

# Highlights from this issue

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Emad El-Omar, Alexander Gerbes and William Grady, *Editor and Deputy Editors*

## Life after bariatric surgery—it's complicated

Bariatric surgery is becoming increasingly common for the management of morbid obesity. While the short-term effects of Roux-en-Y gastric bypass (RYGB) on weight loss and health are clearly beneficial, it is likely that the long-term effects will be complicated. Hull and colleagues have previously shown that the rectal epithelial cell mitosis and crypt size, as well as expression of pro-inflammatory genes including macrophage migration inhibitory factor (MIF), are increased 6 months after RYGB in morbidly obese patients. They now show these potentially pro-tumorigenic effects persist for at least 3 years after RYGB compared with preoperative values and include elevation of the pro-tumorigenic cytokine migration inhibitory factor, which is upregulated following *Apc* loss and which contributes to intestinal epithelial cell homeostasis. These observations suggest patients who have undergone RYGB may be at increased risk for colon neoplasms, and highlight the need for clinical studies of this possible cancer risk (*see page 893*).

## Teduglutide for short bowel syndrome and intestinal failure

Patients with short bowel syndrome (SBS) and intestinal failure depend on parenteral support with fluids, electrolytes, trace elements, vitamins and nutrients but may face potentially life-threatening complications. Recently, hormonal stimulation to augment remnant bowel adaptation has been suggested, with glucagon-like peptide 2 as a key factor. In an open-label non-placebo controlled 21-day phase 2 study, Teduglutide (a glucagon-like peptide 2 analogue) has been shown to increase intestinal wet weight absorption in patients with SBS. In this issue of *Gut*, Jeppesen *et al* conducted the first long-term (24 weeks) randomised placebo-controlled study of Teduglutide in patients with SBS dependent on parenteral support. They found that Teduglutide was safe, well tolerated and led to restoration of intestinal functional and structural integrity through significant intestino-

trophic and pro-absorptive effects. They conclude that Teduglutide has the potential to reduce the burden often seen with parenteral support in patients with SBS and intestinal failure, and could add to the limited clinical treatment armamentarium in treating such patients (*see page 902*).

## Anti-TNF treatment and long-term risk for surgery in newly diagnosed Crohn's patients

The effect of anti-TNF treatment on the long-term risk for surgery in Crohn's disease is unknown. In this issue of *Gut*, Peyrin-Biroulet *et al* conducted the first study that investigated the association between the duration of azathioprine and anti-TNF treatments and the requirement for surgery in patients newly diagnosed with Crohn's disease. The electronic charts of 296 incident cases of Crohn's disease from Nancy University Hospital, France, diagnosed between 2000 and 2008, were reviewed through January 2010. The median follow-up time per patient was 57 months. Anti-TNF treatment was associated with a reduction in the need for surgery while azathioprine had modest efficacy in reducing the risk for long-term surgery in patients newly diagnosed with Crohn's disease (see table) (*see page 930*).

## FOBT deserves more respect

Although guaiac-based faecal occult blood test screening has been shown to be effective in reducing colorectal cancer

mortality, it is commonly criticised for having low sensitivity. This is an important issue for countries that have implemented FOBT based screening programs. In order to address this issue, Zorzi *et al* collected and analysed the interval cancers found by five screening programs to estimate the sensitivity of these programs for detecting colorectal cancer. Their analysis was based on a large study that included the follow-up of 468 306 person-years. They found 126 interval cancers, compared with 572 expected cancers. The proportional incidences were 15.3% and 31.0% in the first and the second interval years, respectively, with an overall episode sensitivity of 78.0% (95% CI: 73.8 to 81.6). Sensitivity was higher for males than females (80.1% vs 74.8%); no differences were observed by age, anatomical site or between programs. Thus, despite the common criticism of low sensitivity, iFOBT-based screening programs showed a high performance in terms of sensitivity as estimated through the IC rates, providing reassurance for the utility of FOBT for colon cancer screening (*see page 944*).

## Hepatology

### Apolipoprotein A5—a new player in NAFLD

Recently, a major influence of Apo A5 on triglyceride metabolism has been described. This interesting study from Austria investigated the role of Apo A5 in non-alcoholic fatty liver disease (NAFLD). Hepatic Apo A5 decreased in patients with NAFLD with weight loss and

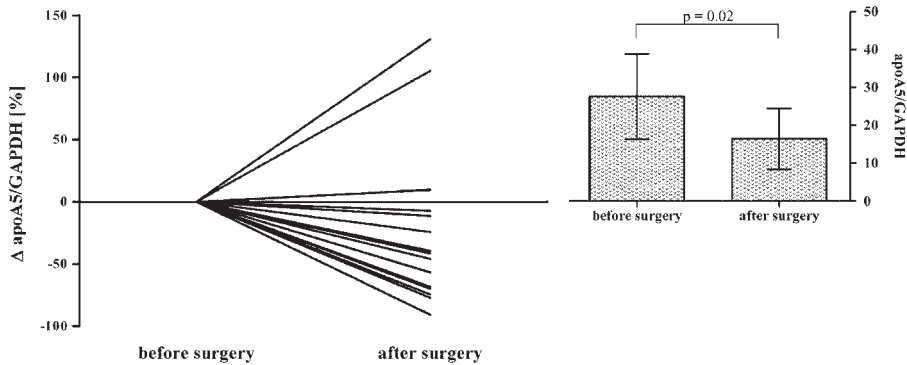
### Predictors of first Crohn's disease—related major abdominal surgery, as determined by multivariate analysis (Cox proportional-hazards regression) after propensity score adjustment

Covariates	HR*	95% CI of HR	P-value†
Crohn's disease behaviour			
B1 (non-stricturing, non-penetrating)	1	—	—
B2 (stricturing)	12.01	5.97 to 24.17	<0.0001
B3 (penetrating)	10.77	4.87 to 23.80	<0.0001
Anti-TNF treatment duration ≤475 days (≈16 months)‡	3.86	1.77 to 8.45	0.0008
Azathioprine treatment duration ≤45 days (≈1.5 months)‡	2.00	1.20 to 3.34	0.008
L2 (isolated colonic disease)	Not retained in the Cox regression model		

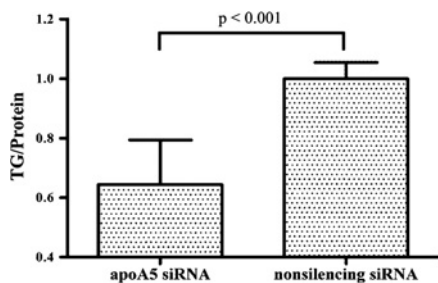
\*HR for the first Crohn's disease—related major abdominal surgery.

†Cox proportional-hazards regression (Stepwise method).

‡Cut-off defined using the ROC analysis described by DeLong *et al*.<sup>12</sup> ROC, receiver operating characteristic; TNF, tumour necrosis factor.



Apo A5 expression decreases in livers of pts with NAFLD following bariatric surgery.



Transfection with Apo A5 siRNA reduces intracellular triglyceride content.

improvement of liver steatosis upon bariatric surgery (figure 1). Apo A5 knock-down in hepatoma cells markedly reduced the triglyceride content suggesting that Apo A5 may play a causal role in hepatic steatosis. Further in vitro data of this study support the contention that PPAR-gamma may be involved in the Apo A5 effects on hepatic triglyceride metabolism (see page 985).

## Low effectiveness of HCC surveillance in the USA

Many patients with hepatocellular carcinoma (HCC) are diagnosed at an advanced stage with few therapeutic options and poor survival. Surveillance strategies aim at detection of HCC at an earlier stage and can improve patient survival. El-Serag and colleagues show in this interesting paper that in the real world very few patients receive the recommended surveillance and those who do have some survival benefit. They investigated a cohort of almost 1500 Veterans Administration patients infected with Hepatitis C, a major cause of HCC, who had been diagnosed with HCC. Surveillance using AFP or ultrasound within 2 years preceding HCC diagnosis was associated with a lower mortality risk (see table 1). Importantly, only six per cent received six-monthly surveillance as recommended by acknowledged guidelines. Thus, in clinical practice adherence to standard-of-care surveillance is poor (see page 992).

Effects of HCC surveillance by AFP or ultrasound in 24 months preceding HCC diagnosis on survival of patients

Surveillance in 0–6 months	Surveillance in 7–24 months	Number of Patients (%)	Median survival (days)	1-Year survival rate	3-Year survival rate	5-Year survival rate	p Value
No	No	332 (22.4%)	130	31.9%	15.4%	11.4%	ref
No	Yes	207 (14.0%)	192	40.6%	19.8%	14.9%	0.06
Yes	No	361 (24.4%)	282	44.3%	19.0%	10.6%	0.01
Yes	Yes	580 (39.2%)	368	50.3%	21.9%	13.0%	<0.01

p Values obtained from Cox proportional hazards analyses.