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Coloproctologie

Geen rol voor routinematig peroperatieve echografie ter opsporing levermetastasen

Background Intraoperative ultrasonography during open surgery for colorectal cancer may be useful for the detection of unrecognized liver metastases. Laparoscopic ultrasonography (LUS) for the detection of unrecognized liver metastasis has not been studied in a randomized trial. This RCT tested the hypothesis that LUS would change the TNM stage and treatment strategy.

Method Patients with colorectal cancer and no known metastases were randomized (1 : 1) to laparoscopic examination (control or laparoscopy plus LUS) in three Danish centres. Neither participants nor staff were blinded to the group assignment.

Results Three hundred patients were randomized, 150 in each group. After randomization, 43 patients were excluded, leaving 128 in the control group and 129 in the LUS group. Intraoperative T and N categories were not altered by LUS, but laparoscopy alone identified previously undetected M1 disease in one patient (0·8 per cent) in the control group and three (2·3 per cent) in the LUS group. In the latter group, LUS suggested that an additional six patients (4·7 per cent) had M1 disease with liver (4) or para-aortal lymph node (2) metastases. The change in treatment strategy was greater in the LUS than in the control group (7·8 (95 per cent c.i. 3·8 to 13·8) and 0·8 (0 to 4·2) per cent respectively; P = 0·010), but the suspected M1 disease was benign in half of the patients.

Conclusion Routine LUS during resection of colorectal cancer is not recommended. Registration number: NCT02079389 (http://www.clinicaltrials.gov).

Analyse van microRNAs bij rectumcarcinoom draagt bij aan gevoeligheidsbepaling voor neoadjuvante therapie

Objective The aim of the study was to explore specific microRNAs (miRs) in rectal cancer that would predict response to radiation and identify target pathways that may be exploited for neoadjuvant therapies.
Summary Background Data

Chemoradiotherapy (CRT) response is a predictor of survival in rectal cancer. Studies have demonstrated changes in RNA expression correlate with chemoradiation sensitivity across cancers.

Methods Forty-five rectal cancer patients, partial responders (PR = 18), nonresponders (NR = 13), and complete responders (CR = 14) to CRT, as defined by a tumor regression score, were examined. miRs differentially

expressed, using NanoString microArray profiling, were validated with qPCR. We quantified 1 miR and its downstream targets in patient samples. Chemosensitivity was measured in HCT-116, a human colorectal carcinoma cell line, using inhibitors of SHP2 and RAF.

Results miR-451a, 502-5p, 223-3p, and 1246 were the most upregulated miRs (>1.5-fold change) in a NanoString profiling miR panel. qPCR revealed a decrease in expression of miR-451a in NRs. EMSY and CAB39, both downstream targets of miR-451a and involved in carcinogenesis (shown in TCGA) were increased in NRs (qPCR). Both targets are associated with worse survival in colorectal cancer. Inhibition of miR-451a in HCT-116 cells significantly decreased cell proliferation with treatment of SHP2 and RAF inhibitors.

Conclusions An integrated analysis of rectal cancer miRs may yield biomarkers of radioresistance and offer treatment targets for resensitization.

UPPER GI

De op CT-bepaalde 'number of tumour' correleert met werkzaamheid van neoadjuvante therapie bij slokdarmkanker

Usefulness of computed tomography density of a tumor in predicting the response of advanced esophageal cancer to preoperative chemotherapy. Kohei Wakatsuki et al. Surgery: October 2017 Volume 162, Issue 4, Pages 823–835.
Pubmedid 28709645

Background In Japan, preoperative chemotherapy is considered essential for resectable stage II or III esophageal cancers. It is important to identify nonresponders for preoperative chemotherapy because continuing ineffective chemotherapy is not beneficial for them. We investigated the correlation between the computed tomography number of tumor and the effect of preoperative chemotherapy in patients with esophageal cancer.

Methods This retrospective study included 50 patients receiving preoperative chemotherapy with docetaxel, cisplatin, and 5-fluorouracil for stage II or III esophageal cancer. The computed tomography number of tumor was measured as the mean of Hounsfield Units of the primary lesion on a plain computed tomography measured within a freehand region of interest drawn around the tumor border. For analysis, the patients were classified into responders and nonresponders to chemotherapy, with the pathologic response evaluated using the Japanese and Mandard classification. We analyzed the associations between the computed tomography number of tumor and clinical factors; histopathologic features, including the tumor size, depth of tumor invasion, capillary invasion, Ki-67, p53, and CK5/6 expression; the pathologic response to chemotherapy and prognosis.

Results There was a significant association between the computed tomography number of tumor and the response to chemotherapy. The cut-off value of the computed tomography number of tumor in predicting responders to chemotherapy was 40 Hounsfield Units (area under the receiver operating characteristic curve = 0.73, P = .009); patients with computed tomography number of tumor greater than this value significantly responded to chemotherapy (P = .02 in the Japanese and P = .009 in the Mandard classification) with good postoperative prognosis (P = .04). Only Ki-67 expression among the histopathogic features were associated with the computed tomography number of tumor in histopathologic features (P = .01).

Conclusion The computed tomography number of tumor may be useful to predict the efficacy of preoperative chemotherapy and subsequent prognosis for patients with advanced esophageal cancer.

Rol voor PETscan in de respons evaluatie van inductietherapie bij cT4 slokdarmcarcinoom

Importance of positron emission tomography for assessing the response of primary and metastatic lesions to induction treatments in T4 esophageal cancer+. Tomoki Makino et al. Surgery: October 2017 Volume 162, Issue 4, Pages 836–845

Pubmedid 28711321

Background There is no consensus strategy for treatment of T4 esophageal cancer, and because of this, a better evaluation of treatment response is crucial to establish personalized therapies. This study aimed to establish a useful system for evaluating treatment response in T4 esophageal cancer.

Methods This study included 130 patients with cT4 esophageal cancer without distant metastasis who underwent 18F-fluorodeoxyglucose-positron emission tomography before and after a series of induction treatments comprising chemoradiation or chemotherapy. We evaluated the maximal standardized uptake value and treatment response.

Results The mean ± standard deviation of standardized uptake value in the primary tumor before and after induction treatments were 13.8 ± 4.4 and 5.4 ± 4.1, respectively, and the mean standardized uptake value decrease was 58.4%. The most significant difference in survival between positron emission tomography-primary tumor responders and nonresponders was at a decrease of 60% standardized uptake value, based on every 10% stepwise cutoff analysis (2-year cause-specific survival: 60.2 vs 23.5%; hazard ratio = 2.705; P < .0001). With this cutoff value, the resectability (P = .0307), pathologic response (P = .0004), and pT stage (P < .0001) were associated with positron emission tomography-primary tumor response. Univariate analysis of 2-year cause-specific survival indicated a correlation between cause-specific survival and clinical stages according to TNM classification, esophageal perforation, positron emission tomography-primary tumor response, lymph node status evaluated by positron emission tomography before and after induction treatments, and operative resection. Multivariate analysis further identified positron emission tomography-primary tumor response (hazard ratio = 2.354; P = .0107), lymph node status evaluated by positron emission tomography after induction treatments (hazard ratio = 1.966; P = .0089), and operative resection (hazard ratio = 2.012; P = .0245) as independent prognostic predictors.

Conclusion Positron emission tomography evaluation of the response of primary and metastatic lesions to induction treatments is important to formulate treatment strategies for cT4 esophageal cancer.

HPB

Geen verschil in morbiditeit en overleving tussen verschillende methodes van veneuze reconstructie bij bordeline resectabel pancreascarcinoom

Impact of portal vein infiltration and type of venous reconstruction in surgery for borderline resectable pancreatic cancer (BJS) R. Ravikumar et al. BJS, Oct 2017 – Volume 104 – Issue 11, pages 1539-1548

Pubmedid 28833055

Background The International Study Group of Pancreatic Surgery (ISGPS) recommends operative exploration and resection of pancreatic cancers in the presence of reconstructable mesentericoportal axis involvement. 15

However, there is no consensus on the ideal method of vascular reconstruction. The effect of depth of tumour invasion of the vessel wall on outcome is also unknown.

Method This was a retrospective cohort study of pancreaticoduodenectomy with vein resection for T3 adenocarcinoma of the head of the pancreas across nine centres. Outcome measures were overall survival based on the impact of the depth of tumour infiltration of the vessel wall, and morbidity, in-hospital mortality and overall survival between types of venous reconstruction: primary closure, end-to-end anastomosis and interposition graft.

Results A total of 229 patients underwent portal vein resection; 129 (56·3 per cent) underwent primary closure, 64 (27·9 per cent) had an end-to-end anastomosis and 36 (15·7 per cent) an interposition graft. There was no difference in overall morbidity (26 (20·2 per cent), 14 (22 per cent) and 9 (25 per cent) respectively; P = 0·817) or in-hospital mortality (6 (4·7 per cent), 2 (3 per cent) and 2 (6 per cent); P = 0·826) between the three groups. One hundred and six patients (47·5 per cent) had histological evidence of vein involvement; 59 (26·5 per cent) had superficial invasion (tunica adventitia) and 47 (21·1 per cent) had deep invasion (tunica media or intima). Median survival was 18·8 months for patients who had primary closure, 27·6 months for those with an end-to-end anastomosis and 13·0 months among patients with an interposition graft. There was no significant difference in median survival between patients with superficial, deep or no histological vein involvement (20·8, 21·3 and 13·3 months respectively; P = 0·111). Venous tumour infiltration was not associated with decreased overall survival on multivariable analysis.

Conclusion In this study, there was no difference in morbidity between the three modes of venous reconstruction, and overall survival was similar regardless of tumour infiltration of the vein.

Een derde van patiënten blijkt irresectabel tijdens chirurgische exploratie bij pancreascarcinoom

Background Despite improvements in diagnostic imaging and staging, unresectable pancreatic cancer is still encountered during surgical exploration with curative intent. This nationwide study investigated outcomes in patients with unresectable pancreatic cancer found during surgical exploration.

Method All patients diagnosed with primary pancreatic (adeno)carcinoma (2009–2013) in the Netherlands Cancer Registry were included. Predictors of unresectability, 30-day mortality and poor survival were evaluated using logistic and Cox proportional hazards regression analysis. 16

Results There were 10 595 patients with pancreatic cancer during the study interval. The proportion of patients undergoing surgical exploration increased from 19·9 to 27·0 per cent (P < 0·001). Among 2356 patients who underwent surgical exploration, the proportion of patients with tumour resection increased from 61·6 per cent in 2009 to 71·3 per cent in 2013 (P < 0·001), whereas the contribution of M1 disease (18·5 per cent overall) remained stable. Patients who had exploration only had an increased 30-day mortality rate compared with those who underwent tumour resection (7·8 versus 3·8 per cent; P < 0·001). In the non-resected group, among those with M0 (383 patients) and M1 (435) disease at surgical exploration, the 30-day mortality rate was 4·7 and 10·6 per cent (P = 0·002), median survival was 7·2 and 4·4 months (P < 0·001), and 1-year survival rates were 28·0 and 12·9 per cent, respectively. Among other factors, low hospital volume (0–20 resections per year) was an independent predictor for not undergoing tumour resection, but also for 30-day mortality and poor survival among patients without tumour resection.

Conclusion Exploration and resection rates increased, but one-third of patients who had surgical exploration for pancreatic cancer did not undergo resection. Non-resectional surgery doubled the 30-day mortality rate compared with that in patients undergoing tumour resection.

LEVERCHIRURGIE

Geen verbeterde leverfunctie na transectie leverparenchym na vena porta embolisatie in konijnen

Background Associating liver partition with portal vein ligation for staged hepatectomy induces more extensive liver hypertrophy than ligation alone; however, the mechanisms underlying the accelerated liver regrowth and the functional quality of the hypertrophic liver are presently elusive. This study, therefore, investigated the effect of parenchymal transection on liver volume and function after portal vein embolization in a standardized rabbit model.

Methods Twelve rabbits were subjected to portal vein embolization of the cranial liver lobes and randomized between parenchymal transection of the left lateral liver lobe versus no transection (portal vein embolization only). Liver volume of the nonembolized liver lobe was assessed using computed tomography–volumetry, and liver uptake function was determined by 99mTc-mebrofenin hepatobiliary scintigraphy before and 3 and 7 days after portal vein embolization.

Results The increase in nonembolized liver volume 3 days after portal vein embolization was 2.7-fold greater in the transected group compared with the portal vein embolization only group (56 ± 16% vs 21 ± 12%, respectively, P < .01) and 1.7-fold greater 7 days after portal vein embolization (113 ± 34% vs 68 ± 24%, P < .01). Liver uptake function did not differ between groups before portal vein embolization (8.4 ± 3.7%/min in the transection group vs 8.9 ± 1.6%/min) on day 3 (33.2 ± 4.7% after transection vs 30.3 ± 4.6%/min, respectively) and day 7 after portal vein embolization (42.6 ± 8.4% vs 39.1 ± 5.3%/min, respectively).

Conclusion Parenchymal transection after portal vein embolization increases liver growth in terms of volume but not function. These results indicate that the rapid volume increase observed after associating liver partition with portal vein ligation for staged hepatectomy does not coincide with the clinically more relevant functional increase. Quantitative liver function tests might be essential in associating liver partition with portal vein ligation for staged hepatectomy to better assess the hypertrophy response and improve clinical decision-making.

Simpele cholecystectomie met adjuvante therapie biedt overlevingsvoordeel ten opzichte van uitgebreide resectie bij galblaascarcinoom

Surgical Management of Gallbladder Cancer: Simple Versus Extended Cholecystectomy and the Role of Adjuvant Therapy. Kasumova, Gyulnara G et al. Annals of Surgery; Oktober 2017 – Volume 266 – Issue 4 – p 625-631

Objective To assess if simple cholecystectomy with adjuvant therapy could provide outcomes comparable to extended cholecystectomy.

Background Current guidelines recommend extended/radical cholecystectomy for T2/T3 gallbladder cancer; however, many tumors are discovered incidentally at laparoscopic cholecystectomy.

Methods The national Cancer Data Base 2004 to 2014 was queried for patients with pT2/T3 gallbladder adenocarcinoma who underwent resection. Adjuvant therapy was defined as chemotherapy, with or without radiotherapy, within 90 days of surgery. Baseline characteristics and overall survival were compared by χ2 and Kaplan-Meier method, respectively. One-to-one propensity score matching for receipt of adjuvant therapy was used to account for potential selection bias.

Results A total of 6825 patients were identified. Diagnosis was made predominantly (78.9%) at the time of surgery or on pathology; 31.8% (2168) received adjuvant therapy. The majority, 88.8% (6060), had a simple cholecystectomy. Patients who received adjuvant therapy versus surgery alone were more likely to: be younger, privately insured, have no comorbidities, pT3 disease, positive lymph nodes, positive resection margins, and extended cholecystectomy. After matching, median survival was significantly longer for extended cholecystectomy with adjuvant therapy (23.3 months) than cholecystectomy with adjuvant therapy (16.4 months), which was significantly longer than either simple (12.4 months) or extended (10.7 months) cholecystectomy alone (all log-rank P<0.001).

Conclusions Adjuvant therapy prolongs survival after resection of T2/T3 tumors. Simple cholecystectomy with adjuvant therapy appears to be superior to extended resection alone in the short term and may serve as a potential alternative to re-resection in select high-risk individuals.

BARIATRISCHE CHIRURGIE

Matig positief vijf-jaars effect van gastric sleeve op type 2 diabetes

Laparoscopic sleeve gastrectomy: Effect on long-term remission for morbidly obese patients with type 2 diabetes at 5-year follow up. Marius Nedelcu et al. Surgery: October 2017 Volume 162, Issue 4, Pages 857–862

Background In the short-term, laparoscopic sleeve gastrectomy has been shown to be effective for the treatment of the type 2 diabetes in patients with severe obesity. There are few data with greater follow-up. Our aim was to evaluate the results of laparoscopic sleeve gastrectomy on the control of type 2 diabetes in patients with severe obesity at 5 years at the University Hospital, France.

Methods From a total of 355 patients with severe obesity operated between January 2006 and June 2010, 52 (15%) had a diagnosis of type 2 diabetes before undergoing laparoscopic sleeve gastrectomy.

Results There were 31 females (60%) and 21 males (40%), with a mean age of 51 ± 10 years (range 27–67) with a mean body mass index of 48 ± 10 kg/m2 (range 35–82). The mean duration of type 2 diabetes was 10.8 ± 10.8 years before bariatric operation. The preoperative glycated hemoglobin was

8 ± 2% (range 5.9–12.8) in 45 patients; 17 patients (38%) had levels of glycated hemoglobin ≥9%. Three patients (6%) required insulin alone, 4 (8%) were taking oral antidiabetic medicine and insulin, and the remaining 45 patients (87%) were taking only oral antidiabetic medicines. The complete data regarding weight loss at 5-year follow-up were obtained for 46 patients, yielding an overall follow-up rate of 89%. The prolonged remission of type 2 diabetes achieved at 1 year that persisted at 5 years of follow-up was present in 9 patients (17%). No patient with complete remission of their type 2 diabetes required insulin preoperatively. Improvement of type 2 diabetes was observed in 30 patients (58%) at 1 year, which was maintained for 27 patients (52%) at 5-year follow-up.

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Conclusion Laparoscopic sleeve gastrectomy has demonstrated a moderate efficacy in the treatment morbidly obese patients with type 2 diabetes. Markedly increased preoperative glycated hemoglobin levels, older age, and preoperative need for insulin treatment may be the factors predicting failure of complete remission of type 2 diabetes after laparoscopic sleeve gastrectomy.