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Older Asymptomatic Women Exhibit Patterns of Thumb Carpometacarpal Joint Space Narrowing that Precede Changes Associated with Early Osteoarthritis

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Abstract

In small joints, where cartilage is difficult to image and quantify directly, three-dimensional joint space measures can be used to gain insight into potential joint pathomechanics. Since the female sex and older age are risk factors for carpometacarpal (CMC) joint osteoarthritis (OA), the purpose of this in vivo computed tomography (CT) study was to determine if there are any differences with sex, age, and early OA in the CMC joint space. The thumbs of 66 healthy subjects and 81 patients with early stage CMC OA were scanned in four range-of-motion, three functional-task, and one neutral positions. Subchondral bone-to-bone distances across the trapezial and metacarpal articular surfaces were computed for all the positions. The joint space area, defined as the articular surface that is less than 1.5 mm from the mating bone, was used to assess joint space. A larger joint space area typically corresponds to closer articular surfaces, and therefore a narrower joint space. *We found that the joint space areas were not significantly different between healthy young men and women. Trends indicated that patients with early stage OA have larger CMC joint space areas than healthy subjects of the same age group and that older healthy women have larger joint space areas than younger healthy women.* This study suggests that aging in women may lead to joint space narrowing patterns that precede early OA, which is a compelling new insight into the pathological processes that make CMC OA endemic to women.

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Conflict of Interest Statement

The authors have no financial or personal relationships that could bias this work.

Keywords

thumb CMC; cartilage; joint space; osteoarthritis; joint biomechanics; computed tomography; in vivo

1. INTRODUCTION

Osteoarthritis (OA) is thought to emerge and progress under the influence of abnormal mechanical loading (Griffin and Guilak, 2005). While acute injury can give rise to posttraumatic arthritis as soon as six months post injury, due to abnormal impact that triggers necrotic, apoptotic, and inflammatory activity, or due to ligamentous destabilization that shifts the centers of pressure in the joint to areas of cartilage that are not prepared to bear load (Lotz, 2010), the role of joint biomechanics on the slower and natural progression of idiopathic OA in joints such as the thumb carpometacarpal (CMC) joint remains unknown. Although aging plays a role in reducing the proliferative activity of chondrocytes (Loeser, 2009), OA is no longer considered simply a process of aging, but rather a multifactorial disease, likely linked to systemic—metabolic, genetic, hormonal—or local, i.e. mechanical, susceptibility. Advanced stage OA is characterized by both abnormal cartilage health and abnormal joint biomechanics, but in order to understand the sequence of events that lead to the simultaneous manifestation of these outcomes, the disease should be studied at the early stage and from both aspects—cartilage biology and joint mechanics.

Findings from studies of contact areas in cadaveric thumb CMC joints of varying arthritic stages are not in agreement (Ateshian et al., 1995; Eaton and Glickel, 1987; Eaton and Littler, 1969; Kuczyński, 1974; Napier, 1955; Pellegrini et al., 1993; Pieron, 1973), and a comparative analysis between the contact mechanics of healthy and arthritic-prone joints, which would provide insight into the potential etiology of CMC OA, is missing. Previous cadaver studies are limited by simulated positions and intervention with pressure-sensitive film within the joint space. More recently, joint space measurements from computed tomography images have emerged as a reliable and elegant alternative for studying articular-surface interactions in vivo (Anderst and Tashman, 2003; Marai et al., 2004). This method involves the computation of minimum bone-to-bone distance maps on the articular surfaces of bone models in different positions. The area on an articular surface that is within a specified distance from the mating articular surface is defined as the joint space area, such that an increase in joint space area is an indicator of joint space narrowing, because it signifies closer proximity between the mating articular surfaces. The center of pressure on the joint surface is estimated by computing the weighted center of the joint space area and is referenced as the joint space centroid.

The purpose of this study was to determine if the size of the CMC joint space area and the location of the CMC joint space centroid across different physiological positions differ with sex, age, and OA onset by using the aforementioned computational estimates. As part of a larger study that aims to track in vivo CMC joint biomechanics longitudinally, this investigation should provide baseline evidence against which future findings can be evaluated. We hypothesized that patients with early stage CMC OA would not have

significantly larger joint space areas when compared to healthy controls, since at this stage there is usually little or no radiographic evidence of joint space narrowing (Eaton and Glickel, 1987). We also hypothesized that the joint space centroid would be located more volarly in arthritic patients than in healthy controls, potentially due greater dorsal subluxation, which is associated with CMC OA.

2. MATERIALS AND METHODS

2.1 Subjects

Following approval from our Institutional Review Board, completion of informed consents, and initial screenings for eligibility, 147 subjects—66 asymptomatic men and women of two age groups and 81 patients with early stage OA (Table 1)—were recruited as part of a broader study on CMC joint biomechanics (Halilaj et al., 2014a, 2014b, 2014c, 2014d, 2014e, 2013). Exclusion criteria for the study included pre-existing conditions that could have altered CMC joint morphology or kinematics, such as traumatic injury, hand or thumb surgery, inflammatory arthritis, systemic conditions, e.g. connective tissue disease, metabolic bone disease, signs of CMC OA, other non-OA diseases of the thumb, or pregnancy. Posterior-anterior (PA), lateral, Robert's (Ladd, 2014; Robert, 1936), and bilateral stress X-ray views were taken for each subject and reviewed by a hand surgeon. Early stage OA subjects, who presented with localized pain at the base of the thumb and had one or more positive clinical signs of CMC OA (e.g., positive grind test), were screened and staged according to a modified Eaton staging system (Eaton and Glickel, 1987). The modified staging system classifies as stage 0 patients who have no radiographic evidence of any arthritis and as stage 1 those who have minimal evidence, including minimal or no joint space narrowing, minimal contour changes, no derbis, as well as minimal or no subluxation. Only patients in stages 0 and 1 were included (Fig. 1).

2.2 Imaging Protocol

The dominant hands of the asymptomatic subjects and the affected hands of the symptomatic subjects were imaged with a 16-slice clinical computed tomography (CT) scanner (GE LightSpeed 16, General Electric, Milwaukee, WI) at tube settings of 80 kVp and 80 mA, slice thickness of 0.625 mm, and in-plane resolution of at least 0.4 mm × 0.4 mm. The positions included a splinted neutral position, three functional positions—lateral key pinch, jar grasp, and jar twist—and four thumb range-of-motion positions: flexion, extension, abduction, adduction. For the neutral scan, wrist and thumb positions were standardized with a modified Rolyan® Original adjustable wrist and thumb spica-splint brace (Patterson Medical, Bolingbrook, Illinois). Custom-made mechanical fixtures were used to standardize wrist and thumb posture in the other positions (Fig. 2). Subjects were advised not to apply any load during the functional positions included in this study.

2.3 Joint Space Measurements

The outer cortical surfaces of the trapezium and first metacarpal were segmented from the neutral CT volumes with commercial software (Mimics v.13.1, Materialise, Leuven, Belgium) and exported as meshed surfaces. Six-degree-of-freedom bone kinematics from the neutral position to each of the remaining seven positions were determined automatically

with a markerless bone registration algorithm that utilizes the bone models from the neutral scan and tissue-classified image volumes from all the scans (Marai et al., 2006). The articular surface area (ASA) on each bone was manually selected by following the visible lining of cartilage on the subchondral surface. Bone-to-bone distance maps on the metacarpal and trapezium were computed by using a combined distance-field and meshed-surface representation of the bone models for each of the scanned positions (Marai et al., 2004) (Fig. 3). The areas on the trapezium and metacarpal within a threshold of 1.5 mm from the mating bone were computed and defined as the joint space area (JSA). The 1.5-mm threshold was chosen because it resulted in a JSA that in the neutral position was equal to or smaller than the ASA. Since the trapezial and metacarpal JSAs for a given joint position were not significantly different, only the trapezial JSA was considered for the analysis presented here. To address the effect of joint size, the JSA was expressed as a percentage of the ASA. The centroid of the JSA weighted linearly by the bone-to-bone distance, which is an approximation of the center of pressure in the joint, was computed and its location was expressed in terms of the dorsal-volar (DV) and radial-ulnar (UR) components of both the trapezial and metacarpal segment coordinate systems. These coordinate systems were centered at the saddle points of the articular surfaces and aligned with the principal directions of curvature, or the concavities and convexities, of the saddle-shaped articular surfaces (Halilaj et al., 2013). DV and UR were normalized by the square root of the articular surface area to account for bone-size differences.

2.4 Statistical Analysis

A correlated error general linear model was used to determine the effects of sex, age, and OA on the JSA, as well as on the trapezial and metacarpal DV and UR components of the joint space centroid. The Holm test was used to determine statistical significance, which, after adjusting for multiplicity, was set at $p = .05$. Based on inspection of model residuals, a normal distribution was selected for all the variables. Results are presented as means with 95% confidence intervals in the figures and means with standard deviations in the text.

3. RESULTS

Overall, trends indicated that JSA differences between age and health groups were not similar in men and women (Fig. 4). The JSAs of healthy young and older men were not different in any of the positions ($p > .645$) (Fig. 4a). The JSAs of arthritic men, however, were approximately 28% larger in the neutral position ($p = .008$), 33% larger in jar grasp ($p = .001$), and 31% larger in jar twist ($p = .046$) than the JSAs of healthy older men (Fig. 4a). Healthy older women had significantly larger JSAs than healthy young women only in extension ($p = .028$), but there were clear trends of higher JSAs when moving from younger to older to arthritic women, in every position (Fig. 4b). Despite the dissimilar effects of age group in the JSAs of men and women, there were no significant differences with sex in the JSAs of young healthy subjects in any of the positions ($p > .178$) (Fig. 4).

The metacarpal joint space centroid was located on the volar half of the metacarpal articular surface and its location was not affected by sex ($p > .171$) or age ($p > .139$), but in 4 of the 8 positions it was located more volarly—closer to the beak—in arthritic women than in

healthy women (Fig. 5). Across all the subjects, the metacarpal joint space centroid was located 1.2 ± 1.3 mm volarly and 1.3 ± 1.6 mm ulnarly in key pinch, 1.5 ± 1.2 mm volarly and 2.5 ± 1.0 mm ulnarly in adduction, 1.4 ± 1.0 mm volarly and 0.6 ± 1.6 mm ulnarly in neutral, 0.7 ± 1.3 mm volarly and 0.2 ± 1.8 mm radially in jar twist, 1.7 ± 1.4 mm volarly and 1.4 ± 1.8 mm radially in flexion. The joint space centroids in arthritic women were located more volarly than in healthy women of the same age group in jar grasp (0.3 ± 0.9 mm in healthy older women and 1.0 ± 1.0 mm in arthritic women, $p = .040$), abduction (0.7 ± 0.8 mm in healthy older women and 1.5 ± 1.0 mm in arthritic women, $p = .033$; UR = 2.8 ± 1.4 mm radially), and in extension (0.6 ± 0.8 mm in healthy older women and 1.4 ± 0.8 mm in arthritic women, $p = .002$; UR = 0.5 ± 1.7 mm ulnarly). In jar grasp, the metacarpal joint space centroid was also located more ulnarly in arthritic men than in healthy men (4.8 ± 1.2 mm radially in healthy older men 3.7 ± 1.5 mm radially in arthritic men, $p = .047$).

The trapezial joint space centroid was located in the central-radial portion of the trapezial articular surface and its location did not differ significantly with sex ($p > .439$), age ($p > .251$), or OA ($p > .328$, except in jar grasp) (Fig. 5). Across all the subjects, the trapezial joint space centroid was located 0.6 ± 1.1 mm dorsally and 0.8 ± 1.5 mm radially in the neutral position, 0.8 ± 1.3 mm dorsally and 1.0 ± 1.8 mm radially in jar twist, 2.0 ± 1.1 mm dorsally and 1.4 ± 1.4 mm radially in extension, 0.4 ± 1.3 mm dorsally and 0.7 ± 1.5 mm radially in key pinch, 1.1 ± 1.1 mm volarly and 1.7 ± 1.6 mm radially in abduction, 1.1 ± 1.2 mm volarly and 1.5 ± 1.3 mm radially in adduction, 1.9 ± 1.3 mm volarly and 0.9 ± 1.6 mm radially in flexion. In the jar grasp position the trapezial joint space centroid was located approximately 1 mm more volarly in arthritic men than in healthy men of the same age group (0.3 ± 0.6 mm volarly in healthy and 1.2 ± 1.0 mm volarly in OA, $p = .002$; UR = 2.1 ± 1.4 mm radially).

4. DISCUSSION

Since abnormal joint loading is considered a contributing factor in the progression of OA (Felson, 2013; Griffin and Guilak, 2005), the purpose of this study was to use joint space measurements to gain insight into CMC joint contact during different positions and to determine if they differ with sex, age, and OA onset. Our study design included healthy men and women of two age groups, as well as patients with early stage CMC OA who reported pain and had one or more positive clinical signs of CMC OA, but exhibited little or no radiographic evidence of joint space narrowing. Using in vivo sequential computed tomography methods, we found that subjects with early CMC OA are characterized by significantly larger CMC joint space areas and more volar joint space centroids, in some of the scanned positions, when compared to healthy subjects of the same age group. We also observed a pattern of larger joint space areas in older than in younger healthy women. Additionally, we found that the CMC joint space centroid is typically located on the radial quadrants of trapezium and on the volar quadrants of the metacarpal, which correspond to previously reported areas of cartilage wear.

Larger joint space areas are typically indicative of a narrower joint space, although in unique cases they can be indicative of better congruence. To confirm that the larger joint space areas that were observed in this study are representative of narrower joint spaces, we also

examined the distribution of the minimum bone-to-bone distances within the JSA, across all the positions. This analysis (Figure 6) yielded similar trends, i.e., lower mean bone-to-bone distances in the joints of arthritic subjects than in the joints of healthy controls and lower mean bone-to-bone distances in the joints of older women than in the joints of younger women, across all the positions. Joint space narrowing is the leading criterion for staging in thumb CMC OA, as it represents loss of articular cartilage, but our findings indicate that cartilage loss may start much earlier than is detectable clinically.

Our findings on the locations of the CMC joint space centroids are consistent with some findings reported in literature on the approximate locations of CMC joint contact. Previous studies have reported that CMC cartilage starts to degenerate on the volar side of the metacarpal (beak) (Koff et al., 2003; Xu et al., 1998), which is consistent with the metacarpal joint space centroid being located more volarly in subject with early OA than in healthy subjects of the same age group. The central location of the trapezial joint space centroid and volar-central location of the metacarpal joint space centroid in the neutral position is in agreement with findings from Ateshian et al. (Ateshian et al., 1995). We found that the joint space centroids of both the trapezium and metacarpal were located on the volar-radial side during abduction, which is in agreement with findings from Pieron (Pieron, 1973), Napier (Napier, 1955), and Kuczynski (Kuczynski, 1974), but not in agreement with the findings of Ateshian et al. (Ateshian et al., 1995) who reported the contact areas to be on the volar-ulnar side of the joint. The later study, however, reported that some of the tested specimens could not be placed in full abduction, which would reasonably result in a more ulnar contact area. We found that the trapezial joint space centroid was located volar-radially and the metacarpal joint space centroid was located volar-ulnarly during adduction, which is in disagreement with the dorsal, dorsal-radial patterns in the trapezium and ulnar patterns in the metacarpal reported by Ateshian et al. (Ateshian et al., 1995). We found that both the trapezial and metacarpal joint space centroids were located volar-radially during flexion, whereas Ateshian et al. found them to be located volar-ulnarly. We found the trapezial joint space centroid to be located dorsal-radially and the metacarpal joint space centroid central-volarly during extension, whereas Ateshian et al. reported dorsal-ulnar trapezial and volar-ulnar metacarpal contact areas. Eaton and Littler (Eaton and Littler, 1969) reported dorsal contact areas in the CMC joint during key pinch, whereas Pieron (Pieron, 1973) and Ateshian et al. (Ateshian et al., 1995) reported volar contact areas. These mixed results may not be significantly different from our finding of a central joint space centroid with standard deviations spanning dorsally and volarly.

It is also important to note that some of these differences may be due to differences in the experimental setup, e.g. the cadaver thumbs in the study by Ateshian et al. were subjected to 25 N of load during key pinch, whereas the subjects in our study did not apply any load. It is important to note the following study characteristics when placing our results in context with the current and future literature. First, we have not measured joint contact directly, but have inferred it from bone-to-bone distance maps. One of the limitations of our CT image-based methodology, which allows the accurate measurement of bone position, is that it is not capable of directly imaging cartilage. Second, we used healthy and early OA subjects, while most previous studies have analyzed arthritic cadaveric specimens. Therefore, a direct comparison between our findings and previously published findings is not possible. Third,

joint space narrowing as measured here could be a result of cartilage softening, instead of cartilage loss, especially if the joint is loaded during scanning. In the positions used in this study, however, the joints were not loaded. Additionally, diurnal fluctuations in cartilage thickness and the effect of thumb usage prior to scanning could potentially interfere with the results. Intra-subject variations are smaller than we can measure with a resolution of $0.4 \text{ mm} \times 0.4 \text{ mm}$ 0.625 mm and smaller than the significant differences that we are reporting. Fourth, this is a cross-sectional study, therefore the direct effects of aging and OA cannot be determined with certainty. Along the same lines, it is worth noting that the higher joint space areas in older when compared to younger women constitute a trend, not a statistically significant finding, albeit a consistent trend throughout the eight positions that were analyzed. Last, to address concerns of longitudinal coordinate system variability, due to articular shape changes with age and OA progression, in future follow-up studies of joint space centroids we will use the coordinate systems generated at baseline, aligning the bone models using whole-bone landmarks.

While additional longitudinal studies are needed for further confirmation, the findings presented here improve the current understanding of CMC joint pathomechanics by suggesting that women, who are more predisposed to CMC OA than men, exhibit patterns of joint space narrowing with aging. Joint space narrowing is indicative of cartilage loss. Further attention should be placed on determining whether the rate of cartilage loss due to aging is indeed different between men and women, and if so, on determining the source of such differences. Hormonal fluctuations, for example, may affect cartilage metabolism in women. The clinical significance of a 1 mm shift in joint space centroid remains to be explored by further analysis, but the ability to acquire these data is promising for longitudinal studies that aim to bring to light the complex relationship between OA progression and joint mechanics. Ultimately, information on joint space areas and centroids in healthy individuals and patients at different stages of CMC OA should inform and refine surgical procedures that transfer load bearing in the CMC joint in order to hinder the rapid progression of the disease.

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Figure 1.

A modified Eaton staging system was used where subjects with no radiographic evidence of any arthritis are classified as Stage 0, whereas subjects with no joint narrowing (compared to adjacent joints), no debris, but minimal contour changes and minimal or no subluxation are classified as Stage 1 – only subjects in Stage 0 or 1 were included in the study.

Figure 2.
3-D rendering of the CT scans of the hand of one subject in all the scanned positions: a) neutral, b) key pinch, c) jar grasp, d) jar twist, e) abduction, f) adduction, g) flexion, h) extension, with the mechanical fixtures used to standardize the positions.

Figure 3.

A healthy and an arthritic CMC joint, where the color intensity represents bone-to-bone distance between the trapezium (TPM) and the metacarpal (MC1), in a resting key pinch position, illustrating that the joint is closer, i.e., the joint space is narrower, in OA subjects than in healthy controls. The joint space area is defined as the area where the bone-to-bone distance is less than or equal to 1.5 mm (yellow), whereas the joint space centroid (in black) is defined as the distance-weighted centroid of the joint space area.

Figure 4.

The mean ($\pm$ SD) joint space areas (JSAs) across all the scanned positions in a) men and b) women. In men only OA had an effect on the JSAs, whereas in women there was a trend of both age and OA affecting the JSAs.

Figure 5.

The metacarpal (upper) and trapezium (lower) articular surfaces with the mean ($\pm$ SD) joint space centroids for each group, shown here in their original (not normalized) location; the centroids were located more volarly in arthritic patients than in age-matched healthy controls in three of the scanned positions.

Figure 6.

The mean probability density functions of the bone-to-bone distances within the 1.5 mm joint space area for each study group, confirming that the trends observed in the JSA are indicative joint space narrowing. These distributions indicate that the mean bone-to-bone distance within the 1.5 mm area is lower in older women than in younger women, and lower in arthritic women than in healthy women of the same age group. In men, however, age has no effect on the bone-to-bone distance distribution, but early OA is associated with lower bone-to-bone distances.

Table 1Mean ($\pm$ SD) ages of the participating subjects divided by group

Group	Age (yrs.)
Young Men (n=16)	24.7 $\pm$ 4.5
Young Women (n=16)	24.9 $\pm$ 3.3
Older Men (n=16)	53.8 $\pm$ 8.7
Older Women (n=18)	56.0 $\pm$ 6.7
Early OA Men (n=34)	60.6 $\pm$ 7.1
Early OA Women (n=47)	53.3 $\pm$ 6.2