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Endoscopic intermuscular dissection for deep submucosal invasive cancer in the rectum. Is this the dawn of the endoscopic cancer surgeon?

Referring to Moons LM et al. p. 993–998

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Over the last 15 years, the paradigm concerning treatment of colorectal neoplasia has shifted massively, with a progressive move away from conventional surgery towards less invasive endoscopic techniques. What was once a feared and controversial approach is now standard of care and, for benign pathology, endoscopic resection has become accepted as the best approach, even for very large and challenging lesions, with surgery being restricted to cases where endoscopic approaches have failed. The techniques used have also progressed, from piecemeal endoscopic mucosal resection (EMR) towards en bloc resection using a submucosal dissection technique (e.g. endoscopic submucosal dissection [ESD]). This has enabled the endoscopist to be confident in the completeness of the resection, with R0 resections becoming possible. With this shift has come a challenge around whether more invasive early cancers can also be managed in a similar manner.

The currently accepted position has been that, whilst early Sm1 invasion can be managed endoscopically, more invasive changes require surgery The main problem that has hindered the endoscopic resection of deeper invasion (≥Sm2) has been concern around the risk of lymph node metastasis (LNM). However, the absolute level of risk has recently been challenged, and a large meta-analysis has suggested that, in the absence of lymphovascular invasion, tumor budding, or poor differentiation, this may be as low as 1.3% [1]. This raises a challenge: ESD can achieve good R0 resection in Sm1 tumors in up to 92% of cases, but the rate drops when deeper invasion is present to as low as 62% [2]. This has led to the question of whether a different approach could be taken.

Moons et al. in this issue of *Endoscopy* have reported a case series of 67 patients with suspected deep submucosal invasive rectal cancer who were treated endoscopically [3]. In their study, an endoscopic dissection between the inner circular and outer longitudinal muscles was performed. The approach was successful in 96% of cases, with an R0 resection achieved in 81% of the resections. Overall, 45% of cases lacked any high risk features and were considered to be curative resections. Only minor adverse events were encountered.

This study opens up many questions. It challenges the paradigm that Sm2 and Sm3 disease is not endoscopically curable and suggests a new way of approaching suspected early invasive disease. The authors raise the suggestion that the technique should be viewed as an attractive endoscopic local staging technique that can achieve an adequate resection technique where ESD would be unlikely to be successful.

On first reading this work, it can feel challenging. It is effectively advocating for a technique that actively facilitates the endoscopic resection of Sm2 and Sm3 disease, which goes against the established European guidelines to which we strive to adhere [4]. But should we be so quick to dismiss these possi-

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bilities? It was not so long ago that a similar position was taken around EMR and ESD, yet these approaches have become the standard of care over a relatively short time-period. If the emerging, recent, and detailed work around the risk of LNM is correct, we may by subjecting patients to further invasive treatment that carries a greater risk than doing nothing.

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It is the nature of research to challenge established truths, and it should not be overlooked simply because it challenges our current beliefs. This study does not claim to be definitive and it does leave unanswered some important questions. In particular, the learning curve for these techniques is not described and it is unclear how long it would take for an experienced endoscopist skilled in ESD to acquire such skills. Furthermore, the follow-up period in this study was very limited and a much larger study with a longer follow-up period would be needed to ascertain with confidence whether the more recent suggestions are indeed correct and these patients do not subsequently have an unacceptably high risk of developing LNM. It is also unclear where it could fit into existing treatment pathways, alongside transanal endoscopic microsurgery (TEMS) and ESD.

It is clear that case selection is vital and high degrees of skill in in vivo diagnostic techniques will be necessary in deciding what type of lesion would be suitable for this approach. It seems improbable that this can be seen as a simple staging technique. Procedure times were not reported in this study, but procedures are likely to be time-consuming and require the patient to undergo a general anesthetic. Therefore, such approaches should be viewed as significant interventions and potentially definitive treatment, and not simply as a "big biopsy." Along similar lines, protocols around the roles of adjuvant treatments, such as chemoradiotherapy, in supporting this organ-sparing approach have not been established and would require randomized controlled trials to investigate them. This is important as there is some evidence that adjuvant therapy may be beneficial after local excision using existing techniques [5], and the combination of this new approach with adjuvant therapy may achieve similar outcomes to conventional mesorectal excision.

This is not the only recent study that has investigated the endoscopic treatment of early colorectal cancer. A retrospective analysis of 604 patients treated with colorectal ESD for submucosally invasive cancer included 207 noncurative resections. Over a median follow-up of 30 months, tumor recurrence and disease-specific survival rates were no different between those who underwent surgical treatment and those followed up with endoscopy [6]. Most significantly, the team found that submucosal invasion of greater than 1000 µm was not an independent predictor of LNM in the absence of other adverse histologic predictors. This is supportive of the experiences of Moons et al. and reflects the reality that the endoscopist is progressively moving into the realm of treating cancer, and techniques are needed for better managing such lesions. With an aging population with multiple co-morbidities, organ-preserving techniques that can be applied in this patient group are needed.

This study opens up a new avenue for improving the quality of the endoscopic resection specimen and makes it possible to confidently resect lesions that it would not have been possible to resect with a conventional ESD approach. It is likely that, as more work is done on the technique, problems not encountered in this relatively small series will be uncovered and refinements in the technique will make it more effective in challenging lesions. I question whether it may also be a good approach for managing scarred benign recurrences, where previous attempts at endoscopic resection have failed and the submucosal space has been compromised.

It is my belief that, in moving forward, we should be both optimistic and cautious. A bright new future could be around the corner with the potential for many patients to avoid invasive and destructive surgery, but it is early and there are still clouds on the horizon. We are effectively redefining what we, as endoscopists, mean by "early neoplasia." Whilst caution is essential, this could be an important step for the therapeutic endoscopist into a new paradigm in early cancer surgery.

Competing interests

The authors declare that they have no conflict of interest.

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