Table 2 Two marker haplotype frequencies, transmission, and association statistics for *CARD4* (caspase recruitment domain family, member 4) in inflammatory bowel diseases

Variation	Haplotype*	$f_{controls}$†	f_{cases}†	p Value‡	f_T§	f_{NT}§	p Value¶	D′**
rs2075822 +	1 – 1	0.771	0.762	0.846	0.455	0.486	0.094	0.91
ND_1+32656	1 – 2	0.042	0.040		0.140	0.101		
	2 – 1	0.013	0.015		0.026	0.057		
	2 – 2	0.174	0.184		0.380	0.357		
ND_1+32656+	1 – 1	0.784	0.775	0.727	0.473	0.519	0.719	0.98
rs2907748	1 – 2	0.002	0.002		0.011	0.011		
	2 – 1††	0.006	0.004		0.014	0.008		
	2 – 2	0.208	0.220		0.503	0.462		

*Allele 1 is defined as the major allele.
†Frequencies of haplotypes in cases and controls estimated by the expectation maximisation algorithm using COCAPHASE.[6]
‡Global significance value obtained after 10 000 permutations with COCAPHASE.
§Frequencies of transmitted (f_T) and non-transmitted (f_{NT}) haplotypes observed using TDTPHASE.[6]
¶Global significance value obtained after 10 000 permutations with TDTPHASE.
**D′ value as a measure of linkage disequilibrium in the control sample.
††Protective haplotype previously identified by McGovern and colleagues.[2]

polymorphisms analysed. While LD was incomplete in the British,[2] there was strong LD in the German patients (table 2). ND_1+32656 could therefore be a population specific marker for an as yet unidentified causative variant in the vicinity. Replication in other British and European samples will be necessary to further examine the role of *CARD4* variants in IBD susceptibility.

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A Franke, A Ruether, N Wedemeyer
Institute for Clinical Molecular Biology, Christian-Albrechts-University, Kiel, Germany

T H Karlsen
Medical Department, Rikshospitalet University Hospital, Oslo, Norway

A Nebel, S Schreiber
Institute for Clinical Molecular Biology, Christian-Albrechts-University, Kiel, Germany

Correspondence to: Dr S Schreiber, Institute for Clinical Molecular Biology, Christian-Albrechts-University, Schittenhelmstrasse 12, 24105 Kiel, Germany; s.schreiber@mucosa.de

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Preliminary data on the use of intraductal optical coherence tomography during ERCP for investigating main pancreatic duct strictures

Optical coherence tomography (OCT) is an optical imaging technique that uses infrared light reflectance and produces high resolution microstructural cross sectional images of tissues in vivo.[1–3] The OCT probe can be inserted inside a standard transparent endoscopic retrograde cholangiopancreatography (ERCP) catheter. To date, only the epithelium of the main pancreatic duct (MPD) has been examined by OCT in humans in three studies: one post mortem[4] and two ex vivo.[5 6] The aim of the present prospective pilot study was to assess the feasibility of intraductal OCT in vivo during an ERCP procedure, its ability to identify changes in MPD wall structure in vivo, and its ability to differentiate non-neoplastic from neoplastic tissue in the presence of MPD strictures.

Fifteen consecutive patients with documented or suspected MPD strictures at a previous computed tomography scan or magnetic resonance cholangio-pancreatography (MRCP) were investigated by endoscopic ultrasonography (EUS) and ERCP; the two procedures were done at the same time under propofol sedation. Mean age of the patients was 61.9 years (range 38–78); there were 11 men and four women. Fine needle aspiration biopsy (FNAB) was planned during EUS when pancreatic neoplasia was suspected; intraductal OCT followed by brush cytology was scheduled during ERCP in all cases when the MPD stricture was confirmed. OCT findings were compared with EUS, cytology (FNAB and/or intraductal brushing), and histopathological findings in those undergoing surgical pancreatic resection. All patients gave informed consent to the endoscopic procedures and the institutional ethics committee approved OCT use in humans.

A near focus OCT probe (Lightlab Imaging, Westford, Massachusetts, USA) was used with a penetration depth of about 1 mm, resolution of approximately 10 μm, and outer diameter of 1.2 mm. An MPD stricture was confirmed by EUS and/or ERCP in 12 of 15 patients. The three patients in whom the stricture was not confirmed were excluded from the study. EUS findings suggested a neoplastic lesion in seven cases, chronic pancreatitis with segmental MPD stricture in three, neuroendocrine tumour compressing the MPD in one, and normal tissue in the remaining case. EUS guided FNAB was performed in eight patients with findings suggesting neoplasia or neuroendocrine tumour. Three patients with neoplastic findings were judged unfit for surgery at EUS. In 10 cases, MPD segments not affected by the stricture showed normal morphology at ERCP, with mild upstream dilatation (4–6 mm); in two cases with EUS findings suggesting chronic pancreatitis, minimal ductal changes were also documented at ERCP.

Both intraductal OCT and brush cytology were performed in 11 patients; in one patient with adenocarcinoma the stricture was too tight to pass the ERCP catheter upstream of the lesion. FNAB findings confirmed the diagnosis of adenocarcinoma and neuroendocrine tissue in all cases. Brush cytology was concordant with FNAB findings in 4/6 patients with pancreatic adenocarcinoma (66.7%) and negative for neoplastic cells in the five cases in which EUS findings did not suggest ductal adenocarcinoma. Five patients were operated on and pancreatic adenocarcinoma and neuroendocrine tumour were confirmed in the surgical specimens. OCT imaging showed a recognisable three layer structure in cases with a normal MPD and chronic pancreatitis whereas in all cases with ductal adenocarcinoma the layer structure was totally unrecognisable (fig 1).

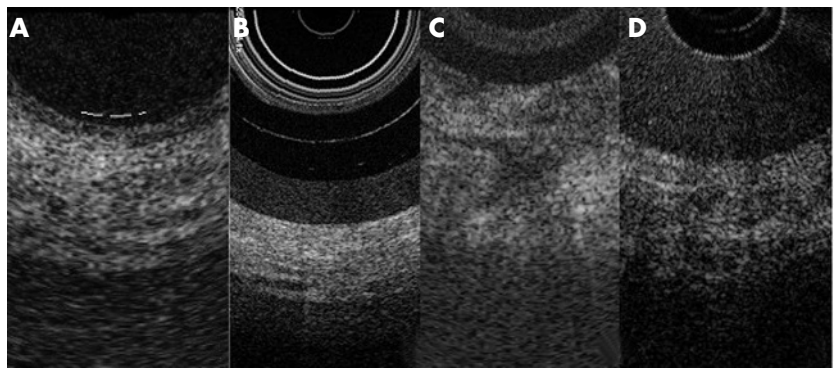

Figure 1 Magnification of an optical coherence tomography (OCT) image from a segmental stricture of the main pancreatic duct with non-neoplastic and neoplastic stricture, with the OCT probe outside (A, B) and inside (C, D) the endoscopic retrograde cholangiopancreatography catheter.

Concordance of OCT and brush cytology with the final diagnosis in patients with non-neoplastic strictures was 100% for both techniques; in the presence of a neoplastic MPD stricture, values were 100% and 66.7%, respectively.

In conclusion this pilot study showed that OCT is feasible during ERCP, could distinguish a non-neoplastic from a neoplastic MPD wall with a diagnostic accuracy superior to brush cytology, but appeared to be unable to discriminate between a normal structure and chronic pancreatitis ductal changes.

P A Testoni, A Mariani, B Mangiavillano, P G Arcidiacono, E Masci
Division of Gastroenterology and Gastrointestinal Endoscopy, University Vita-Salute San Raffaele, Scientific Institute San Raffaele, Milan, Italy

Correspondence to: Dr P Alberto Testoni, Division of Gastroenterology and Gastrointestinal Endoscopy, University Vita-Salute San Raffaele, Scientific Institute San Raffaele, Via Olgettina 60, 20132, Milan, Italy; testoni.pieralberto@hsr.it

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Prognostic value of the lymph node ratio in node positive colon cancer

Surgery is the primary treatment of non-metastatic colon cancer. En bloc removal of the colon with its associated mesenteric lymph nodes is essential. However, the number of lymph nodes reported with colectomy varies widely and may be a result of variation in the actual number of regional lymph nodes, surgical technique, or the thoroughness of the pathologist in finding lymph nodes. The number of lymph node metastases is an important negative prognostic factor and is used in stratification schemes for clinical trials.[1]

Recent studies have emphasised the fact that examining a greater number of nodes increases the likelihood of correct staging and is associated with better survival, after controlling for the number of nodes involved.[2] Hence, the Will Rogers phenomenon may profoundly affect the reported outcome of colon cancer.[3] Indeed, experienced teams often perform meticulous and extensive lymph node dissection, which increases the probability of finding nodes. This not only affects the expected outcome but may also influence decisions on adjuvant treatments. Patients with inadequate lymph node resection could therefore receive less efficient adjuvant treatment. Berger *et al* reported that the ratio of metastatic to examined lymph nodes (the lymph node ratio (LNR)) may decrease the amount of stage migration, and is an important prognostic factor in colon cancer, using four LNR groups.[3]

We compared directly the UICC staging system in node positive colon cancer (metastases in 1–3 (pN1) versus in 4 or more (pN2) regional lymph nodes) to LNR based staging, using two prognostic groups. Data were extracted from the surveillance, epidemiology, and end results (SEER) 9 registries.[4] Selection criteria were histology confirmed primary colorectal cancer, diagnosed between 1988 and 1997, surgically resected, and node positive disease. Data from 26 181 patients were included in the study, of which 3941 received radiotherapy. Median number of examined nodes was 10. The number of positive nodes increased with the number of nodes examined (pairwise correlation coefficient $= 0.36$; $p<0.0001$).

The endpoint of the study was cause specific survival. The number of events was 14 121, with a median follow up of 92 months. The optimal cut off (LNR1 *v* LNR2), determined using the Nagelkerke's r^2 index, was 0.4. In the Cox multivariate analysis, LNR appeared to be a strong independent risk factor ($p<0.0001$), next to sex, age at diagnosis, race, marital status, tumour size, level of cancer infiltration (pT), histological grade, number of positive nodes, and number of nodes removed. Comparison between the LNR and UICC pN stage was performed using Kaplan-Meyer survival estimates and log rank tests (fig 1). The group of patients with LNR1 and LNR2 had a five year cause specific survival of 56% and 25%, respectively. In comparison, pN1 and pN2 stages displayed a five year cause survival of 54% and 28%, respectively. Hence prognostic separation using LNR was 31% compared with 26% using the UICC pN stage.

Therefore, we propose using the LNR in future staging systems for colon cancer, in stratification schemes for clinical trials, and to compare interinstitutional treatment results.

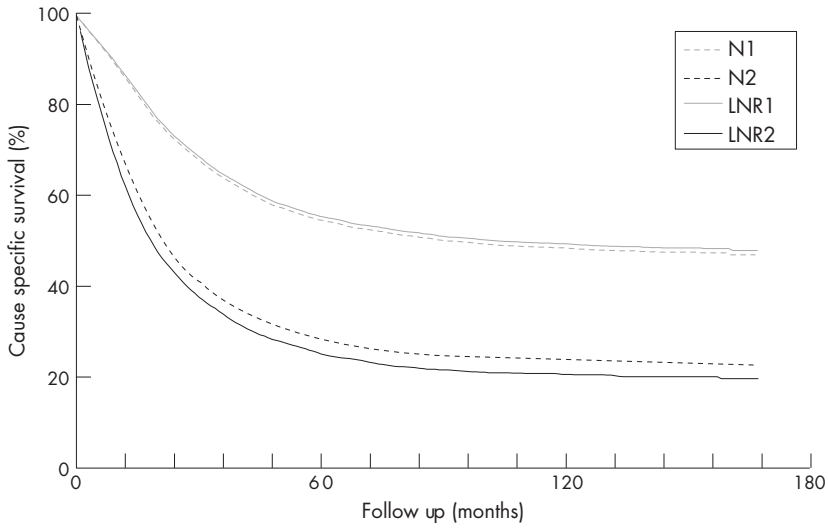

Figure 1 Prognostic value of a number based (N1–2) compared with a ratio based (LNR 1–2) staging system in colon cancer. LNR, lymph node ratio.

M De Ridder, V Vinh-Hung, Y Van Nieuwenhove, A Hoorens, A Sermeus, G Storme
Academic Hospital of the Free University of Brussels, Oncology Centre, Brussels, Belgium

Correspondence to: Professor M De Ridder, Academic Hospital of the Free University of Brussels, Oncology Centre, Laarbeeklaan 101, B-1090 Brussels, Belgium; Mark.Deridder@az.vub.ac.be

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Could the GI tract be a better portal for antibody therapy?

Reinisch and colleagues (*Gut* 2006;**55**:1138–44) recently reported that the infusion of fontolizumab, an anti-interferon γ antibody, into patients with Crohn's disease was generally well tolerated with encouraging clinical responses. Unfortunately, not all first trials with therapeutic antibodies go as well as