

Crohn's Disease: advantages of the Konos-S surgical technique

Doença de Crohn: vantagens da técnica cirúrgica de Konos-S.

Enfermedad de Crohn: ventajas de la técnica quirúrgica Konos-S

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Abstract

Introduction: Crohn's Disease (CD) belongs to the group of diseases called Inflammatory Bowel Diseases (IBD). CD is an inflammatory disease characterized by idiopathic, local and chronic nonspecific inflammation, currently the real cause is still unknown. The recurrence of anastomosis after intestinal resection is one of the most significant problems in the management of CD, recently a new surgical technique was described and used to reduce recurrence, the Konos-S technique described by Konos et al. (2011). **Objective:** To carry out a systematic review of the literature to describe Crohn's disease and the use of the Konos-S surgical technique for the treatment of the disease. **Methodology:** This study is a systematic review of the literature on the main search platforms for scientific articles: ScienceDirect, PubMed, SciELO, BIREME, from 2011 to 2022, 18 articles were selected. **Results and Discussion:** Kono and colleagues introduced into surgery their unique surgical technique to reduce the risk of surgical recurrence of the anastomosis is a hand-stitched end-to-end functional antimesenteric anastomosis. Some clinical studies have demonstrated the effectiveness of the technique in significantly reducing anastomotic and endoscopic recurrence, as it is able to preserve innervation and blood supply, important factors for proper healing of the anastomosis, with a lower risk of reoperation. However, more research is needed to universally validate Konos-S surgery for patients with an indication, as the treatment approach must be personalized for CD cases and complications must be analyzed individually for the patient.

Keywords: Chron's Disease; Surgical technique; Konos- S; Health teaching.

Resumo

Introdução: A Doença de Crohn (DC) pertence ao grupo de doenças denominadas Doenças Inflamatórias Intestinais (DII). A DC é uma patologia inflamatória caracterizada por inflamação idiopática, local e crônica inespecífica, atualmente a real causa ainda é desconhecida. A recorrência de anastomose após ressecção intestinal é um dos

problemas mais significativos no manejo da DC, recentemente uma nova técnica cirúrgica foi descrita e utilizada para reduzir a recorrência, a técnica de Konos-S descrita por Konos et al. (2011). Objetivo: Realizar uma revisão sistemática da literatura para descrever a doença de Crohn e o uso da técnica cirúrgica Konos-S para o tratamento da doença. Metodologia: Este estudo é uma revisão sistemática da literatura nas principais plataformas de busca de artigos científicos: ScienceDirect, PubMed, SciELO, BIREME, de 2011 a 2022 foram selecionados 18 artigos. Resultados e Discussão: Kono e colegas introduziram na cirurgia sua técnica cirúrgica única para reduzir o risco de recorrência cirúrgica da anastomose é uma anastomose antimesentérica funcional término-terminal costurado à mão. Alguns estudos clínicos demonstraram a eficácia da técnica em reduzir significativamente a recorrência anastomótica e endoscópica, pois é capaz de preservar a inervação e o suprimento sanguíneo, fatores importantes para a cicatrização adequada da anastomose, com menor risco de reoperação. No entanto, mais pesquisas são necessárias para validar universalmente a cirurgia Konos-S para pacientes com indicação, uma vez que a abordagem de tratamento deve ser personalizada para cada caso de DC e que as complicações devem ser analisadas individualmente para cada paciente. **Palavras-chave:** Doença de Chron; Técnica cirúrgica; Konos- S; Ensino em saúde.

Resumem

Introducción: La Enfermedad de Crohn (EC) pertenece al grupo de enfermedades denominadas Enfermedades Inflamatorias Intestinales (EII). La EC es una enfermedad inflamatoria caracterizada por inflamación inespecífica idiopática, local y crónica, actualmente aún se desconoce la causa real. La recurrencia de la anastomosis después de la resección intestinal es uno de los problemas más importantes en el manejo de la EC, recientemente se describió y utilizó una nueva técnica quirúrgica para reducir la recurrencia, la técnica Konos-S descrita por Konos et al. (2011). Objetivo: Realizar una revisión sistemática de la literatura para describir la enfermedad de Crohn y el uso de la técnica quirúrgica Konos-S para el tratamiento de la enfermedad. Metodología: Este estudio es una revisión sistemática de la literatura sobre las principales plataformas de búsqueda de artículos científicos: ScienceDirect, PubMed, SciELO, BIREME, de 2011 a 2022, se seleccionaron 18 artículos. Resultados y discusión: Kono y sus colegas introdujeron en la cirugía su técnica quirúrgica única para reducir el riesgo de recurrencia quirúrgica de la anastomosis: una anastomosis antimesentérica funcional de extremo a extremo cosida a mano. Algunos estudios clínicos han demostrado la eficacia de la técnica para reducir significativamente la recurrencia anastomótica y endoscópica, ya que es capaz de preservar la inervación y el riego sanguíneo, factores importantes para la correcta cicatrización de la anastomosis, con un menor riesgo de reintervención. Sin embargo, se necesita más investigación para validar universalmente la cirugía Konos-S para pacientes con una indicación, ya que el enfoque del tratamiento debe personalizarse para los casos de EC y las complicaciones deben analizarse individualmente para el paciente. **Palabras clave:** Enfermedad de Chron; Técnica quirúrgica; Konos – S; Enseñanza en la salud.

1. Introduction

Crohn's Disease (CD) belongs to the group of diseases called Inflammatory Bowel Diseases (IBD)¹. CD is an inflammatory disease characterized by idiopathic, local and chronic non-specific inflammation, currently the real cause is still unknown, but there are many theories as to what could be the focus of the disease. The most recent ones point to the immune system and bacteria as the main causes due to a dysregulated immune reaction to the intestinal microbiota (Actis et al., 2019; Ramos & Papadakis, 2019; Chang, 2020; Cushing & Higgins, 2021).

A recent estimate suggests that 1.3% (3 million individuals) of the US population is diagnosed with IBD.³ Crohn's disease is a chronic disease with an annual incidence ranging from 3 to 20 cases per 100,000. The average onset of the disease is at age 30 and has 2 peaks, first between the ages of 20 and 30 and then a smaller peak around age 50. Crohn's disease is more common in the industrialized world, particularly in North America and Western Europe, although the incidence is increasing in Asia and South America. In Brazil, the prevalence of IBD was 38.2 per 100,000 inhabitants, DC was 14.1 per 100,000/ inhabitants/year) (Van Rheenen et al., 2021; Atreya & Siegmund, 2021).

Crohn's disease is one of the two main subtypes of inflammatory bowel disease (IBD), along with ulcerative colitis. The disease has an unpredictable clinic, characterized by periods of active inflammation and outbreaks of symptoms that are separated by periods of quiescence or remission, with different complications and variable responses to treatment. Typical symptoms experienced in CD include abdominal pain and cramping, (common) diarrhea, blood in the stool, fever, fatigue, reduced appetite, and weight loss. Inflammation in Crohn's disease is transmural, affecting the entire thickness of the intestinal wall, this chronic and recurrent inflammation in the gastrointestinal (GI) tract can be in any portion of the tract, although it

usually occurs in the ileum and colon (Veauthier & Hornecker, 2018; Roda et al., 2020; Chang, 2020; Cushing & Higgins, 2021).

In addition to the symptoms described above, the presence of intestinal inflammation alone can produce several symptoms. These include abdominal pain, diarrhea, fecal urgency, intestinal bleeding, and weight loss. These symptoms significantly impact the patient's quality of life, functional capacity, and emotional state. Generally speaking, treatment falls within either medical or surgical approaches and is largely determined by patient demographics, disease location, disease severity, and presence of complications. In practice, this involves a thorough clinical, biochemical and endoscopic evaluation of all patients to allow for an individualized approach to therapy (Veauthier & Hornecker et al., 2018; Gajendran et al., 2018; Rubin et al., 2020).

Given the previously described pathophysiological models for IBD, it is not surprising that the basis of IBD therapy is based on manipulation of the immune system or gut microbiota. Major classes of drugs used in the treatment of CD include corticosteroids, aminosalicilate or 5-aminosalicylic acid (5-ASA) compounds, antibiotics, immunomodulators, and the new biological class of drugs that specifically target the cytokine pathways that are upregulated in IBD. . The objective is to control the symptoms, the inflammatory reaction, the healing of the mucosal lesions, keep the disease in remission as long as possible and improve the patient's quality of life (Fragoulis et al., 2019; Adamina et al., 2020; Rubin et al., 2020).

Despite recent innovations in the medical treatment of CD through the emergence of new and more potent drugs, the majority of CD patients (70-80%) will still require one or more surgeries during their lifetime (from Buck van Overstraeten et al. 2012). Surgery is indicated in symptomatic patients with CD who do not tolerate, and do not respond to, or do not comply with medical treatment (Adamina et al., 2020; Lightner et al., 2020). Anastomotic recurrence after intestinal resection is one of the most significant problems in the management of CD, in this context, the choice of surgical approach is essential to evaluate the risk-benefit in each situation and should be as limited as possible. Recently, a new surgical technique has been described and used to reduce recurrence, the Konos-S technique, described by Konos et al. (2011). Thanks to this procedure, they concluded that the Kono-S anastomosis appears to be effective in preventing surgical recurrence of anastomosis and that it is more advantageous compared to other anastomoses as it is able to preserve both innervation and blood supply. important factors in the proper healing of the anastomosis. Therefore, the objective of this work is to review the Kono-S surgical technique in the treatment of Crohn's disease.

2. Methodology

This study is a systematic literature review, with a qualitative approach, with interpretation and analysis of the elements obtained. The guiding question of the study was: "What are the main advantages of using the Konos-S surgical technique in patients with Crohn's disease", after which the following subsequent steps were taken to identify the theme, select the pertinent hypothesis or question of research, the criteria for inclusion and exclusion, definition of information and clinical studies to be included in this review study, interpretation of results and presentation of the review with synthesis of knowledge were defined (Pereira et al., 2018).

2.1 1st Step: identification of the topic and selection of the research question

First, the theme was defined to start the elaboration of the integrative review and proceed to the subsequent stages of the study, the guiding question was formulated (Mendes et al., 2008). Thus, in relation to the chosen theme, the guiding question was: What are the benefits of using the Konos surgical technique in Crohn's disease?

2.2 2nd Stage: criteria for sample selection

The research was carried out from the survey of scientific articles found in the main search platforms for scientific articles: ScienceDirect, PubMed, Scientific Electronic Library Online (SciELO) and Latin American and Caribbean Center for Health Sciences Information (BIREME) and NCBI. Using the descriptors present in the Descriptors in Health Sciences (DeCS) which are: Crohn's disease, Treatment of Crohn's disease, Surgery, Konos-S Technique, in Portuguese and English with the Boolean operator "e" in all bases, eventually associating the terms with the use of quotation marks (""). Considering the need to perform a broader search, these keywords and the Boolean operator were always used in the search field related to the abstract. These descriptors were combined in order to find as many publications as possible suitable for the review. The review was done from December 2021 to February 2022.

2.3 3rd Stage: identification of pre-selected and selected studies

For the collection of articles, the search limits were chosen (free full text, 11 years, humans) to specify the results and thus collect pertinent information to support the theme in question. Thus, in the first search, 33 articles were found in Search I, after applying the filters in Search II, the search returned articles and from these, 29 articles were selected for the systematic review. In the SCIELO database, no article was found based on the Search II criteria. After the selection, the titles, keywords and abstracts of all publications resulting from the investigation carried out by the search strategy were carefully read in order to analyze the texts adequate to the previously established inclusion criteria and filters. All 18 selected articles were read in full to properly verify the purpose of the study, including clinical studies, cohort studies, reviews and meta-analyses.

2.4 4th Stage: analysis and interpretation of results

In the last phase, the articles were analyzed and discussed in order to extract all the information that was relevant to the research for the formulation of the work, and all the questions were raised and propositions for the writing of the scientific work were made for the sedimentation of knowledge.

2.5 5th Stage: presentation of the knowledge synthesis

In this phase, the synthesis of the results was carried out through the analysis of the scientific material from the evaluation of the results and conclusions drawn from the selected articles. The document's formulation authorizes readers to assess the veracity of the procedures used in carrying out the review in question.

3. Results and Discussion

In the present study, 18 articles were selected, Table 4 shows the distribution of articles, according to authors, titles and type of study, all of these articles were published in the ScienceDirect, PubMed, Bireme and Lilacs databases. In keeping with the natural history of the disease, the percentage of CD patients requiring surgery remains dramatically high: up to 80% of patients undergo surgical treatment, but such treatment is non-curative. In fact, the rate of postoperative recurrence varies according to current definitions: clinical, endoscopic, radiological and surgical recurrence. Population studies suggest that without maintenance therapy, up to 90% of patients will experience a relapse of their condition at some stage, making complications and the need for surgical intervention more likely (Aniwan; Loftus, 2021).

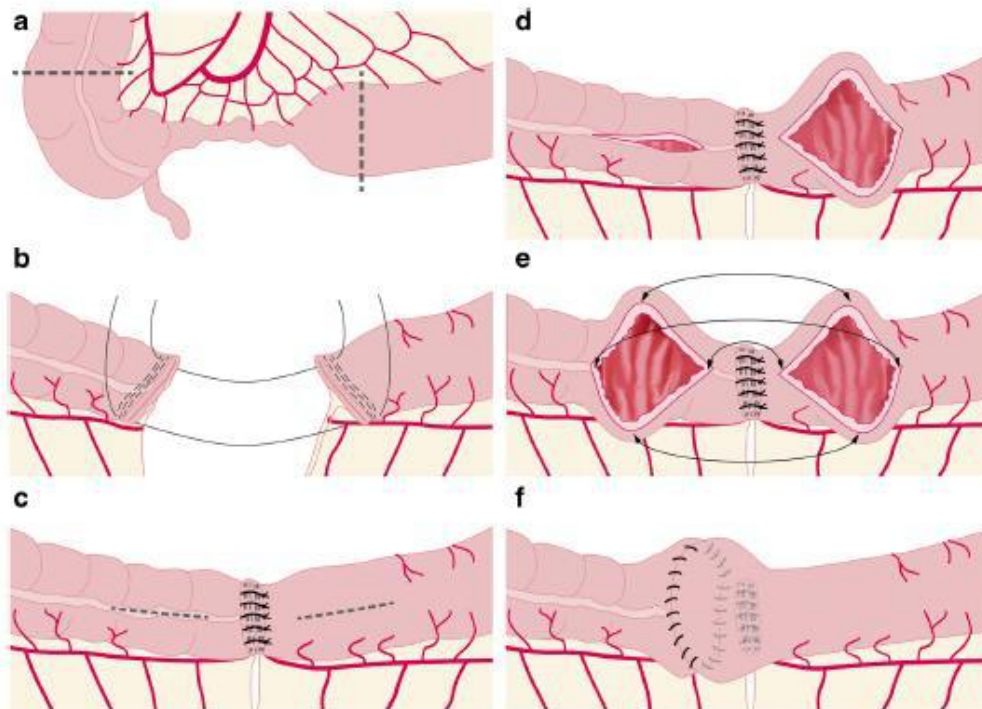
Post-surgical endoscopic recurrence of CD is established as the appearance of mucosal lesions observed through ileocolonoscopy and classified according to the Rutgeerts score. This classification is widely used in cases of ileocolic resection and was recently updated in 2014, where the classification i0 (absence of lesions in the distal ileum), i1 (aphthoid

erosions/ulcers in a number less than or equal to 5), i2a (lesions restricted to the anastomosis, including anastomotic stricture), i2b (more than 5 erosions or aphthoid ulcers where normal mucosa or larger ulcers can be seen in isolated areas), i3 (diffuse inflammation with aphthoid erosions/ulcers) and i4 (diffuse inflammation with larger ulcers, nodules or strictures). This classification can be associated as follows: in patients with scores i0 or i1, symptomatic recurrence is less than 10% at 10 years, while CD patients with scores i3 and i4 are associated with a clinical recurrence of almost 100% at the end of Four years (Alshantti et al., 2021).

Anastomotic recurrence after intestinal resection is one of the most significant problems in the management of CD. In September 2003, Kono and colleagues at Asahikawa a University Medical Hospital in Japan introduced their unique surgical technique to reduce the risk of surgical anastomotic recurrence (Kono-S anastomosis) in patients with CD involving the small or large intestine. His approach was later adopted at several other medical institutions in Japan, in May 2010, this procedure was introduced at the University of Chicago and later at the University of Washington. (Kono et al., 2011)

The Kono-S anastomosis is defined as a functional hand-stitched antimesenteric end-to-end anastomosis. This surgical procedure consists of cutting the intestine with a cutter so that the mesentery side is located in the center of the stump after the intermediate mesentery has been cut close to the intestine. Both stumps are sutured together to create a support column to maintain the diameter and dimension of the anastomosis. Longitudinal enterotomies are performed on the antimesenteric sides of the 2 segments of the intestine. The side-to-side antimesenteric anastomosis is then performed transversely (Figure 1). Thanks to this procedure, Kono et al. concluded that the Kono-S anastomosis appears to be effective in preventing surgical recurrence of anastomosis in CD (Kono et al., 2016; Kono & Fichera, 2020).

Figure 1: Scheme of the Konos-S Surgical Technique.

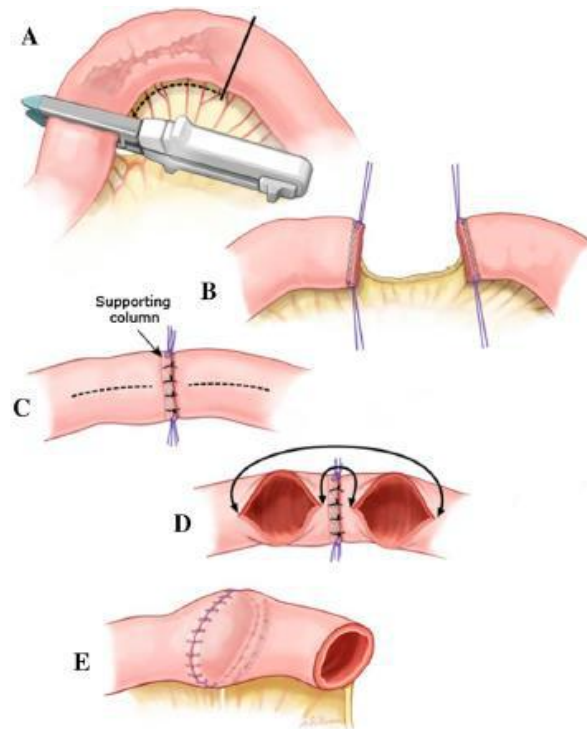


A) The mesentery is divided into the mesenteric wall of the intestine. B) The intestine is sectioned using a linear stapler so that the mesentery is in the middle of the staple line and at a 90° angle to it. C) The staple lines are sutured transversely to create a supporting column that must support the eventual dimension of the anastomosis. D) Longitudinal enterotomies of 7 cm in length are then performed in the antimesenteric aspect, starting 1 cm from the supporting column and the anastomosis is then created transversely in a hand-stitched fashion. The back wall using a double layer continuous way, the front wall using a single layer continuous suture. F) Pale lines indicate the mesenteric side below the anastomosis with the supporting column that is created with the proximal and distal bowel stumps (Horisberger et al., 2021).

The theoretical advantages of the Kono-S anastomosis include preservation of innervation as well as blood supply, both of which are important factors in proper healing of the anastomosis. Blood flow to the intestine is reportedly decreased by more than 50% in CD patients due to the action of the neuronal peptide vasodilator (calcitonin gene-related peptide). Decreased blood flow is associated with recurrence at the anastomotic site. The Kono-S anastomosis is a combination of stapled and hand-stitched techniques, several studies suggest that this technique results in a dramatic reduction in surgical relapse.

A particular aspect of the Kono-S anastomosis is the preservation of the mesentery. Reasoning based on the premise that this preserves vascular and nerve supply to the remaining resection margin (Figure 2). However, the literature also argues that the mesentery is the underlying factor in the disease process and a more radical resection of the mesentery is appropriate. Given the potential importance of the mesentery and the fact that mesenteric preservation is an integral part of the Kono-S technique, some principles of Kono-S anastomosis make anatomical and pathological sense and may explain this low surgical recurrence.

Figure 2: Surgical Technique of Kono-S Anastomosis.



A - Intestinal resection; B) Each intestinal stump is reinforced with sutures. C) Both stumps are sutured together to create a support column to maintain the diameter and dimension of the anastomosis. D) The side-to-side antimesenteric anastomosis is then performed transversely. And the support column is located between the anastomosis and the mesentery when the anastomosis is completed. Source: Dasharathy et al., 2021.

From a surgical point of view, the recurrence of CD should be considered an inevitable consequence. In this context, the choice of surgical approach is essential to assess the risk-benefit in each situation and should be as limited as possible. Therefore, the objective of this work is to carry out a review on Crohn's disease and the use of the Kono-S technique in the treatment of the disease.

Studies show that endoscopic evaluation after ileocolic resection in the absence of medical treatment, the postoperative endoscopic recurrence rate is about 65% to 90% at 12 months and 80% to 100% at 3 years; at the same time, without medical therapy, recurrence is about 20% to 25% per year. Another significant problem is that new drugs (i.e.,

biological drugs) do not change the rate of surgical treatment of CD, even if biological therapy improves disease management and short-term surgery, remission rates, and long-term impact. of this therapy is still unknown (Actis et al., 2019).

For this reason, there is growing interest in the role of surgery in preventing CD recurrence. Anastomotic configuration and extent of mesenteric resection may play a role in postoperative recurrence (POOR). Side-by-side ileocolostomy has been widely adopted due to the fact that it is an easy and reproducible surgical technique. The large anastomotic lumen prevents fecal stasis and bacterial overgrowth. However, high-level evidence of such anastomotic entry configuration at the level of the neoterminal of the ileum represents the critical diameter of the entire anastomosis and precisely this is the most frequent site of recurrence (Adamina et al., 2020).

Recently, a new surgical technique called anastomosis (Kono-S) was described to try to reduce anastomotic recurrences arising on the mesenteric side, which is the ileocolic anastomosis (Kono-S). The Kono-S anastomosis is defined as a functional, end-to-end, hand-stitched antimesenteric anastomosis. The mesentery of the intestinal segment to be excised is initially sectioned at the mesenteric border of the intestinal wall using a vessel-sealing system in order to prevent unnecessary devascularization and denervation of the residual intestine, thereby maintaining an adequate blood supply. as the neural control for local anastomosis (fichera et al., 2012; Katsuno et al. 2015; Bislenghi et al., 2022).

Posteriorly The intestine is sectioned with a linear stapler in such a way that the mesenteric side remains located in the center of the stump, at a 90° angle to the mesentery being manipulated. Both ends of the stump should be reinforced with 3/0 braided lactide polyglycolide (Vicryl). Before starting the anastomosis process, the stumps must be sutured by 4 or 5 stitches together so that they can form a support column, hence the name Kono-S, as a support, which the objective of the technique is to maintain the orientation and large diameter of the anastomosis lumen. Longitudinal enterotomies of approximately 7-8 cm are then performed to obtain a transverse lumen on the antimesenteric side, 0.5-1 cm from the supporting column to further enhance the supporting effect of the column on the anastomosis (Kono et al., 2011; Kono et al., 2011; Kono et al., 2016; Katsuno et al., 2015; Bislenghi et al., 2022)

The anastomosis is then created transversely using the hand-stitching technique with continuous one- or two-layer Vicryl 3/0 sutures, which will culminate in a large anastomosis, in addition to a rigid and stable support to avoid mechanical deformation and functional constriction of the anastomotic lumen compared to a "posterior bone" of the anastomosis. Since the recurrence occurs mainly on the mesenteric side of the anastomosis, the Kono technique is capable of eliminating the mesentery from the anastomotic surface, and maintaining the innervation and vascularization of the intestine, both factors are related in the process of recurrence and consolidation of the anastomosis. anastomosis (Peltrin et al., 2020; Kellil et al., 2021).

On the other hand, the "support column" that was formed maintains the shape of the original intestine and preserves a wide lumen, preventing distortions and stenosis due to recurrence. The studies considered show a low rate of surgical recurrence (0-3.4%), significantly lower especially when compared to a conventional anastomosis and an acceptable rate of post-surgical complications (Kono et al., 2011; Kono et al., 2016; Kono ; Ficheira, 2021) Other positive points of this innovative surgical technique already mentioned above include preservation of blood flow and innervation, both factors associated with a high risk of anastomosis recurrence in DC (Reynolds et al., 2021; Dasharathy et al., 2021).

Table 1 - Selected articles.

Autores	Título	Ano de publicação	Tipo de Estudo
LUGLIO, G. et al. 2020.	Surgical prevention of anastomotic recurrence by excluding mesentery in Crohn's disease: the SuPREMe-CD study-a randomized clinical trial.	2020	Randomized clinical trial
KATSUNO, Hidetoshi et al.	Novel antimesenteric functional end-to-end handsewn (Kono-S) anastomoses for Crohn's disease: a report of surgical procedure and short-term outcomes.	2015	Case Report
FICHERA, A.; ZOCCALI, M.; KONO, T.,	Antimesenteric functional end-to-end handsewn (Kono-S) anastomosis. Journal of gastrointestinal surgery.	2012	Case Report
KONO, T.; FICHERA, A. Clinics in colon and rectal surgery, v. 33, n. 06, p. 335-343, 2020.	Surgical Treatment for Crohn's Disease: A Role of Kono-S Anastomosis in the West.	2020	Surgical technique
DASHARATHY, S. S.; LIMKETKAI, B. N.; SAUK, J. S.	What's New in the Postoperative Management of Crohn's Disease?.	2021	Review
ALSHANTTI, A. et al.	The role of Kono-S anastomosis and mesenteric resection in reducing recurrence after surgery for Crohn's disease: a systematic review. .	2021	Review
GERMER, C. T.; REIBETANZ, J.	Kono-S-Anastomose vs. ileokolische Seit-zu-Seit-Klammernahtanastomose	2020	Retrospective observational study
LUGLIO, G.; KONO,	Surgical Techniques and risk of postoperative recurrence in CD: a game changer?	2021	Review
LUGLIO, G. et al. v. 24, n. 11, p. 1213-1214, 2020b.	Preventing recurrence in Crohn's disease: the Kono-S anastomosis with two-layer technique. Techniques in Coloproctology,	2020b	Retrospective observational study
KONO, T. et al.	A new antimesenteric functional end-to-end handsewn anastomosis: surgical prevention of anastomotic recurrence in Crohn's disease	2011	Surgical technique
KONO, T. et al., 2016.	Kono-S anastomosis for surgical prophylaxis of anastomotic recurrence in Crohn's disease: an international multicenter study.	2016	Randomized clinical trial
COFFEY, C. J. et al. 2018.	Inclusion of the mesentery in ileocolic resection for Crohn's disease is associated with reduced surgical recurrence.	2028	Retrospective observational study
SHIMADA, N. et al.	Surgical recurrence at anastomotic site after bowel resection in Crohn's disease: comparison of Kono-S and end-to-end anastomosis..	2019	Retrospective observational study
KELLIL, T. et al.	Surgical features to reduce anastomotic recurrence of Crohn's disease that requires reoperation: a systematic review.	2021	Review
PELTRINI, R. et al.	Kono-S anastomosis after intestinal resection for Crohn's disease.	2020	Review
SHIMADA, N. et al.	Surgical recurrence at anastomotic site after bowel resection in Crohn's disease: comparison of Kono-S and end-to-end anastomosis..	2019	Retrospective observational study
NG, C. H. et al.	Kono-S anastomosis for Crohn's disease: a systemic review, meta-analysis, and meta-regression.	2021	Review e meta-analysis
BISLENGHI, G. et al.	Totally stapled Kono-S anastomosis for Crohn's disease.	2022	Review

Source: Prepared by the authors from: ScienceDirect, PubMed, SciELO, Bireme and NCBI.

The initial retrospective study by Kono et al (2011) compared 69 patients who underwent Kono-S anastomosis between 2003 and 2009 with 73 patients who underwent hand-stitched end-to-end anastomosis (n = 424) and stapled or sutured

side-by-side anastomosis between 1993 and 2003. They found that the median endoscopic recurrence score in the Kono-S group was lower than in the conventional anastomosis group, the risk of reoperation was also lower in the Kono-S group (0 vs. 15%, $p = 0.0013$) (74). Kono et al. reported similar findings in a group of 187 patients undergoing Kono-S anastomosis in Japan and the USA. The cumulative surgical recurrence rate at 5 and 10 years was 1.7%, with surgical recurrence occurring in only two Japanese patients (Luglio et al., 2021; Luglio et al., 2020; Luglio et al., 2020b;)

A survey by Konos et al (2015) at a center in Japan showed that the mean endoscopic recurrence score (Rutgeerts score) was i2 at 5 years after Kono-S anastomosis, which was significantly lower than in patients undergoing conventional treatment anastomotic procedures (i3). In our study, 65% of patients did not develop surgical recurrence after bowel resection, although they were not on anti-TNF therapy, with a median follow-up of 60 months (range, 12-138). While the role of anti-TNF after surgical resection remains unproven, Kono-S anastomosis should be strongly considered in CD patients who are not candidates for anti-TNF therapy due to adverse effects loss of effectiveness or financial reasons.

Preliminary results comparing the Kono-S anastomosis with conventional surgical techniques show a significant reduction in endoscopic recurrence score (mean Rutgeerts score 2.6 vs 3.4; $P < 0.008$) and surgical recurrence rate (0% vs 15%; $P < 0.0013$), although the data were not randomized or controlled. During the study period, a total of 79 CD patients were finally enrolled and randomized into the Kono group (36 subjects, 50% male, mean age 34 years (Mean 25–50), mean disease duration 101 months, and the Conventional group. [43 subjects, 51.1% men, mean age 43 years (Mean 27-60), mean disease duration 105 months (Luglio et al., 2020).

Most patients had undergone previous surgery (52% vs 65%, respectively for the 2 groups; $P = 0.4$). CD length was 41cm (Mean 34-52) in the Kono group versus 48cm (Mean 38-55) in the Conventional group ($P = 0.2$). Regarding the behavior of CD, fistulization was found in 16 (44.4%) patients in the Kono group versus 19 (44.2%) individuals in the Conventional group ($P = 0.98$). The restrictive behavior was presented by 15 (41.7%) and 16 (37.2%) patients in the respective groups ($P = 0.68$), while the stricture/fistulizing form was present in 5 (13.9%) and 18 (8.6%) patients, respectively ($P = 0.2$). Preoperative treatment was performed during the 6 months before surgery. The laparoscopic approach was used in 52.7% of the cases in the Kono group and in 51.2% of the cases in the Conventional group ($P = 0.8$) (Luglio et al., 2020).

After 6 months, 8 patients in the Kono group (22.2%) and 27 patients in the conventional group (62.8%) had endoscopic recurrence (Rutgeerts score i2). The mean Rutgeerts score (0-4) after 6 months was 0.92 1.05 in the Kono group versus 2.06 1.31 in the Conventional group ($P < 0.001$). In addition, a severe postoperative endoscopic recurrence (Rutgeerts score i3) occurred in 13.8% of Kono versus 34.8% of the Conventional group, but none of the subjects in the Kono group had a Rutgeerts score of i4 (Luglio et al., 2020; Peltrini et al., 2020)

After 18 months of surgery all patients underwent colonoscopy at 18 months found that an endoscopic recurrence (Rutgeerts score i2) occurred in 9 patients in the Kono group (25%, also including patients with endoscopic recurrence at 6 months) and 29 in the Conventional group. (67.4%, of whom 27 had known endoscopic recurrence at 6 months) with a mean Rutgeerts score (0–4) of 1.05 1.06 in the Kono group versus (2.30 1.32) in the conventional (Luglio et al., 2020; Kellil et al., 2021)

Postoperative clinical recurrence was evaluated after 12 months, 3 patients in the Kono group and 8 patients in the Conventional group had clinical recurrence (8% vs 18%). After 24 months, 4 patients in the Kono group and 13 patients in the Conventional group had clinical recurrence (11.1% vs. 30.2%). In Kaplan-Meyer analysis, patients with Kono-S anastomosis had a higher recurrence-free survival rate than patients with anastomosis, postoperative surgical recurrence after 24 months occurred in only 2 patients in the conventional group (4.6%), but none of the Kono group, the postoperative results, there were no differences in terms of duration of surgery, days for flatulence, stool, length of stay (Shimada et al., 2019; Luglio et al., 2020).

Another point that reinforces the importance of this surgery was proven in the recent study by Coffey et al (2018) who demonstrated, for the first time, that the inclusion of the mesentery as part of intestinal resection is associated with a reduction in surgical recurrence. The authors compared surgical recurrence in 2 cohorts: in cohort A (30 patients), standard ileocecal resection was performed, cutting the mesentery close to the intestinal wall; in cohort B (34 patients), the mesentery that supplies the affected ileocecal segment was fully mobilized and resected along with the intestine. The cumulative reoperation rate in cohort A was 40%, while in cohort B it was only 2.9%. Most recurrences occurred within 2 years after surgery. Mesentery-sparing resection was therefore recognized as an independent risk factor for surgical recurrence.

A recent randomized controlled trial was able to demonstrate a reduction in postoperative endoscopic and clinical recurrences 2 years postoperatively, with Kono-S anastomosis being the only variable associated with reduced risk of endoscopic recurrence on multivariate analysis. These findings were confirmed in a meta-analysis including 9 studies and 676 patients, showing an endoscopic examination recurrence rate of 5% after a median follow-up of 12 months (Luglio et al., 2020; Ng et al., 2021).

The present randomized clinical trial by Luglio et al. (2021) was able to demonstrate that the Kono-S anastomosis is associated with a lower rate of endoscopic recurrence after 6 months (22.2% in the Kono group and 62.8% in the Conventional group). and 18 months (25% vs 67.4%, respectively), with less endoscopic recurrence after 6 months and after 18 and a lower rate of clinical recurrence both after 12 and 24 months. Analysis showed that surgical recurrence-free survival at 5 and 10 years the rate was 98.6%. However, this study remains limited by its retrospective nature and comparison with a historical cohort, by differences in study populations at baseline, by the absence of randomization, and by significant differences in post-operative treatment. Similar limitations affect a more recent Kono-S versus end-to-end anastomosis comparative study done in 2019 (Shimada et al., 2019).

Shimada et al (2019) showed that the new anastomotic configuration, Konos-S reduced the risk of anastomotic leak after resection compared technique with hand-stitched end-to-end anastomosis and the surgery-free survival rate was 5 years at the site. of anastomosis with Konos-S was significantly high at 95% (95% CI, 0.90-1.00). An additional advantage of the Konos-S is that the lumen on the mesenteric side does not need to be sutured. Mesenteric intestinal wall suturing is one of the main factors involved in anastomosis leakage in the hand-stitched end-to-end anastomosis technique, especially in patients with CD, the thickened fat pad hinders the vision necessary for suturing in this region. Avoiding suturing in this area helps reduce anastomotic leakage, the Konos-S technique, despite being more complicated, does not extend the operating time, and in the present study, it was associated with low rates of surgical recurrence at the anastomotic site and anastomotic leakage.

In another study, a total of 79 patients were randomized between 2015 and 2017: 36 patients in the Kono group and 43 patients in the conventional group. Both groups of patients did not differ in demographics or manifestation of Crohn's disease (fistulant Crohn's disease: Kono-S: 44.4% vs. conventional: 44.2%; $p = 0.98$), the route of surgical access ($p = 0.8$) and the rate of drug recurrence prophylaxis ($p = 0.15$). Regarding the primary outcome, 8 patients in the Kono-S group (22.2%) vs. 27 patients in the conventional group (62.8%) had endoscopic recurrence with a Rutgeerts score ≥ 2 (odds ratio (OR) = 5.91, 95% confidence interval (CI): 2.17-16.05, $p < 0.001$). In regression analysis, Kono-S anastomosis was the only variable significantly associated with reduced endoscopic Crohn's recurrence (OR=0.19; 95% CI: 0.08–0.74; $p < 0.001$) (Germer; Reibetanz, 2020).

A systematic review of 9 studies, including 896 patients, that examined the results of Kono-S anastomosis, Overall, surgical recurrence was lower in the Kono-S anastomosis group compared with the standard anastomosis. Recurrence ranged from 0-3.4% after a median follow-up of 35 months compared to 15-24.4% after a median of 60 months for standard anastomosis. Endoscopic recurrence was significantly lower in the Kono-S group compared to the standard anastomosis group. The results showed a mean Rutgeerts Score of 1.05 ± 1.06 at 18 months for the Kono-S group compared to 2.30 ± 1.32 in

the conventional group. A Rutgeerts score above i.2 was observed in 9/36 patients (25%) after a Kono S anastomosis compared with 29/43 (67.4%) in the conventional anastomosis group (Alshantti et al., 2021).

4. Final Considerations

The endoscopic recurrence score of CD patients who were operated on with the Kono-S technique was lower than in the conventional anastomosis group, the risk of reoperation was also lower in the Kono-S group. In the included studies, the mean endoscopic recurrence rate ranged from 5% to 30% after a mean follow-up of 12 months, 60 months to 10 years. In addition, other studies have shown that the inclusion of the mesentery as part of intestinal resection is associated with a reduction in surgical recurrence.

Mesentery-sparing resection was therefore recognized as an independent risk factor for surgical recurrence, so the Kono-S technique, despite being more complicated, does not extend the operating time, and in the present study, it was associated with low rates. surgical recurrence at the anastomotic site and anastomotic leak. The Kono technique may play a key role in those patients who can no longer receive biological drugs due to adverse effects or lack of treatment efficacy, but more efforts are needed to obtain higher levels of evidence.

For this reason, an institutional survey (NCT02631967) and a prospective randomized multicenter study (NCT03256240) are underway to evaluate the Kono-S anastomosis in CD in preventing endoscopic and surgical recurrences when compared to conventional side-by-side anastomosis. Therefore, further research needs to be done to universally validate the Kono-S surgery for patients with indication, always emphasizing that the treatment approach should be comprehensive and personalized for CD cases and that all symptoms of recurrence and complications should be analyzed individually so that the choice of treatment strategy is beneficial for the patient.

This study concluded that this technique appears safe and may benefit the recurrence rate, but cautioned that included studies were scarce and that higher-level global multicenter studies are needed. A larger multicenter randomized trial (NCT03256240) and (NCT02631967) is currently underway, recruiting patients from the US and Europe, who fully substantiate and establish the role of the Kono-S anastomosis in the impact of the natural history of CD, this study is comparing the Kono-S anastomosis. S anastomosis with the other techniques, when this study is completed, it may provide more definitive answers about the impact of the Kono-S anastomosis on the natural history of CD after ileocolic resection. Therefore, new double-blind randomized clinical trials should be carried out by different centers to ensure and affirm the benefits of this surgery.

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