

# Game Changers

## ADVANCES IN LAPAROSCOPIC PANCREATIC SURGERY

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Distal pancreatectomy involves removal of the tail and body of the pancreas, with or without the spleen. The number of distal pancreatectomies performed in Northern Ireland has been increasing over the last number of years, in no small part due to the increasing number of incidental lesions detected radiologically. Additionally there is now recognition of the potential for malignant transformation within certain cystic tumours.

Traditional distal pancreatectomy involves an open procedure with a laparotomy via rooftop incision. Recent developments in laparoscopic technology, in particular laparoscopic energy devices for dissection and staplers for dividing the pancreas, have enabled surgeons to develop techniques for performing distal pancreatectomy with a minimally invasive approach<sup>1</sup>. A Cochrane review found that the laparoscopic approach was associated with a 2.43 day reduction in length of stay (MD -2.43 days, 95% CI -3.13 to -1.73), with no other statistically significant differences, although it should be noted that this was based on observational studies<sup>2</sup>.

Where laparoscopic distal pancreatectomy was previously a novel approach, in Northern Ireland it is now first choice in all patients if technically feasible. Where to next? Around the world laparoscopic and robotic Whipples procedure is the new novel technique - watch this space!

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## WILL SGLT2 INHIBITORS PROVE TO BE A 'MULTIPLE' GAMECHANGER?

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Type 2 diabetes (T2D) causes microvascular and macrovascular disease<sup>1</sup>. Diabetic kidney disease is the leading cause of end-stage renal disease worldwide and associated with significant cardiovascular morbidity and mortality<sup>2</sup>.

The kidney plays an important role in glucose homeostasis. The proximal tubule employs two sodium glucose co-transporters for glucose reabsorption from glomerular filtrate – SGLT1 and SGLT2. SGLT2 accounts for 90% of glucose

reabsorption and is markedly upregulated in T2D. This, along with other renal and extra renal mechanisms, contributes to the persistent hyperglycaemia seen in T2D, making SGLT2 a pragmatic drug target<sup>3</sup>.

SGLT2 inhibitors (empaglifozin, canaglifozin, dapaglifozin) are approved for treatment of T2D. Improved glycaemic control is achieved by reducing renal glucose reabsorption with a resultant increase in urinary glucose excretion<sup>3</sup>. The US FDA has mandated that new oral T2D medications undergo clinical trials to assess cardiovascular safety<sup>4</sup>. The EMPA-REG OUTCOME trial demonstrated the cardiovascular benefits of empaglifozin (versus placebo) in patients with T2D with established cardiovascular disease<sup>5</sup>.

SGLT2 inhibitors may have other benefits including weight loss, lower blood pressure, reduced levels of serum uric acid, improved lipid profiles, lower plasma volume and decreased albuminuria<sup>3</sup>. The EMPA-REG OUTCOME trial also reported long-term renal effects of empaglifozin in patients with T2D and established cardiovascular risk. Patients who received empaglifozin, in addition to standard care, had a significantly lower risk of progression to macroalbuminuria, doubling of the serum creatinine level and initiation of dialysis compared to placebo, although renal death and incidental microalbuminuria were not affected<sup>4</sup>.

The renoprotective effects of SGLT2 inhibitors are attributed to their ability to reduce renal hyperfiltration, by vasoconstriction of the afferent arteriole resulting in reduced intraglomerular pressure<sup>5</sup>. The renal benefits seen in the EMPA-REG OUTCOME trial may be due to the combined reduction in intraglomerular pressures as a result of SGLT2 mediated vasoconstriction of the afferent arteriole and RAAS drugs vasodilating the efferent arteriole<sup>4</sup>. A subsequent trial, CANVAS-R has demonstrated the renal benefits of canaglifozin over placebo in patients with T2D and heart disease, albeit with an increased risk of amputation<sup>6</sup>.

SGLT2 inhibitors have been shown to be safe. Genital and urinary infections are the most frequently reported adverse effects, associated with the increased urinary excretion of glucose<sup>3</sup>. SGLT2 inhibitors are not associated with significant hypoglycaemia<sup>7</sup>. Some cases of euglycaemic diabetic ketoacidosis have been reported, but this is less of a concern in T2D<sup>3</sup>. Nephrologists are studying whether SGLT2 inhibitors can slow progression of chronic kidney disease while cardiologists are interested in these drugs to improve heart failure outcomes. SGLT2 inhibitors may be a useful treatment of diverse medical conditions.

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