Ultrathin colonoscopy can improve complete preoperative colonoscopy for stenotic colorectal cancer: a prospective observational study.

Related Articles

Ultrathin colonoscopy can improve complete preoperative colonoscopy for stenotic colorectal cancer: a prospective observational study.

Dig Endosc. 2020 Aug 31;:


Abstract

OBJECTIVES: Preoperative colonoscopy is often incomplete for stenotic colorectal cancers (CRC). This prospective observational study aimed to evaluate the ability of an ultrathin colonoscope (UTC) to inspect the whole colon by passing through the stenotic CRC.

METHODS: All patients who underwent preoperative colonoscopy for stenotic CRCs at Shizuoka Cancer Center were examined for eligibility. If a standard colonoscope (PCF-H290ZI) could not pass because of a stenosis, the patients were recruited. All of eligible patients were prospectively enrolled when informed consent could be obtained, and complete colonoscopy was attempted again using an UTC (PCF-PQ260L). Patients with stent placement and those requiring right hemicolecotomy were not recruited. Primary endpoints were pass-through and cecal intubation rates. The detected synchronous neoplasias (adenomas and cancers) and their pathological findings after resection were evaluated.

RESULTS: A total of 100 patients were enrolled between September 2017 and February 2019. The mean age was 65.6 ± 10.8 years, and 59% were male. The pass-through and cecal intubation rates were 67% (67÷100) and 58% (58÷100), respectively. Synchronous lesions located proximal to the stenoses were detected in 65.5% (38÷58) of the complete colonoscopies, with a total of 86 lesions, including 18 advanced neoplasias with three invasive cancers.

CONCLUSION: When standard colonoscopy cannot pass through stenotic CRC, ultrathin colonoscopy can be considered as an option to inspect the whole colon proximal to the stenosis because treatment strategy can potentially be changed by detecting synchronous neoplasias proximal to the stenosis before surgery.

Comparison of treatment strategies for splenic flexure colon cancer: Reply to Wang et al.

Related Articles

Comparison of treatment strategies for splenic flexure colon cancer: Reply to Wang et al.

Colorectal Dis. 2020 Aug 31;:

Authors: Hajibandeh S, Hajibandeh S, Hussain I, Zubairu A, Akbar F, Maw A

Abstract

In response to the comment regarding "several mistakes in grouping the patients into LH or SC arms", we should highlight that we defined each technique based on the segment of colon removed, ligation of the relevant arteries, and type of anastomosis. Unlike what was understood by the correspondence authors, our definitions have never been based on lymphadenectomy.

Factors Associated with Fibrosis during Colorectal Endoscopic Submucosal Dissection: Does Pretreatment Biopsy Potentially Elicit Submucosal Fibrosis and Affect Endoscopic Submucosal Dissection Outcomes?

Related Articles

Factors Associated with Fibrosis during Colorectal Endoscopic Submucosal Dissection: Does Pretreatment Biopsy Potentially Elicit Submucosal Fibrosis and Affect Endoscopic Submucosal Dissection Outcomes?
Flyer: Digestion. 2020 Aug 31;:1–9


Abstract

BACKGROUND: Submucosal fibrosis observed during colorectal endoscopic submucosal dissection (ESD) is an important factor related to incomplete resection. Biopsy is generally accepted as having the potential to elicit submucosal fibrosis, but few reports have presented definitive proof. This study investigated the relation between submucosal fibrosis and colorectal ESD outcomes and assessed factors related to fibrosis, including pretreatment biopsy.

METHODS: After reviewing 369 records of colorectal ESD performed between January 2011 and December 2016, we assessed the relation between fibrosis and ESD outcomes. Multiple logistic regression analysis revealed fibrosis risk factors.

RESULTS: Severe fibrosis was related significantly to ESD outcomes such as the mean procedure time (p

CONCLUSIONS: Pretreatment biopsy causes submucosal fibrosis resulting in prolonged procedure times and incomplete resection. These findings suggest important benefits of avoiding biopsy before ESD.

PMID: 32866955 [PubMed — as supplied by publisher]

Fluorophore-conjugated Helicobacter pylori recombinant membrane protein (HopQ) labels primary colon cancer and metastases in orthotopic mouse models by binding CEA-related cell adhesion molecules.

Related Articles

Fluorophore-conjugated Helicobacter pylori recombinant membrane protein (HopQ) labels primary colon cancer and metastases in orthotopic mouse models by binding CEA-related cell adhesion molecules.

Transl Oncol. 2020 Aug 28;13(12):100857


Abstract

HopQ is an outer-membrane protein of Helicobacter pylori that binds to human carcinoembryonic antigen-related cell-adhesion molecules (CEACAMs) with high specificity. We aimed to investigate fluorescence targeting of CEACAM-expressing colorectal tumors in patient-derived orthotopic xenograft (PDX) models with fluorescently labeled recombinant HopQ (rHopQ).

Western blotting, flow cytometry and ELISA were performed to determine the efficiency of rHopQ binding to CEACAMs. rHopQ was conjugated to IR800DyeCW (rHopQ-IR800). Nude mice received orthotopic implantation of colon cancer tumors. Three weeks later, mice were administered 25 μg or 50 μg HopQ-IR800 and imaged 24 or 48 h later. Intravital images were analyzed for tumor-to-background ratio (TBR). Flow cytometry and ELISA demonstrated binding of HopQ to CEACAM1, 3 and 5.

Dose-response intravital imaging in PDX models demonstrated optimal results 48 h after administration of 50 μg rHopQ-IR800 (TBR = 3.576) in our protocol. Orthotopic models demonstrated clear tumor margins of primary tumors and small regional metastases with a mean TBR = 3.678 (SD ± 1.027). rHopQ showed specific binding to various CEACAMs in PDX models. rHopQ may be useful for CEACAM-positive tumor and metastasis detection for pre-surgical diagnosis, intra-operative imaging and fluorescence-guided surgery.

PMID: 32866936 [PubMed — as supplied by publisher]

RUNX1 regulates TGF-β induced migration and EMT in colorectal cancer.

Related Articles

RUNX1 regulates TGF-β induced migration and EMT in colorectal cancer.


Authors: Lu C, Yang Z, Yu D, Lin J, Cai W

Abstract

Colorectal cancer (CRC) was one of the most malignant tumors worldwide due to its metastasis. Epithelial-to-mesenchymal transition (EMT) plays an important role in CRC migration, and transforming growth factor-β (TGF-β) works as a dominating cytokine in CRC EMT process. Here, we originally identified RUNX1 as an important factor among TGF-β induced EMT in CRC.

We found that RUNX1 was overexpressed with the treatment of TGF-β, accompanied with enhanced cancer cell migration and EMT which was characterized by up-graded N-Cadherin levels. Vice versa, knockdown of RUNX1 attenuated the migration ability of TGF-β induced CRC cells. In addition, decreased expression of N-Cadherin suggested that EMT was also attenuated after knocking down RUNX1. Similar decrease was observed in EMT regulator snail family transcriptional repressor 1 (SNAI1). And the knockdown effect of RUNX1 cannot be reversed by the addition of TGF-β. Moreover, we observed that RUNX1 expression was higher in CRC tumor tissues than in normal epithelial tissues. The enhanced expression was detected in cancer cell nucleus. These results revealed RUNX1 could regulate colorectal cancer migration via TGF-β signaling pathway, and RUNX1 might serve as a potential target for preventing CRC metastasis.

PMID: 32866710 [PubMed — as supplied by publisher]
Synthesis of flutamide-conjugates.

Related Articles

Synthesis of flutamide-conjugates.
Bioorg Med Chem Lett. 2020 Aug 28;:127507
Authors: Medina-Rojas JC, Castillo-Rodríguez IO, Martínez-Klimova E, Ramírez-Ápan T, Hernández-Ortega S, Martínez-García M

Abstract
In this paper, we designed and extended modification basing on the flutamide structure. A series of flutamide-conjugates were obtained with methyl bromoacetate and ethylenediamine. Through the synthesis of two conjugates with 3,5-bis(dodecyloxy)benzoate derivatives, these flutamide conjugates were tested for anticancer activity. Among the compounds tested, the flutamide-conjugates showed good inhibition activity against cancer cell lines U-251, PC-3 and K-562. The conjugates showed a better inhibitory effect than free flutamide and did not show activity against normal COS-7 monkey kidney fibroblast cells. It was also observed that the flutamide conjugates had an inhibitory effect against human colorectal adenocarcinoma HCT-15.

PMID: 32866675 [PubMed — as supplied by publisher]

Lnc-FAM84B-4 acts as an oncogenic lncRNA by interacting with protein hnRNPK to restrain MAPK phosphatases-DUSP1 expression.

Related Articles

Lnc-FAM84B-4 acts as an oncogenic lncRNA by interacting with protein hnRNPK to restrain MAPK phosphatases-DUSP1 expression.
Cancer Lett. 2020 Aug 28;:

Abstract
The mitogen activated protein kinase (MAPK) pathway has been reported to be involved in many cancer developments. Normally, MAPK activity is self-limited between rapid phosphorylation and dephosphorylation. In abnormal conditions, however, this dynamic equilibrium is broken, triggering tumor-suppressing or -promoting roles. While dual-specificity MAPK phosphatases (MKP/DUSPs) are important for cascade control in MAPK pathway, their role in colorectal cancer (CRC) remains largely unknown. Here, we investigated Lnc-FAM84B-4 and DUSP1 to systematically elucidate their underlying roles in MAPK singling pathway and functions in CRC. Uregulated Lnc-FAM84B-4 was identified by re-mining CRC microarray. Functional assays were performed in vitro and in vivo. RNA-Seq, RNA pull-down, and RIP assays were used to investigate the mechanisms of Lnc-FAM84B-4 in regulating expression of DUSP1. The results indicated that Lnc-FAM84B-4 regulates MAPK pathway by restraining DUSP1 expression. Mechanistically, RNA pull-down followed by mass spectrum determined hnRNPK functions as a binding partner of Lnc-FAM84B-4 in mediating DUSP1 expression. Our findings demonstrate the important role of Lnc-FAM84B-4-hnRNPK-DUSP1 axis in CRC development, and suggest a therapeutic target for CRC treatment.

PMID: 32866608 [PubMed — as supplied by publisher]

Epidermal growth factor (EGF)-based activatable probe for predicting therapeutic outcome of an EGF-based doxorubicin prodrug.

Related Articles

Epidermal growth factor (EGF)-based activatable probe for predicting therapeutic outcome of an EGF-based doxorubicin prodrug.
J Control Release. 2020 Aug 28;:
Authors: Kim HY, Um SH, Sung Y, Shim MK, Yang S, Park J, Kim ES, Kim K, Kwon IC, Ryu JH

Abstract
One of the most promising approaches for the treatment of colorectal cancer is targeting epidermal growth factor receptor (EGFR). Comprehensive research has led to significant clinical outcomes using EGFR-targeted anticancer drugs; however, the response to these drugs still largely varies among individuals. The current diagnostic platform provides limited information that does not enable successful prediction of the anticancer performance of EGFR-targeted drugs. Here, we developed an EGFR-targeted activatable probe for predicting therapeutic efficacy of EGFR-targeted doxorubicin prodrug in colorectal cancer therapy. The EGF-conjugated fluorescence-activatable probe (EGF-probe) and EGF-conjugated doxorubicin prodrug (EGF-prodrug) were both fabricated using peptide substrates that can be dissociated by lysosomal enzymes, and thus share an intracellular mechanism of action. We demonstrated that after EGFR-mediated endocytosis, lysosomal enzymes de-quench the fluorescence of EGF-probe and activate the cytotoxicity of EGF-prodrug. When evaluated in vivo, EGF-probe yielded an outstanding cancer-specific imaging ability with reduced background signals. EGF-prodrug also successfully targeted the tumor and promoted cancer cell death. We tested different colorectal cancer cell types to investigate the correlation between the fluorescence recovery efficiency of EGF-probe and the cytotoxicity of EGF-prodrug. Strong correlations were observed both in vitro and in vivo. The actions of EGF-probe and EGF-prodrug were dependent on the inherent lysosomal activity of the cell type rather than its EGFR expression level. Our proposed approach using EGF-probe and EGF-prodrug may overcome the major drawback of the conventional theranostic platform and
provide great opportunity for successful personalized cancer therapy.

PMID: 32866592 [PubMed — as supplied by publisher]

Superior outcomes of nodal metastases compared to visceral sites in oligometastatic colorectal cancer treated with stereotactic ablative radiotherapy.

Related Articles

Superior outcomes of nodal metastases compared to visceral sites in oligometastatic colorectal cancer treated with stereotactic ablative radiotherapy.


Abstract

BACKGROUND: Stereotactic ablative radiotherapy (SBRT) is a radical option for oligometastatic colorectal cancer (CRC) patients, but most data relate to visceral metastases.

METHODS: A prospective, multi-centre database of CRC patients treated with SBRT was interrogated. Inclusion criteria were ECOG PS 0–2, ≤ 3 sites of disease, a disease free interval of > 6 months unless synchronous liver metastases. Primary endpoints were local control (LC), progression free survival (PFS) and overall survival (OS).

RESULTS: 163 patients (172 metastases) were analysed. The median FU was 16 months (IQR 12.2 — 22.85). The LC at 1 year was 83.8% (CI 76.4% — 91.9%) with a PFS of 55% (CI 47% — 64.7%) respectively. LC at 1 year was 90% (CI 83% — 99%) for nodal metastases (NM), 75% (63% — 90%) for visceral metastases (VM). NM had improved median PFS (9 vs 19 months) [HR 0.6, CI 0.38 — 0.94, p = 0.032] and median OS (32 months vs not reached) [HR 0.28, CI 0.18 — 0.7, p = 0.0062] than VM, regardless of whether the NM were located inside or outside the pelvis. On multivariate analysis, NM and ECOG PS 0 were significant good prognostic factors. An exploratory analysis suggests KRAS WT is also a good prognostic factor.

CONCLUSION: Nodal site is an important prognostic determinant of SBRT that should incorporated into patient selection. We hypothesise this may have an immunoediting basis.

PMID: 32866563 [PubMed — as supplied by publisher]


Related Articles


Ann Intern Med. 2020 Sep 01,:Authors: Lu MT, Raghu VK, Mayrhofer T, Aerts HJWL, Hoffmann U

Abstract

BACKGROUND: Lung cancer screening with chest computed tomography (CT) reduces lung cancer death. Centers for Medicare & Medicaid Services (CMS) eligibility criteria for lung cancer screening with CT require detailed smoking information and miss many incident lung cancers. An automated deep-learning approach based on chest radiograph images may identify more smokers at high risk for lung cancer who could benefit from screening with CT.

OBJECTIVE: To develop and validate a convolutional neural network (CXR-LC) that predicts long-term incident lung cancer using data commonly available in the electronic medical record (EMR) (chest radiograph, age, sex, and whether currently smoking).

DESIGN: Risk prediction study.


PARTICIPANTS: The CXR-LC model was developed in the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial (n = 41 856). The final CXR-LC model was validated in additional PLCO smokers (n = 5615, 12-year follow-up) and NLST (National Lung Screening Trial) heavy smokers (n = 5493, 6-year follow-up). Results are reported for validation data sets only.

MEASUREMENTS: Up to 12-year lung cancer incidence predicted by CXR-LC.

RESULTS: The CXR-LC model had better discrimination (area under the receiver-operating characteristic curve [AUC]) for incident lung cancer than CMS eligibility (PLCO AUC, 0.755 vs. 0.634; P LIMITATION: Validation in lung cancer screening trials and not a clinical setting.

CONCLUSION: The CXR-LC model identified smokers at high risk for incident lung cancer, beyond CMS eligibility and using information commonly available in the EMR.

PRIMARY FUNDING SOURCE: None.

PMID: 32866413 [PubMed — as supplied by publisher]
Additional outreach effort of providing an opportunity to obtain a kit for fecal immunochemical test during the general health check-up to improve colorectal cancer screening rate in Japan: A longitudinal study.

Authors: Fujita M, Fujisawa T, Hata A

Abstract

OBJECTIVES: A sufficient screening rate is indispensable to optimize the positive impact of colorectal cancer (CRC) screening. This study aimed to evaluate the effect of an additional outreach of providing an opportunity to obtain a kit for fecal immunochemical test (FIT) during the general health check-up to increase CRC screening rate.

METHODS: This was a longitudinal study using pre-existing data in Kujukuri Town, Japan. The town provided CRC screening in the fiscal year (FY) 2017 using an existing procedure for all beneficiaries of the National Health Insurance, whereas in FY 2018, an additional outreach effort was made to only those with an even number of age (exposed group), who were offered an opportunity to obtain a kit for FIT at the time of general health check-ups but not to those with an odd number of age (control group). To estimate the effectiveness, generalized estimating equation (GEE) with individuals as clusters was performed.

RESULTS: In total, 3,530 individuals were included (1,708 in the control group and 1,822 in the exposed group). GEE showed significant interaction between the groups (control and exposed) and FYs (2017 and 2018) (p