



## EDITORIAL

## Pediatric Crohn's Disease and Surgery: Another Tool for the Treatment of a Complex Disease



### Doença de Crohn e Cirurgia Pediátrica: Outra Ferramenta para o Tratamento de uma Doença Complexa

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The article by Lourenço et al<sup>1</sup> in this issue of GE reports the experience of a Portuguese tertiary center on surgery in pediatric Crohn's disease. Some specificities concerning manifestations and management of pediatric IBD patients should be highlighted to better understand different aspects of this problem.

Inflammatory bowel disease (IBD), a chronic and relapsing condition, develops during childhood or adolescence in up to 25% of patients.<sup>2,3</sup>

As among adults, the phenotypic spectrum in Crohn's disease (CD) is wide but with some particularities: in children the phenotype is more often extensive and aggressive than in adults; the most common type is inflammatory, followed by fistulizing and structuring disease; also unique to pediatric-onset disease is the potential for linear growth impairment and delayed sexual development already at disease onset or as a complication of undertreated inflammation.<sup>4</sup>

As a consequence of these particularities treatment options also differ from adults patients and are an indirect demonstration of the severity of the disease. It is therefore clearly important to diagnose and treat pediatric patients early in order not only to induce and maintain remission, but also to address nutritional deficiencies, ensure normal growth, avoid complications and change the course of disease if possible, especially when factors suggestive

of poor outcome are identified. The majority of pediatric patients require long-term maintenance medication (immunomodulatory and biologics agents). Unfortunately these medications have been associated with several side effects, and some patients may have to discontinue therapy due to treatment-related complications or loss of efficacy creating additional problems.<sup>5</sup>

The cumulative risk of progression to complicated CD looks similar to adults, but because of early onset of disease, children are more likely to have undergone surgery by young adulthood. Pigneur, et al. found that by the age of 30 years, the risk of surgical resection was  $48 \pm 5\%$  and  $14 \pm 2\%$  in pediatric and adult onset CD, respectively.<sup>6</sup>

It is evident that for some patients surgery is inevitable (intestinal perforation, stenotic fibrosis with occlusion) and sometimes done in an emergency setting not in the best conditions. For a small group of pediatric patients it can be the first option of treatment and done in a planned way (prepubertal, localized disease to terminal ileum and growth delay, for example).<sup>5</sup>

Minimally invasive surgery is being increasingly applied in pediatric patients with IBD and proved to be feasible, safe and effective if performed by surgeons with expertise in this field.<sup>7</sup> Cosmetic results are satisfactory, a very important issue in patients perspective. This is also the experience in our center with 12 CD patients submitted to laparoscopic surgery in the last 10 years with no complications, rapid recovery and good functional outcome (unpublished data).

It is very well known that recurrence of the disease after surgery is probable and only a matter of time, with

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clinical and endoscopic recurrence rates of 2–25% and 65–90% respectively, within one year.<sup>8</sup> In a pediatric population Hansen et al. found a cumulative clinical recurrence rate at 1, 5 and 10 years of 50%, 73% and 77% respectively.<sup>9</sup> With this in mind and in contrast to adult CD patients, children usually start maintenance therapy after surgically induced remission despite conflicting results in the literature and lack of pediatric prospective controlled trials on the prophylactic effect of biologicals and/or immunomodulators after surgery for CD. The recent pediatric guidelines on medical management of CD recommend that thiopurines should be used as first choice drug for post-operative maintenance therapy and that anti-TNF-agents can be an option in selected patients.<sup>5</sup>

Despite this proactive attitude, recurrence at the site of anastomosis still occurs. Because clinical signs of recurrence often occur in an advanced stage of the disease, endoscopy surveillance is mandatory after surgery and ileocolonoscopy should be performed 6–12 months after resection to guide treatment adjustment.<sup>5,10</sup> In POCER study, involving adult patients, endoscopic evaluation showed a clear advantage of systematic evaluation at 6 months with treatment adaptation for low and high risk patients.<sup>11,12</sup> This is the strategy that we have been using in our center in the last 10 years.<sup>13</sup> The endoscopic surveillance and step-up in medical treatment according to recurrence looks even more important in the pediatric CD patients considering their young age, predictability of a long duration of the disease and the imperious necessity to avoid another intestinal resection. Re-scope is a sensitive issue for families and they are often reluctant to subject their children to uncomfortable bowel preparation and anesthesia. Sometimes they propose to postpone the procedure based on favorable evolution but the advantage of the colonoscopy should be explained.

In the retrospective study presented by Lourenço et al.,<sup>1</sup> 8 patients were treated by classic surgery without major complications during a period of 11 years. The results confirm that surgery was safe, inevitable in some patients and scheduled in others. The indication for surgery was not different from the results of other pediatric series. The pre and postoperative treatment was very heterogeneous. Clinical recurrence after surgery was seen only in one patient but the follow-up time ranged from 2 months to 7 years. In this cohort of patients only clinical recurrence was evaluated because patients were not submitted to endoscopic surveillance. This is an important point for reflection because anastomotic recurrence is silent in the majority of patients and should be appropriately seen by endoscopy considering the therapeutic implications. Seven of 8 patients, were submitted to azathioprine and infliximab after surgery and it would be interesting to see the effect of these medications in the prevention of endoscopic recurrence. Because of the small number of patients involved no other conclusions can be drawn and this is also the problem of other published pediatric series reinforcing the importance of collaborative studies among centers.

Considering the complexity of pediatric IBD patients they should be treated in tertiary pediatric

gastroenterology centers by multidisciplinary teams including pediatric gastroenterologist, surgeon with special interest on IBD, interventional radiologist, pathologists and anesthesiologists able to offer the best treatment in each moment. In the best interest of the patient the treatment should always be individualized, considering the benefit-risk of each option and based on the existing evidence. As pediatricians we should not accept “less than the best” in the treatment of this vulnerable and complicated population.

## References

- Lourenço R, Azevedo S, Lopes AI. Surgery in pediatric Crohn disease: case series from a single tertiary referral center. *GE Port J Gastroenterol*. 2016;23:191–94.
- Benchimol EI, Fortinsky KJ, Gozdyra P, Van den Heuvel M, Van Limbergen J, Griffiths AM. Epidemiology of pediatric inflammatory bowel disease: a systematic review of international trends. *Inflamm Bowel Dis*. 2011;17:423–39.
- Cosnes J, Gower-Rousseau C, Seksik P, Cortot A. Epidemiology and natural history of inflammatory bowel diseases. *Gastroenterology*. 2011;140:1785–94.
- De Bie CL, Paerregaard A, Kolacek S, Ruemmele FM, Koletzko S, Fell JM, et al. Disease phenotype at diagnosis in pediatric Crohn’s disease: 5-year analyses of the EUROKIDS Registry. *Inflamm Bowel Dis*. 2013;19:378–85.
- Ruemmele FM, Veres G, Kolho KL, Griffiths A, Levine A, Escher JC, et al. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn’s disease. *J Crohns Colitis*. 2014;8:1179–207.
- Pigneur B, Seksik P, Viola S, Viala J, Beaugerie L, Girardet JP, et al. Natural history of Crohn’s disease: comparison between childhood- and adult-onset disease. *Inflamm Bowel Dis*. 2010;16:953–61.
- Pini-Prato A, Faticato M, Barabino A, Arrigo S, Gandullia P, Mazzola C, et al. Minimal invasive surgery for paediatric inflammatory bowel disease: personal experience and literature review. *World J Gastroenterol*. 2015;21:11312–20.
- Renna S, Camma C, Modesto I, Cabibbo G, Scimeca D, Civitavecchia G, et al. Meta-analysis of the placebo rates of clinical relapse and severe endoscopic recurrence in postoperative Crohn’s disease. *Gastroenterology*. 2008;135:1500–09.
- Hansen L, Jakobsen C, Paerregaard A, Qvist N, Wewer V. Surgery and postoperative recurrence in children with Crohn disease. *J Pediatr Gastroenterol Nutr*. 2015;60:347–51.
- Van Assche G, Dignass A, Reinisch W, van der Woude CJ, Sturm A, De Vos M, et al. The second European evidence-based consensus on the diagnosis and management of Crohn’s disease; special situations. *J Crohns Colitis*. 2010;4:63–101.
- De Cruz P, Kamm MA, Hamilton AL, Ritchie KJ, Krejany S, Gorelik A, et al. Optimising post-operative Crohn’s disease management: best drug therapy alone versus colonoscopic monitoring with treatment step-up. The POCER study. *Gastroenterology*. 2013;144:S164.
- De Cruz P, Kamm MA, Hamilton AL, Ritchie KJ, Krejany EO, Gorelik A, et al. Efficacy of thiopurines and adalimumab in preventing Crohn’s disease recurrence in high-risk patients – a POCER study analysis. *Aliment Pharmacol Ther*. 2015;42:867–79.
- Santalha M, Santos S, Tavares M, Amil Dias J, Trindade E. Endoscopic recurrence after surgery on paediatric Crohn’s disease. *AGH*. 2013;4:28–31.