

## IN BRIEF

## OESOPHAGUS

**Endoscopic myotomy non-inferior to surgical myotomy for idiopathic achalasia**

Current treatment options for achalasia include endoscopic pneumatic dilation and surgical laparoscopic Heller's myotomy (LHM). A multicentre, randomized trial compared LHM plus Dor's fundoplication with the less-invasive peroral endoscopic myotomy (POEM) in patients with idiopathic achalasia. The primary endpoint of clinical success at the 2-year follow-up was observed in 83.0% of the 112 patients undergoing POEM and 81.7% of the 109 patients undergoing LHM plus Dor's fundoplication. Thus, POEM was non-inferior to LHM plus Dor's fundoplication ( $P=0.007$  for non-inferiority). 44% of patients who underwent POEM and 29% of patients who underwent LHM plus Dor's fundoplication had reflux oesophagitis at the 2-year follow-up.

**ORIGINAL ARTICLE** Werner, Y. B. et al. Endoscopic or surgical myotomy in patients with idiopathic achalasia. *N. Engl. J. Med.* **381**, 2219–2229 (2019)

## NASH

**Obeticholic acid for the treatment of NASH**

There are currently no approved therapies for nonalcoholic steatohepatitis (NASH). In a planned month-18 interim analysis of a multicentre, randomized, double-blind phase III study of the use of obeticholic acid, a farnesoid X receptor agonist, in the treatment of NASH, patients with NASH who had stage F2–F3 fibrosis received oral placebo ( $n=311$ ), obeticholic acid 10 mg ( $n=312$ ) or obeticholic acid 25 mg ( $n=308$ ). The fibrosis improvement primary endpoint ( $\geq 1$  stage with no worsening of NASH) was met by 12% of patients in the placebo group, 18% of patients receiving obeticholic acid 10 mg ( $P=0.045$ ) and 23% of patients receiving obeticholic acid 25 mg ( $P=0.0002$ ). An alternative primary endpoint of NASH resolution with no worsening of fibrosis was not met. Serious adverse events were similar across the groups. Thus, obeticholic acid 25 mg significantly improved fibrosis in patients with NASH and the study is ongoing to assess clinical outcomes.

**ORIGINAL ARTICLE** Younossi, Z. M. et al. Obeticholic acid for the treatment of non-alcoholic steatohepatitis: interim analysis from a multicentre, randomised, placebo-controlled phase 3 trial. *Lancet* **394**, 2184–2196 (2019)

## LIVER CANCER

**Combined TACE and sorafenib for HCC treatment**

Transarterial chemoembolization (TACE) and sorafenib have both been shown to prolong survival in patients with unresectable hepatocellular carcinoma (HCC), but previous trials assessing the combination of TACE and sorafenib have been unable to show clinical benefit compared with TACE alone. Now, Kudo et al. report results from a randomized, multicentre prospective trial of TACE plus sorafenib compared with TACE alone in patients with unresectable HCC. Patients were randomized either to treatment with TACE plus sorafenib before and after TACE ( $n=80$ ) or to a group that received TACE without addition of sorafenib ( $n=76$ ). Median progression-free survival was significantly longer ( $P=0.006$ ) in the combination group (25.2 months) than in the TACE without sorafenib group (13.5 months). Median time to untreatable progression (a TACE-specific endpoint) was also significantly longer ( $P=0.02$ ) in the combination group (26.7 months) than in the TACE without sorafenib group (20.6 months).

**ORIGINAL ARTICLE** Kudo, M. et al. Randomised, multicentre prospective trial of transarterial chemoembolisation (TACE) plus sorafenib as compared with TACE alone in patients with hepatocellular carcinoma: TACTICS trial. *Gut* <https://doi.org/10.1136/gutjnl-2019-318934> (2019)

## DIAGNOSIS

**Deep-learning AI for neoplasia detection in Barrett oesophagus**

A new study has developed and validated a deep-learning computer-aided detection (CAD) system that can detect neoplasia in patients with Barrett oesophagus with higher accuracy than endoscopists.

Endoscopic surveillance of oesophageal carcinoma in patients with Barrett oesophagus is typically performed using high-definition white light endoscopy (HD-WLE). However, failed detection of early neoplasia is still a problem owing to the rare incidence of progression. “Endoscopists in daily practice can struggle with the recognition of early neoplasia during Barrett surveillance endoscopies,” explains first author Jeroen de Groof.

One option to improve the accuracy of surveillance is with artificial intelligence, in which CAD systems recognise patterns in images. The new study was conducted by the ARGOS consortium, consisting of the Eindhoven University of Technology and centres

for Barrett oesophagus referrals in the Netherlands. “Our group previously reported two studies that described the development of a clinically inspired CAD system that detected early neoplasia on HD-WLE images,” says de Groof. In the latest work, deep-learning techniques were applied to overcome human perceptual biases in preselecting the features for detection, which have restricted previous CAD systems.

The new CAD system was developed using 1,704 high-resolution images of confirmed early neoplasia and non-dysplastic oesophagus from 669 patients with Barrett oesophagus. “The CAD system was tested using two external datasets and the results were then benchmarked against performance of general endoscopists,” reports de Groof. The CAD system outperformed the panel of 53 endoscopists from 4 countries in accuracy (88% versus 73%), sensitivity (93% versus 72%) and specificity

## IMAGING

**High-definition medicine: modelling NAFLD in 3D**

3D spatially resolved geometrical and functional models have provided novel insights into the progression of nonalcoholic fatty liver disease (NAFLD) in a new study. This high-definition approach revealed changes in the complex 3D tissue organization during the course of NAFLD, with specific morphometric features correlated with disease progression.

“Important tissue characteristics such as cell polarity, biliary network connectivity and the spatial context of hepatocytes and non-parenchymal cells cannot be assessed quantitatively using 2D-histology,” explains author Marino Zerial. In a collaborative effort as part of the Liver Systems Medicine LiSyM programme funded by the German Federal Ministry of Education and Research, the researchers developed a pipeline for imaging liver tissue at high resolution and in 3D.

A combination of multiphoton imaging, 3D digital reconstructions and computational simulations were used to generate spatially resolved geometrical and functional models of human liver tissue. These models covered different stages of NAFLD, including simple steatosis and early nonalcoholic steatohepatitis (NASH), and were compared with normal livers and liver from individuals who were healthy obese.

The investigators identified spatially distributed morphological alterations that could be used as biomarkers in NAFLD, such as size distribution of lipid droplets, nuclear texture in hepatocytes and bile canaliculi (BC) morphology. 3D reconstructions revealed that the BC network was disrupted in NAFLD, including increased BC radius and reduced connectivity in the pericentral region. Finally, computational simulations of biliary fluid dynamics predicted