PROSTATE CANCER

# You've got a friend online

The first study to empirically assess psychological morbidity and emotions expressed by men newly diagnosed with prostate cancer who use online cancer support groups using artificial intelligence has been published in *PLoS One*. Participation in these groups decreased psychological stress and long-term engagement improved emotional well-being. Thus, men with newly diagnosed prostate cancer might benefit from joining an online support group.

In this study, the researchers used artificial intelligence to extract and analyse activities of men with prostate cancer using online support groups in order to assess the reasons that these men joined, the emotions they expressed and the variation in deep emotions from diagnosis through to recovery, which could indicate psychological morbidity. To extract this data, the investigators extended the Patient-Reported Information Multidimensional Exploration (PRIME) framework. PRIME automatically detected relevant data (emotions expressed and mentions of adverse effects) from 277,805 conversations that were conducted by 18,496 patients in ten globally available, high-volume online support groups. This data collection enabled the creation of an emotion and adverse-effect profile for each patient who took part in the groups. The reasons for joining the online support group were assessed using natural language processing and machine-learning-based automatic topic extraction.

Four distinct reasons for joining a support group were identified: diagnosis; treatment; adverse effects; and cancer recurrence. Information on treatment was the most common reason for joining a group (61.72%). The most frequently expressed emotions in the first post were open and interested (which were classed as positive) and afraid and hurt (which were classed as negative). When expressed emotions were analysed in the context of the reasons for joining, 'interested' was associated with adverse effects, 'positive' was expressed by men whose reason for joining was diagnosis, and all reasons except adverse effects were associated with expressing 'afraid' as an emotion. Joining for adverse effects was associated with increased emotions related to 'hurt' and 'sad'.

Evaluation of emotional fluctuations showed that negative emotions reduced in intensity after 12 months. For all reasons for joining except cancer recurrence, negative emotions were significantly reduced at 12 months after joining compared with at 1 month. Joining after treatment was associated with higher negative emotion intensity than joining before treatment, even at 12 months despite a reduction in negative emotions for both groups.

These results suggest that clinicians should inform newly diagnosed patients about online support groups as they can improve the psychological well-being of men with prostate cancer.

*Louise Stone*

**ORIGINAL ARTICLE** Adikari, A. et al. Can online support groups address psychological morbidity of cancer patients? An artificial intelligence based investigation of prostate cancer trajectories. *PLoS One* https://doi.org/10.1371/journal.pone.0229361 (2020)

KIDNEY CANCER

# AKI induces pRCC

New research, published in *Science Translational Medicine*, shows that acute kidney injury (AKI) is associated with increased risk of developing papillary renal cell carcinoma (pRCC) and tumour relapse. These results suggest that pRCCs with no apparent association with known risk factors could be related to AKI episodes and that AKI prevention and risk stratification protocols should be developed.

Analysis of data from patients with RCC and monitoring for 1 year before diagnosis showed that 16.2% had an AKI episode, corresponding to 420 AKI episodes per 10,000 person-years. Nationwide data from Denmark showed that subsequent incidence of RCC among patients with AKI was 0.06% the first year after AKI diagnosis and 0.1% >1 year after the first AKI episode. Incidence of previous AKI episodes was significantly increased in patients diagnosed with pRCC but not for those diagnosed with clear cell RCC. In particular, type 2 pRCC development was associated with previous AKI.

Postoperative AKI after tumour resection for localized pRCC was associated with significantly decreased 5-year recurrence-free survival, and multivariate analysis showed that postoperative AKI was positively correlated with recurrence in single-centre and multicentre analyses.

Mechanistically, assessment of AKI-activated signalling pathways showed that decreased expression of mTOR, β-catenin and VHL and increased expression of NOTCH1 were associated with advanced pRCC stage. Differences in the expression of distinct AKI-related signalling pathways were seen between type 1 and type 2 pRCC; mTOR, β-catenin and VHL were increased in type 1 pRCC, whereas increased NOTCH1 was associated with type 2 pRCC. Increased expression of NOTCH1 was associated with worse prognosis and was found to be a crucial prognostic factor for type 2 pRCC.

In vivo, long-term follow-up monitoring of wild-type mice that underwent ischaemia–reperfusion injury (IRI) showed that development of type 1 and 2 pRCC was time dependent. At 4 weeks after IRI, no tumours were visible, but at 12 and 36 weeks 55.6% of mice had papillary adenomas. At 36 weeks, 22.2% of mice showed pRCC; mice that did not undergo IRI did not develop tumours. Lineage tracing of tubular epithelial cells (TECs) at the single-cell level revealed that >95% of type 1 and 2 papillary tumours were monoclonal in origin. Induction of overexpression of *Notch1* in PAX8$^+$ TECs plus IRI caused accelerated development of pRCC in transgenic mice. *Notch1* overexpression in renal progenitors plus IRI resulted in the development of type 2 pRCC tumours. Blocking endogenous AKI-induced NOTCH1 activation led to fewer tumours developing.

In vitro, overexpression of NOTCH1 in human renal progenitor cells caused a pRCC-like phenotype, increased cell proliferation and resulted in aberrant mitosis. In tissue samples from patients with AKI, nuclear expression of NOTCH1 was observed in tubular cells, particularly CD133$^+$ cells. Single-cell RNA sequencing showed that the transcriptome of human renal progenitor cells was similar to PT1, which is the putative cell of origin of human pRCC.

Together, these data suggest that AKI is a risk factor for the development and recurrence of pRCC in humans and that NOTCH1 overexpression could be the mechanism by which pRCC is induced after AKI. Thus, AKI prevention and risk stratification programmes should be developed to prevent and monitor the development of pRCC after AKI.

*Louise Stone*

**ORIGINAL ARTICLE** Peired, A. J. et al. Acute kidney injury promotes development of papillary renal cell adenoma and carcinoma from renal progenitor cells. *Sci. Transl Med.* **12**, eaaw6003 (2020)