Possible association of single nucleotide polymorphisms in the 3' untranslated region of HOXB9 with acetabular overcoverage


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Objectives
Excessive acetabular coverage is the most common cause of pincer-type femoroacetabular impingement. To date, an association between acetabular over-coverage and genetic variations has not been studied. In this study we investigated the association between single nucleotide polymorphisms (SNPs) of paralogous Homeobox (HOX9) genes and acetabular coverage in Japanese individuals to identify a possible genetic variation associated with acetabular over-coverage.

Methods
We investigated 19 total SNPs in the four HOX9 paralogs, then focused in detail on seven of those located in the 3' untranslated region of HOXB9 (rs8844, rs3826541, rs3826540, rs7405887, rs2303485, rs2303486, rs79931349) using a case-control association study. The seven HOXB9 SNPs were genotyped in 316 subjects who had all undergone radiological examination. The association study was performed by both single-locus and haplotype-based analyses.

Results
The genotype and allele frequencies of the five HOXB9 SNPs showed significant association with acetabular over-coverage compared with controls (rs7405887 OR = 3.16, p = 5.29E-6, 95% CI 1.91 to 5.25). A significant difference was also detected when haplotypes were evaluated (OR = 2.59, p = 2.61E-5, 95% CI 1.65 to 4.08). The two HOXB9 SNPs (rs2303485, rs2303486) were associated with decreased acetabular coverage (rs2303485 OR = 0.524, p = 0.0091, 95% CI 0.322 to 0.855; rs2303486 OR = 0.519, p = 0.011, 95% CI 0.312 to 0.865).

Conclusions
The five HOXB9 SNPs (rs8844, rs3826541, rs3826540, rs7405887, rs79931349) were associated with acetabular over-coverage. On the other hand, the two SNPs (rs2303485 and rs2303486) were associated with the lower acetabular coverage. The association of rs2303486 would be consistent with the previous study. Therefore, the HOXB9 SNPs might be involved in the morphogenesis of acetabular coverage, and could be an independent risk factor for developing pincer-type femoroacetabular impingement.

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Article focus
To date, an association between acetabular over-coverage and genetic variations has not been studied. We investigated the association between single nucleotide polymorphisms (SNPs) of paralogous HOX9 genes and acetabular over-coverage.

Key messages
The HOXB9 SNPs might be involved in the morphogenesis of acetabular coverage, and could be an independent risk factor for developing pincer-type femoroacetabular impingement.

Strengths and limitations
Strengths: This is the first report on the association of genetic variations in acetabular over-coverage. The HOXB9 SNPs showed significant association with acetabular over-coverage compared with controls.