Long term toxicity after radiotherapy for prostate cancer
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Purpose or Objective
Prostate cancer (Pca) patients can experience a significant decline in quality of life due to late toxicity after external beam radiotherapy (EBRT). Development of normal tissue complication probability (NTCP) models for late toxicity could predict the risk of toxicity after radiotherapy for Pca. The main purpose of this prospective cohort study was to develop comprehensive NTCP-profiles for Pca patients treated with radiotherapy.

Material and Methods
Dosimetric data of 302 Pca patients treated in the University Medical Center Groningen between 2006 and 2010 were collected. Patient reported questionnaires were prospectively used to score toxicity according to the Radiation Therapy Oncology Group criteria. Baseline clinical data were retrospectively acquired from patient files; age, androgen deprivation therapy (ADT), acetylsalicylic acid tablet use, other anticoagulants agents use, pretreatment TURP and diabetic disease. All patients have been treated with EBRT to 78 Gy (39 fractions of 2 Gy). The median follow-up was 60 months (range 4-120 months).

The following toxicity symptoms were investigated in this model: rectal blood loss, fecal incontinence (requiring daily use of pads), obstruction (requiring daily use of laxatives) and abdominal cramping or pain. Multivariable logistic regression analysis was used to analyze dose volume effects and NTCP models were developed.

Results
The discriminating ability of the model was described by the area under the receiver operating characteristic curve (AUC). The discrimination slope was calculated as the absolute difference between the mean predicted NTCP value for patients with and without the outcome. Finally, the gain and intercept of the model calibration were calculated, and the calibration was evaluated using a Hosmer-Lemeshow test which was not significant in any of the models, indicating a good agreement between observed and expected outcomes.

Rectal bleeding was significantly associated with V70 rectal wall (volume of rectal wall receiving 70 Gy) \( p=0.015; \ OR=1.081 \ (1.016-1.152) \), anal canal V30 (volume of anal canal receiving 30 Gy) \( p=0.010; \ OR=1.022 \ (1.005-1.040) \) and aspirin use \( p=0.011; \ OR=3.215 \ (1.463-7.065) \). AUC=0.70 \ (0.60-0.79). Fecal incontinence was significantly associated with anal canal V10 (volume of anal canal receiving 10 Gy) \( p=0.021; \ OR=1.040 \ (1.002-1.080) \) and patient age \( p=0.005; \ OR=1.140 \ (1.033-1.258) \). AUC=0.76 \ (0.65-0.87).

Conclusion
We developed a comprehensive set of NTCP-models that can be used to predict the most relevant rectal toxicities in prostate cancer radiotherapy. The resulting NTCP-profiles can be used for radiotherapy treatment dose optimization. In addition, these NTCP-profiles can be used in the future for model-based selection of patients for proton therapy, based on \( \Delta \)NTCP-profiles.