

Is 'frozen shoulder' a genetic condition? Study finds links to specific genes

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Frozen shoulder, or adhesive capsulitis, is a common cause of shoulder pain and immobility. New findings point to specific genes associated with an increased risk of this condition, reports the *Journal of Bone &*

Joint Surgery.

The risk genes are associated with nearly a sixfold increase in the odds of developing frozen shoulder—a stronger association for most known clinical risk factors, according to the new research by Mark T. Langhans, MD, Ph.D., of Hospital for Specialty Surgery, New York. The authors believe their findings may lend new insights into the causes, prevention, and treatment of adhesive capsulitis.

Genome-wide association study finds 'significant loci' affecting frozen shoulder risk

Patients with adhesive capsulitis develop painful and progressive loss of shoulder motion with associated pain. Frozen shoulder is one of the most common shoulder conditions, occurring in up to 10% of people at some time in their lives. Although the exact cause is unclear, frozen shoulder sometimes occurs after an injury, surgery, or other condition that reduces shoulder mobility. Loss of motion results from fibrosis (scarring or thickening) of the capsule around the shoulder joint.

Certain clinical factors are associated with an increased risk of frozen shoulder, including diabetes, thyroid disease, and smoking. Recent studies have suggested that risk is also higher in people with affected relatives—suggesting a possible genetic predisposition. Dr. Langhans and colleagues performed a [genome-wide association study](#) to identify [specific genes](#) that might be related to the risk of frozen shoulder.

Data studied from large British database

The study used data from a large British database, the UK Biobank, which includes genetic and health data on approximately 500,000 patients. The analysis focused on 2,142 patients with adhesive capsulitis compared to those without this diagnosis. Possible genetic associations

were adjusted for other factors, including sex, diabetes, thyroid disease, history of shoulder dislocation, and smoking.

The study identified three significant loci for frozen shoulder. The strongest association was found for gene variants located at a site called WNT7B. This finding was consistent with previous studies that reported a possible link between WNT7B and frozen shoulder, along with several other orthopedic-related conditions. Weaker associations were also found for two previously unreported genetic loci located near genes for POU1F1 and MAU2.

All three associations remained significant after adjustment for other factors. Together, the three variants carried nearly a sixfold increase in the odds of developing frozen shoulder. That was greater than the risk associated with diabetes (about four-fold) or thyroid disease (less than two-fold), and second only to smoking (about 11-fold).

New insights could lead to a new development

The findings may lend new insights into the development of adhesive capsulitis. In particular, [genes](#) located at WNT7B have been shown to be expressed in bone-forming cells (osteoblasts) and to be involved in regulating fibrosis, along with a wide range of other functions. The two newly reported loci, POU1F1 and MAU2, are involved with [cell division](#), which might lend clues into the cellular mechanism by which frozen shoulder develops.

The researchers note some key limitations of their analysis, including the need for further studies of genetic associations in groups other than the white, British population that predominates in the UK Biobank.

Meanwhile, the new study identifies several gene loci with the ability to predict a clinically relevant risk of frozen [shoulder](#). Dr. Langhans and

colleagues conclude that "refining the genetic risk metric and including it in a larger clinical model could allow patients at risk for future adhesive capsulitis to be identified, leading to efforts at prevention, early diagnosis, and ultimately improved outcomes."

More information: Scott Kulm et al, Genome-Wide Association Study of Adhesive Capsulitis Suggests Significant Genetic Risk Factors, *Journal of Bone and Joint Surgery* (2022). [DOI: 10.2106/JBJS.21.01407](https://doi.org/10.2106/JBJS.21.01407)

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