GWAS for tumour size, grade, stage, and age in NMIBC patients in the West Midlands Bladder Cancer Prognosis Programme

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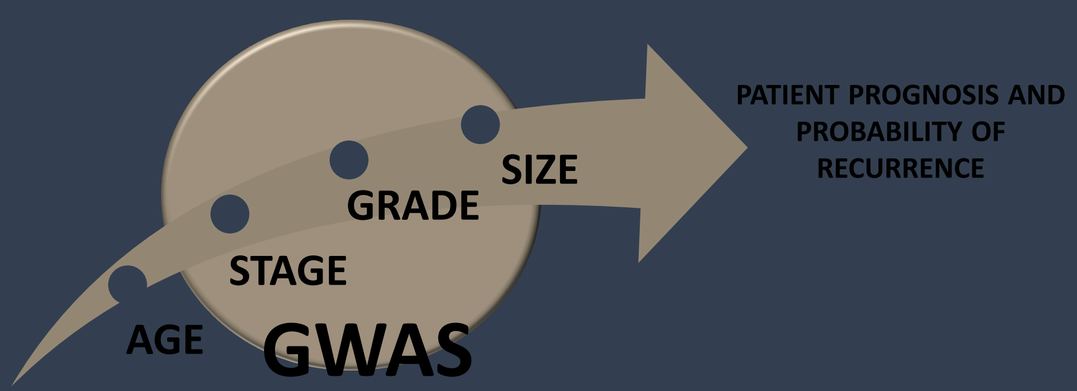
BACKGROUND

- Non-muscle invasive bladder cancer (NMIBC) exhibits high recurrence and progression rates, causing significant burden on patients and healthcare systems.
- Current disease prognostic tools make use of tumour characteristics at the time of diagnosis, but fail to make an accurate prognosis on per-individual level.



- We have performed a genome-wide association study (GWAS) aimed to investigate potential associations with tumour **size, stage, grade,** and **age** at the time of diagnosis that could increase precision of prognostic tools used in clinical practice.

METHODS

Setting:

653 patients from the West Midlands Bladder Cancer Prognosis Programme (BCPP) had their biological samples genotyped and passed quality control procedures.

Analysis:

Eagle v2.3.2 was used to estimate haplotypes, followed by imputation with IMPUTE2, using 1000 Genomes Phase 3 data as a reference panel. Single-nucleotide polymorphisms (SNPs) were tested using SNPTEST v2.5.2 for associations with all endpoints (tumour size (continuous (cm) and categorical (sample mean as a cut-off) outcome), stage (Tis and T1 vs Ta), grade (G3 vs G2 and G1), age (continuous (years) and categorical (sample mean as a cut-off)), filtering for minor allele frequency (MAF>0.01%) and imputation accuracy (info>0.3). Promising findings were tested in a sample of the Netherlands Bladder Cancer Study (NBCS).

RESULTS

61 novel associations across all outcomes have yielded genome-wide significance (p<5*E-08), corresponding to 29 distinct loci. In a meta-analysis of both cohorts, one SNP showed a promising association with tumour size, (rs180940944 (ß=0.9 cm, p=2.92E-09)), which is situated in an intronic region of the *NBEA* gene.

CONCLUSIONS

Our study adds novel findings to the current knowledge regarding associations between genetic variation and NMIBC characteristics at the time of diagnosis. Such findings may be useful for improving prognostication.

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