Leading article

Norwegian moratorium on transanal total mesorectal excision

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The survival of patients with rectal cancer has improved over the past 30 years[1]. Standardization of total mesorectal excision (TME) with or without neoadjuvant treatment has decreased local recurrence risks. Transanal TME (TaTME) was introduced to improve access to the pelvis in difficult to reach scenarios (such as obese men), with the promise of better margins and specimen quality[2]. From January 2015 to December 2017, some 110 TaTME procedures were performed in Norway. Surgery for primary rectal cancer is undertaken in approximately 20 hospitals, four of which mainly did TaTME, but treatment of locally recurrent disease is centralized to one hospital in each of four health regions. In April 2018, the Norwegian Radium Hospital in Oslo reported a new, unexpected pattern of recurrences that occurred early after TaTME, giving rise to significant concerns. An immediate snapshot analysis was presented to the treatment centres at a national meeting.

At least ten local recurrences (9·5 per cent) have been diagnosed, but the complete data are not currently available and the follow-up period is limited. The time to recurrence was short, a median of 11 months after surgery. Only a few cases involved technical problems that were described in the operation reports (for example entering an incorrect dissection plane). The recurrence pattern after TaTME was characterized by rapid, multifocal growth in the pelvic cavity and sidewalls, different from that typically observed after conventional surgery. Indeed, over the same interval, by comparison, the Norwegian Colorectal Cancer Registry[3] found only 3·4 per cent local recurrence following TME. A national audit is under way to confirm these observations and to elucidate reasons for this unexpected, serious issue; these are unclear but may involve educational, technical and oncological issues. Yet the surgeons at the four large-volume hospitals, who are experienced in laparoscopic and transanal endoscopic surgery, were trained in TaTME at international workshops in England and Spain. One centre had international proctoring during the introduction of TaTME and two other centres reported to the TaTME registry in the UK[4].

To date, studies on TaTME have focused mainly on surrogate oncological endpoints observed at the time of surgery, such as specimen quality, circumferential resection margin involvement and the free distal margin[4]. End-stage oncological parameters, including overall survival, disease-free survival and local recurrence, have yet to be clarified[5]. Recurrence rates after TaTME were estimated at 4 per cent in one systematic review, and 2·8–8·9 per cent (high volume *versus* low volume centres)[6], and 0–5·9 per cent in another[7]. The possibility of local recurrences related to the rectal transection and air flow during dissection from the perineum cannot be evaluated by examining the specimen; they can be assessed only by scrutinizing technical issues, such as the tightness of the purse-string suture.

Neoadjuvant chemoradiotherapy might protect patients from tumour regrowth. In Norway, guidelines are based on the disease stage and the predicted circumferential resection margin. Decisions regarding neoadjuvant therapy are made independently of the planned procedure or approach, and currently about 30 per cent of patients receive it[3]. Neoadjuvant therapy was given to a much higher proportion (58 per cent) of patients in the TaTME registry[4]. Adjuvant chemotherapy is not administered routinely to patients with stage I–III rectal cancer in Norway. Are these issues factors contributing to the unusually high recurrence rate observed following TaTME in Norway? It seems unlikely as many countries have similar guidelines and the pattern of recurrence is unusual.

This report highlights some fundamental challenges to introducing and implementing new surgical techniques. The introduction of new pharmaceutical drugs is strictly regulated, and involves testing in phase I studies (safety and dose ranging), phase II studies (efficacy) and phase III RCTs to document effectiveness. In contrast, no such regulations apply to surgical techniques. Randomized trials in surgery depend on the willingness of the surgical community to subject new treatment options to rigorous scientific evaluation in the absence of legal regulations. The history of surgery is rich with examples of new procedures that incur unexpected

problems; an example is the increase in common bile duct injuries in the early phase of laparoscopic gallbladder surgery[8,9]. The introduction of surgical techniques poses considerable methodological challenges, as RCTs may be possible to address only 25 per cent of the surgical research questions[10,11]; TME became accepted as the standard of surgery for rectal cancer based on institutional and national registry studies. However, there are good examples of well-designed RCTs, including the CLASICC trial, COLOR I and II trials, and the ROLARR trial. TaTME is currently being studied within the COLOR III trial and compared with laparoscopic rectal cancer surgery[2]. Like ROLARR and other trials, participants have to document that they have performed a minimum number of procedures of sufficient quality. This precondition is warranted to avoid a greatly needed trial being compromised owing to lack of experience. The observation that local recurrences increased after TaTMEs might, to some extent, be due to the learning curve, which is inevitable in the introduction of a complex procedure. Thus, the learning curve associated with the introduction of a new technique probably represents the most challenging phase. There is a risk of bringing a potentially beneficial surgical technique into discredit but, more importantly, of causing serious harm to patients. Adverse outcomes after the use of new health technologies may vary from minor to serious, or even lethal, consequences. Notably, a New York State memorandum read: 'a learning curve is not a valid justification for patient injury'[12].

At present, it seems that the learning curve is the Achilles heel of surgical innovation when experience increases most at the individual or institutional level by treating a limited number of patients. There is a need to define the standard for responsible surgical innovation, and to formulate comprehensive procedures for introducing new surgical techniques in an accountable process. This requires scientific endeavour based on informed patient consent such as that defined in the IDEAL (Idea, Development, Exploration, Assessment, Long-term Follow-up) framework. As modern surgery is becoming increasingly complex and based on more sophisticated technology, the surgical community has an obligation to take this initiative and to audit carefully for harm. In December 2018, because of these concerns, the Norwegian Colorectal Cancer Group recommended a temporary halt to the performance of TaTMEs for rectal cancer, whereas the Norwegian health authorities declared a national moratorium for TaTME until the national audit is complete. Other countries should consider the issue in the context of local practices and results.

Disclosure

The authors declare no conflict of interest.

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