Predicting risk of recurrence after surgery for colorectal cancer.

PRESENTER: **Mikail Gögenur**

INTRO

Risk of recurrence after colorectal cancer surgery is the main driver of long-term morbidity and mortality.

Following curative intended surgery, up to 15-20% of patients will experience recurrence. Knowing which patients will have a low risk of recurrence could decide which type of surgery a patient should undergo, where an older frail patient with low risk of recurrence could be offered a small resection, instead of the standard approach of removing large portions of the bowel. However, presently no tools exist to predict which patients are at risk of recurrence at the preoperative setting.

METHODS

A CDM was built from the validated Danish Colorectal Cancer Group (DCCG) Database, containing 99% of all colorectal cancer surgeries in Denmark since 2001. Recurrence was estimated in the DCCG database by applying the validated algorithm by Lash et al. ATLAS and OHDSI prediction-level package was used to create patient-level prediction models using preoperatively available variables to predict risk of recurrence. We applied the LASSO logistic regression model using default settings and a three-fold cross validation.

RESULTS

- From 2001-2019, 25,290 patients underwent surgery with curative intent for colorectal cancer in Denmark.
- 5,717 experienced a recurrence event.
- The PLP was able to predict patients at elevated risk using only preoperatively known variables with risk of recurrence (AUROC: 0.65 (0.63-0.66), PRROC: 0.34), with good calibration and a Brier score of 0.17

Preoperative variables can decently predict the risk of recurrence after surgery for colorectal cancer.

Increased risk can be taken into consideration for clinical decision-making to identify patients that might benefit from:

preoperative treatment

smaller resections

increased postoperative monitoring
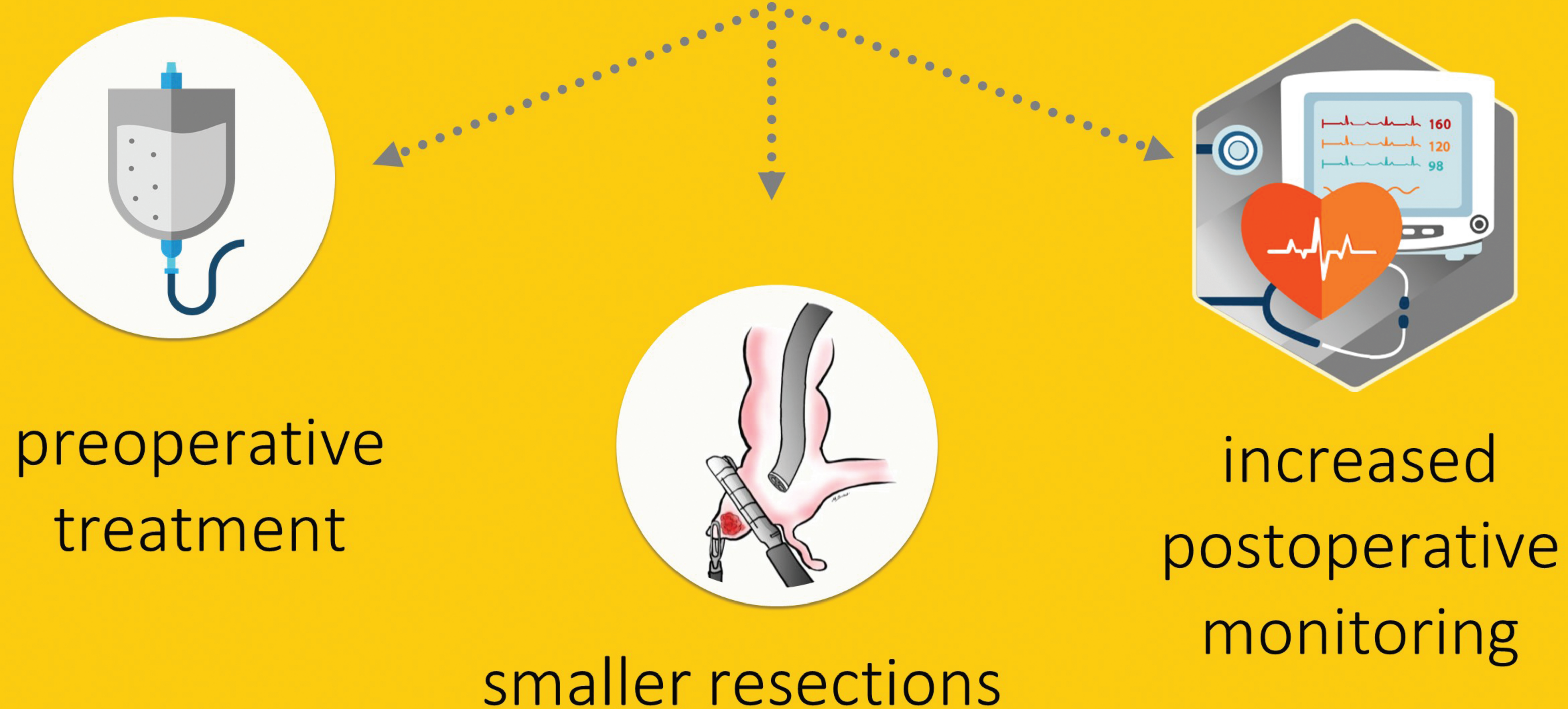
TOP 5 COVARIATES ASSOCIATED WITH RISK OF RECURRENCE

Name	Value
Low association to risk of recurrence	
Age group 90-94	-0.75
Local macroradical excision of colorectal tumor	-0.39
T1 category	-0.39
Age group 85-89	-0.36
N0 category	-0.35
High association to risk of recurrence	
Transanal endoscopic microsurgery	0.66
Stent insertion into colon	0.49
Emergency operation	0.42
Age group 40-44	0.22
Age group 35-39	0.21

CLINICAL USE OF PREDICTION MODELS

In the clinical setting, the absolute risk of recurrence is valuable, why we note that our model had a good calibration despite subpar discrimination.
A patient's individual prediction can be used in the multidisciplinary team (MDT) meeting prior to surgery as well as with the patient in a preoperative discussion on treatment planning.

- For a young patient presenting with a high risk of recurrence, the patient could be offered extensive surgery with an intensive surveillance program and adjuvant chemotherapy.

- For an elderly patient presenting with a low risk of recurrence, the decision could be to contain the disease for now with a local procedure considering the possible complications of a large resection with the risk of developing recurrence.

THE WAY FORWARD

Our model had a decent discrimination with a good calibration, but is not ready for clinical usage.
Even though that DCCG contains some genomics information, we know that a deep phenotypical understanding of the tumor microenvironment is needed to adequately predict risk of recurrence. Incorporating this in our CDM is in our pipeline.

Mikail Gögenur, Viviane Lin, Adamantia Tsouchnika, Eldar Allakhverdiiev, Andreas Weinberger Rosen, Karoline Bendix Bräuner, Julie Sparholt Walbech, Ismail Gögenur

CENTER FOR SURGICAL SCIENCE
REGION ZEALAND
ZEALAND UNIVERSITY HOSPITAL

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