Variation within the *MMP3* Gene as a Risk Factor for Achilles Tendon Pathology in a British Population

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Objective Achilles tendon pathology (ATP) is a multifactorial condition with a recognised genetic component. The MMP-3 enzyme regulates extracellular matrix homeostasis by degrading various types of collagens. The matrix metalloproteinase 3 (*MMP3*) gene has previously been associated with the risk of developing ATP in a South African Caucasian population. The purpose of this study was to determine whether the *MMP3* rs679620 variant that was associated with ATP in South Africans was also a risk factor for ATP in a recently recruited British Caucasian population. We also sought to establish, in a preliminary manner, whether the variant was associated with additional clinicopatholigical characteristics of our cohort.

Methods 252 (121 cases with ATP and 131 asymptomatic controls) British Caucasian participants were recruited for this case-control genetic association study. All participants were genotyped for the *MMP3* G/A rs679620 variant using TaqMan technology. Data was analysed using chi-squared and ANOVA tests with significance set at $p<0.05$.

Results There was no significant ($p=0.349$) difference in genotype distribution frequency between the ATP and control groups. However, when we restricted our analysis to include only individuals with Achilles tendon rupture, we found a significant ($p=0.029$) difference in genotype distribution frequency between this group (AA, 31.4%; AG, 31.4%; GG, 37.1%) and the controls (AA, 26.7%; AG, 54.2%; GG, 19.1%). Furthermore, we found that male participants with tendinosis and the GG genotype had significantly ($p=0.007$) thicker Achilles tendons compared to the AG and AA genotypes.

Conclusion This study shows that the *MMP3* rs679620 variant was not associated with ATP when the condition was analysed as a single clinical entity. However, we did show that the GG genotype was significantly associated with both the risk of Achilles tendon rupture and

increased tendon width in males with tendinosis. Although these data show some contrasts with a previously published study in South Africans they do enhance our understanding of the role of the *MMP3* rs679620 variant in predisposing to Achilles tendon injury.