The prevalence of calcifications at the origin of the extensor carpi radialis brevis increases with age

Running Title: THE PREVALENCE OF ECRB CALCIFICATIONS

ABSTRACT

Background: Enthesopathy of the extensor carpi radialis brevis origin [eECRB] is a common idiopathic, non-inflammatory disease of middle age that is characterized by excess glycosaminoglycan production and frequently associated with radiographic calcification of its origin. The purpose of our study was to assess the relationship of calcification of the ECRB and advancing age.

Methods: We included 28,563 patients who received an elbow radiograph and assessed the relationship of calcifications of the ECRB identified on radiograph reports with patient age, sex, race, affected side, and ordering indication using multivariable logistic regression.

Results: Calcifications of the ECRB were independently associated with age (OR: 1.04; p<0.001); radiographs ordered for atraumatic pain (OR: 2.6; p<0.001) or lateral epicondylitis (OR: 5.5; p<0.001); and Hispanic ethnicity (OR: 1.5; p<0.001) and less likely to be found at the left side (OR: 0.68; p<0.001). Similarly, incidental calcifications of the ECRB, those on radiographs not ordered for atraumatic pain or lateral epicondylitis, were independently associated with age (OR: 1.03; p<0.001) and Hispanic ethnicity (OR: 1.5; p<0.024) and less likely to be found on the left side (OR: 0.71; p<0.001).

Conclusions: We observed that about nine percent of people have ECRB calcification by the time they are in their sixth decade of life and calcifications persist in the absence of symptoms which supports the idea that eECRB is a common, self-limited diagnosis of middle age.

Level of Evidence: Level II; Retrospective prognostic study
Keywords: extensor carpi radialis brevis; lateral epicondyle; calcification; enthesopathy; tennis elbow; lateral epicondylitis; radiograph; prevalence
Tennis elbow and lateral epicondyritis are two common terms that refer to enthesopathy of the extensor carpi radialis brevis origin (eECRB). eECRB is an idiopathic, non-inflammatory disease that presents with pain over the lateral elbow. The condition occurs primarily in patients 35 to 54 years of age and is self-limited (1-4). On histology eECRB is characterized by excess glycosaminoglycan production (mucoid degeneration) (5-7). Calcification of the extensor carpi radialis brevis [ECRB] origin at the lateral epicondyle is common with eECRB and these calcifications might be permanent (5, 8-11).

Given that eECRB is common and often associated with calcifications, radiographic calcification of the extensor carpi radialis brevis (ECRB) might be expected to accumulate with age. In this sense the prevalence of calcification of the ECRB origin with age may serve as a surrogate for the cumulative lifetime prevalence of eECRB.

Our study tested the primary null hypothesis: the prevalence of ECRB calcifications is not associated with age accounting for other factors. Secondarily, we tested the null hypothesis: the prevalence of incidental calcifications of the ECRB is not related to age accounting for other factors.
METHODS

Study design and population

After obtaining IRB approval, we searched the patient data registry of two tertiary care hospitals for all patients who had an elbow radiograph with at least two views (CPT codes 73070 and 73080) between January 1, 2005 and January 1, 2015. We included every patient greater than 18 years old who received an elbow radiograph at one of the two institutions. All patients with cancelled radiographs, radiographs completed at an outside institution, incomplete radiograph reports or radiographs ordered for a clinical mass or malignancy were excluded. All 28,563 eligible patients were included in this study. We only included the first elbow radiograph report for each patient to comply with the statistical assumption of independence.

Outcomes

Our primary outcome measure was calcific enthesopathy around the lateral epicondyle. We searched the first elbow radiograph report of every eligible patient for mention of calcifications, enthesopathy, the lateral epicondyle or the common extensor tendon, including synonyms and common misspellings: 4,983 (17%) reports were flagged and 1,236 (4.3%) of these patients had probable calcifications or changes at the lateral epicondyle not likely caused by trauma, inflammatory diseases, and/or arthritis. We then manually reviewed the complete report text of all 1,236 patients with probable changes in the extensor tendon and found that 958 patients had an impression of calcification of the extensor tendon, 220 had findings consistent with calcifications of the extensor tendon, and 58 did not have calcifications within the extensor tendon. To assess the accuracy of our text search we randomly sampled 100 patients identified as
not having calcifications of the extensor tendon at the lateral epicondyle and manually reviewed
the report text for each patient. None of the 100 patient reports we reviewed had mention of
extensor tendon calcification within their reports. To assess the accuracy of the radiology reports,
two research fellows reviewed the elbow radiographs of 100 randomly selected patients with
reported calcifications of the ECRB and 100 patients without reported calcifications. Of the 100
patients with calcifications in their report, 81 patients had calcifications about the lateral
epicondyle on their radiograph. Of the 100 without calcifications noted in the report text, 8
patients had calcifications on their radiographs.

Our secondary outcome measure was incidental (i.e. non-symptomatic) common extensor
tendon calcifications, which included all radiographs not ordered to assess lateral epicondylitis or
atraumatic elbow pain.

Our explanatory variables were age as a continuous variable, and sex, race, affected side,
and the primary ordering indication for the radiograph as categorical variables. We identified
patient age, sex, and race from the medical record and extracted the indication from the
radiology report text.

The primary ordering indication for an elbow radiograph was determined by searching
the “indications” section of each elbow radiograph report. When the primary ordering indication
was unclear (n = 36), the indication was manually reviewed. We identified patients who had an
indication of lateral epicondylitis or atraumatic elbow pain to determine which calcifications
were incidental or asymptomatic. We included patients with primary ordering indications of
arthritis, tendinopathies, other painful conditions or isolated stiffness and/or swelling in a group
called atraumatic pain. There were 16,564 (58%) radiographs ordered to assess trauma or follow-
up of a surgery for trauma; 10,154 (36%) radiographs were ordered to assess atraumatic elbow
pain; 949 (3.3%) radiographs did not have an ordering indication in the report, 522 (1.8%) were ordered for lateral epicondylitis or a synonym; and 374 (1.3%) radiographs were ordered for a diagnosis that did not fit into another category, e.g. – foreign body, evaluation of dialysis fistula, neuropathy. (Appendix A, Table I)

Statistical analysis

We report frequencies with percentages for categorical variables and mean with standard deviation (SD) for continuous variables.

We used multivariable logistic regression analysis to assess the association between each explanatory variable and the response variables while adjusting for potential confounding. We report the odds ratio (OR), standard error (SE), and p-value for the regression analyses; a two-tailed p-value below 0.05 is considered significant.

Baseline characteristics

The eligible patients averaged 50 (SD=18) years of age; 52% were men; and 75% were white. Radiology reports addressed the right elbow in 13,568 (48%) patients, the left elbow in 12,716 (45%) patients, and in 2,279 (8%) patients the report did not identify a side or described bilateral elbows. The most common ordering indication was trauma (Table I). Symptomatic and incidental calcifications peaked in prevalence when patients were 60 to 80 years of age. In our study population, 1,178 of 28,563 patients (4.1%, 95% confidence interval [95% CI], 3.9 – 4.4) had elbow radiograph reports describing elbow calcifications within the extensor tendon. When we excluded all patients with radiographs ordered for lateral epicondylitis or atraumatic pain
(37% [10,676 out of 28,563]) we found that 486 of 17,887 patients had incidental extensor tendon calcifications identified on radiograph (2.7%, 95% CI, 2.5 – 3.0; Table II).
RESULTS

Age (OR 1.04; p < 0.001; 4% increase in likelihood per year over age 18); radiographs ordered for atraumatic pain (OR 2.6; p < 0.001) or lateral epicondylitis (OR 5.5; p < 0.001); and Hispanic ethnicity (OR 1.5; p < 0.001) were independently associated with calcifications of the ECRB. The left elbow (OR 0.68; p < 0.001) was less likely to have calcifications of the ECRB.

(Table III and Figure 1)

Age (OR 1.03; p < 0.001; 3% increase in likelihood per year over age 18) and Hispanic ethnicity (OR 1.5; p < 0.024) were independently associated with incidental calcifications of the ECRB. Incidental calcifications were less likely to be found in the left ECRB (OR 0.71; p < 0.001; Table III and Figure 1).
DISCUSSION

Calcifications about the lateral epicondyle are associated with eECRB and thought to be permanent (5, 8-11). The prevalence of calcification on elbow radiograph may reflect the cumulative lifetime incidence of clinical eECRB. We found that each year of age increases the odds of having ECRB calcifications. We also found that calcifications are more common on the right lateral epicondyle and in people of Hispanic ethnicity.

Our study has certain limitations. First, our retrospective cohort study design can only identify a relationship between age and calcification; it cannot address the specific cause of calcification. Second, we relied on reports written by the radiologists at the two institutions we reviewed. In the reports we reviewed, the calcifications of the ECRB were not systematically described with the same language as all radiologists from our two institutions were included. To ensure we captured all reports mentioning calcification of the ECRB, we included search terms for calcification or the ECRB and all synonyms and any common misspellings.

Third, we relied on searching report texts to identify the affected side and radiograph ordering indication. Based on manual review of the identified reports we are confident our search terms accurately identified indication and the affected side listed in the reports. However, we believe our estimate of incidental calcifications is conservative because we excluded all patients with atraumatic pain or epicondylitis as an indication. The one-word ordering indication “pain” was very common and we had no way of knowing what part of the elbow the ordering provider referred to so we assumed all radiographs ordered for “pain” could represent eECRB. This may have led to exclusion of patients with symptomatic medial epicondylitis or ulnar neuropathy with incidental calcific enthesisopathy. Fourth, we relied on radiologists reporting calcifications in each radiograph and there may be inter-radiologist variability of which we are unaware. The text
descriptions were reasonably accurate on manual review of the radiographs, but there is some
degree of error introduced by variation of radiographic interpretation. Some radiologists may
omit commenting on calcifications which would decrease the prevalence. In addition, when
double-checking radiographs, we used a different software system to view the DICOM images
than the radiologists. It is possible that the radiologists were able to see calcifications that we
could not see because they had a superior DICOM viewing platform. We do not anticipate that
any over or under call would be significantly different than other institutions and or bias the
prevalence based on age, side, race or ordering indication. Fifth, there may be differences in the
quality of the radiographs read by radiologist in this study as our cohort includes patients who
received radiographs over a ten-year period. Sixth, the majority of our cohort was white and
lived in the [redacted] and therefore these results might not be generalizable to
all populations or geographical regions. However, these limitations are counterbalanced by the
number of patients in our research database. The large number of patients, radiologists, and
institutions mitigates variation of radiographic interpretation and reporting. In addition, the large
number of patients allows for a more robust statistical analysis than studies with smaller patient
cohorts.

We found all calcifications of the ECRB were predicted by advancing age, the right
element and Hispanic ethnicity. Previous studies were set up to suggest that calcifications of the
ECRB are related to symptomatic eECRB. For instance, Edelson et al documented calcification
on CT scans in 3 of 20 patients with no elbow symptoms and 6 of 10 patients with long-standing
element symptoms \((p = 0.003)\), but there was no difference in patients with symptoms for less than
one year \((p = 0.73)\) \((9)\). Similarly, Levin et al compared ultrasound images of 25 elements with
symptoms of eECRB to 32 asymptomatic elements and found calcifications of the common
extensor tendons (OR 6.2; p < 0.05) and adjacent bone irregularity (OR 4.8; p < 0.05) were associated with symptoms. However, patients with symptomatic elbows were significantly older than asymptomatic elbows (10). It is difficult to compare our radiographic prevalences to prevalences based on symptoms such as Hamilton et. al., (twice as common on the right side; similar numbers of men and women) (1) and Owens et al (fewer black patients) (12). In our opinion, the racial findings are likely spurious because most of the patients were white.

Secondarily we found that incidental calcifications of the ECRB were predicted by advancing age, the right elbow and Hispanic ethnicity. The association of age with calcification supports the theory that the pathophysiological changes persist and accumulate in aging populations even as the symptoms resolve (Table II and Figure 1). This is supported by other studies of the extensor tendon. Zeisig et al who found persistent changes in 13 of 20 sonograms of the extensor origin after resolution of symptoms (11). Jaén-Díaz examined the common extensor tendon using ultrasound in 240 patients and noted that 48% with changes remembered symptoms consistent with eECRB compared to 2% in patients with normal elbows (p < 0.001) (13). Van Leeuwen et al studied MRI signal changes of the ECRB and found that age was independently associated with ECRB enthesopathy (OR 1.04; p < 0.001) and that the prevalence of signal changes increases to 16% in patients over age 71 (14). MRI changes are likely more often detected than calcifications and this is probably a more accurate reflection of the prevalence of eECRB.
CONCLUSION

The observation that about nine percent of the population have calcifications of the ECRB origin by the time they are in their sixth decade of life supports the idea eECRB is a common, self-limited disease of middle age (1, 2, 9, 11, 13). Combined with similar MRI data and the weight of current best evidence, patients can be counseled that evidence to date support the concept that eECRB is common and self-limiting.


FIGURE LEGENDS

Figure 1: Prevalence of calcification of the extensor carpi radialis brevis and incidental calcifications of the extensor carpi radialis brevis versus age.

Table I: Baseline characteristics of study population.

Table II: Prevalence of calcifications of the ECRB with age.

Table III: Predictors of common extensor tendon calcifications.

Appendix A: Indication search strings.