Familial Clustering of Thumb Carpometacarpal Osteoarthritis in a Large Statewide Cohort

Nikolas H. Kazmers MD MSE[1], Cathy Gavile PhD[1], Huong D. Meeks PhD[2], David Z Yu MS[2], Kendra A. Novak BS[3], Tyler Barker PhD[4], Michael J Jurynec PhD[1]

(1) University of Utah Department of Orthopaedics; (2)Huntsman Cancer Institute – Utah Population Database; (3) University of Utah School of Medicine; (4) Intermountain Healthcare

INTRODUCTION

- The pathogenesis of thumb carpometacarpal osteoarthritis (CMCOA) is partly genetic, however the exact genes and the increased risk of undergoing future surgery conferred to a family member of an affected individual remains unclear.

- Therefore, our primary purpose was to quantify the elevation in familial risk of thumb CMC OA among first-, second-, and third-degree relatives of affected individuals.

- Secondarily, we identified demographic and comorbidity risk factors associated with thumb CMCOA.

MATERIALS & ETHODS

- Patients diagnosed with, and surgically treated for, thumb CMCOA were identified by searching the Utah Population Database (UPDB).
  - The UPDB is a comprehensive statewide database with comprehensive genealogical records that contains pedigrees dating back to the early 1800s which are linked to 31 million medical records for 11 million patients from 1996 to the present.

- Thumb CMCOA patients were mapped to pedigrees to identify high-risk families with an increased incidence of thumb CMCOA relative to control pedigrees, as defined by a familial standardized incidence ratio ≥ 2.0.

- The magnitude of familial risk of thumb CMCOA in related individuals was calculated using Cox regression models with Huber-White sandwich estimator of variance of regression parameters to correct for the non-independence of observations within families.

- Association of thumb CMCOA risk factors was analyzed using conditional logistic regression.

RESULTS

- We identified 4227 affected individuals linked to 550 unrelated high-risk pedigrees with increased incidence of thumb CMCOA.

- Familial risk of thumb CMCOA was significantly elevated among individuals with an affected first-degree (RR 3.66, 95% CI 2.73 to 4.90; p < 0.001) or third-degree relative (RR 1.19, 95% CI 1.01 to 1.40; p < 0.001), but not second-degree relative (RR 1.25; 95% CI 0.89 to 1.76; p = 0.197).

- Independent of familial involvement, White race, non-Hispanic ethnicity, obesity, and current or past tobacco use were associated with a significantly greater risk of thumb CMCOA (Table 1).

Table 1: Risk Factors Associated with Thumb CMC OA

Factor	Relative Risk (RR)	95% Confidence Interval		P-value
		Lower Limit	Upper Limit	
Race (Non-white vs. White)	0.41	0.33	0.51	< 0.001
Race (Unknown vs. White)	4.80	3.95	5.83	< 0.001
Ethnicity (Hispanic vs. Non-Hispanic)	0.85	0.78	0.93	< 0.001
Ethnicity (Unknown vs. Non-Hispanic)	0.69	0.59	0.82	< 0.001
Alcoholism diagnosis (Yes vs. No)	0.99	0.83	1.18	0.873
Diabetes diagnosis (Yes vs. No)	0.95	0.88	1.03	0.182
Obesity diagnosis (Yes vs. No)	1.33	1.23	1.43	< 0.001
Current or past tobacco use (Yes vs. No)	1.41	1.31	1.52	< 0.001
Had at least one FDR with thumb CMC OA (Yes vs. No)	3.39	2.70	4.26	< 0.001
Had at least one SDR with thumb CMC OA (Yes vs. No)	1.18	0.83	1.65	0.355
Had at least one TDR with thumb CMC OA (Yes vs. No)	1.18	1.00	1.39	0.056

Note: Both sexes included in this analysis.

Abbreviations: FDR - first degree relative. SDR - second degree relative. TDR - third degree relative.

CONCLUSIONS

- These findings further support a genetic basis for thumb CMCOA.

- First-degree relatives of affected individuals had a 3.66-fold greater risk of undergoing surgery for thumb CMC OA.
- We also identified White race, non-Hispanic ethnicity, obesity, and tobacco use as independent demographic and comorbidity risk factors.

- Sequencing of high-risk pedigrees is underway to identify specific genetic variants associated with thumb CMCOA, which may guide the development of improved therapeutic strategies in the future.

ACKNOWLEDGEMENTS

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