Is the significant risk of perioperative complications associated with radical surgery following non-curative endoscopic submucosal dissection for early colorectal cancer still acceptable?

We read the interesting study by Spadaccini *et al*, which compared the oncological outcomes between patients who received either a clinical follow-up or radical surgery following a non-curative endoscopic submucosal dissection (ESD), finding no difference in terms of tumour recurrence after a follow-up of 30 months.[1]

The current guidelines indicate radical surgery following non-curative ESD.[2] However, the risk factors for residual disease after ESD have been investigated only in retrospective surgical series, and colorectal surgery is associated with a significant chance of complications or stoma formation, especially in patients at higher surgical risk.[3] A query of the dataset of the COVID-CRC study (17 938 patients undergoing colorectal cancer surgery between 2018 and 2021)[4] identified 103 patients who underwent surgery following a non-curative ESD. As shown in table 1, in 64.1% of the cases no residual disease was found after surgery. Of these patients, 18.3% underwent a loop ileostomy formation (requiring a subsequent operation), 9.1% were admitted to intensive care and 10.6% experienced a severe complication (Clavien-Dindo grade 3 or higher). Among the 37 patients (35.9%) who had a residual disease on the surgical specimen, the majority (64.9%) only had local residual disease with no positive lymph nodes (table 1).

Even in our 'real-life' series, most patients underwent unnecessary major surgery. It is understandable that 35.9% is still too high a risk of residual disease after non-curative ESD. On the other hand, 65.1% of patients could have undergone an organ-sparing treatment after the endoscopic procedure. As shown by Spadaccini *et al*, the risk of residual cancer is even lower in tertiary centres (19.8%). Even from a surgeon's perspective, one cannot help but wonder whether radical surgery and its risks can still be justified in all patients, or it could be considered an overtreatment, at least in a proportion of cases.

A common effort of endoscopists and surgeons will be necessary to create a prospective, international, multicentre, real-life registry of patients undergoing non-curative ESD. The role of histological features and patient's risk factors as predictors of residual disease (local or nodal) should be reassessed to create a new algorithm of tailored treatment for patients who receive what is now considered a non-curative ESD. Adequate benchmarks of the quality of the ESD should be identified, and pathways of centralisation to referral centres should be created. By doing so, the risk of unnecessary radical surgery will be reduced while assuring good oncologic outcomes. A similar approach has been successfully adopted in cases of a clinical complete response after neoadjuvant therapy for rectal cancer, with no evidence of worse oncological outcomes in those who have undergone watchful surveillance.[5]

Table 1 Comparison of the clinical, histological and perioperative variables according to the presence of residual cancer on the surgical specimen

Variables	Overall sample (N=103)	No residual cancer (N=66)	Residual cancer (N=37)	P value*
High volume centre (>100 cases/year)	55.3	59.1	48.7	0.41
Mean age in years (SD)	66.7 (10.6)	67.8 (10.4)	65.0 (11.0)	0.10
Male gender, %	46.6	47.0	46.0	0.92
Mean BMI in kg/m^2 (SD)	25.4 (3.4)	25.7 (2.7)	25.2 (3.8)	0.69
Location, %				
Right or transverse colon	36.1	36.4	21.6	0.12
Left colon	31.1	30.3	32.4	0.82
Rectum	37.8	33.3	46.0	0.20
Depth of invasion, %				
sm1	31.1	42.4	10.8	<0.001
sm2	17.5	16.7	18.9	0.77
sm3	46.6	37.9	62.2	0.023
>sm	4.8	3.0	8.1	0.34
Tumour budding, n (%)	98 (44.9)	53 (47.5)	33 (40.5)	0.54
	(N=101)	(N=56)	(N=33)	
Lymphovascular invasion, %	19.8	21.9	16.2	0.61
	(N=101)	(N=57)	(N=32)	
R1, %	60.4	55.4	69.4	0.20
G3, %	2.0	3.2	0	0.31
Residual disease on surgical specimen				
Only local residual disease	–	–	64.9	–
Only positive lymph nodes	–	–	21.6	–
Local residual disease and positive lymph nodes	–	–	13.5	–
ASA score ≥3, %	19.4	16.7	24.3	0.43
Minimally invasive surgery, %	93.2	90.9	97.3	0.42
Conversion to open surgery, %	2.1	1.7	2.8	0.86
Loop ileostomy, %	23.2	18.3	31.4	0.20
Postoperative intensive care, %	6.8	9.1	2.7	0.41
Surgical complications, %	18.4	22.7	10.8	0.19
Severe complications, %	8.7	10.6	5.4	0.48
Mean length of stay in days (SD)	6.9 (3.3)	7.3 (3.7)	6.2 (2.2)	0.024

Severe complications were defined as Clavien-Dindo grade 3 or higher.
*Kruskal-Wallis test for the continuous variables and χ^2 test for the categorical variables.
ASA, American Society of Anesthesiologists; BMI, body mass index.

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