BACKGROUND AND RATIONALE

Pancreatic cancer is the fourth leading cause of cancer death worldwide and is predicted to become the second most common cause within the next few years [1]. Prognosis is poor, with overall 5-year survival at best around 9% [2]. The only chance of either cure or long-term survival is surgical resection delivered with systemic chemotherapy, which can increase 5-year survival to up to 30-40% [1]. Surgery only confers unequivocal survival benefit if the cancer is removed with microscopically clear margins; clinicians must therefore be confident before proceeding that delivering this outcome is feasible for an individual. Unfortunately, 80% of patients present with either locally advanced or metastatic disease precluding this approach [2]. Those that are resectable will undergo major abdominal surgery from which the overall rate of morbidity is up to 80% and mortality ranges from 3-10% [1, 3, 4]. A patient's fitness to both survive and recover from surgery is therefore another critical constraint on offering curative treatment. In this context, it is the combination of patient selection for surgery, technical expertise and the standard of peri-operative care that determine outcomes of pancreatic cancer surgery.

Incremental progress has been made in all three of these domains and work is ongoing to further improve approaches. In terms of patient selection, conclusive research is needed on issues including the optimal sequencing of surgery and chemotherapeutic for upfront resectable tumours, if and how individual tumour biology influences management strategies, if and when any preoperative biliary drainage is necessary in those who are fast-tracked for surgery. In terms of operative advances, 'artery first', 'uncinate first', 'triangle resection', 'arterial

divestment', 'radical antegrade modular pancreatosplenectomy', 'distal pancreatectomy with coeliac axis resection' techniques have arisen in addition to venous, arterial and multi-visceral resection in attempts to increase operability and the rate of microscopically clear resections. The minimally invasive laparoscopic and robotic techniques popularised in other areas of abdominal surgery have extending into pancreatic cancer surgery. These may offer improved patient recovery and facilitate increased uptake and timeliness of adjuvant therapy. However, determining if benefits materialise and harm is avoided whilst techniques are standardised and learning curves overcome is crucial for research. In terms of peri-operative care standards, multidisciplinary management with intensivists, interventional and endoscopic interventionalists have significantly improved management of postoperative complications, but developing guidelines and refining algorithms is fertile territory for ongoing research.

It has been well documented that specialist centres with an embedded multidisciplinary approach offer more patients surgery for pancreatic cancer and with better outcomes [5, 6]. However, even across specialist centres decision making, techniques and outcomes are highly variable [4, 7]. Data synthesis and meta-analysis that allow accurate comparison of differences across both institutions and interventions are vital to provide all stakeholders with robust evidence to inform decision making. Multiple systematic reviews of abdominal surgery have demonstrated inconsistent and heterogeneous outcome reporting, with definitions of morbidity, mortality and outcome differing widely reflecting a lack of adequate standardisation[8-12]. This can have a number of detrimental effects: Outcomes of clinical trials can fail to advise clinical practice [13], heterogeneity of outcome

measures makes data synthesis across studies challenging and effective systematic review and meta-analysis may be prevented [14]. A lack of standardised outcome measures can also mean selective outcome reporting may occur [15, 16] biasing any conclusions from a trial with researchers selecting outcomes relevant to their needs rather than the needs of patients and practising clinicians [17-19]

We expect that the issues will also be applicable in in the field of pancreatic cancer surgery and that development of a focused clinical core outcome set would be beneficial and support ongoing data standardisation.

THEORETICAL FRAMEWORK

A solution to outcome reporting heterogeneity can be provided by core outcome sets (COS)[20]. A COS represents the minimum outcomes that should be reported in research of a specific condition. The World Health Organisation (WHO) began work on standardisation of outcomes for cancer trials in the 1970s, but since then the most notable work has been undertaken by the Outcome Measures in Rheumatology Initiative (OMERACT) and the Core Measures in Effectiveness Trials (COMET) initiative [21]. Through the work of these initiatives COS are now widely accepted as part of robust trials methodology as they allow meaningful comparison between separate trials for the same condition and ensure research reports on the outcomes agreed as most important by patients and clinicians. COS are centred on promoting research for patient benefit. With their value proven, work in core outcomes sets has focused most recently on how to refine methodology and make robust recommendations on how to develop 'good quality' core outcome sets. The has

culminated in the production of the COMET Handbook 1.0[21], the COS-STAR statement [22] and the COS-STAD recommendations [23].

This project is registered with the COMET initiative (https://www.comet-initiative.org/Studies/Details/2431) and will be conducted in line with the best practice recognised in these documents.

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