Radboud Research Round
Tumors of the digestive tract

Paper Awards 2020

Propensity Score–Matched Analysis Comparing Minimally Invasive Ivor Lewis Versus Minimally Invasive Mckeown Esophagectomy

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Grard A. P. Nieuwenhuijzen, MD, PhD,¶ and Camiel Rosman, MD, PhD*

Introduction: Totally minimally invasive esophagectomy (TMIE) is increasingly used in treatment of patients with esophageal carcinoma. However, it is currently unknown if McKeown TMIE or Ivor Lewis TMIE should be [performed in pat]ients in whom both procedures are oncologically feasible.

[This s]tudy was performed in 4 high-volume Dutch esophageal [cancer centers] between November 2009 and April 2017. Prospectively [collected data fr]om consecutive patients with esophageal cancer localized [in the esop]hagus or gastroesophageal junction undergoing McKeown [TMIE or Ivor L]ewis TMIE were included. Patients were propensity score [matched for age], body mass index, sex, American Society of Anesthesiol[ogists classificat]ion, Charlson Comorbidity Index, tumor type, tumor loca[tion, tumor sta]ge, neoadjuvant treatment, and the hospital of surgery. The [primary outcome] parameter was anastomotic leakage requiring reintervention [and the s]econdary outcome parameters were operation characteristics, [lymph nodes], complications, reinterventions, reoperations, length of stay, and mortality.

Adhesion-related readmissions after open and laparoscopic surgery: a retrospective cohort study (SCAR update)

Pepijn Krielen, Martijn W J Stommel, Pille Pargmae, Nicole D Bouvy, Erica A Bakkum, Harold Ellis, Michael C Parker, Ewen A Griffiths, Harry van Goor, Richard P G ten Broek

Summary

Background Adhesions are the most common driver of long-term morbidity after abdominal surgery. Although laparoscopy can reduce adhesion formation, the effect of minimally invasive surgery on long-term adhesion-related morbidity remains unknown. We aimed to assess the impact of laparoscopy on adhesion-related readmissions in a population-based cohort.

Methods We did a retrospective cohort study of patients of any age who had abdominal or pelvic surgery done using laparoscopic or open approaches between June 1, 2009, and June 30, 2011, using validated population data from the [National] Health Service. All patients who had surgery were followed up until Dec 31, 2017. The primary [outcome w]as the incidence of hospital readmissions directly related to adhesions in the laparoscopic and [open group]s at 5 years. Readmissions were categorised as directly related to adhesions, possibly related to [adhesions, or read]missions for an operation that was potentially complicated by adhesions. We did subgroup [analy]sions by anatomical site of surgery and used Kaplan-Meier analyses to assess differences in [the g]roups. We used multivariable Cox-regression analysis to determine whether surgical approach [was an independent] and significant risk factor for adhesion-related readmissions.
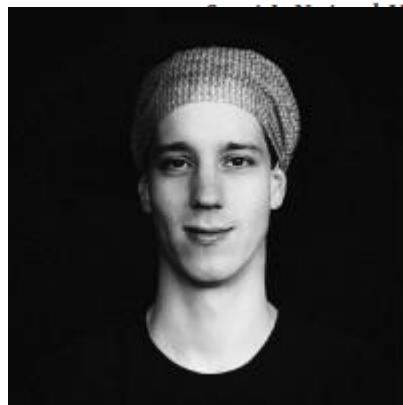
[Findings Between Ju]ne 1, 2009, and June 30, 2011, 72270 patients had an index abdominal or pelvic surgery, of whom [21519 (29·8%) had l]aparoscopic index surgery and 50751 (70·2%) had open surgery. Of the 72270 patients who had [surgery, 2527 patien]ts (3·5%) were readmitted within 5 years of surgery for disorders directly related to adhesions, [11541 (16·0%) for di]sorders possibly related to adhesions, and 9436 (13·1%) for operations potentially complicated by [adhesions. Of 21]519 patients who had laparoscopic surgery, 359 (1·7% [95% CI 1·5–1·9]) were readmitted for [disorders directly re]lated to adhesions compared with 2168 (4·3% [4·1–4·5]) of 50751 patients in the open surgery cohort (p<0·0001). 3443 (16·0% [15·6–16·4]) of 21519 patients in the laparoscopic surgery cohort were readmitted for [disorders possibly rel]ated to adhesions compared with 8244 (18·2% [17·8–18·6]) of 50751 patients in the

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ORIGINAL ARTICLE – COLORECTAL CANCER

The Impact of Primary Tumor Location in Synchronous Metastatic Colorectal Cancer: Differences in Metastatic Sites and Survival

Nelleke P. M. Brouwer, Bsc[1], Dave E. W. van der Kruijssen, MD[2], Niek Hugen, MD, PhD[1], Ignace H. J. T. de Hingh, MD[3], Iris D. Nagtegaal, MD[4], Rob H. A. Verhoeven, PhD[1,5], Miriam Koopman, MD[2], and Johannes H. W. de Wilt, MD[1]

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Purpose. We explored differences in survival between [...]

0.71–0.76). The survival disadvantage for RCC remained present, even in cases with metastasectomy for liver-only [...]

Detection of Barrett's oesophagus through exhaled breath using an electronic nose device

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MESSAGE

Timely detection of oesophageal adenocarcinoma (OAC) and even more so its precursor Barrett's oesophagus would contribute to decrease OAC incidence and ...lity. An accurate, minimally-invasive screening ...d for BO for widespread use is currently not ...le. In a proof-of-principle study in 402 patients, ...veloped and cross-validated a BO prediction model ...volatile organic compounds (VOCs) analysis with ...ctronic nose device. This electronic nose was able ...inguish between patients with and without BO ...ood diagnostic accuracy (sensitivity 91% specificity ...and seemed to be independent of proton pump ...or use, the presence of hiatal hernia, and reflux. ...echnique may enable an efficient, well-tolerated, ...ensitive and specific screening method to select high-risk individuals to undergo upper endoscopy.

by an electronic nose device is based on pattern recognition and resembles mammalian olfaction (figure 1).[6 7] The Aeonose (the eNose company, Zutphen, the Netherlands) consists of three metal-oxide sensors and uses chemical to electrical interfaces to measure subtle VOC profiles of different diseases in exhaled breath. Data were analysed by an artificial neural network in a supervised fashion to identify data classifiers to extract breath print differences between patients with BO, gastro-oesophageal reflux disease (GORD), and controls. Leave-10%-out cross-validation of data was performed after training the artificial neural network to make sure the prediction model generated was disease-specific. More details on the methods and the electronic nose technology can be found in the online supplementary file.[8 9]

Targeted Optical Imaging of the Glucagonlike Peptide 1 Receptor Using Exendin-4-IRDye 800CW

Marti Boss[1], Desiree Bos[1], Cathelijne Frielink[1], Gerwin Sandker[1], Selen Ekim[1], Camille Marciniak[2], Francois Pattou[2], Go van Dam[3], Sanne van Lith[1], Maarten Brom[1], Martin Gotthardt[1], and Mijke Buitinga[4]

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The treatment of choice for insulinomas and focal lesions in ...nism (CHI) is surgery. However, intraoperative ...llenging. This challenge could be overcome ...orescence imaging, which provides real-time ... high spatial resolution. Here, a novel method ...red (NIR) fluorescence imaging of glucagon-...r (GLP-1R)–positive lesions, using the GLP-1 ...led with IRDye 800CW, was examined in vitro ... A competitive binding assay was performed ...r lung (CHL) cells transfected with GLP-1R. ...was determined in BALB/c nude mice bearing ...LP-1R xenografts. In vivo NIR fluorescence ...-1R xenografts was performed. Localization ...pancreatic islets of BALB/c nude mice was

Although preoperative imaging is essential for tumor detection before surgical cancer treatment, translating this information into the operating room is often challenging. Intraoperative optical imaging can provide real-time detection of tumor lesions and thereby contribute to optimal surgical procedures (*1*).

Insulinomas, insulin-producing neuroendocrine tumors arising from stem cells or pancreatic β-cells, are the most common cause of endogenous adult hyperinsulinemic hypoglycemia (*2*). Persistent hypoglycemia also occurs in neonates and is in most cases caused by congenital hyperinsulinism (CHI). There are 2 subforms of this disease: focal CHI, caused by focal adenomatous islet cell hyperplasia, and diffuse CHI, resulting from diffuse involvement of pancreatic β-cells (*3*). Symptoms of insulinomas and CHI, caused by

Article

CD276-Positive Circulating Endothelial Cells Do Not Predict Response to Systemic Therapy in Advanced Colorectal Cancer

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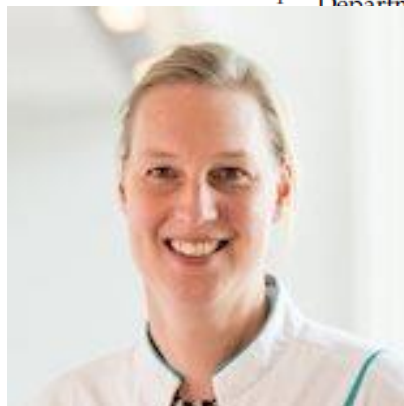
Assessment of individual tumor buds using keratin immunohistochemistry: moderate interobserver agreement suggests a role for machine learning

J. M. Bokhorst [1] · A. Blank[2] · A. Lugli [2] · I. Zlobec[2] · H. Dawson[2] · M. Vieth[3] · L. L. Rijstenberg[1] · S. Brockmoeller[4] ·
M. Urbanowicz[5] · J. F. Flejou[6] · R. Kirsch[7] · F. Ciompi[1] · J. A. W. M. van der Laak [1,8] · I. D. Nagtegaal[1]

g is a promising and cost-effective biomarker with strong prognostic value in colorectal cancer. However,
ited to interobserver variability persist. Such variability may be reduced by immunohistochemistry and
d tumor bud selection. Development of computer algorithms for this purpose requires unequivocal
dividual tumor buds. As such, we undertook a large-scale, international, and digital observer study on
or bud assessment. From a pool of 46 colorectal cancer cases with tumor budding, 3000 tumor bud
re selected, largely based on digital image analysis algorithms. For each candidate bud, an image patch
5 μm) was extracted from a pan cytokeratin-stained whole-slide image. Members of an International Tumor
ortium (n = 7) were asked to categorize each candidate as either (1) tumor bud, (2) poorly differentiated
neither, based on current definitions. Agreement was assessed with Cohen's and Fleiss Kappa statistics.
showed moderate overall agreement between observers (0.42 and 0.51), while Cohen's Kappas ranged
from 0.25 to 0.63. Complete agreement by all seven observers was present for only 34% of the 3000 tumor bud

Multimodal CEA-Targeted Image-Guided Colorectal Cancer Surgery using ^{111}In-Labeled SGM-101

Jan Marie de Gooyer[1,2], Fortuné M.K. Elekonawo[1,2], Desirée L. Bos[1], Rachel S. van der Post[3], André Pèlegrin[4], Bérénice Framery[5], Françoise Cailler[5], Alexander L. Vahrmeijer[6], Johannes H.W. de Wilt[2], and Mark Rijpkema[1]

ABSTRACT

Purpose: Intraoperative image guidance may aid in clinical decision-making during surgical treatment of colorectal cancer. We developed the dual-labeled carcinoembryonic antigen–[redacted] ^{111}In-DTPA-SGM-101, for pre- and intra-[redacted] cancer. Subsequently, we investi-[redacted] biodistribution and multimodal [redacted] and assessed the clinical feasibility [redacted] cancer samples, paving the way for [redacted].

[redacted]101 was conjugated with p-isothio-[redacted]inepentaacetic acid (DTPA) and [redacted]. The biodistribution of 3, 10, 30, [redacted]GM-101 was assessed in a dose [redacted]e mice with subcutaneous LS174T [redacted]ved by a study to determine the [redacted] Mice with intraperitoneal LS174T tumors underwent micro-SPECT/CT imaging and fluorescence image–guided resection. In a final translational experiment, we

incubated freshly resected human tumor specimens with the tracer and assessed the tumor-to-adjacent tissue ratio of both signals.

Results: The optimal protein dose of [^{111}In]In-DTPA-SGM-101 was 30 µg (tumor-to-blood ratio, 5.8 ± 1.1) and the optimal timepoint for imaging was 72 hours after injection (tumor-to-blood ratio, 5.1 ± 1.0). In mice with intraperitoneal tumors, [^{111}In]In-DTPA-SGM-101 enabled preoperative SPECT/CT imaging and fluorescence image–guided resection. After incubation of human tumor samples, overall fluorescence and radiosignal intensities were higher in tumor areas compared with adjacent nontumor tissue ($P < 0.001$).

Conclusions: [^{111}In]In-DTPA-SGM-101 showed specific accumulation in colorectal tumors, and enabled micro-SPECT/CT imaging and fluorescence image–guided tumor resection. Thus, [^{111}In]In-DTPA-SGM-101 could be a valuable tool for preoperative SPECT/CT imaging and intraoperative radio-guided localization and fluorescence image–guided resection of colorectal cancer.

Earlier Paper Award sessions

- 2014: Lauranne Derikx (Department of Gastroenterology)

Prior Colorectal Neoplasia Is Associated With Increased Risk of Ileoanal Pouch Neoplasia in Patients With Inflammatory Bowel Disease

- 2015: Robbert Weren (Department of Genetics)

A germline homozygous mutation in the base-excision repair gene *NTHL1* causes adenomatous polyposis and colorectal cancer

- 2017-2018: Daniel Garza (Department of Bioinformatics)

Towards predicting the environmental metabolome from metagenomics with a mechanistic model

Daniel R. Garza[1], Marcel C. van Verk[2,3], Martijn A. Huynen[1] and Bas E. Dutilh[1,2]*

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