors, such as inertial measurement units (IMU) and accelerometers, is becoming increasingly popular in OA research. A scoping review found an exceptional increase over the last 5 years[64]. Wearables, when properly processed and calibrated, provide the possibility to more easily measure biomechanics in clinical practice or OA self-management, and the ability to acquire biomechanics data in many participants in a time efficient manner.

For data acquisition over a long duration, an activity monitor, usually a single sensor, is secured at a convenient location. Lisee *et al.*[65] used a hip-worn accelerometer that classified each 60-s epoch for its type of activity and measured the cadence when walking. After ACL reconstruction, participants spent 17% less time walking, especially at a moderate-to vigorous-intensity. Using a thigh-worn accelerometer, activities of women with knee OA did not differ from their non-OA peers[66]. To feedback cumulative joint load based on activity classification, a smartphone app was co-created with OA patients and healthcare providers[67]. The app uses the built-in smartphone accelerometer, with joint load estimations for each activity derived from previous studies. Though preliminary, we consider this a very promising tool to support OA self-management.

IMUs can be used to measure joint kinematics during gait. Validation for a full IMU setup (i.e., an IMU for each body segment, up to 15 in total[68]) has been further established this year[68,69], enabling a more accessible way of performing biomechanical evaluations. Several studies used different subsets of a full IMU sensor setup to demonstrate the presence of joint kinematic differences in knee OA and hip OA[70–74]. Besides overall joint kinematics, specific kinematic targets like trunk lean/center of mass position[68] or knee varus thrust[75] can be feasibly tracked with IMUs, making IMUs useful for targeted biomechanics studies in OA.

Therapeutic reduction of joint load might be achieved by adapting a movement pattern that avoids high impact or prolonged loading. Gait retraining to achieve this has been successful[76], but feedback is required for an individual to sustain new walking styles. Wouda *et al.*[77] used a single foot-worn IMU and a dedicated algorithm to calculate walking direction and real-time Foot Progression Angle (FPA). In a study by Xia *et al.*[78], the FPA sensor was built into the sole of the shoe, and together with a haptic device (vibrator), they showed that participants could control FPA very precisely (within 3°) on a treadmill.

Although manipulating FPA does affect the KAM and therefore the joint load, it remains an indirect measure and might not hold for every person with knee OA. Unfortunately, a direct estimation of the KAM seems not possible using wearables alone. Machine Learning might be able to bypass the need for force plates and biomechanical models. Wang and colleagues delivered an impressive study that demonstrated the real-time estimation from just two ankle-worn IMUs. An Artificial Neural Network was trained with 78 persons with knee OA and 12 asymptomatic persons[79]. The IMUs were linked to a smartphone, and the artificial neural network was run in the cloud. Excellent correlation ($r^2 > 0.94$) between the estimated KAM and the lab-derived KAM was achieved, including validation with toeing-in and toeing-out. After independent replication, this approach could become an important tool in gait retraining. Boswell *et al.*[80] applied machine learning to estimate KAM. Using frontal kinematics of gait as input, the artificial neural network predicted peak KAM ($r^2 = 0.85$). This approach could be applied to estimate KAM from frontal plane video recordings, enabling point-of-care mechanical diagnostics in knee OA. This again highlights that machine learning in combination with wearables (Fig. 1) are promising tools for more easily obtaining meaningful biomechanical measures.

Biomechanics in OA treatment

Given the important role of biomechanics in OA onset and progression, biomechanics interventions continued to be investigated this year - see OARSI Year in Review Rehab for more detail. In addition, where clinical trials often focus on pain and function as a study outcome, a growing number of studies are incorporating biomechanical outcomes into their study design. Various data acquisition methods and modelling modalities are used, although the use of wearables and machine learning is still limited (Fig. 1). Below we outline several key papers in which biomechanical outcomes have been included in intervention studies.

A systematic review found that in healthy individuals, both toe-in and toe-out gait reduced KAM and KAM angular impulse compared to natural gait, while in individuals with knee OA, only toe-out gait appeared to reduce these gait parameters[81]. Using standing MRI, a small amount of lateralization of contact for both toe-out and toe-in postures in individuals with mild knee OA was found[82], indicating accurate analyses of joint kinematics during gait may be needed to reveal more subtle changes. Another study considered other gait modifications such as trunk lean and medial knee thrust and concluded that addressing multiple gait modifications in future study designs might demonstrate a more optimal reduction in KAM[83].

One way to conduct preliminary explorations of different or novel types of interventions without the undue burden of conducting clinical trials is through the use of musculoskeletal modelling simulations. Biomechanics data from eight healthy participants was used to simulate the effect of three different designs of a tricompartmental unloader brace[84]. All three brace simulations showed reduced knee joint loads of 30–50% at knee flexion angles of more than 30 °, providing proof-of-concept and informing the design of these novel braces.

The effects of an existing medial offloader brace was evaluated *in vivo* with fluoroscopy while individuals with knee OA performed their usual gait both with and without the brace on[85]. With the brace on, mean joint space width increased 1.6 (±0.8) mm at both heel strike and contralateral toe off. Use of fluoroscopy in a gait laboratory represents recent advances in technology that make it possible to measure the effects of biomechanical interventions such as braces, where previously instruments were not precise enough to detect such changes.

Several RCTs were published this year that evaluated the efficacy of various biomechanical interventions in knee OA. One crossover RCT ($n = 24$) of three types of knee braces worn for 3 months each found an unloader brace with both valgus and external rotation functions to be more comfortable and to decrease KAM both at baseline and after treatment (with brace donned), however interpretation of the results are limited by a carryover effect[86]. An RCT investigating footwear with individually adjustable external convex pods attached to the outsole (compared to control shoes) showed reduced pain in the treatment group of limited clinical relevance and mildly increased velocity and step length compared to controls[87]. An RCT of minimalist footwear in women with knee OA that had previously shown reduced KAM and KAM impulse after 6 months[88] conducted secondary analyses to explain the mechanism of reduction of KAM[89]. They found no association with other lower limb joint kinematics and frontal moments, center of pressure displacement, or FPA, concluding specifically that changes in KAM were not related to increased hip moments or ankle inversion angles. RCTs of lateral wedge insoles were also published this year. One study compared 12 weeks of lateral wedge insole wear to neutral insoles and found lateral wedge insoles were no more effective than neutral insoles at reducing KAM and KAM impulse[90]. A second RCT compared 6 weeks of insole wear to an ankle foot orthosis, and found lateral wedge insoles to be less effective than the ankle foot orthosis at reducing KAM and KAM impulse, though the between-group differences were of doubtful clinical relevance[91].

High tibial osteotomy is a common surgical approach to correct severely abnormal biomechanics in individuals with or at risk for knee OA. This year, a study of 50 individuals who underwent a biplanar open wedge technique with rigid plate fixation demonstrated a mean correction in frontal plane alignment of approximately 14°[92]. Moreover, improved cartilage scores were noted in 38% of participants, and various synovial markers of inflammation were reduced by 14–49%. Another study investigating unilateral medial open wedge high tibial osteotomy with internal fixation in 36 participants showed a frontal plane correction of approximately 7 °, but also reduced effusion-synovitis volume, KAM and KAM impulse, and shorter T2 relaxation times in the medial tibiofemoral joint[93,94]. Together, these studies suggest that the surgical correction of severe varus alignment may result not only in biomechanical improvements but also in improvements in inflammation and cartilage health. Taken together, these studies demonstrate the potential of incorporating pre-post biomechanical outcomes into OA clinical trials to better understand the mechanisms underpinning effects (or lack thereof) for various interventions.

Conclusion

In this narrative review we reported on emerging evidence in four key topics: (i) joint-level biomechanics; (ii) computational modeling; (iii) wearable technology; and (iv) mechanics as outcomes in clinical research. Computational and experimental innovations have enabled more detailed analyses of cartilage load. There was a main focus on knee OA, including a prominent role of ACL research. Although generally with small sample sizes, *in silico* single scale models were used to evaluate clinically relevant questions. Multi-scale *in silico* models yield valid estimates of cartilage loads and are a promising tool for further assessing cartilage structure and function. The use of wearable sensors is becoming increasingly popular in OA research, enabling low cost measurements in the free-living environment and providing feedback for gait retraining. Machine learning is used to extract higher fidelity estimates of cartilage load from lower fidelity information. Clinical trials increasingly incorporate biomechanical outcomes into their study design. These results further elucidate the role that mechanics plays in OA onset and progression, and to harness its potential as an effective treatment target. Since most recent advancements in the field of biomechanics in OA are at the level of proof-of-principle, future research should continue on this path of innovation, but also aim to develop clinical workflows that would allow inclusion of precision biomechanics into large scale studies.

Author contributions

All authors performed the literature search and review, selected the articles, identified themes, summarized results and wrote the manuscript.

Conflict of interest

The authors have no conflict of interest.

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