Common bile duct stones—cut or stretch?  


Endoscopic sphincterotomy (ES) is the standard method for dealing with common bile duct stones and is superior to balloon dilation (EPBD) in the short term. However, long-term outcomes of ES and EPBD are similar, with rates of re-dilation of 4%–7% and 5%–11% respectively for ES and EPBD. The long-term costs (VdR) are 2.8% for EPBD and 1.2% for ES and the VdR cost of EPBD is only 1.1%.

This study was designed to compare the long-term outcomes of EPBD and ES in a prospective randomised multicentre trial comparing 128 patients with bile duct stones <1.5mm (167 men, mean age 67.7 years, range 26–91). The study was adequately powered and the evaluation parameters were duct clearance, number of sessions required and complications occurring up to 30 days. Both techniques achieved duct clearance well (100% for ES and 99.3% for EPBD) with a similar number of sessions and equal procedure times. There was no overall difference in complications (11.8% for ES and 14.5% for EPBD) and no deaths occurred. While bleeding only occurred in the ES group (2 patients), pancreatitis, mostly mild, was more common in the EPBD group (10.9% vs 2.8%, p<0.02). In contrast, biliary infection was more common in the ES group (7.6% vs 3.6%, p=NS).

This study shows what can be done to provide a strong evidence base for therapeutic endoscopic practice. It confirms that EPBD is not superior to the established technique of sphincterotomy but only long term follow up will tell whether there is a difference between the procedures in recurrence rate for stones and effects on sphincter of Oddi function. For the time being EPBD should probably be reserved for those at high risk of bleeding form sphincterotomy.

Natalizumab for active Crohn’s disease  


Natalizumab, a α4 integrin-inhibitor of lymphocyte trafficking, is effective for active Crohn’s disease, although its role in the treatment strategy for active disease remains unclear. The migration of leukocytes from the circulation into the intestinal submucosa and their activation are mediated in part through α4 integrins. There are two types of receptor, α4β1 and α4β7, both of which are upregulated in Crohn’s disease. Natalizumab (Antegren, Elan Pharmaceuticals and Biogen), a humanised monoclonal antibody against α4 integrin, proved promising in two pilot studies of patients with active Crohn’s and active UC.

This double blind, placebo controlled trial of natalizumab was performed in 748 patients with moderate-to-severe Crohn’s disease (CDAI 220–450) in 35 centres throughout Europe. Randomisation was complex: two infusions of placebo (n=63), one of 3mg/kg and one of placebo (n=68), two infusions of 3mg/kg (n=66), or two of 6mg/kg (n=51). 10–25% of patients in the four groups had fistulising disease and 49–63% were on steroids, although patients on prednisolone >25mg/d, or methotrexate were excluded. The primary endpoint was remission (CDAI <150) at 6 weeks and the patients given 2mg/kg infusions did no better than placebo (remission rates 27%, 29%, 44%, and 31% respectively for the four groups). The highest remission rate was 44% and response rate (ΔCDAI −70) 71%, achieved in the group given two 3mg/kg infusions. Natalizumab was well tolerated (although up to 20% had an influenza type syndrome) and ancillary measures (BDQ score) were consistent with the clinical response.

This study is both encouraging and disappointing. The primary endpoint (only) showed a benefit for two 3mg/kg infusions. Secondary analyses showed benefit for other doses at different endpoints in the short term (up to 12 weeks after two infusions 4 weeks apart). The effect is partial, perhaps because neutrophils express α4β1, only after leaving the circulation and long term safety remains to be established. Chronic inhibition of α4 integrin may have undesirable effects on haemopoiesis or mucosal immunity, even though there was no increase in infections in the current study. One is left with the impression that natalizumab helps some patients, but more slowly than infliximab, and for a short period only. The real question for the biologics, is whether it works in the third of patients who do not respond to infliximab. The answer may be a long time coming.

Iron deficiency—an open question?  


Iron deficiency anaemia (IDA) is common; population surveys have found IDA in 2–5% of men and postmenopausal women and iron deficiency alone in about twice this number. Investigation of IDA thus accounts for a significant part of a gastroenterologist’s workload. Recent BSG guidelines recommend an upper endoscopy and colonoscopy or barium enema for most cases other than menstruating women. Increasingly laboratories are routinely reporting ferritins or other measures of iron status and gastroenterologists are being asked to investigate patients who are iron deficient but not anaemic. The yield from investigating such patients is not clear and the need for more research was highlighted in the guidelines. Ioannou et al have analysed data on haemoglobin and iron status first collected in a large US population survey (NHANES) 30 years ago and followed up 10 years later. About 2% (n=143) were anaemic and iron deficient and 8% (n=710) were only iron deficient. Over the next two years 18 were diagnosed with gastrointestinal malignancy (GI), mainly colorectal (13). None of the 442 premenopausal women with anaemia or iron deficiency alone developed a GI malignancy. In comparison 6% of the men and postmenopausal women with an IDA did, giving a relative risk of developing GI cancer of 31 compared to those not anaemic or iron deficient. In contrast the risk of GI cancer in those iron-deficient but not anaemic (n=221) was only 1%, a relative risk of 5. This rose to 2.3% if only those aged 65 or over were considered. It was notable that only 5 of the 13 colorectal cancers were in women, and no cancers were seen in those over 50 requiring some form of colorectal cancer screening.

This study shows that investigation of people incidentally found to be iron deficient will have a low yield of GI malignancy. Nevertheless, with colorectal cancer screening about to start in the UK the bottom line perhaps is that unexplained iron deficiency in those over 50 requires some form of colorectal cancer screening.

Hepatocellular carcinoma surveillance: is risk stratification the way forward?  


Hepatocellular cancer (HCC) meets several of the criteria for surveillance. However, the likely cost effectiveness of screening...
patients with cirrhosis for HCC remains controversial. Velazquez and colleagues prospectively followed 463 patients with Child-Pugh class A or B cirrhosis to identify 38 HCC over a period of 38 months. The predictive value of different risk factors was evaluated. According to the contribution of each of these factors to the final model, a score ranging between 0 and 4.72 points was constructed as follows: Score = 1.65 (if prothrombin time was ≤75%) + 1.41 (if age was ≥55 years) + 0.92 (if the platelet count was <75 × 10^9/l) + 0.74 (if anti-HCV was positive). The cumulative risk for HCC at 4 years was 2.3% in the low risk group (score <2.33) compared with 30.1% in the high risk group (score >2.33). These findings are promising steps forward in clarifying the target population for HCC surveillance. The model identifies two groups with strikingly different orders of risk. Age cut off used in the study may not be applicable in a population with a high prevalence of hepatitis B virus infection often acquired at an early age. The score was validated using the split sample technique in this study and it is desirable to validate the model in an independent population.