Random biopsies taken during colonoscopic surveillance of patients with longstanding ulcerative colitis: low yield and absence of clinical consequences

van den Broek FJ, Stokkers PC, Reitsma JB, Boltjes RP, Ponsioen CY, Fockens P, Dekker E.

Am J Gastroenterol 2014; 109(5):715-22.

http://www.ncbi.nlm.nih.gov/pubmed/21427710

This retrospective European study of 466 colonoscopies in 167 patients over a 10 year period for surveillance of ulcerative colitis found that random biopsies are low-yield for detection of neoplasia, with 6% of the colonoscopies with neoplasia having found that neoplasia by random biopsy, while 94% of the colonoscopies yielding a biopsy diagnosis of neoplasia included targeted biopsies. They further report that of the four patients having a diagnosis of UC-associated neoplasia on random biopsy, only one of these had clinical consequences. Their study raises the question of the necessity and cost-effectiveness of random biopsies for UC surveillance.

Cthrc1 overexpression is an independent prognostic marker in gastric cancer

Gu L, Liu L, Zhong L, Bai Y, Sui H, Wei X, Zhang W, Huang P, Gao D, Kong Y, Lou G.

Human Pathol 2014; 45(5):1031-8.

http://www.ncbi.nlm.nih.gov/pubmed/24746208

This immunohistochemical study found overexpression of Cthrc1, a marker of arterial injury, in gastric cancer as compared to controls. Expression levels were based on a combined score of percent positivity and staining intensity. High Cthrc1 expression was found in 108 of 166 gastric cancers (65%) and positively correlated with AJCC stage, depth of invasion, lymph node involvement, lymphovascular space involvement, and recurrence. High Cthrc1 expression was also correlated with poorer overall survival and disease-free survival as compared to low expression, and was an independent prognostic factor for survival.

Validation study of the Esohisto consensus guidelines for the recognition of microscopic esophagitis (histoGERD Trial)

Schneider NI, Plieschnegger W, Geppert M, Wigginghaus B, Hoess GM, Eherer A, Wolf EM, Rehak P, Vieth M, Langner C.

Human Pathol 2014; 45(5):994-1002.

http://www.ncbi.nlm.nih.gov/pubmed/24746203

This prospective European trial included 1071 patients undergoing upper endoscopy for unselected reasons, of which 452 reported symptoms of esophageal disease, and 503 were taking a PPI. The histology was assessed according to the Esohisto guidelines, which incorporate basal cell hyperplasia, papillary elongation, dilation of intercellular spaces, and intraepithelial eosinophils, neutrophils, and mononuclear cells to result in a combined severity score of normal or mild or severe microscopic esophagitis. 352 (33%) patients had normal histology, 423 (40%) had mild microscopic esophagitis, and 296 (28%) had severe microscopic esophagitis. Changes of the squamous epithelium were more common than inflammatory infiltration overall. Of 450 patients with normal esophagus on endoscopy (modified LA Grade N), 42% had mild microscopic esophagitis and 17% had severe microscopic esophagitis, indicating higher sensitivity of histology over endoscopy for esophagitis detection. The authors conclude that histology is correlated with symptoms and endoscopic impression of GERD and that esophageal biopsy should be obtained routinely for patients undergoing upper endoscopy for evaluation of GERD.

Matched biopsy and resection specimens of gastric and gastroesophageal adenocarcinoma show high concordance in HER2 status

Wang T, Hsieh ET, Henry P, Hanna W, Streutker CJ, Grin A.

Human Pathol 2014; 45(5):970-5.

http://www.ncbi.nlm.nih.gov/pubmed/24656529

A study of gastric and GEJ adenocarcinomas HER2 status in biopsy as compared to resection specimens, including 128 patients with paired samples. IHC was performed in all cases and in situ hybridization was performed if IHC was equivocal (2+) on either biopsy or resection or in discrepant cases. HER2 overexpression was found in 18 cases (14%) with a concordance rate between biopsy and resection of 96%. Five discrepant cases included overexpression in biopsy alone in 2 cases and in resection alone in 3 cases. The majority of the discrepant cases (80%) showed tumor heterogeneity, defined as 3+ or 2+ staining in 10% to 60% of tumor cells, while only 24% of concordant cases showed tumor heterogeneity.

Correlation of ALOX15 expression with eosinophilic or reflux esophagitis in a cohort of pediatric patients with esophageal eosinophilia

Matoso A, Allen D, Herzlinger M, Ferreira J, Chen S, Lu S, Fabre V, Monahan R, Yang D, Noble L, Mangray S, Resnick MB.

Human Pathol 2014; 45(6):1205-12.

http://www.ncbi.nlm.nih.gov/pubmed/24742828

This immunohistochemical study found that ALOX15 was expressed in 90.5% of pediatric patients with at least one esophageal biopsy containing at least 15 eosinophils per high-power field (eosinophilic esophagitis group) as compared to 44% expression in the control gastroesophageal reflux group. ALOX15 positive GERD cases tended to have a higher average number of peak eosinophils per high-power field. For patients with more than 15 eos/HPF in the distal esophagus only, the sensitivity of ALOX15 for detecting EoE is only 81.2%, and the specificity is only 50%.

Barrett's esophagus translational research network (BETRNet): the pivotal role of multi-institutional collaboration in esophageal adenocarcinoma research

Abrams JA, Appelman HD, Beer DG, Berry LD, Chak A, Falk GW, Fitzgerald RC, Ginsberg GG, Grady WM, Joshi BP, Lynch JP, Markowitz S, Richmond ES, Rustgi AK, Seibel EJ, Shaheen NJ, Shyr Y, Umar A, Wang KK, Wang TC, Wang TD, Yassin R.

Gastroenterology 2014; 146(7):1586-90.

http://www.ncbi.nlm.nih.gov/pubmed/24768332

Commentary on the rationale, development, efficiencies, and individual contributions of a multi-institutional collaboration in esophageal adenocarcinoma research, allowing opportunities for multi-faceted projects which aim to answer “Big” questions.

PTEN loss and KRAS activation leads to the formation of serrated adenomas and metastatic carcinoma in the mouse intestine.

Davies EJ, Durban VM, Menie V, Williams GT, Clarke AR.

J Pathol 2014; 233:27-38.

http://www.ncbi.nlm.nih.gov/pubmed/24293351

The investigators inserted mutant Kras and PTEN genes under VillinCreER control that could be activated by treatment with Tamoxifen. When the inserted mutated Kras and PTEN genes were activated in wild type mice the small bowel villi became hyperplastic and hyperproliferative, apparently driven by activation of the PI3'K pathway. In longer term studies of the aged mice serrated polyps (hyperplastic polyps and sessile serrated adenomas) developed in the small bowel and ultimately led to the development of small bowel adenocarcinomas. The authors suggest that this murine model may be valuable in the study of the serrated pathology of colonic adenocarcinoma in humans, and feel that further studies of the contribution of PTEN mutations in human colon cancer arising via the serrated pathway are warranted.

Outcomes of children after esophagogastroduodenoscopy for chronic abdominal pain.

Thakkar K, Chen L, Tessier ME, Gilger MA.

Clin Gastroenterol Hepatol 2014; 12:963-9.

http://www.ncbi.nlm.nih.gov/pubmed/24016631

This prospective cohort study studied children between the ages of 4 and 18 years who underwent initial upper endoscopy to evaluate clinically significant chronic abdominal pain of unknown etiology of at least 2 month duration. The study included only otherwise healthy children (patients with a history of reflux esophagitis were included) and required that at least one biopsy of the esophagus, stomach and duodenum be performed. The investigators report a diagnostic yield of 38% based on histologic findings in the 290 studied children. A median of 9 biopsies were obtained (mean = 10). Diagnoses included reflux esophagitis (21%), eosinophilic esophagitis (4.5%), eosinophilic gastroenteritis 4.1%), H. pylori gastritis (2.8%), celiac disease (0.6%), Crohn disease (0.3%) and chemical gastritis (0.3%). A multivariate logistic regression model of clinical features predictive of finding a pathologic condition included black race, male gender and the presence of two or more "alarm features" (e.g., nighttime awakening due to pain).

Lymph node revealing solutions in colorectal cancer: should they be used routinely?

Horne J, Bateman AC, Carr NJ, Ryder I.

J Clin Pathol 2014; 67:383-88.

http://www.ncbi.nlm.nih.gov/pubmed/24493650

This comprehensive review covers the utility and drawbacks of the use of fat clearing agents as an aid for lymph node recovery in colectomy specimens, with special emphasis on rectal resections after chemoradiation therapy. The authors have performed an exhaustive review of published articles in this area and summarize the available data regarding the number of additional nodes recovered, the effect on staging, and the size of the additional nodes recovered. They also describe the limitations of the published literature in terms of the variety of primary node dissection methods, and the toxicity and time and cost of the use of clearing agents. The authors conclude that the use of a clearing agent composed of glacial acetic acid, ethanol, water and formalin has promise for rectal resection specimens in terms of better patient management.

Cancer risk after resection of polypoid dysplasia in patients with longstanding ulcerative colitis: a meta-analysis.

Wanders LK, Dekker E, Pullens B, Bassett P, Travis SPL, East JE.

Clin Gastroenterol Hepatol 2014; 12(5):756-64.

http://www.ncbi.nlm.nih.gov/pubmed/?term=Cancer+risk+after+resection+of+polypoid+dysplasia+in+patients+with+longstanding+ulcerative+colitis%3A+a+meta-analysis

This meta-analysis included 376 patients from 10 published studies who developed a polypoid dysplastic lesion at a mean of 15.7 after diagnosis of IBD. After a mean follow-up period of 54.4 months following endoscopic removal of the polypoid lesion (total follow-up 1704 years) 9 of the 376 patients (5.3 per 1000 patient years of follow-up) developed invasive colorectal cancer, while 100 patients developed additional polypoid or flat dysplastic lesions (65 per 1000 patient years of follow-up). The prevalence of PSC was only reported in 5 of the 10 studies which included 224 patients, 15 of which were reported to have PSC. The authors conclude that while the risk of invasive cancer development over the short term of follow-up is low, the relatively high risk of additional dysplasia suggests that patients with polypoid dysplastic lesions should be monitored closely by follow-up colonoscopy.

Microscopic colitis and colorectal neoplastic lesion rate in chronic nonbloody diarrhea: a prospective, multicenter study.

Tontini GE, Pastorelli L, Spina L, Fabris F, Bruni B, Clemente C, de Nucci G, Cavallaro F, Marconi S, Neurath MF, Neumann H, Tacconi M, Vecchi M.

Inflamm Bowel Dis 2014; 20(5):882-91.

http://www.ncbi.nlm.nih.gov/pubmed/24681653

This study examined the prevalence of microscopic colitis and associated risk of colorectal neoplasia among 265 patients who presented with chronic non-bloody diarrhea in a metropolitan area of Northern Italy. The authors report that either lymphocytic or collagenous colitis was diagnosed in 43 (16%) patients in the study group. Although the majority (73%) of the remaining patients had negative colonoscopic and histologic exams, 17 (6%) were diagnosed with inflammatory bowel disease, eight (3%) with colonic adenocarcinoma, and the remainder with a variety of other inflammatory diseases (e.g. diverticulitis). The overall number of subjects screened in order to diagnose one new case of microscopic colitis was 6.2. This number dropped to 2.3 in patients >80 years of age, reflecting a statistically significant age-dependent increase in the incidence of microscopic colitis with each decade after 40. The rate of microscopic colitis diagnosis was only 4% in patients under 40, but was 19% in patients 40 and older. Only two neoplastic lesions (conventional adenomas) were detected in patients with microscopic colitis compared with 36 conventional adenomas, 5 adenomatous polyps with serrated features, 4 hyperplastic polyps and 8 adenocarcinomas in the remaining patients. Thus, the rate of colonic neoplasia was lower in patients with microscopic colitis compared to the rest of the study group. The authors also point out that, although chronic non-bloody diarrhea is not typically considered to be a warning sign for malignancy, the presence of adenocarcinoma in eight study patients underscores the importance of colonoscopic examination of patients with unexplained diarrhea.

Elastic scattering spectroscopy as an optical marker of inflammatory bowel disease activity and subtypes.

Rodriguez-Diaz E, Atkinson C, Jepeal L, Berg A, Huang CS, Cerda SR, O'Brien MJ, Bigio IJ, Farraye FA, Singh SK.

Inflamm Bowel Dis. 2014; 20(6):1029-36.

http://www.ncbi.nlm.nih.gov/pubmed/24798637

Elastic scattering spectroscopy (ESS) is an optical endoscopic technique that uses absorption spectra measured by fiberoptic probes to evaluate micromorphologic features of mucosae, including nuclear size, crowding, chromatin quality, and organelle density in real time, without

generating microscopic images. The authors tested the potential utility of ESS for diagnosing inflammatory bowel disease, detecting disease activity, and distinguishing between ulcerative colitis and Crohn disease. Elastic scattering spectroscopy measurements were collected from 30 patients with a clinical diagnosis of Crohn disease, 18 with ulcerative colitis, and 46 control patients undergoing screening colonoscopy. The authors report that ESS distinguished patients with inflammatory bowel disease from patients in the control group with 93% sensitivity and 91% specificity. They also found that ESS readings accurately differentiated active from inactive colitis and correctly classified ulcerative colitis and Crohn disease in the majority of cases. They conclude that ESS may prove to be a clinically useful optical biomarker for the diagnosis and classification of inflammatory bowel disease.

Higher quality of molecular testing, an unfulfilled priority: results from external quality assessment for KRAS mutation testing in colorectal cancer.

Tembuyser L, Ligtenberg MJ, Normanno N, Delen S, van Krieken JH, Dequeker EM.

J Mol Diagn 2014; 16(3):371-7.

http://www.ncbi.nlm.nih.gov/pubmed/24631467

This quality assessment study evaluated the accuracy of genotyping and result reporting in KRAS mutation testing of colorectal cancer. A total of 1050 specimens were tested by 105 laboratories. Genotyping errors occurred in 48 (5%) cases and included false positives, false negatives, and incorrect mutation identified. Deficiencies in reports issued by participating laboratories included absence of patient identifiers, and failure to mention exact genotype found and/or clinical impact of the detected genotype, type and sensitivity of method used, and specific mutations evaluated.

Mortality and causes of death in Crohn's disease: results from 20 years of follow-up in the IBSEN study.

Hovde Ø, Kempski-Monstad I, Småstuen MC, Solberg IC, Henriksen M, Jahnsen J, Stray N, Moum BA.

Gut 2014; 63:771-5.

http://gut.bmj.com/content/63/5/771.abstract

Results from patients enrolled over a four-year period in the 1990s from the Inflammatory Bowel South-Eastern Norway study (IBSEN) show that there was no significant difference between Crohn's patients and controls in overall mortality (13.9% versus 12.7%, p=0.578) or deaths from cancer over a 20-year period. Median age at diagnosis was 28 years and diagnoses were re-evaluated at 1-, 5-, and 10-year visits.

Commentary: Interval cancer: nightmare of colonoscopists.

Haug U, Regula J. Gut 2014; 63:865-6.

http://gut.bmj.com/content/63/6/865.extract

References the two articles below on reasons for colorectal cancer to occur in the time interval between scheduled screenings (interval cancer, postcolonoscopy CRCs or PCCRCs). The US study of pooled data from 58 interval CRCs (1980-1999) found new CRC (occurring at least 3 years after colonoscopy, no significant adenoma in the same anatomic segment at prior exam) to be 24% of cases. Missed lesions (within 3 years, no significant adenoma in same segment) are 52%, incomplete adenoma resections are 19% and failed biopsies (previously suspected lesion) are 5%. The Dutch study of 147 such cases (1996-2005) shows 14% new CRC, 58% missed lesions, 9% incomplete adenoma resection, and 20% to be inadequate examination or inappropriate surveillance per Dutch postpolypectomy guidelines. The commentary points out that quality of colonoscopies has steadily increased over time, and the majority of PCCRCs were due to suboptimal quality of colonoscopy.

Colorectal cancers soon after colonoscopy: a pooled multicohort analysis

Robertson DJ, Lieberman DA, Winawer SJ, Ahnen DJ, Baron JA, Schatzkin A, Cross AJ, Zauber AG, Church TR, Lance P, Greenberg ER, Martínez ME.

Gut 2014; 63:949-56.

http://gut.bmj.com/content/63/6/949.abstract

Postcolonoscopy colorectal cancers are preventable: a population-based study

le Clercq CMC, Bouwens MWE, Rondagh EJA, Bakker CM, Keulen ETP, de Ridder RJ, Winkens B, Masclee AAM, Sanduleanu S.

Gut 2014; 63:957-63.

http://gut.bmj.com/content/63/6/957.abstract

Juvenile-like (inflammatory/hyperplastic) mucosal polyps of the gastrointestinal tract in neurofibromatosis type 1

Agaimy A, Schaefer IM, Kotzina L, Knolle J, Baumann I, Ströbel P, Vieth M..

Histopathology 2014; 64: 777-86.

http://www.ncbi.nlm.nih.gov/pubmed/?term=Juvenile-like+(inflammatory%2Fhyperplastic)+mucosal+polyps+of+the+gastrointestinal+tract+in+neurofibromatosis+type+1

This study describes inflammatory (juvenile-like) polyps in four male patients with NF-1 (ages 23-65 years). Two patients had multiple polyps. An additional 11 such cases were identified by literature review. The etiology is unknown but could represent NF-1 inactivation, NF-1-associated vasculopathy, or mucosal prolapse related to a motility disorder.

Overexpression of FOXC1 correlates with poor prognosis in gastric cancer patients

Xu Y, Shao QS, Yao HB, Jin Y, Ma YY, Jia LH.

Histopathology 2014; 64: 963-70.

http://www.ncbi.nlm.nih.gov/pubmed/?term=Overexpression+of+FOXC1+correlates+with+poor+prognosis+in+gastric+cancer+patients

This study reports higher levels of FOXC1 (a member of the forkhead box transcription factor family) by RT-PCR and IHC in gastric cancer than in non-cancer tissues. In addition, high FOXC1 expression correlates with decreased survival, differentiation, stage, depth of invasion, nodal metastasis, and distant metastasis, all to statistically significant degrees.

Ewing sarcoma of the small bowel: a study of seven cases, including one with the uncommonly reported EWSR1–FEV translocation

Milione M, Gasparini P, Sozzi G, Mazzaferro V, Ferrari A, Casali PG, Perrone F, Tamborini E, Pellegrinelli A, Gherardi G, Arrigoni G, Collini P, Testi A, De Paoli E, Aiello A, Pilotti S, Pelosi.

Histopathology 2014; 64: 1014-26.

http://www.ncbi.nlm.nih.gov/pubmed/?term=Ewing+sarcoma+of+the+small+bowel%3A+a+study+of+seven+cases%2C+including+one+with+the+uncommonly+reported+EWSR1%E2%80%93FEV+translocation

A detailed report of seven cases of primary Ewing sarcoma of the small bowel (ileum). One tumor demonstrated a EWSR1-FEV rearrangement and the remainder exhibited the more common EWSR1-FLI1 rearrangement. The patient with FEV rearrangement was alive after 15 years with multiple recurrences controlled by surgery alone. EWSR1-FLI1 patients had a mean survival of 14 months.

Debating Deposits: An Interobserver Variability Study of Lymph Nodes and Pericolonic Tumor Deposits in Colonic Adenocarcinoma

Rock JB, Washington MK, Adsay NV, Greenson JK, Montgomery EA, Robert ME, Yantiss RK, Lehman AM, Frankel WL.

Arch Pathol Lab Med 2014; 138:636-42.

http://www.archivesofpathology.org/doi/abs/10.5858/arpa.2013-0166-OA

A reproducibility study on the pathologic distinction of positive nodes from tumor deposits as per AJCC 7th edition criteria, with assessment of microscopic features thought to be useful versus actually used. The latter include, in rank order, round shape, thick capsule, peripheral lymphoid follicles, peripheral lymphocyte rim, size greater than 3 mm, admixed lymphocytes, residual LN in surrounding fibroadipose tissue, possible subcapsular sinus, tumor in nearby lymphovascular channels, and contiguous lymphovascular channels. For the 25 difficult metastases described, there was complete agreement for 44% of cases and nonagreement (no clear consensus) for 16% of cases.

A clinicopathologic study of 24 cases of systemic mastocytosis involving the gastrointestinal tract and assessment of mucosal mast cell density in irritable bowel syndrome and asymptomatic patients.

Doyle LA, Sepehr GJ, Hamilton MJ, Akin C, Castells MC, Hornick JL.

Am J Surg Pathol 2014; 38:832–43.

http://www.ncbi.nlm.nih.gov/pubmed/24618605

One primary aim of this study was to determine the utility of GI biopsies for the diagnosis of systemic mastocytosis (SM). Twenty four patients with SM involving the GI tract were compared to 100 asymptomatic patients and 100 patients with IBS. In patients with SM, the most commonly involved site was the colon. The most common GI symptom was diarrhea. Histological involvement can be focal; biopsies were characterized by infiltrates of ovoid to spindle-shaped mast cells in aggregates or sheets in the lamina propria. The authors recommend having a low threshold for using KIT immunohistochemistry as a screening tool to detect subtle aggregates of mast cells, and if present, using CD25 to confirm the diagnosis of SM. Aberrant expression of CD25 is seen in the neoplastic mast cells of SM, but not in non-neoplastic mast cells. Mast cell tryptase has a more limited utility in identifying neoplastic mast cell infiltrates in the GI tract compared to KIT and CD25. One pitfall for not recognizing the mast cell aggregates is concomitantly increased numbers of obscuring eosinophils.

Tropical sprue: revisiting an underrecognized disease.

Brown IS, Bettington A, Bettington M, Rosty C.

Am J Surg Pathol 2014; 38:666-72.

http://www.ncbi.nlm.nih.gov/pubmed/24441659

Tropical sprue (TS) is an acquired chronic inflammatory disorder of the intestinal mucosa affecting residents of and visitors to tropical regions (30 degrees North or South of the equator, e.g., India, Southeast Asia, the Caribbean). The precise etiology of tropical sprue remains mysterious, although an infective cause is favored. Reports of TS have become infrequent and the diagnosis is often not considered, however, TS causes significant morbidity and it is eminently treatable with broad-spectrum antibiotics. In this study, the clinical presentation and histologic findings of 12 TS patients were compared to 150 cases of gluten-sensitive enteropathy (GSE), the condition with which it is most frequently misdiagnosed. Histologic features suggesting TS over GSE are (1) incomplete villous atrophy; (2) involvement of the ileum, often in a more severe manner than the proximal small bowel; and (3) higher numbers of eosinophils in the lamina propria. TS may present with increased duodenal IELs with normal villous architecture (Marsh stage 1). In addition, villous tip accentuation of IELs was not appreciable in this cohort of TS.

Cystic pancreatic neuroendocrine tumors: the value of cytology in preoperative diagnosis.

Morales-Oyarvide V, Yoon WJ, Ingkakul T, Forcione DG, Casey BW, Brugge WR, Fernández-Del Castillo C, Pitman MB.

Cancer Cytopathol 2014; 122(6):435-44.

http://www.ncbi.nlm.nih.gov/pubmed/24591417

Pancreatic cystic neoplasms are composed of a heterogeneous group of tumors with a wide spectrum of biologic behavior, ranging from benign and indolent neoplasms to invasive carcinomas with aggressive behavior resembling conventional ductal adenocarcinoma. Most cystic tumors can be classified as 1 of 3 distinct neoplasms: serous cystadenoma, mucinous cystic neoplasm and IPMN. A small remaining proportion is comprised of secondarily cystic solid neoplasms such as ductal adenocarcinoma, acinar cell carcinoma and neuroendocrine tumors (cPanNET). Once thought rare, it has been established that cPanNETs account

for a large proportion of PanNETs in multiple studies. This study retrospectively evaluated the imaging characteristics, cyst fluid characteristics and cytomorphologic features of histologically confirmed cPanNETs. The authors concluded that cystic neuroendocrine tumors have imaging features overlapping with those of other pancreatic cysts, and the imaging features are insufficiently accurate for the independent diagnosis of cPanNET. Furthermore, both CEA and amylase levels are low with rare exception. The cytomorphology of the cyst fluid cells, however, are key to the accurate diagnosis of cPanNETs. Cytology was the most accurate test for preoperative diagnosis of cPanNETs.

Journals Reviewed (May and June Issues)

Histopathology

Archives of Pathology and Lab Medicine

Modern Pathology

American Journal of Clinical Pathology

Journal of Pathology

Journal of Clinical Pathology

American Journal of Pathology

Human Pathology

Cancer Cytopathology

American Journal of Surgical Pathology

Advances in Anatomic Pathology

Journal of Molecular Diagnostics

Gastrointestinal Endoscopy

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