Relationship of Serum Relaxin to Generalized and Trapezial-Metacarpal Joint Laxity

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Purpose The reproductive hormone relaxin acts to loosen pelvic ligaments in preparation for childbirth and is thought to be a mediator of joint laxity. The purpose of this study was to evaluate the correlation of serum relaxin with radiographic laxity at the trapezial-metacarpal joint and with generalized joint laxity.

Methods We enrolled 289 healthy subjects prospectively. Participants completed a demographic questionnaire and were examined for generalized joint hypermobility using the Beighton-Horan scale. Stress radiographs of the trapezial-metacarpal joint were obtained in 163 subjects (56%). Blood samples were collected, and serum relaxin was measured for 287 subjects using enzyme-linked immunosorbent assay for human relaxin-2.

Results The mean serum relaxin level among all subjects was 1.84 pg/mL (range, 0–45.25 pg/mL). Relaxin was not detectable in 166 of 287 samples, whereas the mean serum relaxin level among the 121 subjects with a detectable relaxin level (of 287 total relaxin samples) was 4.37 pg/mL (range, 0.46–45.25 pg/mL). Mean trapezial-metacarpal subluxation ratio scores were higher among those with a detectable relaxin level compared to those without a detectable relaxin level (0.34 vs 0.30 pg/mL). The average Beighton-Horan laxity score was 1.8 (range, 0–9). There was no correlation between generalized joint laxity measures and serum relaxin levels.

Conclusions In a large volunteer population, we demonstrated a relationship between circulating relaxin and trapezial-metacarpal joint laxity. However, we were unable to show a direct link between serum relaxin and generalized joint laxity. *(J Hand Surg 2013;38A:721–728. Published by Elsevier Inc. on behalf of the American Society for Surgery of the Hand.)*

Type of study/level of evidence Prognostic II.

Key words Hypermobility, laxity, relaxin, stress view, trapezial-metacarpal.

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Laxity and attenuation of the supporting ligaments of the basilar thumb joint has been postulated as a potential cause of trapezial-metacarpal (TM) osteoarthritis.[1] Without joint stability allowing congruent loading of the joint surfaces, abnormal forces on the joint cartilage during grip and pinch may lead to eventual cartilage deterioration and osteoarthritis of the TM joint.

The baseline degree of joint mobility and laxity at the thumb and at other joints varies based on sex and age. It has been shown that female subjects demonstrate higher scores on standardized laxity testing than age-matched male subjects.[2,3] Younger age is also associated with a higher degree of joint laxity, supported by studies of adolescents and young adults as compared to older subjects.[4,5] At the TM joint, greater generalized laxity is associated with higher radiographic laxity with joint stress views.[2] Other studies have shown laxity to be associated with joint injury. Myer et al noted a 5-fold increased risk of anterior cruciate ligament (ACL) rupture in a prospectively followed cohort when knee hyperextension was noted before injury.[6] Cameron et al reported that subjects with generalized joint hypermobility were nearly 2.5 times as likely to have a history of shoulder instability than those without generalized joint hypermobility.[7]

Hormonal factors have been proposed as another mediating factor in joint mobility. Relaxin is a peptide hormone best known for its role in softening the cervix and pelvic ligaments in preparation for parturition.[8] On the molecular level, relaxin binds to its receptor, a membrane protein,[9] and mediates upregulation of matrix metalloproteases, which act to degrade collagen and extracellular matrix. Relaxin has also been shown to mediate expression of vascular endothelial growth factor.[10,11] Relaxin is also produced in nonpregnant women,[12] as well as men,[13] although at far lower levels. Recent studies have shown that relaxin may have a cardioprotective effect in heart failure[14] and that this hormone may act to reverse fibrosis in the kidney.[15] Furthermore, the relaxin knockout mouse is a model of progressive fibrosis, suggesting that relaxin regulates collagen deposition.[16]

Dragoo et al characterized relaxin receptors on ACL fibroblasts and showed weakening of the ACL in response to *in vivo* infusion of relaxin in biomechanical testing in an animal model.[17,18] In a prospective evaluation of 128 female collegiate athletes, those who sustained ACL tears had higher serum relaxin than those who did not.[19] Other investigators evaluated serum relaxin level in relation to knee laxity measured with a KT-1000 arthrometer (MedMetric Corporation, San Diego, CA) and were unable to show a correlation.[20] In light of these conflicting studies, the purpose of this study was to prospectively evaluate a large group of volunteer subjects of both sexes and across a range of ages, to determine whether there was an association between relaxin levels and standardized measures of generalized laxity and radiographic basal thumb laxity.

MATERIALS AND METHODS

Subject recruitment and power analysis

After obtaining institutional review board approval and informed consent, we recruited 289 subjects within 2 local university communities. We prospectively enrolled 135 men and 154 women. The average age was 47 years (range 18–91 y). Subjects were divided by sex into 3 age groups: 18 to 39 years, 40 to 59 years, and 60 years or greater. Exclusion criteria were subjects with diagnoses of TM osteoarthritis, inflammatory arthritis, collagen vascular disease, current musculoskeletal injury, and pregnant or lactating women, as these factors may affect joint laxity independently.

A power analysis was performed to estimate the number of subjects required to detect differences by sex, age, and the interaction between sex and age. The analysis was based on clinical data indicating a large effect for laxity by sex ($d = 0.83$). Data were not available regarding differences in laxity by age group; hence, the analysis was based on a medium effect size[21] ($f = 0.25$). To detect $r = 0.30$, given alpha $= 0.05$ and power $= 0.80$, a total of 84 subjects would be required (14 per group). Because relaxin levels may not be detectable in all subjects, a larger number of subjects were enrolled.

Study information

Each subject was evaluated for generalized joint laxity using the Beighton-Horan index, a 9-point scale evaluating joint mobility by testing elbow, metacarpophalangeal, and knee hyperextensibility; ability to passively oppose each thumb to the ipsilateral forearm; and trunk flexibility[22] (Figs. 1, 2). Each person also filled out questionnaires that covered medical comorbidities.

Stress view radiographs of the bilateral TM joints were obtained for the first 163 subjects, using a previously described technique in which a posteroanterior radiograph is obtained while the subject presses the parallel thumbnails as well as the interphalangeal and metacarpophalangeal joints together.[23] Radiographs were not obtained in the rest of the cohort, which was enrolled at a separate institution. The stress view sub-