Tendon and ligament-associated gene variants and history of soft tissue injury in elite male rugby athletes.

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Introduction

There is a genetic component to tendon and ligament injuries which is highly likely to be polygenic in nature (1). Elite rugby has one of the highest reported injury incidences of any professional sport with some of the most severe injuries affecting tendons and ligaments (1). Thus, this study investigated if suspected tendon and ligament injury-associated polygenic profiles of elite rugby athletes (RA) with a history of prior tendon and ligament injury differed from RA with no history of injury. We hypothesised that tendon and ligament injury-associated genotypes and polygenic profiles would be overrepresented in RA with a history of soft tissue injury compared to RA with no history of injury.

Method

Participants were from the RugbyGene project, comprising elite male RA (185 white males; mean (standard deviation) height 1.86 (0.07) m, mass 102 (12.6) kg, age 26.4 (5.1) yr) competing at an elite level in rugby union (n = 165) and league (n = 20) in the UK, Ireland, Italy and South Africa. Soft-tissue injury history was collected using a self-reported injury history questionnaire. PCR of genomic DNA was used to determine genotypes using TaqMan probes, and total genotype scores (TGS) from 13 polymorphisms were calculated, then groups were compared using χ^2 and odds ratio (OR) statistics. In addition, multifactor dimensionality reduction (MDR) and inferred haplotype analysis were used to identify genetic interactions.

Results

For *MMP3* rs679620, the C allele was more common in the tendinopathy group (TD) compared to the non-injured tendon group (NIT) (63.5% vs 50.0%, *P* = 0.02, OR = 1.62, 95% CI = 01.00-2.60) (Fig. 1). However, the C allele was more common in the non-injured ligament group (NIL) compared to the ligament rupture (LR) group (63.7% v 47.9%, P = 0.02, OR = 1.91, 95% CI = 1.09-3.35) (Fig. 1.). For *COL5A1* rs12722 the TT genotype was more common in NIT compared to the tendon rupture group (TR) (25.0% vs. 3.8%, *P* = 0.006, OR 4.35, 95% CI = 0.49-37.01).

TGS differed between NIL and the ligament sprain group (LS) (Fig. 2A)(*U*=1868.50;*P* = 0.02). Receiver operating characteristic curve (ROC) and area under the curve (AUC) analysis confirmed the TGS algorithm could identify LS (AUC = 0.61; 95% CI = 0.52-0.72; *P* = 0.02) (Fig. 2B).

The T-C inferred haplotype frequency of *COL5A1* rs12722 and *COL5A1* rs3196378 respectively, was higher in TR, LS and the all-injured athlete groups compared to NIT, NIL and the all-non-injured group (*P* < 0.01) (Fig. 3). MDR could not identify a model to predict any of the injury groups with a sufficiently powerful cross-validation statistic.

Results

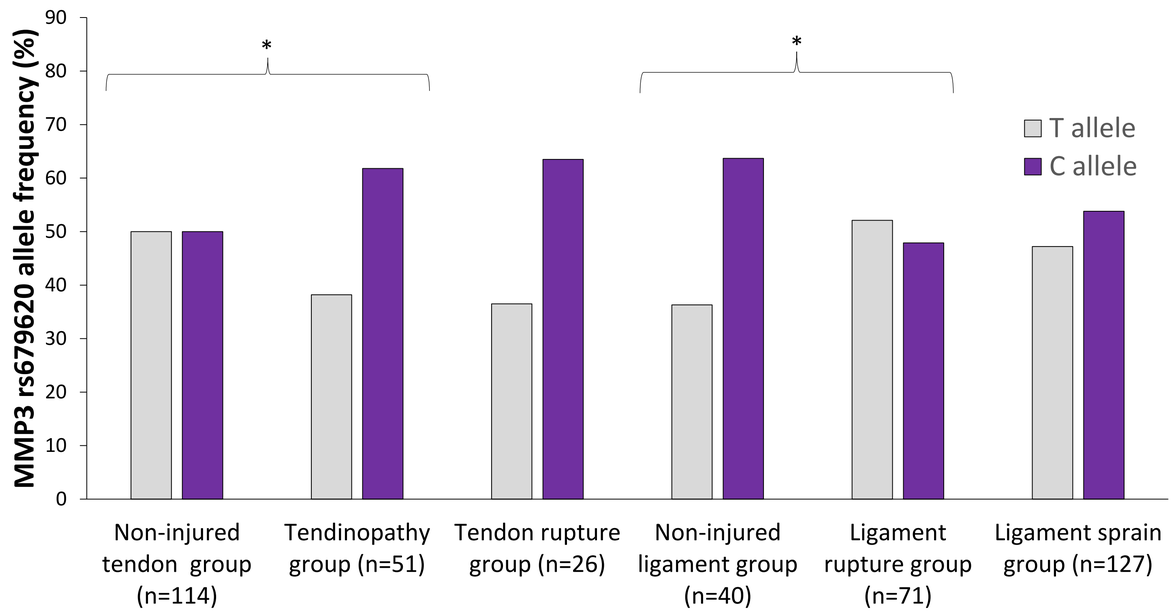

Fig. 1 Genotype frequency of *MMP3 rs679620* for athletes. * (*P* < 0.05).

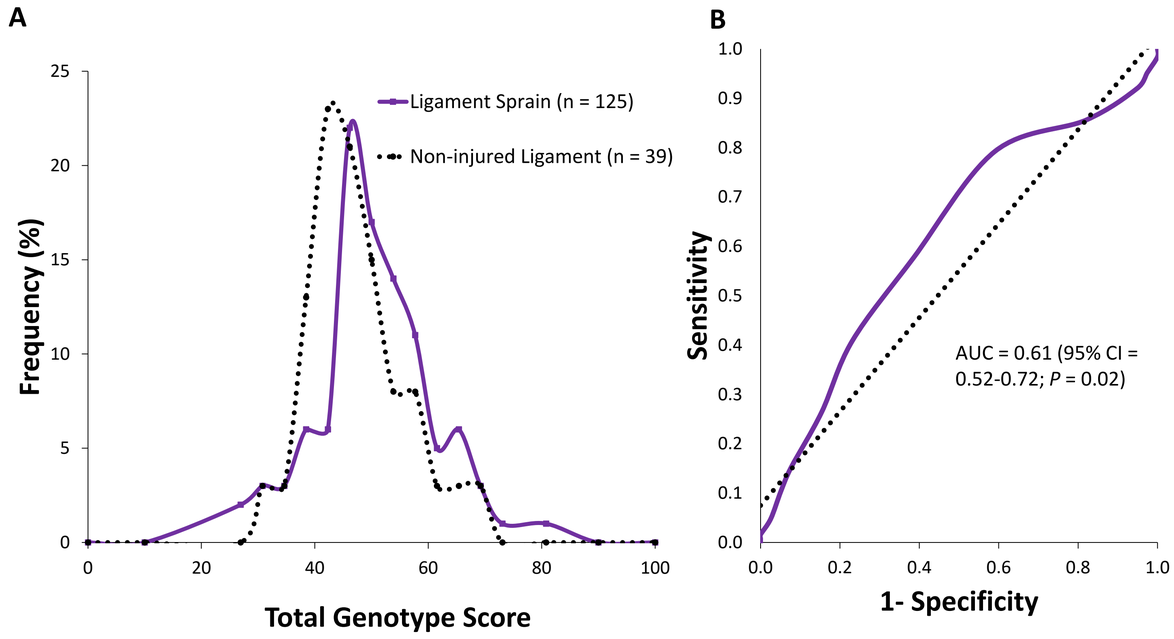

Fig. 2 . Frequency distribution of TGS for NIL (47.1 ± 8.2) and LS (50.3 ± 9.8); *P* = 0.02 (**2A**). Receiver operating characteristic curve displays the ability of the TGS to discriminate NIL from LS. Dotted line = no discrimination. **(2B)** AUC; area under the curve .

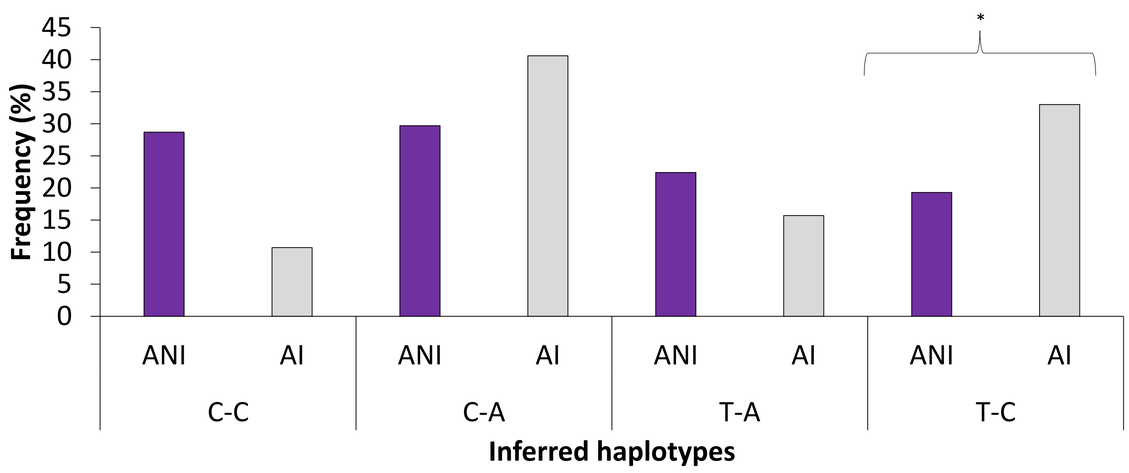

Fig. 3 . Inferred haplotype frequencies derived from *COL5A1* rs12722 and rs3196378. ANI = All non-injured athletes, AI = All injured athletes. *different from ANI (*P* <0.001)

Conclusion

The current data suggests musculoskeletal soft-tissue injury could be influenced by an athlete's genetic predisposition. This study provides further insight into the detailed aetiology of musculoskeletal soft tissue injuries within elite rugby and may, in future, be worthy of consideration for managing the interindividual variability of injury risk in rugby.

References

[1] Brazier, J *et al.*, "Tendon and Ligament Injuries in Elite Rugby: The Potential Genetic Influence," *Sports*, vol. 7, no. 6, p. 138, June. 2019, doi: 10.3390/sports7060138.

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