International Journal of Colorectal Disease (2019) 34:353–354
https://doi.org/10.1007/s00384-018-3197-1

LETTER TO THE EDITOR

"Mesentery-based surgery" to prevent surgical recurrence in Crohn's disease: from basics to surgical practice

Roberto Peltrini[1] · L. Bucci[1]

Accepted: 9 November 2018 / Published online: 11 November 2018

Dear Editor:

Surgery in Crohn's Disease (CD) has always been based on the principle of limiting intestinal resection to the diseased tract as much as possible, thus saving precious centimeter of intestine for the patient. Traditionally, intestinal resection takes place by following the edge of digestive tube, keeping away from the vessels that go into the mesentery and the mesocolon, unlike cancer surgery which obliges the surgeon to respect the oncological principles.

Recent studies have recognized the mesentery as a single anatomical and structural unit with functional properties that plays a role in both physiological and pathological mechanisms [1]. In particular, JC Coffey highlights that the main morphological changes of the mesentery (those detected intraoperatively by the surgeon): fat wrapping (or creeping fat) and mesenteric thickening are correlated with mucosal ulceration and degree of disease severity and that the mucosal ulceration is always confined to the mesenteric margin of the intestine. So he identifies the patobiological link of the disease in this connection: while signs of inflammation and edema extend circumferentially, the ulceration would be the result of the convergence of inflammatory inputs coming from both the submucosa and the mesentery [2].

How this issue can affect surgical practice? In a retrospective study [3], Toru Kono, with his antimesenteric functional end-to-end anastomosis, showed a lesser probability of anastomotic surgical recurrence in patients with CD who underwent Kono-S at 5 years (0% vs 15% $p = .0013$) than who underwent conventional anastomosis. The effectiveness of the new anastomosis in reducing the risk of surgical recurrence seems to be confirmed by the results of a multicenter study [4] where the 5- and 10-year cumulative surgical recurrence rate was 1.8% (95% CI, 0–4.3%) and 1.7% (95% CI, 0–4.2%) in Japanese and the US group respectively. It is possible to explain the low rates of surgical recurrence because, being the mesenteric side of the intestine the original site of anastomotic CD recurrence, to place anastomosis' columns at the mesenteric side should prevent anastomosis distortion and maintain its diameter and dimension. The mesenteric side is placed at the center of the supporting columns, behind the posterior wall of the anastomosis; it is so excluded from the intestinal lumen. Thus, when recurrence of CD starts, it provides stable support which will prevent mechanical deformation. Shimada et al.'s recent study [5] strengthens the effectiveness of this type of anastomosis than classic end-to-end anastomosis in reducing surgical recurrence (3.4% in the Kono-S group and 24.4% in the end-to-end group) with a median follow-up of 54 months.

Data suggest that the increased visceral adipose tissue (VAT) is involved in pathobiology of CD not only at molecular level (positive correlation with C-reactive protein, increase in adiponectin, adipocytokines, TNFα, IL10, and IL6) [6] but also at the clinical level since Li Y associated it with Crohn's disease activity and with an increased risk of postoperative recurrence [7], although it is not entirely clear whether the mesenteric fat hypertrophy is a primary or secondary phenomenon of intestinal inflammation. In his retrospective cohort series, CJ Coffey [8] showed how the inclusion of the mesentery as part of intestinal resection is associated with reduced surgical recurrence (the cumulative rate of reoperation in cohort A, mesentery sparing, was 40% and 2.9% in cohort B, mesentery excised) with a mean follow-up time of 69.9 ± 48.47 months and 51.7 ± 20.98 months, respectively. Furthermore, on a multivariable

✉ Roberto Peltrini
roberto.peltrini@gmail.com

L. Bucci
luigi.bucci@unina.it

[1] Department of General and Specialist Surgery, University of Naples Federico II, Via Pansini 5, 80131 Naples, Italy

analysis, retention of the mesentery was an independent predictor of recurrence requiring surgical intervention ($p = 0.002$) and, between clinicohistopathological features, only the presence of fat wrapping increased the risk of surgical recurrence significantly (HR 4.7, 95% CI $p = 0.003$). He suggested that mesenteric excision could reduce mesenteric inflammatory mesenchymal inputs and, with a greater lymphadenectomy, reduce immunological inputs improving postoperative outcomes. Risk of bleeding and excessive resection of healthy bowel are, in our opinion, not negligible aspects for this surgical approach even if the difference in the length of the resected intestine was not significant ($p = 0.430$, ileum; $p = 0.383$, colon). Then, would the excision of the mesentery result in an increase in postoperative morbidity? It is interesting to note how in EJ de Groof and CJ Buskens' series [9] after proctectomy for CD, perineal complications were more represented in the group of patients underwent close rectal dissection than the group underwent total mesorectal excision (59.5% vs 17.6% $p = 0.007$), as well as healing rates were lower (51.4% vs 88.2% $p = 0.014$) in patients where part of the remaining mesorectum continued, probably, to exert its pro-inflammatory action.

Focus on the mesentery, in addition to intestine, may offer a new interpretation of CD and therefore of its surgical treatment. Further studies are needed to establish higher levels of evidence: currently two RCT (NCT02542904 and NCT03172143) are underway to assess the real benefit of mesentery excision in CD and other two RCT (NCT03256240 and NCT02631967) to assess long-term results about Kono-S anastomosis vs stapled side-to-side anastomosis.

References

1. Coffey JC, O'Leary DP (2016) The mesentery: structure, function, and role in disease. Lancet Gastroenterol Hepatol 1(3):238–247. https://doi.org/10.1016/S2468-1253(16)30026-7
2. Coffey JC, O'Leary DP, Kiernan MG, Faul P (2016) The mesentery in Crohn's disease: Friend or foe? Curr Opin Gastroenterol 32(4): 267–273. https://doi.org/10.1097/MOG.0000000000000280
3. Kono T, Ashida T, Ebisawa Y, Chisato N, Okamoto K, Katsuno H, Maeda K, Fujiya M, Kohgo Y, Furukawa H (2011) A new antimesenteric functional end-to-end handsewn anastomosis: surgical prevention of anastomotic recurrence in Crohn's disease. Dis Colon rectum 54(5):586–592. https://doi.org/10.1007/DCR.0b013e318208b90f
4. Kono T, Fichera A, Maeda K, Sakai Y, Ohge H, Krane M, Katsuno H, Fujiya M (2016) Kono-S anastomosis for surgical prophylaxis of anastomotic recurrence in Crohn's disease: an international multicenter study. J Gastrointest Surg 20(4):783–790. https://doi.org/10.1007/s11605-015-3061-3
5. Shimada N, Ohge H, Kono T *et al.*, Surgical recurrence at anastomotic site after bowel resection in Crohn ' s disease : comparison of Kono-S and end-to-end anastomosis, 2018. https://doi.org/10.1007/s11605-018-4012-6
6. Li Y, Zhu W, Gong J, Zuo L, Zhang W, Gu L, Guo Z, Cao L, Li N, Li J (2014) Influence of exclusive enteral nutrition therapy on visceral fat in patients with Crohn's disease. Inflamm Bowel Dis 20(9):1568–1574. https://doi.org/10.1097/MIB.0000000000000114
7. Li Y, Zhu W, Gong J, Zhang W, Gu L, Guo Z, Cao L, Shen B, Li N, Li J (2015) Visceral fat area is associated with a high risk for early postoperative recurrence in Crohn's disease. Color Dis 17(3):225–234 https://doi.org/10.1111/codi.12798
8. Coffey CJ, Kiernan MG, Sahebally SM et al (2018) Inclusion of the mesentery in ileocolic resection for Crohn's disease is associated with reduced surgical recurrence. J Crohn's Colitis:1–12. https://doi.org/10.1093/ecco-jcc/jjx187
9. de Groof EJ, van der Meer JHM, Tanis PJ *et al*. Persistent mesorectal inflammatory activity is associated with complications after proctectomy in Crohn's disease, J. Crohn's Colitis, 2018. https://doi.org/10.1093/ecco-jcc/jjy131