Game Changers

TRANSANAL ENDOSCOPIC MICROSURGERY – CHANGING THE MANAGEMENT OF EARLY RECTAL CANCER

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Rectal cancer is the fifth most common cancer in adults. While the management of rectal cancer has become increasingly multimodal, surgical excision in the form of anterior resection, or abdomino-perineal excision, remains the primary intervention. There is debate about the optimum surgical approach to early stage rectal cancer (T1,N0), and endoscopically unresectable rectal polyps.

Transanal endoscopic microsurgery (TEM) has emerged as a less invasive alternative to traditional surgery. It is the intraluminal excision of a rectal lesion, with a clear, magnified view, using an operating rectoscope, allowing for organ-preserving surgery. TEM has a number of advantages over radical surgery, including avoidance of stoma, decreased pain, faster recovery, and much shorter hospital stay, typically 24 hours. Importantly, several studies comparing TEM to radical abdominal surgery show no significant difference in recurrence (4-8%), or survival. A recent meta-analysis comparing TEM with standard trans-anal surgery demonstrated a lower rate of margin involvement, decreased tumour recurrence, and reduced specimen fragmentation with TEM.

Careful patient selection is essential. TEM is now an accepted treatment for large benign polyps and early low risk rectal cancers (T1), which have no adverse pathological features. High-risk T1 tumours with poor differentiation and lymphatic involvement are better served with conventional resection. The use of TEM in node negative T2 and T3 tumours is unclear and requires further study. There is a role for TEM in the palliation of those with advanced rectal cancers, that due to co-morbidity, or metastatic disease, are unfit for major resection. As the use of this technique becomes more widespread, there are implications for service planning and training.

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ENDOVASCULAR THERAPY FOR ACUTE ISCHAEMIC STROKE

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Stroke secondary to proximal vascular occlusion has a poor natural history unless rapid recanalization can be achieved. Unfortunately intravenous thrombolysis has modest efficacy at achieving this in the setting of a large clot burden[1]. Endovascular therapy (mechanical thrombectomy) via utilizing a retrievable stent has shown promise to effect the rapid recanalization required.

The Royal Victoria Hospital, Belfast Trust was recently the sole UK recruiting centre for the ESCAPE trial[1], which compared outcome in anterior circulation stroke patients treated with endovascular therapy plus standard care versus standard care alone. Patients were selected into the study based on advanced CT imaging criteria, which had to demonstrate a small core infarct, proximal vascular occlusion and salvageable brain (that is ischemic, but not yet irreversibly infarcted). For patients randomized into the endovascular arm, emphasis was put on procedural speed, with a target CT to groin puncture of <60 minutes and groin puncture to procedure completion of <30 minutes.

The study demonstrated that the rate of functional independence at 90 days from stroke onset increased from 29.3% to 53.0% in the endovascular group and there was a decrease in mortality from 19.0% to 10.4%.

The American Heart Association/American Stroke Association in their updated guidelines has now endorsed endovascular therapy for selected stroke patients[2]. As this therapy becomes standard of care, the challenge for us in Northern Ireland is to fully implement a 24/7 service and to ensure that patients eligible for this treatment are transferred as quickly as possible to benefit from it.

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A NEW DAWN FOR THE TREATMENT OF CYSTIC FIBROSIS

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Cystic Fibrosis (CF) is an inherited, life limiting, multisystem disease characterized by viscid secretions in multiple organ systems. Progressive respiratory failure remains the most common cause of morbidity and mortality with a current median survival of 41 years. The disease affects over 10,000 people in the United Kingdom. The mainstay of therapy is the treatment and reduction of respiratory infections and optimizing nutritional status.

Cystic fibrosis is caused by a defect in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene causing altered chloride and water transport. Over 2,000 different mutations of this gene have been described although not all cause CF. Approximately 50% of patients are homozygous for the ΔF508 mutation.

Ivacaftor (Kalydeco) is the first in a new class of transformative medications known as CFTR Modulators. It improves the transport of chloride across the cell membrane resulting in a significant increase in lung function and a reduction in respiratory infections.[1] It is licensed for use in patients with the G551D and other similar mutations (5-10% of patients).

More recently two positive phase III trials have been completed to assess the efficacy of Ivacaftor along with another CFTR Modulator, Lumacaftor, in patients homozygous for the ΔF508 mutation.[2] This combination therapy (Orkambi) is currently licensed in the US with a European Medicine Agency review expected later in 2015. However, these drugs are expensive and the cost per quality adjusted life year (QALY) for Ivacaftor is between £285,000 and £1,077,000.[3] There are several new CFTR modulators undergoing clinical trials at present.

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