

The Association of Index-to-Ring Finger Ratio With Trapeziometacarpal Joint Osteoarthritis in an Elderly Korean Population

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ABSTRACT. Objective. Index-to-ring finger ratio (IRFR) has been reported to be associated with joint osteoarthritis (OA). We aimed to evaluate the association between IRFR and trapeziometacarpal joint (TMCJ) OA in an elderly Korean population.

Methods. A population-based sample included 604 participants with a mean age of 74.8 years. IRFR was radiographically measured by the ratio of the length of the right second to fourth phalangeal bones (“phalangeal IRFR”) and metacarpal bones (“metacarpal IRFR”), and was visually classified as either type 1 (index finger longer than or equal to ring finger) or type 2 (index finger shorter than ring finger). Odds ratios (ORs) for the presence of OA (Kellgren-Lawrence [KL] grade > 1) and for severe OA (KL grade > 2) were analyzed using logistic regression.

Results. The phalangeal IRFR averaged 91.3%, the metacarpal IRFR 116.7%, and 304 out of 604 participants (50.3%) had type 2 IRFR. We found TMCJ OA in 112 participants (18.5%), and severe TMCJ OA in 33 participants (5.5%). Presence of TMCJ OA was significantly associated with age (OR 1.04; 95% CI 1.01-1.06) and metacarpal IRFR (OR 0.94; 95% CI 0.88-0.99), and severe TMCJ OA with age (OR 1.08; 95% CI 1.03-1.12) and type 2 IRFR (OR 3.07; 95% CI 1.13-8.33).

Conclusion. Radiographic IRFR, specifically metacarpal IRFR, was associated with the presence of TMCJ OA, and visual IRFR with severe TMCJ OA in both elderly Korean men and women. The results of this study suggest that IRFR might serve as an easily measurable biomarker to identify patients vulnerable to TMCJ OA.

Key Indexing Terms: index-to-ring finger ratio, osteoarthritis, trapeziometacarpal joint

Index-to-ring finger ratio (IRFR) is an indicator of prenatal testosterone levels.¹⁻³ The testosterone level measured from amniotic fluid, umbilical cord, or maternal circulation is associated with the IRFR.^{1,4,5} Medical conditions characterized by

atypical androgen activity, such as congenital adrenal hyperplasia, complete androgen insensitivity syndrome, and Klinefelter syndrome, show small IRFR.⁶ From their early prenatal period, males typically have shorter index than ring fingers, whereas the fingers are more equal in length in females.⁷

During the last decade, IRFR has been examined in relation to joint osteoarthritis (OA). In several cohorts, OA of the knee, hip, and hand joints was associated with a low IRFR.⁸⁻¹³ It has been suggested that hormonal mechanisms in the development of the OA^{14,15} may explain this relationship.¹⁰ In another cohort, association with knee injury was found, where better sporting activity and aggressive behavior in groups with low IRFR could risk development of the knee OA.¹¹ OA is one of the most prevalent musculoskeletal diseases, but knowledge of its pathogenesis is still limited.

Arthritic involvement of trapeziometacarpal joint (TMCJ) is common in the elderly and can cause significant pain, weakness, and functional limitations.¹⁶ Previous studies that assessed the association between the IRFR and hand OA evaluated the interphalangeal joints of all fingers.¹¹⁻¹³ However, the phalangeal length change caused by OA can affect the measurement of the IRFR. Indeed, the association attenuated after excluding participants with severe OA of the index and the ring fingers.^{11,12} Unlike other fingers, TMCJ would not affect the IRFR; therefore, examining the relationship between IRFR and TMCJ OA

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would minimize the risk of selection bias caused by excluding index and ring finger OA. We carried out a radiographic study on a large population sample who had participated in a Korean Longitudinal Study on Health and Aging (KLoSHA), investigating health, aging, and common geriatric diseases in an elderly Korean population. The aim of this study was to evaluate the association between IRFR and TMCJ OA.

METHODS

Study population. This study was conducted as a substudy of the KLoSHA. The data were collected from September 2005 to August 2006 from residents of Seongnam City, South Korea. The institutional review board of our hospital approved this cohort-based study (IRB No: B-0508/023-003), and informed consent was obtained from all participants.

Candidates were randomly drawn from a list of all participants aged ≥ 65 years. A total 1118 residents were enrolled in this study by letter and telephone, and 696 (62.3%) residents agreed. We obtained posteroanterior hand radiographs of 680 participants out of the 696 enrolled, by using a picture archiving and communication system (PACS; Agfa Impax, Agfa) and recorded the demographic data. We excluded 60 participants who had a history of hand fracture and another 5 participants diagnosed with rheumatoid arthritis. We also excluded 11 participants who had had amputation of any finger. Therefore, 604 participants were included in the analysis. Their mean age was 74.8 (range 65-96) years, of whom 318 (52.6%) were men and 286 (47.4%) were women (Table 1).

Measurement of IRFR. Radiographs of the right hand were used to determine the IRFR, which was measured using 2 methods. The first method was to radiographically measure the length ratio of the right second to fourth phalangeal bones (length of index phalangeal bone [mm]/length of ring phalangeal bone [mm] $\times 100$, "phalangeal IRFR") and metacarpal bones (length of index metacarpal bone [mm]/length of ring metacarpal bone [mm] $\times 100$, "metacarpal IRFR"). The length from the midpoint of the proximal phalanx base to the distal phalanx tip, and the length from the midpoint of the metacarpal bone base to the metacarpal bone tip were used for the calculations. The second method was a visual classification ("visual IRFR"), which classified the IRFR as either type 1 (soft tissue outline of the index fingertip longer than or equal to that of the ring finger) or type 2 (soft tissue outline of the index fingertip shorter than that of the ring finger; Figure 1).

Assessment of TMCJ OA. The TMCJs were evaluated for osteophytes, joint space narrowing (JSN), sclerosis, and cysts. The joints of the right hand were graded from 0 to 4 for OA according to Kellgren-Lawrence (KL) grades: grade 1, minimal osteophytes; grade 2, definite osteophytes and possible cyst; grade 3, moderate osteophytes, JSN and subchondral sclerosis, and

deformity of bone ends; and grade 4, large osteophytes, severe sclerosis, and severe JSN¹⁷ (Figure 2).

Intra- and interobserver reliabilities of measurements. Before taking the radiographic measurements, we held consensus-building and reliability sessions. The radiologic definitions and measurement landmarks were clarified by 2 observers who were orthopedic surgeons with 7 and 3 years of experience. Reliability sessions used intraclass correlation coefficients (ICCs). They were performed on a random sample of 48 subjects after arriving at sample size estimation calculations. The interobserver reliability was determined by the 2 orthopedic surgeons, who measured the phalangeal IRFR, metacarpal IRFR, visual IRFR, and TMCJ OA grading. Each one was unaware of the other observer's findings. The interobserver reliability of each radiographic measurement was calculated as an ICC value among the 2 observers. The radiographs were assigned for each observer in random order. In addition, one of the observers repeated the above radiographic measurements 3 weeks later, and the intraobserver reliability was confirmed.

Statistical analysis. Prior precision analysis was done to determine minimal sample sizes for reliability testing. A random sample of 48 subjects who were each measured 2 times produced a 2-sided 95% CI with a width of 0.2 when the estimated ICC was 0.8, according to Bonett approximation.¹⁸

Descriptive statistics (mean, SD, and percentages) were used to evaluate the IRFR and the TMCJ OA. A KL grade of 2 was used as a criterion for diagnosis of TMCJ OA, and a KL grade of 3 for severe TMCJ OA.¹⁷ A paired *t* test and ANOVA were done to assess differences in continuous variables, such as radiographic IRFR. Chi-square tests were used to evaluate the differences according to the TMCJ OA grades in categorical variables, such as visual IRFR. Logistic regression analysis was performed to find the odds ratios (ORs) for each variable and the 95% CIs for presence of TMCJ OA and severe TMCJ OA. The diagnostic accuracy of using the IRFRs to detect the TMCJ OA was assessed using a receiver-operating characteristic (ROC) curve analysis. Multivariable logistic regression analysis was performed to find the adjusted OR for TMCJ OA and severe TMCJ OA, with age, gender, phalangeal and metacarpal IRFR, and visual IRFR as independent variables. A variance inflation factor was measured to check the multicollinearity between the independent variables. All statistical analyses were performed using IBM SPSS Statistics version 26.0 for Windows (IBM Corp), and a *P* < 0.05 was considered statistically significant.

Sensitivity analysis. In addition, because of concerns of hand OA possibly affecting the phalangeal and visual IRFRs, we selected those participants without radiographic JSN in the distal interphalangeal (DIP) and/or proximal interphalangeal (PIP) joints of the index and ring finger, and performed the same statistical analysis.

RESULTS

Population characteristics. Radiographic evaluation for TMCJ

Table 1. Characteristics of the study sample according to TMCJ OA.

| | Total, N = 604 | Normal, n = 492 | OA, n = 112 | <i>P</i> |
|-------------------------------|----------------|-----------------|-------------|--------------|
| Age, yrs, mean (SD) | 74.8 (8.4) | 74.3 (9.4) | 77.1 (8.4) | 0.001 |
| Gender, n (%) | | | | 0.53 |
| Male | 318 (52.6) | 256 (52.0) | 62 (55.4) | |
| Female | 286 (47.4) | 236 (48.0) | 50 (44.6) | |
| Phalangeal IRFR, %, mean (SD) | 91.3 (3.3) | 91.4 (3.5) | 90.9 (2.2) | 0.18 |
| Metacarpal IRFR, %, mean (SD) | 116.7 (3.6) | 116.9 (3.5) | 115.8 (4.0) | 0.005 |
| Visual IRFR, n (%) | | | | 0.04 |
| Type 1 | 300 (49.7) | 254 (51.6) | 46 (41.1) | |
| Type 2 | 304 (50.3) | 238 (48.4) | 66 (58.9) | |

Values in bold are statistically significant. IRFR: index-to-ring finger ratio; OA: osteoarthritis; TMCJ: trapeziometacarpal joint.



Figure 1. Posteroanterior hand radiographs were used to calculate the index-to-ring finger ratio (IRFR) through radiographic and visual methods. For the radiographic IRFR, the ratio of the length of the second to fourth phalangeal bones and metacarpal bones were measured to obtain phalangeal IRFR and metacarpal IRFR, respectively (arrows). For the visual IRFR, soft tissue outlines of the index fingertip and of the ring finger were compared. Longer ring finger than index finger (right panel), was defined as type 2 IRFR, and index finger longer than or equal to ring finger was defined as type 1 IRFR (left panel).



Figure 2. TMCJ OA was evaluated from the posteroanterior hand radiographs according to the Kellgren-Lawrence grading system. (A) Grade 1 was defined to have minimal osteophytes. (B) Grade 2 had definite osteophytes (white arrow) and possible cyst (black arrowhead), and was the cut-off for diagnosis of TMCJ OA. (C) Grade 3 had JSN, subchondral sclerosis, and deformity of bone ends, and was the cut-off for severe TMCJ OA. (D) Grade 4 had large osteophytes, severe sclerosis, and severe JSN. JSN: joint space narrowing; OA: osteoarthritis; TMCJ: trapeziometacarpal joint.

OA, according to the KL grade, demonstrated grade 0 in 181 out of the 604 participants (30.0%), grade 1 in 311 (51.5%), grade 2 in 79 (13.1%), grade 3 in 31 (5.1%), and grade 4 in 2 (0.3%). Overall, we diagnosed TMCJ OA (a KL grade of ≥ 2) in 18.5% of them (112 out of 604, 62 men and 50 women), and severe

TMCJ OA (a KL grade of ≥ 3) in 5.5% (33 out of 604, 17 men and 16 women). The correlation between age and presence of TMCJ OA was significant ($P < 0.001$; Table 1).

Interobserver and intraobserver reliability. Interobserver reliabilities of phalangeal IRFR, metacarpal IRFR, visual IRFR,

and TMCJ OA grades were 0.99 (95% CI 0.99-0.997), 0.95 (95% CI 0.91-0.97), 0.96 (95% CI 0.94-0.98), and 0.92 (95% CI 0.86-0.96), respectively, whereas their intraobserver reliabilities were 0.99 (95% CI 0.98-0.99), 0.93 (95% CI 0.88-0.96), 0.92 (95% CI 0.86-0.96), and 0.93 (95% CI 0.88-0.96), respectively (data not shown).

Correlation between IRFR and TMCJ OA. According to the radiographic evaluation, the phalangeal IRFR averaged 91.3% (SD 3.3), and the metacarpal IRFR averaged 116.7% (SD 3.6). According to the visual classification, 300 participants (49.7%) were classified into type 1, and 304 participants (50.3%) into type 2. Their distributions according to the TMCJ OA are shown in Figure 3.

The presence of TMCJ OA was associated with metacarpal IRFR (OR 0.93, 95% CI 0.88-0.98) and type 2 IRFR (OR 1.53, 95% CI 1.01-2.32). The cut-off points of 116.4 for metacarpal IRFR achieved the highest possible sensitivities and specificities in detecting the presence of TMCJ OA. Multivariable regression analysis showed that age (adjusted OR 1.04, 95% CI 1.01-1.06) and metacarpal IRFR (adjusted OR 0.94, 95% CI 0.88-0.99) were the risk factors. Severe TMCJ OA was associated with phalangeal IRFR (OR 0.85, 95% CI 0.72-0.999), metacarpal IRFR (OR 0.90, 95% CI 0.82-0.98), and type 2 IRFR (OR 4.63, 95% CI 1.87-11.43). The cut-off points of 90.8 for phalangeal IRFR and 116.0 for metacarpal IRFR achieved the highest possible sensitivities and specificities in detecting severe TMCJ OA. Multivariable regression analysis revealed that age (adjusted OR 1.08, 95% CI 1.03-1.12) and type 2 IRFR (adjusted OR 3.07, 95% CI 1.13-8.33) were the risk factors (Table 2, Figure 4).

Sensitivity analysis in patients without finger OA. Because index and ring finger OA may affect phalangeal lengths and thus influence the association between the IRFR and TMCJ OA, sensitivity analysis was performed for participants without JSN in the second and the fourth DIP and PIP joints (n = 523, 86.6%). The association of visual IRFR with the presence of TMCJ OA, and that of phalangeal IRFR with severe TMCJ OA shown

in all subjects (Table 2) disappeared in the sensitivity analysis. However, multivariable regression analysis showed similar results with age (OR 1.03, 95% CI 1.002-1.06) and metacarpal IRFR (OR 0.93, 95% CI 0.88-0.99) being the risk factors of TMCJ OA, and age (OR 1.07, 95% CI 1.01-1.12) and type 2 IRFR (OR 4.63, 95% CI 1.21-17.64) being the risk factors of severe TMCJ OA (Supplementary Table S1, available from the authors upon request).

DISCUSSION

In this large population-based study, we observed a significant association between low IRFR and the TMCJ OA. TMCJ OA rates increased with old age and low metacarpal IRFR, and severe TMCJ OA rates increased with old age and type 2 IRFR. Because severe OA in the index and ring fingers might affect phalangeal lengths, we performed a sensitivity analysis after excluding these populations. However, an increase in the risk in populations with low IRFR was still present.

Assessment of the association between IRFR and hand OA has been attempted by some groups using population-based cohorts.¹¹⁻¹³ Haugen et al evaluated phalangeal and metacarpal IRFR to find that hand OA is associated with low phalangeal IRFR, but not with metacarpal IRFR.¹¹ Visual IRFR was assessed by de Kruijff et al, and participants with type 2 IRFR had a 1.64-fold increase in risk for hand OA.¹² Kalichman et al, by defining the hand OA using the number of affected joints and total OA score, also showed that populations with type 2 IRFR are involved with more severe hand OA.¹³ These 3 studies identically evaluated the hand OA in all 5 fingers. Observation of only TMCJ OA in our present study was a novel attempt, and we were able to detect a significant association between IRFR and hand OA.

Patients with TMCJ OA had an 8.4-fold greater risk for other types of hand OA than those without.¹⁹ Correspondingly, severe OA of the index finger could be seen with a higher percentage of our participants having severe TMCJ OA (15 out

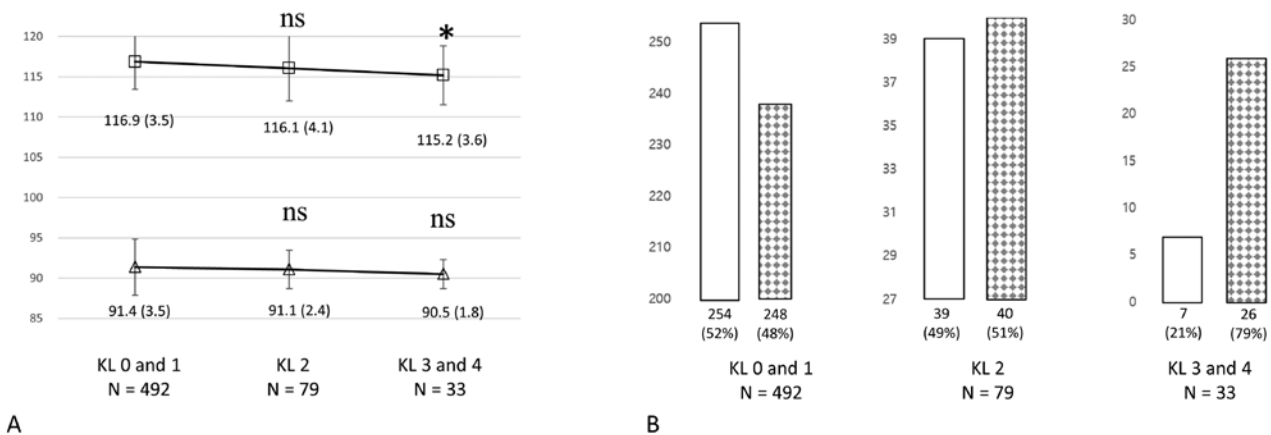


Figure 3. (A) Distributions of the radiographic index-to-ring finger ratio (IRFR) were expressed by triangles (phalangeal IRFR) and squares (metacarpal IRFR) according to the KL grade. The *P* values between the IRFR were calculated using ANOVA, and difference between groups with statistical significance was expressed as asterisk. (B) Distributions of type 1 IRFR and type 2 IRFR (tiles) were expressed in box plot according to the KL grade. Percentages are shown in the parentheses. KL: Kellgren-Lawrence; ns: not significant.

Table 2. Regression outcomes for the presence of TMCJ OA and severe TMCJ OA.

| | Presence, n = 112 | Absence, n = 492 | Univariable Regression Model | | | Multivariable Regression Model | | |
|----------------------------|----------------------|---------------------|------------------------------|-----------|--------------|--------------------------------|-----------|--------------|
| | | | OR | 95% CI | P | Adjusted OR | 95% CI | P |
| Age, yrs, mean (SD) | 77.1 (8.4) | 74.3 (9.4) | 1.04 | 1.02-1.06 | 0.001 | 1.04 | 1.01-1.06 | 0.004 |
| Female, n (%) | 50 (45) | 236 (48) | 0.88 | 0.58-1.32 | 0.53 | 0.89 | 0.58-1.36 | 0.59 |
| Phalangeal IRFR, mean (SD) | 90.9 (2.2) | 91.4 (3.5) | 0.94 | 0.87-1.03 | 0.18 | 0.97 | 0.89-1.06 | 0.56 |
| Metacarpal IRFR, mean (SD) | 115.8 (4.0) | 116.9 (3.5) | 0.93 | 0.88-0.98 | 0.004 | 0.94 | 0.88-0.99 | 0.02 |
| Type 2 IRFR, n (%) | 66 (59) | 238 (48) | 1.53 | 1.01-2.32 | 0.04 | 1.21 | 0.75-1.94 | 0.44 |

| | Severe, n = 33 | Not Severe, n = 492 | Univariable Regression Model | | | Multivariable Regression Model | | |
|----------------------------|-------------------|------------------------|------------------------------|------------|----------------|--------------------------------|-----------|--------------|
| | | | OR | 95% CI | P | Adjusted OR | 95% CI | P |
| Age, yrs, mean (SD) | 80.9 (7.7) | 74.3 (9.4) | 1.09 | 1.04-1.13 | < 0.001 | 1.08 | 1.03-1.12 | 0.001 |
| Female, n (%) | 16 (48) | 236 (48) | 1.02 | 0.50-2.07 | 0.95 | 1.06 | 0.50-2.24 | 0.88 |
| Phalangeal IRFR, mean (SD) | 90.4 (1.7) | 91.4 (3.5) | 0.85 | 0.72-0.999 | 0.048 | 0.95 | 0.79-1.15 | 0.61 |
| Metacarpal IRFR, mean (SD) | 115.1 (3.7) | 116.9 (3.5) | 0.90 | 0.82-0.98 | 0.01 | 0.92 | 0.84-1.00 | 0.05 |
| Type 2 IRFR, n (%) | 26 (81) | 238 (48) | 4.63 | 1.87-11.43 | < 0.001 | 3.07 | 1.13-8.33 | 0.03 |

Values in bold are statistically significant. OR: odds ratio; IRFR, index-to-ring finger ratio; TMCJ: trapeziometacarpal joint.

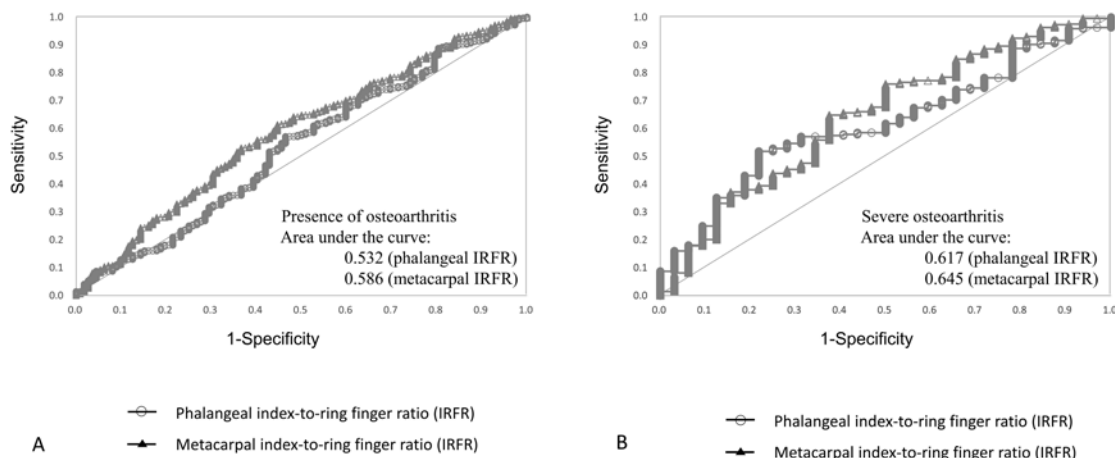


Figure 4. Receiver-operating characteristic curves for the prediction of (A) presence of TMCJ OA, and (B) severe TMCJ OA. IRFR: index-to-ring finger ratio; OA: osteoarthritis; TMCJ: trapeziometacarpal joint.

of 33 participants, 45%) than with TMCJ OA (30 out of 112 participants, 27%; Figure 2). The involvement of index finger OA, which shortens the index finger, can increase the association between the visual IRFR and the TMCJ OA. Indeed, according to the sensitivity analysis after excluding patients with severe OA in the index and the ring fingers, the association between phalangeal IRFR and severe TMCJ OA disappeared in the univariable regression model, as expected from previous literature.^{11,12} However, the association with type 2 IRFR was still present.

The evaluation of IRFR has been made using either the metacarpal bones, phalanges, or visual classification. In a previous study by Robertson et al that evaluated the IRFR from radiographs of 3172 participants, only 84% and 71.3% could be evaluated using the phalangeal and visual measurement, respectively, because of arthritic involvements or malpositioning such as radial or ulnar deviation of wrists or splaying of the fingers, whereas

99% could be evaluated using the metacarpal measurements.²⁰ The phalangeal and visual IRFR may be used in younger populations with less common hand OA and trauma. To examine their associations with hand OA, it is necessary to exclude patients with severe OA in their index and ring fingers.¹¹ The metacarpal IRFR, on the other hand, is not influenced by interphalangeal OA. Therefore, examinations of the association between IRFR and OA would benefit from examining the metacarpal IRFR. A case-control study by Zhang et al found a significant association between metacarpal IRFR and knee OA.⁹ Our study indicates that metacarpal IRFR can better identify patients with TMCJ OA than phalangeal IRFR.

Because the IRFR is a possible indicator of prenatal testosterone exposure, hormonal mechanism on one's vulnerability to joint OA can be deduced. Whereas estrogen is protective from OA in mice, testosterone exacerbates it.¹⁵ Hormone therapies are

suggested to show some preventive effects on knee and hip OA occurrences in humans.^{19,21} Although their effect was unclear in TMCJ OA,²² there is other evidence on the role of hormonal factors in TMCJ OA. For example, an abrupt increase in the prevalence of TMCJ OA could be found in women when they reached postmenopausal status.²² After adjusting for other possible risk factors, such as age and sex, BMI is proportional to TMCJ OA, with an OR of 1.29 per 5-kg/m² increments.¹⁶ Ligamentous laxity in the structures of TMCJ contributes to both the development and aggravation of OA, on which estrogen or relaxin are known to have an effect.²³

This study has some limitations. First, the hand radiographs were taken primarily for the assessment of OA. To assess the IRFR, more appropriate positioning of the hand might have been required.²⁰ However, the ICC calculated for the IRFR measurements showed excellent reproducibility using our radiographic images. Second, the IRFR was measured only in the right hand. In the literature, however, there is evidence that the right-hand measurements better indicate fetal androgenization than the left.⁴ Third, we could not collect other demographic factors from the cohort such as occupation or activity level. As these are associated with IRFR and could influence TMCJ OA prevalence, further analyses should examine them. Fourth, because we used cross-sectional data to examine the relationship of finger length with TMCJ OA, directionality cannot be assessed.

In conclusion, this study of the KLoSHA cohort, conducted with subjects aged ≥ 65 years who were randomly recruited from the general population, shows significant association between low IRFR and TMCJ OA. In both elderly Korean men and women, radiographic—specifically metacarpal—IRFR is associated with the presence of TMCJ OA, and visual IRFR with severe TMCJ OA. These findings suggest that IRFR might serve as an easily measurable biomarker to identify patients vulnerable to TMCJ OA.

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