ISSN 2536-4898

Volume 32

Issue 4

December 2022

Turkish Journal of COLORECTAL DISEASE

Official Journal of the Turkish Society of Colon and Rectal Surgery

www.turkishjcrd.com

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Turkish Journal of Colorectal Disease is an open access, scientific and peer-reviewed journal in accordance with independent, unbiased, and double-blinded peer-review principles of the Turkish Society of Colon and Rectal Surgery.

The journal is published quarterly in March, June, September, and December in print and electronically. The publication language of the journal is English.

This journal aims to contribute to science by publishing high-quality, peer-reviewed publications of scientific and clinical importance that address current issues at both national and international levels.

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The journal scopes epidemiologic, pathologic, diagnostic and therapeutic studies relevant to the management of small intestine, colon, rectum, anus and pelvic floor diseases.

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CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA 2001; 285:1987-91);

PRISMA statement of preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.);

STARD checklist for reporting studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al., for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.);

STROBE statement, a checklist of items that should be included in reports of observational studies;

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

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Results: What were the main findings?

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Reviews should include a conclusion in which a new hypothesis or study about the subject may be posited. Do not publish methods for literature search or level of evidence. Authors who will prepare review articles should already have published research articles on the relevant subject. The study's new and important findings should be highlighted and interpreted in the Conclusion section. There should be a maximum of two authors for review articles.

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Abstract length: Not to exceed 100 words.

Article length: Not to exceed 1000 words.

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Introduction: A brief introduction (recommended length: 1-2 paragraphs).

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Discussion: This section should include a brief review of the relevant literature and how the presented case furthers our understanding of the disease process.

References: See under 'References' above.

Acknowledgments.

Tables and figures.

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Indications

Method

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DOI: 10.4274/tjcd.galenos.2022.2022-2-5
Turk J Colorectal Dis 2022;32:217-228

INVITED REVIEW

The Concept of Complete Mesocolic Excision

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ABSTRACT

Complete mesocolic excision (CME) was introduced into the literature in 2009 for standardization of colon cancer surgery, which had not been established until then, in reality. Based on surgical anatomy and embryology, this concept of oncologic surgery for colon cancer included strict preservation of the mesocolic fascia on either side of the colon by sharp dissection of the interfaces, together with central dissection of the regional lymph nodes by a central ligation of the feeding arteries. CME should be applied to all cancers at any site within the colon. There is clear evidence that CME surgery achieves a higher lymph node yield, a higher quality of plane preservation, a greater distance from the tumor to the central resection line and longer vascular pedicles. In most meta-analyses, the rate of intraoperative bleeding is slightly higher, mainly due to venous bleeding from the branches of Henle's loop, compared to "conventional" surgery. Postoperative complications occur at a similar or slightly higher rate. Postoperative mortality is not increased. There is increasing evidence that long-term oncologic outcome is better with CME. CME has not been implemented in all centers because of a steep learning curve due to the need for full understanding of the anatomical and embryologic background and adequate experience of handling the central intestinal vessels; thus the experience of the surgeon is critical.

Keywords: Complete mesocolic excision, concept, implementation

Introduction

In 2009, we presented the concept of complete mesocolic excision (CME) and put it up for discussion as an alternative to conventional and mostly non-standardized surgery for coloncancer, which was being performed in most institutions globally at that time.[1] This proposition was supported by oncologic outcome figures, which differed markedly from most survival and local recurrence rates published in the literature, at that time. Overall survival data may have been similar, but the difference was more pronounced in advanced or more complex case groups, such as stage 3 disease, T4-tumors and emergencies. In this context, 5-year-survival with stage 3 disease varied from 38.5% to 74%.[2,3]

This was not the first concept presented for improving outcomes in colon cancer surgery and several other reports including above average oncologic long term outcome figures above had been published previously.

Is the Concept of "Complete Mesocolic Excision" Really a New One?

For several decades, Turnbull et al.'s[4] "no-touch isolation technique" was accepted as a major progress in colon cancer surgery. The philosophy was that all the vessels (lymphatics, arteries and veins) supplying or draining the tumor had to be divided ahead of any mobilization or other manipulations of the tumor-bearing colon. Thus, dissemination of tumor cells should be avoided and prognosis improved. This concept resulted from analysis of different outcome figures, when comparing Turnbull's[5] results with those of his colleagues who had mainly used conventional surgery, at the Cleveland Clinics.[4,5] Applying the no-touch isolation technique, 5-years survival was 68.85% for all patients operated for cure, compared to 52.13% with conventional surgery, and 56.84% and 28.06%, respectively, for stage 3 disease. Finally, the illustrations in the publications clearly showed that "conventional surgery", as practiced by Turnbull's et al.[4], only included the pericolic lymph nodes. However, even Turnbull[5] performed just a "high tie", exposing the vascular pedicles by encircling them with the index finger. Then, a clamp was set and the vessels divided afterwards. An appreciable amount of tissue, together with the central lymph nodes, was left behind. The separation of the planes was mainly achieved by blunt finger dissection. The technique performed by Turnbull was accurately reproduced in a video made by Jagelman in the

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Received: 24.02.2022 **Accepted:** 19.03.2022

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1990s, who was a resident of Turnbull and who performed a right hemicolectomy demonstrating the procedure performed by Turnbull, in detail. Finally, Turnbull did not consider the concept of strict plane preservation, and he never did perform a true central vascular tie, at least not for right sided or transverse colon cancer.

Enker et al.[6] had already published enhanced survival from his personal experience in 1979. He called his approach to colon cancer surgery "wide anatomic resection". He described his technique in detail in 1978.[7] In this article, he mainly referred to the supplying arteries to be divided in relation to the site of the tumor, to include all regional lymph nodes. According to his sketches, illustrating the extent of colonic resection and the division of the supplying arteries, his practice in this regard did not differ from ours with CME. For splenic flexure and left sided transverse colon cancer, he even resected more bowel, always including the ascending colon. However, from his wording he did not describe the plane or fascia principle, describing the "adhesions" as "ligaments" to be divided, and he did not give further technical description about how he prepared and dissected the vessels centrally or the extent of dissection. He also called his technique for transecting the arteries "high tie". In this article, he also questioned the feasibility of Turnbull's[5] procedure in every patient.

In the Concord Hospital in Sidney, a dedicated colorectal unit was formed in 1980.[8] From that time on, the group around Bokey et al.[8] changed the technique for operating on colon cancer. They mobilized the colon along the embryologic planes and specifically preserved the posterior mesocolic fascia, as an important principle. Furthermore, they took down the greater omentum from the transverse colon following the interface, predefined if necessary. In this regard, they followed the principles of CME fully. However, there is no mention of a true central tie with exposure of the origin of the colic main arteries in their technical descriptions. They even say that they performed just a high tie. This is supported by their approach to left sided colon cancer, with the following: "The root of the inferior mesenteric artery was not touched, but this vessel was divided after the exit of the left ascending colic artery". Obviously, they always left the central nodes of the main feeding arteries. This is supported by their outcome figures. In their publication in 2003, overall survival of Dukes' C patients was just 43.0%, although they did not separate the results of the two different periods reported. In their paper published in 2015, 5-year survival in stage 3 disease was now 66.3%, but the median lymph node count was no more than 15, compared to 28 in all Erlangen series.[9,10]

Japanese surgeons began to standardize the surgery of colorectal cancer early.[11,12]

In 2012, Kontake et al.[13] published a rate of five-year, overall survival in stage 3 colon cancer of up to 73.0%, for patients operated between 1974 and 2002. Japanese surgeons meticulously performed early dissection of the feeding vessels, did not include the adjoining vascular arcades resulting in shorter bowel length and did not focus on the importance of plane preservation. Nevertheless, their survival figures were excellent. Thus, there had been several technical descriptions approaching the concept of CME without fully capturing the complete concept and they quickly accepted CME as a comprehensive concept.

Finally, Søndenaa et al.[14] from Bergen in Norway was able to achieve a broad consensus amongst an international board of surgeons, most being early adopters of CME surgery.

Key Features and Characteristics of CME

At the beginning of this millennium, there was still a broad variation of oncologic outcome figures following "conventional" curative colon cancer resections. The overall survival data may have been quite similar. However, the results of more complex cases, such as T4-tumors, nodal positive cancer and emergencies differed enormously. Furthermore, the risk of local recurrence was underestimated; it was at least as high as in rectal cancer.

These differences were indicative of the missing standardization of "conventional" colon cancer surgery, at that time. Of course, there were guidelines available in many countries. They included the extent of lymph node dissection and of colonic resection or the recommendation of an en-bloc resection, if adjacent structures or organs were fixed or invaded. However, the recommendations for lymph node dissection, for example, may have described the lymph node stations to be removed but did not give detailed instructions nor of to perform a central dissection adequately. A "high tie" was the common practice adopted at that time. A true central tie of the feeding arteries, flush with the arteries at their points where they arose was not really described or even followed outside of Japan, and the importance of preserving the integrity of the surgical planes was not explicitly mentioned.

The CME concept was frequently only associated with a right, and eventually extended, hemicolectomy. It is correct that on the right side the anatomical conditions are more complex than with the left colon. However, basically the same principles are also applied for the rest of the colon. Furthermore, it is not always realized that CME includes a radical regional lymph node dissection with a central tie of the feeding arteries. We have operated emergencies, such as complete obstructions and perforations, in the same way as

elective cases. Only the decision concerning an anastomosis depended on the sequelae of these complications, mainly on the degree of a diffuse peritonitis, so that in half of the cases an anastomosis was omitted.

CME surgery is based on precise anatomical and sharp dissection along the interface of the embryologic adhesions between the intra-abdominal organs, covered by a continuously running mesenteric fascia and the parietal fascia, which also covers the retroperitoneal organs and the large vessels, namely the aorta and the vena cava (Figure 1). This interface was described by Toldt[15] as the "white line". As frequently, but nevertheless wrongly, indicated, he never described this phenomenon as a fascia. Finally, these two fasciae join at the vascular confluence of the hepatic veins and the vena cava and at the origin of the celiac axis and the superior and inferior mesenteric artery.

Depending on the organ which the mesenteric fascia is covering, it is termed the mesocolic and mesorectal fascia, but also the mesopancreatic fascia, where it extends to the pancreas, and so on. The second step after mobilization of the abdominal organs from the parietal fascia is to take down the adhesions of these mesenteric fasciae fixing, for example the greater omentum to the transverse colon or the mesoduodenum from the ascending mesocolic fascia, to get access to the superior mesenteric vein and artery behind. The dissection along these interfaces is achieved by sharp dissection, at all times, applying permanent traction and counter-traction.

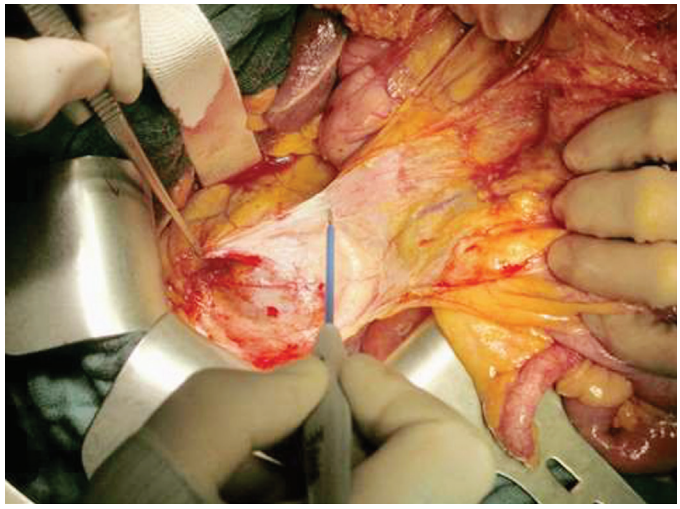

Figure 1. The interface between the parietal fascia on the left-hand side and the mesenteric fascia is divided by sharp dissection with the tip of the cautery. It presents as a white line, as described by Thold[15], already (which can be seen here, too, adjacent caudally to the tip of the cautery). The mesenteric fascia on the right side is covering as a continuously running plane the abdominal organs including the duodenum, next to the cautery. The following steps after complete mobilization will isolate the mesoduodenum from the ascending mesocolon, to get access to the central mesenteric vessels

Only recently anatomists have realized these conditions and interrelations[16] and the respective nomenclature is not yet officially accepted. Finally, the application of CME needs profound knowledge and understanding of these conditions.

During these dissections of the fasciae, the preservation of its integrity is of profound importance. West et al.[17] from Leeds have categorized the quality of specimens related to the integrity or laceration of the mesocolic fascia, which covered the resected colon on either side. They defined "mesocolic plane" as the optimum, an "intermesenteric plane" and a "muscularis propria plane" as the worst case. This has a tremendous impact on survival of the patients. Independent of any other feature and related only to the quality of specimen retrieval, the survive rate in the long run will be reduced by 50% with a stage 3 disease in case of a muscularis propria plane dissection.[17]

Following these principles, the colon and even the entire bowel including the duodenum with the pancreatic head, for right sided cancer is mobilized in such a way that even in very obese patients the tumor bearing colon can be brought forward in front of the abdominal wall, allowing unhindered access to the central vessels feeding the tumor. The compartment involved can now be easily twisted, and will be lying right in front of one's eyes, in a very superficial position. All the central vessels, namely the superior mesenteric vein and artery, will now be safely accessible for right sided cancer. This is essential for the second step of CME, which is the complete clearing of the regional lymph nodes, including the most central ones by a central tie of the arteries feeding the tumor, flush with the central vessels they are arising from. The Japanese term "D3-dissection" is more or less equivalent to our "central tie" procedure.

This procedure was always performed in our department by a lateral to medial approach. Some surgeons prefer the opposite way, exposing the superior mesenteric vein first. This is also the preferred approach of laparoscopic surgeons, some of whom are able to perform CME surgery the same way as we had described. We have never ligated the bowel to either side of the tumor as this maneuver may just disturb the integrity of the colonic fasciae.

In summary, "conventional surgery" for colon cancer was never defined in detail and it included a broad spectrum of variation. Furthermore, CME aims to create a specimen with perfect integrity of the mesosolic fascia on either side of the mesentery, as well complete clearing of the regional lymph nodes, including the most central ones, by a central tie of the feeding arteries flush with the central vessels they arise from. Such specimens should be achieved not just sometimes, but in at least 90% of all operations.

Feasibility of CME in Laparoscopic and Robotic Surgery

The introduction of CME and the evolution of laparoscopic surgery for colon cancer were almost coincidental. This had a degree of negative impact on the acceptance of CME, mainly in Europe, at least in the beginning, and in those departments were the introduction of laparoscopic surgery had first priority. Moreover, strictly following the principles of CME with a laparoscopic operation may be very challenging, both for less experienced surgeons and when operating on obese patients. The feasibility of laparoscopic CME was tested early in South East Asia, not least because there the mean body mass index (BMI) is between 19 and 23 kg/m^2 compared to about 27 kg/m^2 in Middle Europe. Most randomized trials or clinical studies, comparing open versus laparoscopic surgery, were initiated in South East Asia.

Since then, quite a lot of randomized trials and comparative studies have been published on this subject. Recent reviews reveal that in the laparoscopic cohorts operative time is longer, while blood loss and wound infections rates were significantly less and time to flatus, oral feeding, and length of hospital stay were significantly shorter. The 1-, 3-, and 5-year overall survival rates were better, or at least not inferior, in the laparoscopically operated cohorts compared to the open procedure.

Although there are some publications exclusively analyzing T4-tumors and transverse colon cancer, in most studies these entities were excluded or under-represented and the median BMI was mostly below 24 kg/m^2.[18,19] Similar results were achieved, in the meanwhile, by robotic surgery.[20]

Finally, as a result of all these studies it can be concluded that laparoscopic CME surgery of right and left sided cancer may be at least equivalent to open surgery, in terms of outcomes. However, these results are not completely applicable to any patient and to any site along the colon. Patients with a higher BMI and more complex tumors, such as transverse colon tumors including both flexures and locally very advanced cancer, are not yet adequately investigated and should be selected carefully for an eventual laparoscopic approach.

Extent of Colonic Resection

The length of colonic resection for cancer is mainly dependent on the pericolic extent of lymphatic spread of lymph node metastasis and the pattern of arterial blood supply of the colon. As positive lymph nodes are very rarely found beyond a distance of 10 cm to either side of the tumor, this extent of resection would be sufficient. This approach is common practice in Japan (Figure 2). To clear the entire area of possibly involved lymphs we, however, always included the adjacent arterial arcade (Figure 3), as shown in an example with a splenic flexure carcinoma.

With a coecal carcinoma, this will include lymph nodes along the right branch of the middle colic artery, or even the lymph nodes along the right colic artery if there is a suspicion of involvement, even if this is rare. This principle results in a right hemicolectomy for a tumor at that site (Figure 4), an extended right hemicolectomy for hepatic flexure cancer (Figure 5) and a subtotal colectomy for splenic flexure carcinomas (Figure 3).

For cancer of the sigmoid or the descending colon, the distal resection has to be extended to the upper rectal third, because with these tumors the inferior mesenteric artery has to be divided centrally and the pericolic artery may be missing along the distal sigmoid (Sudeck's point) (Figure 6).

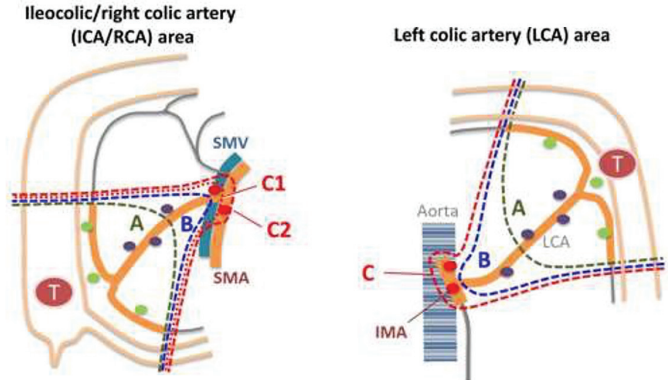

Figure 2. The Japanese Guidelines recommend an ileocecal resection for a cecal carcinoma and a segmental resection for a carcinoma close to the splenic flexure (however, with a central tie of the feeding arteries in case of an advanced tumor)[21]

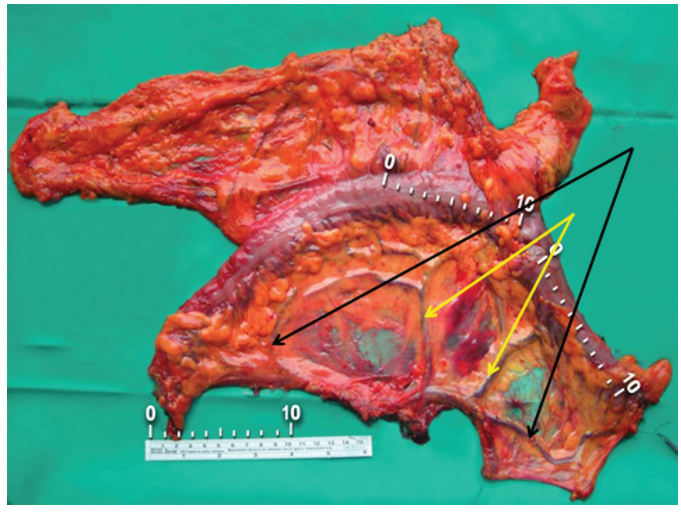

Figure 3. Specimen of a carcinoma right at the splenic flexure. To clear all possibly involved lymph nodes, the vascular arcades to either side (black arrows) of the two main feeding vessels (yellow arrows) are also included into the dissection resulting in a longer specimen. All feeding arteries were ligated, centrally. In Japan, only the two main feeding arteries would be transected

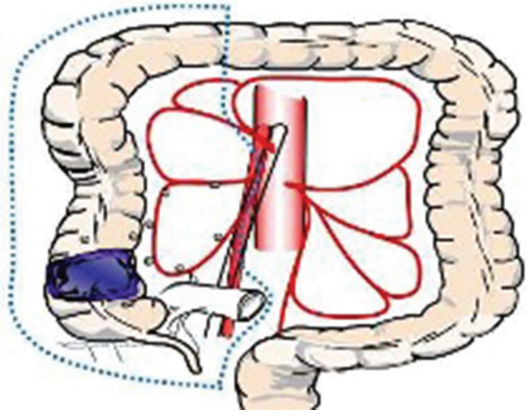

Figure 4. A right sided hemicolectomy is performed for carcinomas of the cecum or the ascending colon

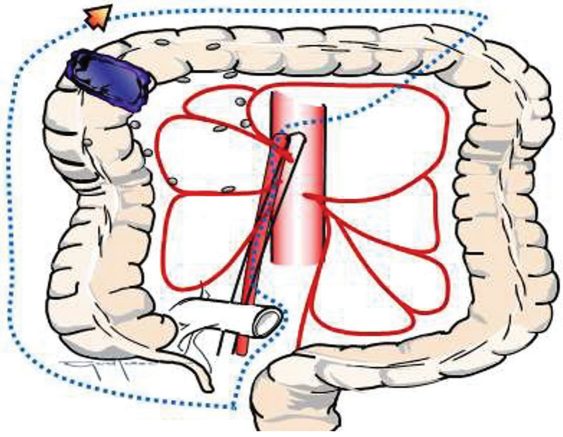

Figure 5. Hepatic flexure carcinomas need a more extended right hemicolectomy with a central tie of the middle colic artery. The arrow close to the tumor is to indicate that the lymph nodes along the right gastroepiploic artery will be not included and need a respective dissection, in addition

Characterisitics of Lymph Node Dissection

The lymphatic spread of a colon cancer follows the arterial blood supply of the colon involved. The venous drainage, which mainly runs parallel to the arteries, is irrelevant in this context. The two sites, were the vein's course is different from the arterial supply are Henle's trunk and the inferior mesenteric vein. With regard to the extent of lymph node dissection, these veins can be ignored.

The eventual involvement of lymph nodes by metastasis cannot be judged just by finger palpation or from its appearance. From clinical experience, suspicious lymph nodes are actually not affected about 50% of the time but, on the other hand, if a lymph node appears to be clear, it will nevertheless be involved about 20% of the time. This raises the question, whether a radical lymph node dissection with a central ligation is always needed or can be omitted in less advanced tumors, as it is common practice in Japan. Of course, it was already practice for T1-tumors with a low-

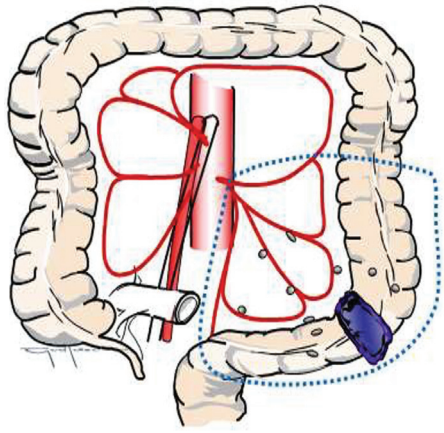

Figure 6. For a tumor of the sigmoid or the descending colon, the distal resection has to be extended to the upper rectal third, because in case of a central tie of the inferior mesenteric artery the arterial perfusion of the distal sigmoid is uncertain, because the continuity of the pericolic artery along this part of the colon may be missing

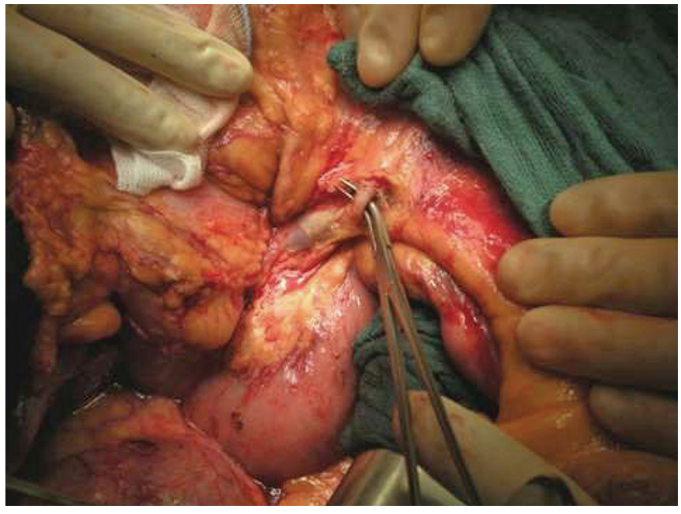

Figure 7. Preparations to cut the right ileocolic artery centrally, which is crossing the superior mesenteric vein from below, quite a common finding. Next, this vessel will be ligated flush with the SMV

risk histology (grading 1,2; L0, <3 cm) to be removed, either endoscopically or by a segmental resection. However, as the risk of lymph node metastasis with a pT1 carcinoma and high-risk features may be 15% or even more, we always performed a radical lymph node dissection. The argument is that in any case a maximum lymph node harvest will be achieved with a very low risk of lymph node metastasis remaining *in situ*. Moreover, the risk of complications in experienced hands will be not increased and there are no functional disadvantages in the long run.[22]

A frequent matter of debate is whether to dissect the most central lymph nodes at all. However, there is a positive correlation between the length of the arterial stump left behind, as determined by a postoperative computed tomography-scan, and the rate of loco-regional recurrence.[23]

In addition, it is still not entirely clear to all surgeons what constitutes a true central tie. Therefore some examples are shown in the Figures 7-9.

Intraoperative Complications

Even with elective conventional surgery for colon cancer, intraoperative complications are rare. First of all, ureteral injuries are well known. Therefore, even now the ureter is isolated and taped by some surgeons, which necessitates the opening of the covering parietal fascia. This maneuver may increase the risk of postoperative bleeding. As strict CME surgery is performed in the interface between the mesenteric fascia and the parietal fascia, the retroperitoneal organs remain well protected without any need to expose, for example, the ureter. Therefore the risk of ureteral lesions is even lower with CME.

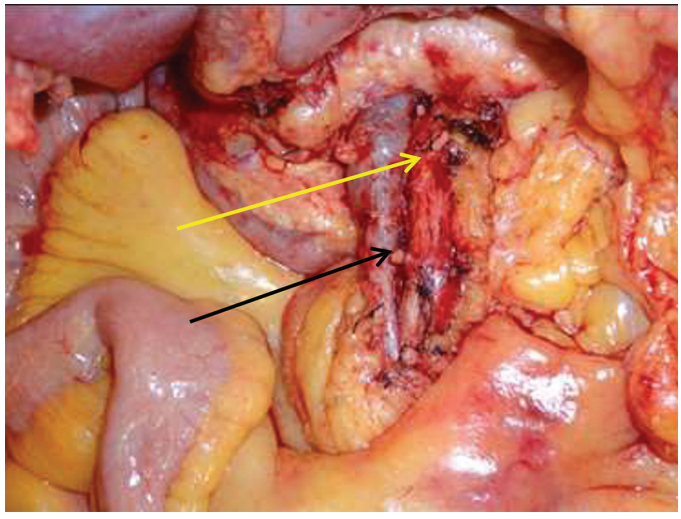

Figure 8. Intraoperative situs after an extended right hemicolectomy for a transverse colon cancer. The middle colic artery (yellow arrow) and the ileocolic artery (black arrow) are divided centrally, each. The stumps are measuring less than 1 cm

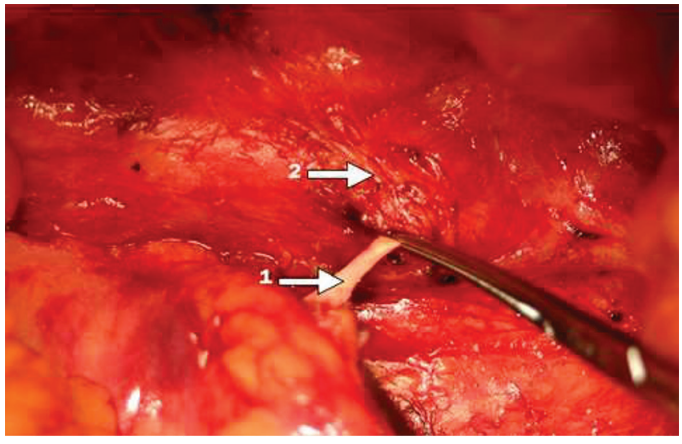

Figure 9. Preparation of the inferior mesenteric artery prior to its transection (arrow 1). The cuff of autonomous nerves covering the artery has been cut peripherally and shaved central-wards. Thus, the entire superior mesenteric plexus (arrow 2) and its function can be preserved with great certainty

Another common intraoperative complication is bleeding from splenic injuries. Its frequency in colorectal surgery is in the range of single figures per thousand. It is, however, much more frequent with transverse colon resections, reaching 3.4%.[24] In more than 90%, these lesions occur during mobilization of the splenic flexure due to splenic tears where the "ligaments" from the colonic flexure are connected to the splenic "capsule" ("Lord's ligaments").[25] These so-called ligaments are simply duplications of the mesenteric fascia which cross the dissection plane during mobilization of the splenic flexure and must be sharply

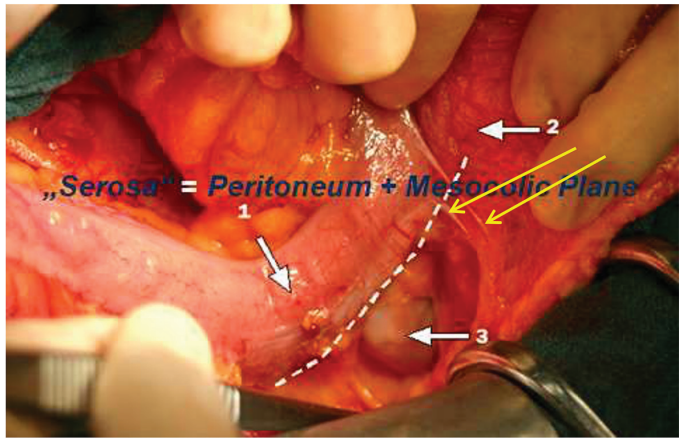

Figure 10. The white dotted line indicates the dissection level between the colonic wall (white arrow 1) and the mesenteric duplications running to the spleen. They have to be divided, sharply (see two yellow arrows). The greater omentum 2) has been taken down, before already. The stomach 3) in the depth of the lesser sac. It should be noted that the so-called serosa includes two layers, the thinned mesocolic fascia and the peritoneum

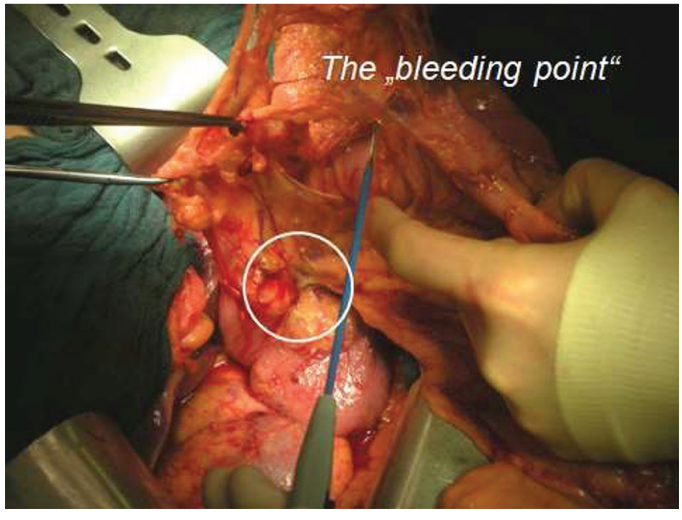

Figure 11. The right superiorcolomic vein is crossing the dissection plane to mobilize the hepatic flexure, completely and finally to expose the superior mesenteric vein. If this confluens is not fully visible but was approached in a funnel like way, instead, in case of an inadvertent bleeding-controlled hemostasis will be difficult

divided right along the colonic wall (Figure 10).

To expose this area safely, the dissection in the interface between the descending mesocolic fascia and the parietal fascia in the "retroperitoneum" should be driven forward cranially, as far as possible below the left side of the pancreas, ahead of the splenic mobilization. Then, the left omentum is detached from the left colon in the respective interface. The omentum should not just be divided. Only now can the splenic flexure be taken down. Finally, exactly following the interfaces between the embryologic fasciae by sharp dissection all the time, the safest approach to avoid splenic injuries is achieved. Again, this is one of the principles of CME surgery.

The most serious intraoperative complication is bleeding from major vessels. Above all, this event is the main contributory factor to increased intraoperative complications in reviews and meta-analyses.[26] This risk exists mainly with right-sided hemicolectomy, and injuries result first of all from tears of the branches of Henle's loop and of the superior mesenteric vein. These lesions can mainly be avoided by being well aware of the detailed anatomy of the gastroepiploic-pancreatic-colic trunk. The demonstration in almost all anatomic textbooks with the right colic vein directly entering the superior mesenteric vein is, in reality, a rare variation that will be found in only about 10% of cases. In the rest, the right colic vein joins the venous trunk and crosses the dissection plane (Figure 11), when exposing the hepatic flexure. During this maneuver, the vessel is at risk of being torn.

Finally, the right gastroepiploic vein must be exposed and all vessels joining from the colon must be dived. Sometimes, even the middle colic vein can be part of Henle's loop. To achieve a sufficient overview, extended mobilization along the embryologic fasciae is recommended, prior to the exposure of these branches. Secondly, once they are completely exposed, any traction on the mesocolon by the assistant must be avoided. If, in spite of all these precautions, a tear occurs, the bleeding can frequently be stopped simply by apply a compress. Sometimes a single vascular stitch may be needed but blind stitches should never be applied. All these measures can only be applied if these vessels have been exposed adequately.

As outlined above, these intraoperative complications can be avoided by consequent CME surgery. In the literature, however, intraoperative complications were more frequent with CME surgery compared to the conventional approach.[26,27]

Iatrogenic superior mesenteric vein injury is called the "peril of high ligation"[28] due to an increased risk of intravascular lesions.[29] In a systematic review by Wang et al.[26], above all intraoperative blood loss was higher, which is directly related to all of the potential pitfalls described above.

Postoperative Complications and Mortality

The rate of postoperative complications in the Department of Surgery in Erlangen is listed in Table 1. About 15 years ago, Bowel Cancer Centers were established in Germany and were to be annually certified by the German Cancer Society. Every year, official reports of a predefined data set indicating the outcome figures of all certified centers are published, including details of postoperative complications.[30] These figures are also shown in Table 1. In a way, both can be regarded as reference values.

Table 1. Postoperative complications in Erlangen (1) and in the certified Bowel Cancer Centers in Germany (n=296)[30]

	Erlangen	All German bowel centers (median)	Cancer center variation
Anastomotic leaks	1.8%	4.13%	0-14.3%
Reoperations	3.9%	8.6%	0-30.0%
Morbidity	21.0%	Not announced	Not announced
Mortality	3.3%	2.04%	0-9.52%

Postoperative leaks are the most striking incident in the postoperative course, which have an impact on postoperative overall morbidity and mortality. In Erlangen, the leak rate was below 2% for many years, although emergencies were always included in the reports. Less than 4% needed reoperation and overall morbidity was just over 20%, resulting in an in-hospital mortality of 3.3%.

In the German Bowel Cancer Centers, there was a broad spectrum of postoperative complications. The leak rates, for example, varied from zero to 14.3% in one center. The median rate was 4.13%. A median of 8.6% of the patients had to be re-operated and median postoperative mortality was 2.04%. In the literature, close to 20 reviews and meta-analyses of CME have been published. According to these, and disregarding some separate publications, the rate of anastomotic leaks and of postoperative mortality is not increased when comparing CME with conventional surgery. If in particular cases complication rates associated with CME surgery may differ from these general trends, one has to look at the absolute figures to understand conflicting data.

Oncologic Outcome (Local Recurrence and Survival)

There is a wrong perception that, in contrast to rectal cancer, local recurrence is rare in colon cancer and usually a manifestation of systemic disease.[31] The rate of local

recurrence after colon cancer surgery is at least as high. In the literature published in the first 15 years of this millennium, local recurrence rates between 4% and 15.5% were reported. The risk was even 2.56 times higher with tumors at the hepatic flexure compared to the ascending colon and 2.0 to 4.42 times more frequent with lymph node metastasis compared to N0-cases, depending on the extent of lymph node involvement.[32] In 61.1% of cases, the recurrence was just a local event without peritoneal or retroperitoneal involvement, implying an option of successful R0-resection of these recurrences.

In our department, overall loco-regional recurrence was 3.6% in the period 1995-2002 and increased with more advanced stages. It was 0.9 % in stage 1 and 9.6% in stage 3. With continuing internal quality control, we were able to reduce this rate further, reaching 2.1% in the following period up to 2009. Still, the highest risk is connected to lymph node metastasis, with 5.7% for pN1 and 18.5% for pN2, compared to 1.5% in N0-cases. It is also increased with T4-tumors, being 15.1% compared to 1.2% with T2-tumors. Even with a local recurrence following operation for a former pN2-tumor, further peritoneal or organ metastasis may be missed. This indicates the importance of true central lymph node dissection, which we may not have performed adequately in all cases.

Until the beginning of this millennium, survival from colon cancer had not improved particularly over the 20 years previously, but was always better than the prognosis for rectal cancer. After curative resection with curative intention, overall colon cancer 5-year-survival was approximately 65% to 75% in the early 1980s,[33] but was reported to vary, at 50.4% and 76.6%, respectively, almost twenty years later.[2,8]

Finally, due to the implementation of Heald and Ryall[34] total mesorectal excison, the awareness of the impact of clear resection margins on oncologic outcome,[35] and the progress made with neoadjuvant radiochemotherapy,[36] the prognosis for rectal cancer became better, but there was no progress at all with prognosis following surgery for colon cancer. For these reasons, survival of rectal cancer patients outpaced colon cancer.[37]

At that time, in our department, cancer related 5-year survival of all colon cancer patients operated from 1978 to 1997, R0-resection, stage 1 to 3 was already 85.5%, and 66.9% for stage 3 disease without any adjuvant chemotherapy.[38] In the period from 2003 to 2009, cancer related survival even increased to 90.6% and to 80.9% for stage 3 disease.[10]

When we published our paper introducing the concept of CME[1] in the same issue of colorectal disease, the chief editor at that time, Haboubi[39] stated that "while these advances were being made in rectal cancer surgery, colonic cancer has been left untouched" and called the principle described "a new paradigm". In the meantime, many papers have been published analyzing oncologic outcome following CME surgery. Obviously, with the application of CME, better oncologic outcome figures are now being achieved. However, in some institutions using CME, surgery survival also improved but did not exceed he figures achieved in earlier years.

We suspect that the concept was not followed sufficiently in these cases. Finally, almost all meta-analyses published in recent years have reported a lower rate of loco-regional recurrence and higher survival rates following CME surgery compared to conventional surgery.[40-42]

Quality Management

Every surgeon should know his personal outcome results, which must include the postoperative complications and long-term results, whatever kind of surgery he is practicing. It is not enough to refer to figures presented in the literature.

The principles of a quality circle can easily be transferred to surgical practice. One provides a guideline, follows the single steps and tries to reproduce the course of a CME procedure, for example. The indispensable basis of all of this, however, is prospective documentation of every case without any selection, using proforma with specified items. Pathologists play an important role in this context, because, apart from their histopathological findings, in colorectal cancer surgery they can also deliver objective criteria to qualify a specimen, including eventual tears of the covering mesocolic fascia, the length of the vascular pedicles, the distance of the tumor to the resection level and many others[17,43] (Figure 12). Thus, benchmark data are available, which can also serve as an orientation. From time to time, this data should be collected and analyzed and deviations must be scrutinized and corrected.

In our department a tumor registry had been established since 1969, fulfilling all the aspects mentioned above. In addition, with every operation for a malignancy, the operating surgeon was anonymously documented. There were only three people who knew the encryption. Every surgeon, however, could get insight into his personal results. The follow-up rate of all patients was 98.5%. Eventually, by strict application of the principles of quality management, we were able to improve our results, period by period (Figure 13).

Furthermore, the survival curves of our patients correlated with the operating surgeon were very close. Only the survival rates achieved by the surgeons in training were slightly worse, because their results still included their learning curve (Figure 14).

How to Implement CME Surgery into One's Own Practice

CME-surgery is more complex and technically demanding than total mesorectal excision. Exposing the vessels to be dissected needs some experience with vascular surgery. However, the principles of any current oncologic surgery demand this knowledge and these techniques of vascular surgery. It should be remembered that CME-surgery is oncologic surgery of the large bowel and it is different from the techniques commonly applied in colorectal surgery.

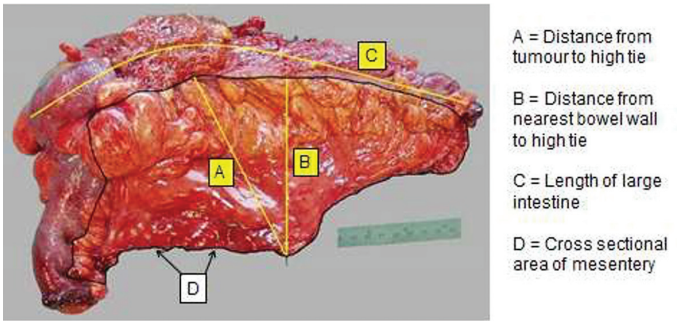

Figure 12. Tissue morphometry, as practiced in the Leeds Institute of Pathology and Molecular Medicine. It is based on photo-documentation of a fresh specimen

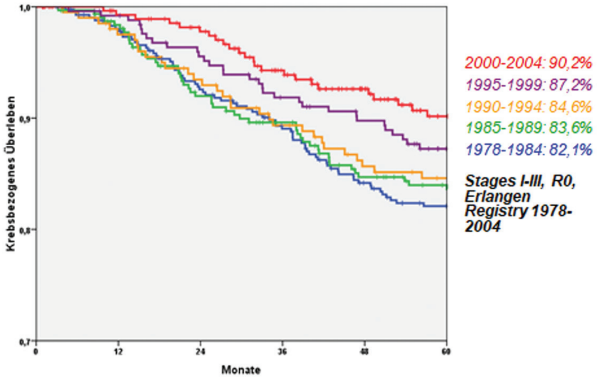

Figure 13. 5-year cancer related survival, achieved in consecutive periods in the Surgical Department of the University in Erlangen

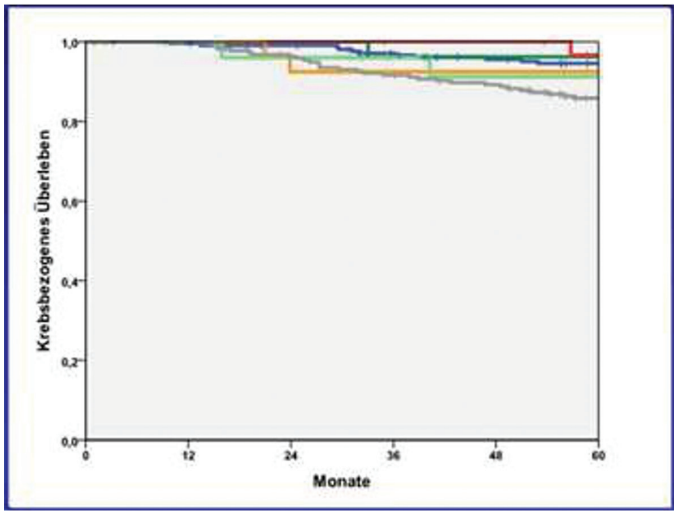

Figure 14. 5-year cancer related survival correlated with the operating surgeons. Each line represents an individual surgeon. They grey line demonstrates the results of all surgeons in training

Strict plane preservation is mandatory and deep and comprehensive knowledge of embryology and anatomy is essential. Therefore, before starting CME, teaching of all these basics and theoretical principles is the first step in implementation. Next, repeated observation of live operations or video-presentations should follow. Only after this can actual operations be performed in the implementing center. Depending on the level of education, a tutor may be needed to assist the surgeon. From personal experience, just one or two surgeons in a department should operate these patients, until the procedure is established. Only then can the technique be adopted by other surgeons.

Even an experienced surgeon has to negotiate a learning curve, as was the case in our team. There is data from Canada analyzing the implementation of laparoscopic right hemicolectomy following the principles of CME. The duration of surgery continued to decrease until the 81st operation. The rate of complications and the yield of lymph nodes were acceptable, from the beginning. However, the range of variations decreased in the same manner as the duration of surgery.[44] Therefore, to recommend a fixed number of CME-operations is unlikely to meet the needs and requirements in all institutions, equally.

The Evidence for Complete Mesocolic Excision

Since 2009, the concept of CME has gained huge interest, worldwide. It is recommended by several national guidelines and the National Comprehensive Cancer Network in the United States, for example.[45] Although some call it the golden standard,[46] others still question its superiority because of limited current evidence[40] and suggest there is a need for randomized trials.

The Web of Science verifies close to 900 peer-reviewed publications referencing the original paper. On the occasion of the twentieth anniversary of colorectal disease, this article was the most frequently cited paper in the history of the journal. Within the last five years, about twenty reviews and meta-analyses have analyzed all papers published on CME reporting outcome data.

There is undisputed agreement that CME achieves a higher lymph node yield, a higher quality of plane preservation and a greater distance from the tumor to the central resection line and longer vascular pedicles, without any relevant functional disadvantages.

Still under debate are eventual intraoperative complications, improvement of postoperative complications, reduction of local recurrence and increased long-term survival.

The review and meta-analysis of Díaz-Vico et al.[41] included 27 publications from 17 countries. The authors conclude that CME improves the quality of the mesocolic resection plane and, more importantly, provides evidence in support of the 3-year DFS and CSS, as well as 3- and 5-year OS benefits of CME, and decreased local and distant recurrence when compared with conventional surgery. Despite the fact that CME is more complex and challenging than conventional surgery, it appears to be a safe and feasible technique in experienced hands. Nevertheless, further high-quality and prospective randomized, multicenter studies encompassing UICC stages 1-3 colon cancer patients would be needed to assess the role of this technique and clarify the potential of CME regarding oncological outcomes in the short and long term before CME can be recommended as the standard of care for primary colon cancer.

Summary and Perspectives

In 1982, Bill Heald published his first paper about total mesorectal excision (TME).[47] Based on the frequency of citations, it took about ten years for this concept to receive broad interest and almost ten more years until it was fully accepted and implemented, worldwide. In the beginning, TME gave rise to the same discussion which occurred some years later about CME. First, that it was not new, then the low local recurrence rates and respective survival rates were questioned, and finally prospective randomized trials were called for before it could be considered the gold standard technique. Compared to TME, the concept of CME is even more complex and technically demanding. Therefore, the resistance was even more pronounced. Nevertheless, it reached wide acceptance within ten years.

The criticism of missing evidence with CME outcome data is just wrong, in our view. The rules of the Canadian Task Force say that a systematic review of prospective cohort studies is consistent with level 2 evidence. In the meanwhile, several such reviews and meta-analyses were performed. The test of this concept by randomized trials is just impossible, as it was with TME. This is because some surgeons are pretending to perform CME-surgery, but do not adhere to the principle fully. The second arm, which would be conventional surgery, is not clearly defined at all. Finally, over the last ten years, even those who disagreed with CME-surgery have adopted surgical techniques which approach the CME-concept. Nevertheless, there are still some open questions. One is the extent of lymph node dissection for cancer of the splenic flexure. Tumors at that site have the worst prognosis compared to the rest of the colon. The concept of CME includes the dissection of the lymph nodes at the inferior edge of the left pancreas and those along the gastroepiploic artery, as well.[48] However, even in our center the 5-year survival of these tumors is just 45%, which indicates that we did not always dissect these additional lymph node stations. Another open question refers to the need of the resection of the adjacent arcades beyond 10 cm to either side of the colon. The T-REX Trial, initiated by Shiozawa et al.[21] from Tokyo, may answer it.

Conclusion

The introduction of TME partially led to a far-reaching centralization of rectal cancer surgery. The same may happen with colon cancer surgery, too. The most challenging task, however, is to test whether, when using quality-controlled CME-surgery, adjuvant chemotherapy will be always needed in lymph node positive cases, if only up to three nodes are involved.[49] The thesis is that these patients will not benefit from adjuvant chemotherapy. Even nowadays, the indication of adjuvant chemotherapy is based on Moertel's trial, published in 1990.[50] The rate of local recurrence in this study was over 20%, which indicates a very poor quality of surgery. Therefore, this 30-year-old dogma may not be valid, if strict CME-surgery is applied.

Peer-review: Externally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

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DOI: 10.4274/tjcd.galenos.2022.2022-9-1
Turk J Colorectal Dis 2022;32:229-237

INVITED REVIEW

Current Management of Colovesical Fistula

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ABSTRACT

A colovesical fistula (CVF) is an abnormal communication between the large bowel and bladder. This complex condition carries significant morbidity and negatively impacts quality of life. The clinical presentation of CVF can vary from symptoms, such as pneumaturia and fecaluria, to life threatening urosepsis. The most common etiology of CVF is diverticulitis. Diagnostic work-up with accurate diagnosis is key for prompt recognition and treatment of this condition. The primary goal of treatment is to remove the diseased colonic segment. Traditionally, open surgical intervention was the preferred surgical approach. Over the last decade, there has been an increasing interest in and use of minimally invasive techniques to treat patients with CVF.

Keywords: Bladder fistula, colovesical fistula, diagnostic work-up, diverticulitis, laparoscopic surgery, surgery, surgical treatment, urinary fistula

Introduction

A fistula is an abnormal anatomic connection between two epithelialized surfaces. The term colovesical fistula (CVF) refers to an abnormal communication between the large bowel lumen and the bladder.[1-3] The most common etiology of CVF is diverticular disease (50-70%), followed by malignancy and inflammatory bowel disease (IBD).[4-8] Diverticulosis is prevalent in Western countries and the incidence of symptomatic diverticulitis is increasing, especially in young patients.[9] It is estimated that 10% to 20% of individuals suffering from diverticulosis develop diverticulitis and approximately 2% of patients progress to complications, such as abscess formation, fistula, stricture with obstruction, or hemorrhage.[10,11] The majority of diverticulitis related perforations and fistulas occur in the sigmoid colon, which is the portion of the large bowel most affected by diverticulitis. CVF is associated with significant morbidities and negatively impacts quality of life for patients. Surgical resection is the main curative modality. However, proper evaluation and diagnosis are of paramount importance to ensure prompt treatment of this condition.

The aim of this article was to provide an overview of the management of CVF in the modern era of surgical care. The information provided to the reader is based on the established literature and on the expert opinion of the senior author, who has over 20 years experience managing patients with complicated diverticulitis and complex colorectal fistulas.

Presentation and Findings

The majority of patients with CVF are symptomatic, albeit the symptoms can range from mild to life threatening. The passage of gas bubbles and/or fecal particles into the urine, termed pneumaturia and fecaluria, respectively, is consistent with large bowel fistula to the urinary system. Other symptoms include dysuria, hematuria, and suprapubic pelvic pain. The majority of urinary fistulas involve the bladder and the sigmoid colon, with a minority of patients presenting with a rectourethral fistula that is often related to prostate cancer and its treatment. Less common is an enterovesical fistula from the small bowel to the bladder. Recurrent urinary tract infections are known sequelae of CVF, with a minority of patients presenting with life threatening urosepsis.

The patient's medical and surgical history can aid in diagnosis. While a prior history of one or more episodes of diverticulitis is often reported by patients, some patients can present with *de novo* fistula without prior documented history of diverticulitis. It is important to solicit from the patient any past history of abdominal surgery, past or current digestive disease, prior radiation therapy to the pelvis, and

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Received: 14.09.2022 **Accepted:** 02.10.2022

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Turkish Journal of Colorectal Disease published by Galenos Publishing House.

history of abdominal or pelvic malignancy. Past obstetrical history should be documented in women to solicit any prior perineal trauma from forceps or vacuum delivery, episiotomy, or tear. Baseline continence level should be recorded along with patient's bowel movement habits.

Physical examination consists of visual inspection of the abdomen for scars, distention, or tenderness. Digital rectal examination and assessment of anal sphincter tone is advisable. In men with prior history of prostate cancer treatment, the addition of anoscopy is recommended, especially if there is suspicion for the possibility of rectourethral fistula, which may be palpated anteriorly within 6 to 8 cm from the anal verge.

Diagnostic Work-up

The diagnostic work-up for CVF include laboratory tests, imaging, and endoscopic examinations. Basic laboratory tests include complete blood count, renal function, urine analysis, and urine culture. Cross sectional imaging is necessary in all patients with suspected urinary fistula. Ultrasound of the abdomen and pelvis is not additionally informative and thus plays very little role in diagnosis of CVF. The preferred study is computed tomography (CT) of the abdomen and pelvis.[12,13] The presence of air in the bladder with pericolonic scarring, inflammation, or clear fistula in a patient without recent urinary catheterization is pathognomonic for CVF (Figure 1-3). CT scan confirms the diagnosis of CVF in addition to providing useful information regarding the presence of acute colonic inflammation and/or pelvic abscess (Figure 4). Magnetic resonance imaging (MRI) scan is another cross-sectional imaging study that can document CVF but in the majority of patients, CT scan is the study of choice with the advantages of being readily available at all institutions with shorter procedure time and lower cost. Furthermore, most surgeons are more comfortable interpreting CT scans than MRI.

Fluoroscopy based studies, such as a cystogram or a gastrografin enema, are useful in documenting the presence and location of the fistula. Cystogram is a simple procedure which can demonstrate the passage of contrast material from the bladder into the large bowel to make the diagnosis of CVF (Figure 5). It is a readily available study in most radiology departments. Gastrografin enema together with injection of contrast transanally, can confirm the diagnosis of CVF, demonstrate the anatomic configuration of the large bowel, and document the presence or absence of any secondary finding, such as a colonic stricture (Figure 6). Both cystogram and gastrografin enema can exclude the presence of a fistula from other parts of the digestive tracts, such the small bowel (enterovesical fistula), which can present with similar symptoms to CVF. Endoscopic examination of the bladder and the colon is advisable in patients with suspected CVF. Both studies can provide information about the fistula and rule out conditions other than diverticulitis, such as IBD or malignancy. Cystogram can exclude malignant causes of CVF. While colonoscopy with straight forward viewing scope rarely shows the fistulous hole on the colonic side, it can pinpoint the general area of the fistula by identifying secondary findings, such as edema, erythema, pus drainage, narrowing of the bowel, and the presence of diverticulosis (Figure 7). Colonoscopy can be of paramount

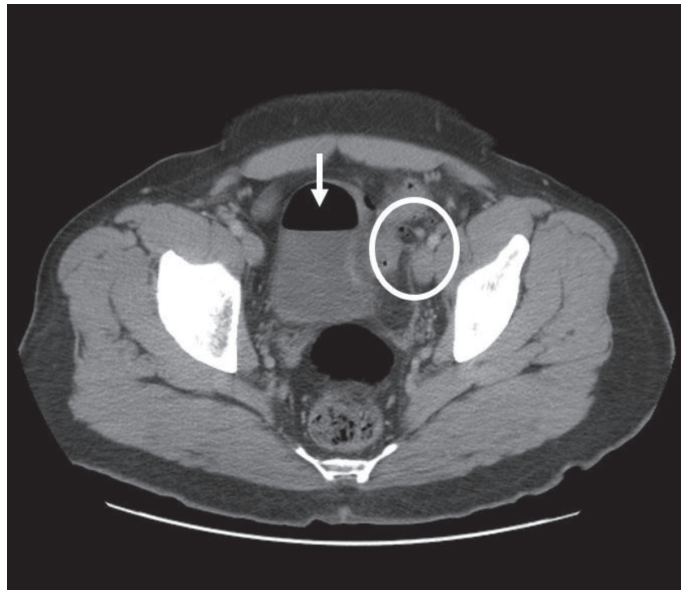

Figure 1. Axial views of CT scan of a patient with recurrent diverticulitis and colovesical fistula. Air fluid level is seen inside the bladder [arrow]. An adjacent inflamed sigmoid colon with diverticulae is noted [circle]
CT: Computed tomography

Figure 2. Coronal views of CT scan of a patient with Crohn's colitis with colovesical fistula. Note inflamed colon [arrow]. Air bubbles are seen inside the bladder
CT: Computed tomography

importance in patients presenting with iatrogenic CVF following prior pelvic surgery (Figure 8). In patients with IBD, such as Crohn's disease, endoscopic examination is necessary to document disease activity in the remainder of the large bowel and terminal ileum in order to determine whether a segmental resection vs. a more extensive colonic resection is needed and to guide medical management by the gastroenterologist. Furthermore, disease activity in the rectum will be documented to aid the surgeon in deciding whether to perform a primary anastomosis to the rectum and/or a diverting stoma. In addition, colonoscopy provides the added value of screening the non-affected area of the colon for neoplastic lesions, such as polyps and tumors.

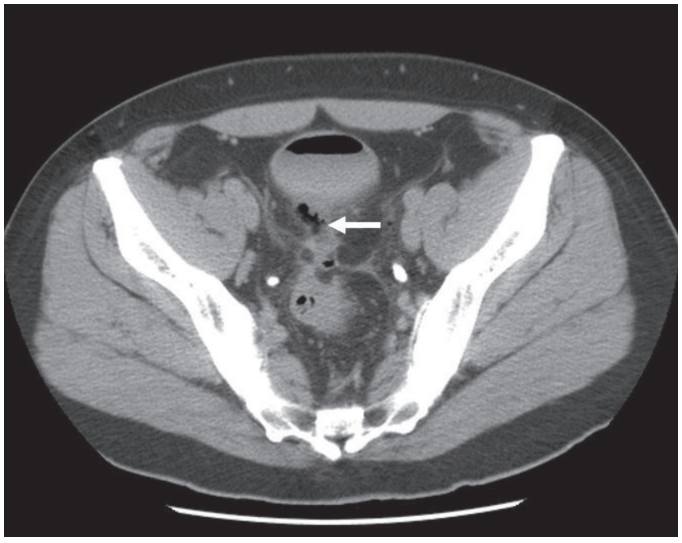

Figure 3. Axial views of CT scan of a patient with recurrent diverticulitis delineating a clear fistulous tract with gas from the colon to the bladder [arrow]
CT: Computed tomography

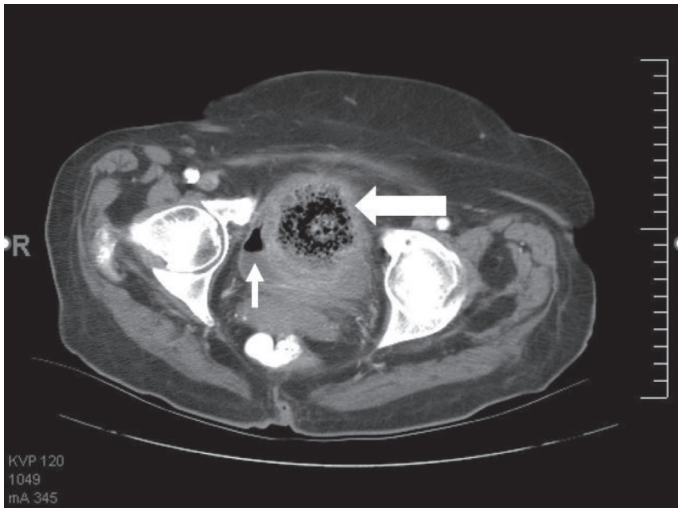

Figure 4. Axial views of CT scan of a patient with diverticulitis and pelvic abscess [wide arrow] with colovesical fistula and air in the bladder [narrow arrow]
CT: Computed tomography

Initial Management and Preparation of the Patient with Colovesical Fistula

The majority of patients with CVF will be symptomatic and require treatment. The mainstay of treatment for this condition is surgical intervention, as medical therapy usually temporizes the symptoms but does not cure the fistula. Surgical intervention is best performed in the

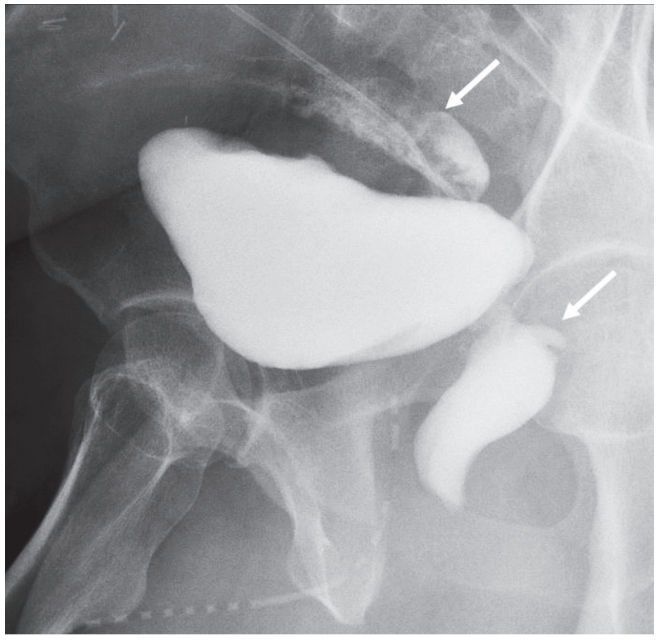

Figure 5. Fluoroscopic cystogram in a patient with a colovesical fistula demonstrates filling of the bladder with passage of contrast into the rectosigmoid area [arrows]

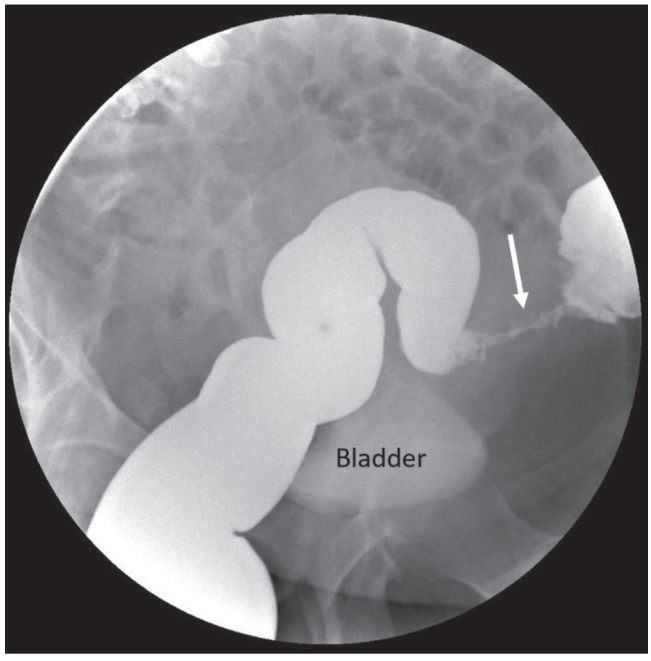

Figure 6. Gastrografin enema in a patient with colovesical fistula reveals a sigmoid stricture. Contrast spillage into the bladder confirms the presence of the fistulous communication

elective setting as rarely CVF requires emergency surgery. The initial management of CVF will include making the proper diagnosis and optimizing the patient for elective surgery. Medical optimization includes control of sepsis while addressing malnutrition and anemia, if present. Patients with urosepsis should receive an appropriate course of antimicrobial therapy and, if a pelvic abscess is present, consideration for percutaneous drainage should be made for any collection larger than 4 centimeters to expedite resolution of acute sepsis. Control of sepsis, and correction of anemia and malnutrition when present can shift the patient to elective surgical intervention under more optimal conditions, which can improve the chances of a minimally invasive approach with less conversion to open surgery and lower rate of stoma formation. When significant colonic inflammation is present in the setting of diverticulitis, a full antimicrobial course and deferring the operation for a minimum of four to six weeks decreases the chances of encountering a hostile abdominopelvic cavity during surgery.

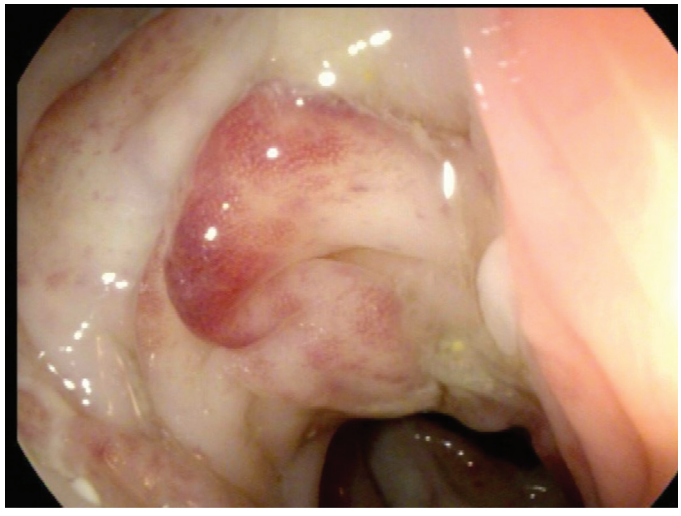

Figure 7. Colonoscopic view of area of colovesical fistula in the sigmoid colon. Noted are the secondary findings of bowel edema and erythema with pus drainage

Figure 8. Endoscopic view of an iatrogenic rectovesical fistula following stapled rectal anastomosis [arrow]. Note the 2 metal staples in the center of the fistula

A urologic consultation is advisable to aid in diagnosis and to provide surgical assistance as required on the day of the operation. If a stoma is contemplated as a possibility by the surgeon, the patient should be evaluated by an enterostomal nurse for skin marking and should be educated about stoma care. Patients with a prolonged history of CVF with numerous prior antimicrobial courses can benefit from an infectious disease review of prior cultures for recommendations of the optimal antimicrobial coverage at time of surgical resection.

A mechanical oral bowel preparation is advisable in all patients. Various bowel preparations are available and the surgeon can administer the standard bowel preparation for colonic resection at their institution. The addition of an oral antibiotics regimen to the bowel preparation can be considered, if it is part of the surgeon's standard bowel preparation for colorectal resection. Their usefulness has been debated over the last few decades. At our institution we do not currently use them.

CVF surgical treatment can be straightforward in some cases, yet very challenging in some patients with prolonged operative time and blood loss. It is advisable to type and cross-match all patients undergoing resection for CVF for 2 to 4 units of packed red blood cells, depending on the level of preoperative hemoglobin.

Surgical Care and Technique

Intraoperative

Operative interventions for CVF can be challenging. We typically schedule these cases as the first case in the morning. The operating room is set up for a minimally invasive operation. Trays of open instruments and retractors are made available in the room in case conversion to open surgery is needed.

All operations are performed in the lithotomy position under general endotracheal anesthesia. Both arms are tucked and safely padded (Figure 9). We advise for a bilateral transversus abdominis plane block, as part of the postoperative pain management protocol. It is best performed under ultrasound guidance prior to surgical incision. An orogastric tube is inserted to decompress the stomach and it is removed at the completion of the surgical procedure. Intravenous antibiotics are administered, along with chemical deep venous thrombosis prophylaxis with subcutaneous injection of unfractionated heparin or low molecular weight heparin.

The first phase of the operation consists of cystoscopy with bilateral ureteral catheters placement for intraoperative

identification and protection of the ureters. While most CVFs involve the dome of the bladder, some inflammation may extend to the area of the trigone. Furthermore, some patients may have significant inflammatory changes in the retroperitoneum, away from the area of the fistula. Prior retroperitoneal perforation with abscess from diverticulitis or Crohn's disease may lead to retroperitoneal fibrosis which can render the ureter susceptible to laceration during the division of the sigmoid vascular pedicle or the mobilization of the left colon (Figure 10). Ureteral catheters can allow the surgeon to identify the ureter by visualization and/or palpation. In cases with significant fibrosis, ureteral catheters can also facilitate detection of intraoperative ureteral laceration, which can be promptly repaired.

After insertion of ureteral catheters, the abdomen is prepped and draped in the usual sterile fashion. As the majority of CVFs involve the rectosigmoid colon, the room set-up is geared towards a standard left sided resection. For the last two decades, the senior author has been advocating for a minimally invasive approach for CVF.[14,15] A minimally invasive approach, for example with laparoscopic surgery, yields significant short and long-term patient benefits, such as faster recovery, less postoperative complications, and lower rates of incisional ventral hernia and adhesive small bowel obstruction.[16] With advanced laparoscopic expertise, CVF can be treated with keyhole surgery. In this article, we will focus on the laparoscopic approach, as laparoscopic equipment is readily available at most hospitals. In addition, most of the available literature on minimally invasive techniques for CVF concerns laparoscopic surgery with a paucity of data on robotic surgery. However, with the gradual global adoption of robotic surgery, the robot may play an increasing role in the treatment of CVF in the future.

For laparoscopic resection, a 4-trocar technique is favored: 5 or 10 mm infraumbilical trocar for the camera, 5 mm trocars in the right upper quadrant and in the left mid-lower abdomen as working ports for the surgeon and the assistant, and 12 mm right lower quadrant trocar for the use of the endoscopic stapler (Figure 11). For specimen extraction site, there are three possibilities: A transverse left lower quadrant incision (extending the 5 mm trocar site), a limited infraumbilical midline, or a short Pfannenstiel incision. For the majority of our resections, we use a transverse left lower quadrant extraction site.

A variety of laparoscopic approaches have been described. After obtaining laparoscopic access, we start from a medial to lateral approach making a mesocolic window by opening the retroperitoneum, starting at the sacral promontory. Retrograde dissection identifies the left ureter and the vascular pedicle to the rectosigmoid. For a sigmoid resection, division of the sigmoidal vessels is achieved with an energy sealing

Figure 9. Lithotomy position with patient secured to the table and both arms tucked and well padded

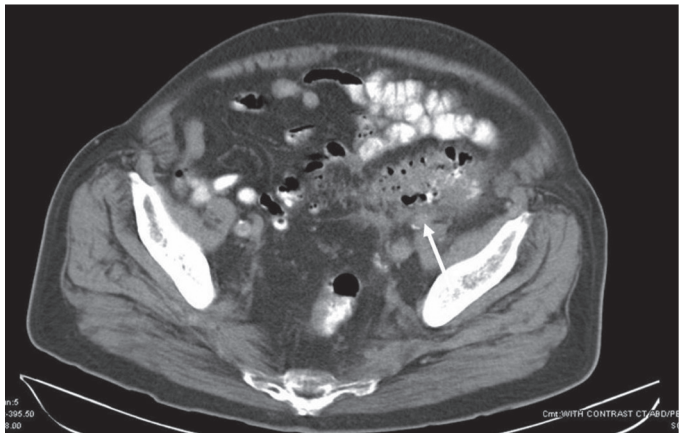

Figure 10. Sigmoid diverticulitis with perforation into the retroperitoneum surrounding the iliac vessels and left ureter [arrow]

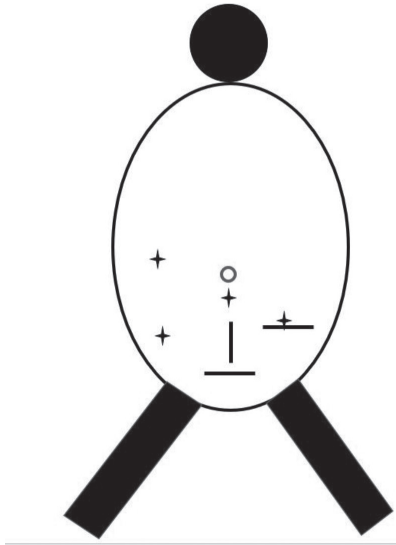

Figure 11. Trocar site placements [stars] and potential specimen extraction site [lines]

device. In case of an anterior resection, the vascular division and sealing is at the level of inferior mesenteric vessels. The retroperitoneum is dissected further by lifting the mesocolon anteriorly. Following that step, the proximal descending colon is dissected from a lateral to a medial approach by incising the left lateral gutter and going towards the sigmoid colon. Once the area of inflammation is reached, attention is directed anteriorly to the area of the bladder fistula (Figure 12). Using blunt dissection by horizontal sweeping of the laparoscopic instrument back and forth across the fistula, the bladder is separated from the large bowel. In cases where blunt dissection is not sufficient, the fistula is divided with an energy sealing device or electrocautery. The bladder is inspected carefully. Often there are inflammatory changes at the site of the fistula without an identifiable obvious hole in the bladder. Gentle debridement and irrigation of the area of inflammation is performed allowing the affected area to heal by secondary intention. If a clear fistulous hole is noted with visualization of the bladder lumen (Figure 13), a one to two layers repair of the bladder is done with absorbable sutures. Next, the upper rectum is transected in an area of soft and pliable bowel using an endoscopic stapler. Splenic flexure mobilization is conducted in select cases, if needed for a tension free anastomosis. The specimen is exteriorized through an extraction site exposed by a wound protector. The descending colon is divided extracorporeally at an area of soft and non-thickened large bowel and the specimen is sent for histologic evaluation (Figure 14). The anvil of a circular EEA stapler is inserted in the cut end of the descending colon after purse stringing the bowel with a suture. The bowel is reduced internally and the extraction site is closed. A stapled end to end colorectal anastomosis is performed under direct visualization. The integrity of the anastomosis is checked with the air leak test. In our practice we also perform flexible endoscopy to directly visualize the intraluminal aspect of anastomosis. Areas of bleeding are controlled with endoscopic clips and the anastomosis is checked for completeness and good vascularity. A surgical drain is left anterior to the anastomosis, behind the bladder. Fecal diversion with ileostomy is uncommon in our practice but considered in select cases based on the surgeon's judgement.

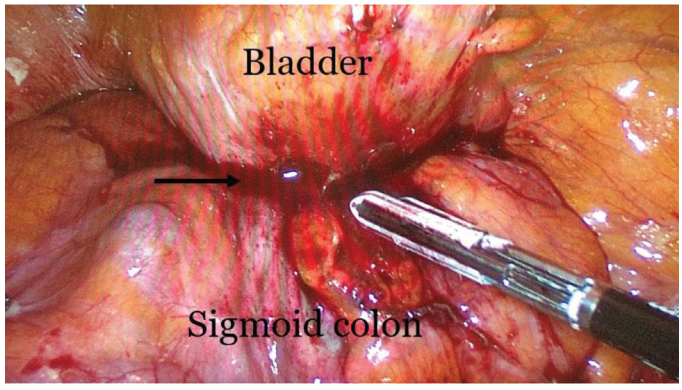

Figure 12. Intraoperative view of colovesical fistula involving the sigmoid colon [arrow]

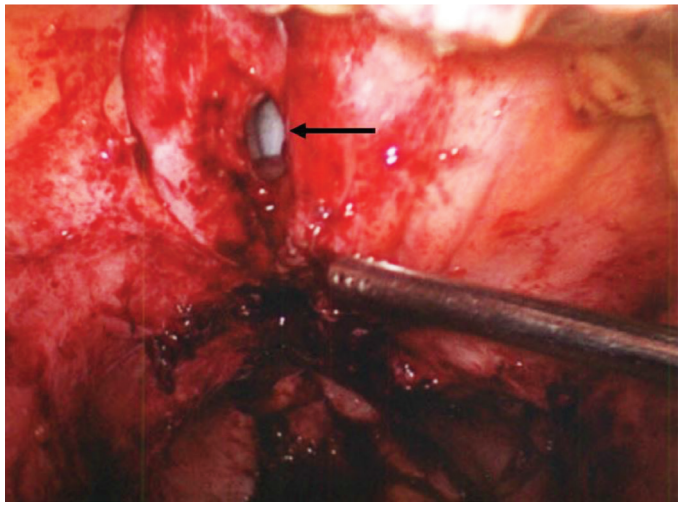

Figure 13. Intraoperative view of the bladder lumen with urinary catheter [arrow]

Postoperative Care

The patient is admitted to the ward and started on a full liquid diet within six hours of the operation. Early ambulation is encouraged and intravenous fluid maintenance is infused at a low rate, avoiding fluid overload. Pain control is achieved with non-steroidal anti-inflammatory medications and paracetamol, with the addition of narcotics medications if needed. Deep venous thrombosis chemical prophylaxis is administered subcutaneously during the hospitalization and continued after discharge for two weeks. The urinary bladder catheter is kept on average for 7-10 days, at which time a

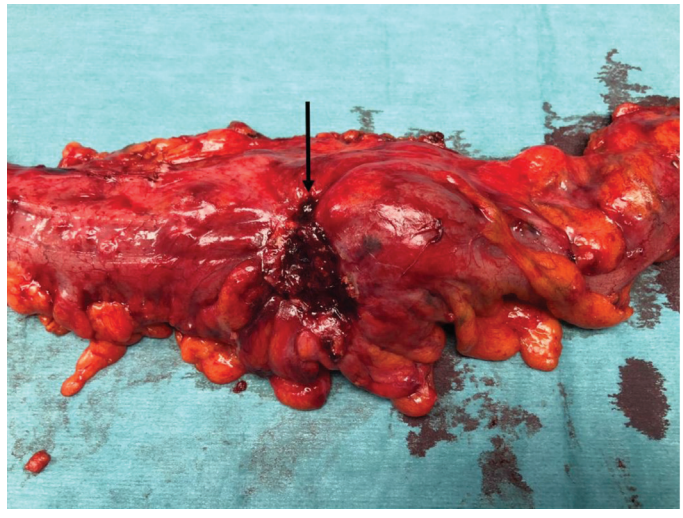

Figure 14. Sigmoid colon specimen with area of the large bowel involved by the fistula [arrow]

contrast cystogram is performed in radiology to confirm healing before catheter removal. Antibiotics are continued while the urinary catheter is in place. The surgical drain is kept until the drainage amount is less than 30 mL in 24 hours, and then removed.

Discussion

Colorectal fistulas carry significant morbidity and negatively impact the quality of patient's life. Several types of colorectal fistulas have been classified and these include CVF, colovaginal, coloenteric, colocutaneous, rectourethral, and rectovaginal fistulae. The senior author previously reported his experience at a tertiary center with this spectrum of conditions in the modern surgical era.[17] The focus of this article was to provide the reader with a framework of how to approach CVF, based on data available in the literature and the two decades experience of the senior author treating this condition.

Until recently, the majority of CVF cases have been surgically treated with an open approach. In a recent retrospective review of over 500 cases of CVF documented in the American College of Surgeons National Surgical Quality Improvement Program data base, only 29.7% of the cases were operated laparoscopically.[18] In this retrospective study open surgery was an independent risk factors for complications. For nearly two decades, the senior author has advocated a minimally invasive technique to treat CVF, previously reporting his experience with laparoscopic surgery and subsequently robotic surgery.[14,15] CVF can be safely approached with a minimally invasive technique. In his initial series on laparoscopic surgery for CVF, the senior author compared the results of patients who underwent laparoscopic surgery for diverticulitis with colonic fistulas [group 1: (n=21), of whom 15 (71.4%) had CVF] with patients with diverticulitis but without fistula [group 2: (n=21)].[14]

There was no difference between groups in terms of demographics. Intraoperative outcome was similar between groups. Median operative time and median blood loss was similar in both groups (group 1 vs. group 2: 240 vs. 260 minutes, p=0.36, and 150 mL vs. 150 mL, p=0.94). No difference was noted in intraoperative complications or the need for diverting stoma (group 1 vs. group 2: 0 vs. 5%, p=1.0, and 5% vs. 5%, p=1.0). Conversion rate to open surgery was 0% in group 1 vs. 10% in group 2 (p=0.48). Similarly, postoperative outcome was similar between groups. Median length of stay was 4 days in both groups (p=0.17). Overall complications rate was 38% in group 1 compared to 33% in group 2 (p=1.0). Readmission rate was 10% in group 1 vs. 5% in group 2 (p=1.0). Reoperation rate was 10% in both groups (p=1.0). There was no mortality in either group and 100% of the patients with CVF healed their fistula at last follow-up. The conclusions drawn from this initial experience was that laparoscopic surgery in patients with diverticulitis complicated by colonic fistulas including CVF is technically feasible with low conversion rate, low stoma rate, low readmission and need for reoperation, and with 100% success in healing the fistula. Furthermore, the overall intraoperative and postoperative results are similar to patients operated laparoscopically for diverticulitis without fistula.[14]

Table 1 summarizes results of several studies published in the last decade on laparoscopic and/or endoscopic repair of CVF.[14,19-24] Mean operative time ranged from 135 to 240 minutes. Mean estimated blood loss varied from 75 to 267 milliliters. Conversion rates to open surgery were reported to be between 0 and 46%. Mean length of stay ranged from 4 to 10 days. The majority of patients healed the fistula after laparoscopic repair.

Data on the use of robotic surgery for colonic fistula including CVF remains scarce. Currently most published data consists of case reports or video presentations. The senior author reported his initial experience with the robotic approach for colonic fistulas in 2015.[15] Eleven patients with colonic fistulas including six with CVF (54.5%) were operated robotically. Conversion rate to open surgery was 18%. Stoma formation rate was 18%. Median operative time was 250 minutes with a median blood loss of 250 milliliters. No intraoperative complications were noted. Median length of stay was 7 days with 27% complication rate. The readmission rate was 9%. All patients healed their fistula at last follow-up. The conclusion of this study was that patients with colonic fistulas including CVF can be treated by the robotic approach with 100% healing rate and acceptable operative times and blood loss. However, in comparison to the laparoscopic experience of the senior author, the conversion rate was higher and length of stay longer but it was unclear whether these results were attributable to the early learning curve of the senior author with robotic surgery at the time and/or the small number of patients in the study.[15] In 2014, Maciel et al.[25] published their experience with laparoscopic and robotic surgery for CVF. During their study period, 55 patients were operated laparoscopically for CVF and 20 patients underwent robotic surgery for CVF. The two groups were similar demographically. Two patients in the robotic group had colovaginal fistula in addition to the CVF. Mean total operative time was shorter in the laparoscopic group compared to the robotic group (181.7 minutes vs. 274.8, p=0.001). The complication rate was similar in both groups, 29.1% in the laparoscopic group and 20% in the robotic group (p=0.69). Mean estimated

Table 1. Results of several studies published in the last decade on laparoscopic and/or endoscopic repair of CV

Study	Patient number, (n)	Mean age (years)	Type of surgery	Mean operative time (minutes)	Mean blood loss (mL)	Conversion rate, (%)	Mean length of stay (days)	Reoperation within 1 month, (n)	Anastomotic leak, (n)	Non-healing of bladder
Martinolich et al.[19]	49	60	49 lap	152	162	46	6	0	NR	0
Kawada et al.[20]	1	76	Combined lap and cystoscopic	NR	NR	0	NR	0	0	0
Velayos et al.[21]	1	69	Novel device for endoscopic closure	NR	NR	-	-	0	0	0
Marney and Ho[22]	15	63	15 lap	135	75	33.3	6	0	0	0
Abbass et al.[14]	15	49	15 lap	240	150	0	4	0	0	0
Badic et al.[23]	28	68	14 lap 14 open	206	NR	43	10	0	0	0
Spector et al.[24]	34	62	21 lap 13 open	145	267	0	6	1	1	2

Lap: Laparoscopic, NR: Not reported

blood loss was 187.7 milliliters in the laparoscopic group compared to 101.3 milliliters in the robotic group (p=0.06). Conversion rate was higher in the laparoscopic group (14.6% vs. 0%, p=0.001). The mean length of stay was similar in both groups (4.6 days vs. 3.5 days, p=0.08). No mortality was noted in the study. One patient in each group developed colocutaneous fistula postoperatively, with recurrence of CVF in one patient in the laparoscopic group. The overall conclusions of the study were that the robotic approach was feasible in patients with CVF with longer operative time compared to the laparoscopic techniques but similar blood loss, complication rates, and length of stay. However, patients operated robotically had significantly lower conversion rate. In view of the limited data on robotic surgery for CVF and difference in results in the above cited studies, more research is needed with larger number of patients to determine the outcome of laparoscopic and robotic surgery for patients in CVF.

Conclusion

CVF is a complex colorectal condition, which carries significant morbidity and negatively impacts quality of life. Proper evaluation starting with an accurate history and physical examination is the initial step in the management of the patients. Prompt recognition of CVF by imaging study is the initial necessary phase prior to treatment. CT scan of the abdomen and pelvis is the preferred diagnostic modality and this can be supplemented with fluoroscopy-based contrast study, such as cystogram and gastrografin enema. Endoscopic evaluation with cystoscopy and colonoscopy are helpful adjuncts to confirm the diagnosis and provide useful information on the etiology of CVF and disease activity. Surgical resection of the diseased segment of colon remains the mainstay of treatment in the 21st century. Patients can benefit from laparoscopic surgery. Additional data is needed on robotic surgery to determine its outcome compared to laparoscopic surgery. Due to the challenging aspect of CVF, surgical intervention should be conducted by experienced surgeons with advanced surgical skills and robust clinical judgment, in order to optimize the outcome for the patient with CVF.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.O., M.A.A., Concept: M.O., M.A.A., Design: M.O., M.A.A., Data Collection or Processing: M.O., M.A.A., Analysis or Interpretation: M.O., M.A.A., Literature Search: M.O., M.A.A., Writing: M.O., M.A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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DOI: 10.4274/tjcd.galenos.2022.2022-1-2
Turk J Colorectal Dis 2022;32:238-244

RESEARCH ARTICLE

Anal Fissure Patients: Before Treatment, First Consider Irritable Bowel Syndrome, Defecation Disorder and Psychopathology

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ABSTRACT

Aim: The exact etiology of anal fissure (AF) remains unclear but it appears that constipation and stress may instigate AF. Little is known about the role of functional bowel disorder and psychopathology in AF. The aim of this study was to investigate the comorbidity of irritable bowel syndrome (IBS) in AF and its effect on quality of life (QoL).

Method: This was a cross-sectional observational study. Ninety-six AF patients (76 female; 79.2%) with a mean age of 36.54±14.98 years were recruited. The Rome 3 Criteria were applied to diagnose IBS, functional constipation (FC) and no functional gastrointestinal disorder (NoGIS). Depression, anxiety, stress level, stressful life events and QoL were evaluated.

Results: Of the AF patients, 42.7% had IBS, 36.4% had FC, and 20.8% had noGIS. Furthermore, 59% had defecation disorder, characterized by obstructive defecation symptoms. Patients with IBS tended to have more anteriorly located AF (IBS: 40.5%, FC: 24.1%, NoGIS: 7.1%; p=0.053). IBS patients had a significantly higher anxiety score (p=0.021). More severe depression predicted IBS (p=0.009) and IBS predicted more severe depression score (p=0.027). Depression, pain symptom severity and IBS were the most important negative factors affecting QoL (p<0.05).

Conclusion: IBS, FC and defecation disorder are frequent comorbidities in patients with AF. IBS especially and defecation disorder caused a more anxious emotional state, resulting in a decreased QoL. Depression and pain symptom severity appeared to have a greater negative effect on QoL than the other symptoms of AF itself.

Keywords: Anal fissure, irritable bowel syndrome, defecation disorder, psychopathology, quality of life

Introduction

Anal fissure (AF) is a benign anorectal problem even though it can cause significant pain and a negative quality of life (QoL).[1-3] Approximately 40% of patients who present with acute AFs progress to chronic AFs resulting in frequent hospital visits and a high economic cost.[4] However, the exact etiology and natural history is still not well understood and the optimal therapy algorithm for AF is still controversial.

Fissure can be either primary or secondary to predisposing factors, including inflammatory bowel disease, tuberculosis, human ımmunodeficiency virus (HIV), anal cancer, and/or prior anal surgery.[5] The majority of primary acute AFs is thought to be due to the passage of hard stools or diarrhea. Impaired bowel function and defecation disorder might be common among these patients.[6] However, data are limited concerning the risk factors and associated comorbidities of this disorder, although these additional illnesses can further affect the care of this patient population.[7]

Irritable bowel syndrome (IBS) is a common gastrointestinal disorder characterized by abdominal pain and symptoms of constipation, diarrhea or both. Rome classification divides IBS into subtypes based on the predominant stool pattern. IBS-constipation (IBS-C), a subtype of IBS and functional constipation (FC) are described as two major functional diseases according to the Rome III consensus conference.[8]

Poster presentation in ESCP's 13th Scientific and Annual Meeting 26-28 September 2018 in Nice, France.

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Received: 18.01.2022 **Accepted:** 13.04.2022

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Turkish Journal of Colorectal Disease published by Galenos Publishing House.

However, the pathophysiology of IBS and constipation is broad and includes abnormalities involving motility, visceral sensation, brain-gut interaction, and psychosocial distress.[9] Psychosocial factors, such as depression and anxiety, have been shown to be associated with functional gastrointestinal disorders, such as IBS and constipation but, little is known about the impact of functional bowel disease in the complex etiology of AF.[10] The aim of this study was to investigate the comorbidity of IBS and defecation disorder in AF and what impact, if any, these coexisting disorders have on AF.

Materials and Methods

Patient Recruitment

Patients with AF were recruited from the department of surgery. The study protocol was approved by the Bolu Abant İzzet Baysal University Faculty of Medicine Institutional Ethics Committee (approval number: 2014/06-57, date: 25.02.14). Informed consent was obtained from all patients.

Surgical Assessment

Diagnosis of AF, physical examination and clinical evaluation of all patients was performed by an expert colorectal surgeon. AF was categorized as primary and secondary and those deemed to be suffering from secondary AF (coexisting IBD, tuberculosis, HIV, anal malignancy, active cancer treatment, anal incontinence) were excluded from the study. Chronic AF was diagnosed when non-healing symptoms were present for more than six weeks and there were signs of chronicity on examination (hypertrophied anal papillae, keratinous edges, sentinel pile and/or visible sphincter fibres at the base). Visual analog scale (VAS) for pain and bleeding was used for the assessment of the severity of symptoms of AF.

A Turkish validated, self-administered, 27-item symptom questionnaire, which was based on the Rome III criteria, was used to identify IBS, FC and no functional gastrointestinal disorder (NoGIS).[11] IBS was defined as recurrent abdominal pain of at least three days per month in the last three months, associated with two or more of the following criteria: related to defecation; associated with a change in frequency of stool; and associated with a change in the form (appearance) of stool. Patients who did not meet any of these criteria were accepted as NoGIS patients.

In addition, according to the same questionnaire, defecation disorder was recorded according to the presence of two or more of the following: (i) straining; (ii) sensation of incomplete evacuation; (iii) sensation of anorectal obstruction/blockage; and (iv) manual manoeuvres to facilitate in more than 25% of defecations.

Psychiatric and Quality of Life Assessment

Patients underwent psychological testing at the time of their first clinic visit. Depression and anxiety severity was evaluated with the self-rated Hospital Depression and Anxiety Scale (HAD). The validated Turkish version was used in this study.[12] Stress level was evaluated by two different questionnaires. The first was the Turkish validated form of the self-rated Perceived Stress scale measuring the stress level in the previous month by asking 10 questions, with higher scores indicating higher perceived stress level.[13] Stressful life events were also evaluated by the Sorias Life Events Questionnaire which assesses for 107 stressful life events, including those causing economic, health, relationship, and emotional stress, that occurred in the last one year.[14] Finally, QoL was measured with the Turkish validated form of self-rated SF-36 questionnaire.[15]

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) for Windows, version 22.0, was used for all statistical analyses (SPSS Inc., Chicago, IL, USA). Patients with and without IBS were accepted as constituting internal control and no healthy controls were included. The primary outcome measures were functional gastrointestinal disorder frequency, depression, anxiety, stress level and QOL. Chi-square test, Student's t-test or Mann-Whitney U test were used according to the normality of distribution of data assessed by Kolmogorov-Smirnov test. Pearson's correlation analysis was used to assess the correlations. Binary logistic regression analysis was done to analyze which independent variables (age, sex, fissure type, pain VAS, HAD score) predicted IBS presence. General linear models were created to predict HAD score and subscales of SF-36 QoL scores. Statistical significance was accepted at a p-value of <0.05.

Results

Patient's demographic, symptom severity, fissure type and location data are shown in Table 1. Mean age for the whole cohort was 36.5±14.9 years with a sex distribution of 20 men (20.8%) and 76 women (79.2%). Mean disease duration was 32 months and the most common symptoms were pain (98%), with a mean VAS of 7.5 and bleeding (86%) with a mean VAS of 3.8. Patients with acute fissure tended to have a higher pain VAS score than chronic fissure patients (6.93±2.60 vs. 5.55±2.49, p=0.053). All patients had a primary fissure with no previous surgery for AF. The most common fissure location was posterior (48.8%). The proportions of anterior, anterior + posterior and lateral fissure locations were 28.7%, 20% and 2.5% respectively. More than half (51%) had an additional colorectal disease (20 hemoroid and 29 pruritis ani).

In total, 42.7% of AF patients had IBS, 36.5% had FC and 20.8% had NoGIS. None of these patients were screened for functional gastrointestinal disease (FGID) before, so their

Table 1. Comparison of demographic variables of anal fissure patients with IBS, FC and with no functional gastrointestinal disorder symptom

Demographics	IBS + (group 1) (n=41)	FC + (group 2) (n=35)	NOGIS (group 3) (n=20)	X^2/t/z	p	Post-hoc
Age (years)	35.73 ±14.99	32.69±12.45	45.37±16.37	7,591	**0.022**	1=2<3
Sex						
Male	8 (19.5%)	8 (22.9%)	4 (20/0%)	0.139	0.933	1=2=3
Female	33 (80.5%)	27 (77.1%)	16 (80/0%)			
Disease duration (months)	29.70±62.96	25.91±39.61	47.68±68.45	2,390	0.303	1=2=3
Fissure type						
Acute	3 (7.3%)	10 (28.6%)	3 (15.0%)	6,192	**0.045**	1>2
Chronic	38 (92.7%)	25 (71.4%)	17 (85.0%)			
Fissure location						
Anterior	15 (40.5%)	7 (24.1%)	1 (7.1%)	12,457	**0.053**	1>3
Posterior	17 (45.9%)	15 (51.7%)	7 (50.0%)			
Anterior + posterior	5 (13.5%)	5 (17.2%)	6 (42.9%)			
Lateral	0 (0.0%)	2 (6.9%)	0 (0.0%)			
Symptoms						
Pain VAS	5.18±2.29	6.85±2.47	5.15±2.68	9,231	**0.009**	2>1=3
Bleeding VAS	3.61±2.74	4.21±2.50	3.41±2.18	1,262	0.532	1=2=3
Additional anorectal disease	18 (43.9%)	18 (51/4%)	12 (65/0%)	2,398	0.302	1=2=3
Defecation disorder	27 (69.2 %)	26 (78.8%)	1 (5.0%)	-	<0.001	1=2<3

Mean ± standard deviation and t or z values are given according to the normality of distribution of continuous variables. n (%) and X^2 value are given for categoric variables and p<0.05 is accepted for statistical significance. IBS: Irritable bowel syndrome, FC: Functional constipation, NoGIS: No functional gastrointestinal disorder, VAS: Visual analog scale

diagnosis was made for the first time with this study. FC was associated with acute (28.6%) and IBS was associated with chronic (92.7%) fissure development (p=0.045). Pain VAS was significantly higher in the FC patients (FC: 6.85, IBS: 5.18, NoGIS 5.15, p=0.009). Patients with IBS tended to have a more anteriorly located AF (IBS: 40.5%, FC: 24.1%, NoGIS: 7.1%, p=0.053).

Psychiatric data are given in Table 2. Forty-eight patients (50%) were found to have either an anxiety disorder or a depressive disorder. Among these 48 patients, 42 (87.5%) had a depressive disorder, while six (12.5%) had an axiety disorder. It is notable that only 12 (25%) were on antidepressant medication at the time of inclusion in the study. IBS patients had a higher anxiety score (p=0.021) and their QoL was significantly worse on four out of eight of the SF-36 subscales (p<0.05).

Defecation disorder was defined according symptom questionnaire. According to these questions, 59% were found to have a defecation disorder with no gender difference (61.6% in females, 47.4% in males, p=0.260) (Table 1). Defecation disorder was characterized by obstructive defecation symptoms. Digitation symptom severity was found to be associated with a higher VAS bleeding score (r=0.238, p=0.027). The FC ratio was much higher (79.4% vs 46.6%, p=0.002) in patients with a defecation disorder while IBS ratio did not differ (68.4% vs. 51.9%, p=0.112). Patients with a defecation disorder were significantly more anxious (p=0.010) with a higher number of stressful life events (p=0.042), a higher distress score (p=0.004) and a higher adaptation score (p=0.048). Half of their QoL scores (physical and emotional role limitations, vitality, mental health scores) were also significantly lower than non-defecaton disorder patients (all; p<0.05).

The binary logistic regression model was significant (Omnibus test=0.006, Hosmer-Lemeshow test=0.668) and explained 23.9% of the variance (Nagelkerke R^2=0.239). Only HADD score predicted being in the IBS group (p=0.009, B=-0.162).

A general linear model was created to predict HADD score where IBS presence, age, sex, disease duration, pain VAS and stress score were entered as independent variables. The model explained 48.9% of the variance (R^2=0.489) and

Table 2. Comparison of psychiatric variables of anal fissure patients with IBS, FC and with no functional GIS symptom (NOGIS)

Psychiatric variable	IBS + (group 1) (n=41)	FC + (group 2) (n=35)	NOGIS (group 3) (n=20)	X^2/t/z	p	Post-hoc
HADA	8.97±4.67	7.61±4.86	5.31±4.11	4,109	**0.021**	1>3
Anxiety present	18 (45.0%)	10 (29.4%)	3 (15.8%)	5,137	0.070	1=2=3
HADD	7.42±4.32	5.47±4.02	5.25±4.05	2,557	0.084	1=2=3
Depression present	21 (55.3%)	15 (44.1%)	6 (37.5%)	1,173	0.425	1=2=3
PSS-14	20.48±6.97	18.70±6.24	17.63±5.79	1,388	0.255	1=2=3
Number of stressful life events	5.43±5.10	3.93±3.39	2.79±2.75	3,543	0.170	1=2=3
Distress score	284.05±273.66	203.76±187.87	151.14±158.05	2,956	0.228	1=2=3
Adaptation score	254.05±245.46	183.38±168.14	132.93±139.44	3,193	0.203	1=2=3
GH	15.38±4.23	15.17±3.21	15.36±3.25	0.556	0.757	1=2=3
PF	24.71±4.74	25.40±4.97	25.77±4.69	0.844	0.656	1=2=3
RLP	6.20±1.54	6.80±1.47	7.26±1.32	7,636	**0.022**	1<3
RLE	4.33±1.22	5.02±1.12	5.40±0.82	11,622	**0.003**	1<2=3
SF	7.24±2.22	7.34±2.37	8.52±1.61	4,309	0.116	1=2=3
P	7.00±1.98	6.92±2.18	8.22±1.64	6,611	**0.037**	1=2<3
V	13.55±4.45	14.74±3.88	15.72±3.28	2,992	0.224	1=2=3
MH	18.94±5.55	19.97±5.10	22.73±2.97	3,738	**0.028**	1<3

Mean ± standard deviation and t- or z-values are given according to the normality of distribution of continuous variables. n (%) and X^2 value are given for categoric variables and p<0.05 is accepted for statistical significance. HADA: Hospital Anxiety and Depression Scale-anxiety score, HADD: Hospital Anxiety and Depression Scale-depression score, PSS-14: Perceived Stress Scale score, GH: General health, PF: Physical function, RLP: Role limitations physical, RLE: Role limitations emotional, SF: Social function, P: Pain, V: Vitality, MH: Mental health

HADD was signicantly predicted by the presence of IBS (p=0.027, B=1.684) and stress score (p<0.001, B=0.398).

In other general linear models, QoL subscales scores were entered as dependent variables and age, sex, HAD score, pain VAS, fissure type and IBS presence were entered as independent variables. Physical function was predicted by age (p=0.009) and HADD score (p=0.007); physical role limitation was predicted by HADD (p<0.001) and pain VAS (p=0.022); emotional role limitation was predicted by HADD (p<0.001), pain VAS (p=0.023) and IBS presence (p=0.001); social function was predicted by HADD (p<0.001) and pain VAS (p=0.058); pain was predicted by HADD (p=0.001) and pain VAS (p<0.001); vitality was predicted by HADD (p<0.001); mental health was predicted by HADD (p<0.001).

Discussion

The present study showed that almost half of the patients with AF also had IBS and approximately two-thirds had a defecation disorder, characterized by obstructive defecation symptoms. The presence of IBS presence was associated with chronic fissure development while FC seemed to be associated with acute fissure development. AF patients with IBS were more anxious, with poorer QoL compared to patients with no IBS. All subscales of the SF-36 QoL tool were negatively predicted by depression severity and some subscales were negatively predicted by pain severity, rather than other clinical aspects of AF, such as fissure type and location. To the best of our knowledge, this is the first study invesigating the prevalance and effect of IBS and defecation disorder in AF patients.

Most surgeons and published expert opinions describe AF as "common", but there is scarce published epidemiologic data and the causative factors for AF are poorly understood.[6] By understanding the associated risk factors or coexisting disorders, prevention and treatment could be improved. It is well known that associated constipation is the most common factor causing chronic AF. However, constipation is a very broad spectrum and it can be classified as obstructed defecation disorder, slow-transit constipation, constipation-predominant IBS and FC.[16] These classifications are not mutually exclusive and significant overlap exists, but IBS is the most common of these disorders. Although worldwide prevalence of IBS is 10-15%, there is no epidemiologic data about the prevalance of IBS in AF.[17] Surprisingly few data exist on the interplay between AF and IBS, and what impact this comorbidity has on the presentation and course of AF.

Interestingly, none of our patients had been questioned about IBS prior to this study, had not been diagnosed with IBS, and had not received any specific treatment for it, despite the proportion of AF patients with IBS being 43% in this cohort.

The most common location of primary AF is posterior midline (90%). However, we found that the presence of IBS was associated with a more frequent anterior fissure location in this study. The posterior region receives less than half of perfusion in comparison to the rest of the anal canal and reduced anodermal blood flow associated with hypertonicity of the internal anal sphincter is the most common accompanying physiology in AF.[18] However, manometric studies have shown that up to 50% of patients with AF do not have increased anal pressures.[19] Anterior midline location is rare and accounts for up to about 25% of primary fissures in women (particularly postpartum women) and about 8% of primary fissures in men. Up to 3% of patients present with both primary anterior and posterior fissures simultaneously.[20] The cause of these other locations is not well known. These patients are typically women with anterior midline AF, which, in small studies, has been associated with vaginal delivery, external sphincter injury/dysfunction, rectocele, and rectoanal intussusception.[21] In this study, although we had a female preponderence in the cohort, no gender difference was found in terms of fissure location. So, IBS seemed to be associated with anterior fissure development in this cohort.

Approximately 40% of patients who present with acute AF progress to chronic AF.[5] Over the years, the pathophysiological mechanisms of the persistance and chronicity of AF have not been identified. According to the present study, the presence of IBS seemed to be associated with chronic fissure development while fuctional constipation seemed to be associated with acute fissure development. Apart from that, in IBS patients, no significant difference in pain symptom severity was reported but pain intensity was found to be significantly higher in FC patients compared to IBS patients, probably due to acute fissure.

Defecation disorder may also play a role in patients with AF or hemorrhoids.[6] Whether these disorders are secondary to defecation disorder or are responsible for the abnormal defecatory act remains conjectural. In the present study, more than half of the AF patients had a defecation disorder characterized by obstructed defecation symptoms. However, we do not know whether these findings are related to dyssynergic defecation or anatomical abnormality, such as rectocele, intussusception, or AF per se, since we did not perform manometric or radiological evaluations.

Furthermore, there was no difference in terms of fissure location or severity of fissure-related symptoms between patients with and without a defecation disorder, except for the higher ratio of FC in defecation disorders patients. Although there was no difference in terms of IBS prevalance in patients with and without defecation disorder, defecation disorder patients were much more anxious and stressed with a lower QOL. Thus, stress and related anxiety seems to be asociated with defecation disorder and FC seems to be associated with the development of AF. However, it could it be that AF and the associated painful defecation and bleeding may also result in defecation disorders and FC, which may produce stress and anxiety as well. Prospective cohort studies may be needed to evaluate this cause-effect relationship.

As mentioned, in this study, it was found that AF patients had a higher frequency of FGID-like FC, obstructed defecation disorder and IBS. Although many studies have focused on the intensity of psychological parameters in FGID subtypes and have shown significant associations between FGID symptoms and psychological factors, frequently no difference was found in terms of psychiatric comorbidity between subjects with different FGID subtypes.[22] However, we found that IBS patients had statistically significant higher anxiety levels than FC patients, although depression has been shown to be associated with constipation. Defecation disorder patients were also more anxious and stressed compared to non-defecation disorder patients.

Although there are many studies showing significant associations between IBS symptoms, psychological factors and psychiatric comorbidity, our study is the first to investigate this association in AF patients. Previous studies have shown that mood disorders, anxiety and somatization were the most common psychiatric comorbidities in IBS patients.[23] These psychosocial factors were shown to be associated with increased IBS symptom severity, impaired QOL, and visceral hypersensitivity.[24] In our patient group, patients with IBS were more anxious with a lower QoL compared to patients with no IBS. All subscales of the SF-36 were predicted negatively by depression severity and some subscales were negatively predicted by pain severity rather than the other clinical aspects of the disease, such as fissure type and location. The presence of IBS and stress level predicted depression severity in this patient group to a greter degree than the other clinical variables, while depression severity also predicted having IBS. Thus, there seems to be a mutual interaction between stress, depression, presence of IBS and QOL. Of course this result does not explain the old dilemma of whether depression causes IBS or IBS causes depression; it only indicates a bi-directional relationship between the two.

The link between psychosocial factors and gastrointestinal function (motility, sensation, inflammation) is through the brain-gut axis, implying bidirectional communication between the gastrointestinal tract and the brain, through neural, neuroimmune and neuroendocrine pathways. Stress has an impact on important physiological functions of gut through sympathetic overactivation causing abnormalities in gut motility, secretion, visceral sensitivity, mucosal blood flow and intestinal microbiota, leading to the development of a broad array of FGID's.[25] So, surgically correctable anorectal disease and disorders of the brain-gut axis, such as IBS, may be two clinically distinct entities that are mutually exclusive. Given this observation, we argue that patients referred for management of AF should be screened and treated for FGID's, such as IBS, FC and defecation disorder, before considering surgical treatment.

Study Limitations

Our study is limited by a relatively small cohort size and there was no follow-up in this cohort study so, no cause-effect relationships can be drawn. The small number of cases may also be insufficient to make a robust association between IBS with constipation and the occurrence of chronic AF through its association with increased anxiety. In addition, FGID subtypes were defined according to a self-rated questionnarie. The Rome III criteria for FGID separates IBS with constipation and FC into separate entities and excludes a diagnosis of FC in patients satisfying the criteria for IBS. Recent studies, however, suggest that there is a lack of symptom profile specificity and much diagnostic overlap exists between these groups, and that they might be part of the same condition, with patients located along a spectrum of pain/discomfort severity.[26,27] We have also found an overlap between these FGID subtypes, although no manometric or radiologic study was done to show objective evidence for defecation disorders. Furthermore, our data reflected a subset of treatment-seeking individuals and, therefore, our findings may not be generalized to primary care settings or community populations. Lastly, some of our patients were on antidepressant medication at the time of inclusion in the study, which might cause a change in bowel movements, but this was a small percent (25%) and most of the patients were free of medication at time of inclusion.

Conclusion

Our findings suggest that assessment of IBS symptoms and obstructed defecation symptoms may be an important part of the evaluation of AF. Recognition of IBS/subtypes and obstructed defecation disorder that may be more amenable to conservative treatments may be necessary before proceeding with more invasive treatment modalities in AF, since psychological symptoms like anxiety are frequent features in IBS. Also, psychological factors including cognitive (anxiety sensitivity) and emotional (depression) elements seem to be as important as somatic symptoms (severity of AF) in predicting QoL in these patients. Thus, a concept of the biopsychosocial model of illness may integrate all possible accountable factors for the pathogenesis and clinical expression of AF. These findings further solidify the recommendation of non-operative management for AF. However, additional evidence is needed to support this approach in clinical care. Thus, future prospective studies which focus on the effect of surgical or non-surgical treatment to show if the findings persisted or resolved upon healing of the so-called resultant fissure would help to resolve this question.

Ethics

Ethics Committee Approval: The study protocol was approved by the Bolu Abant İzzet Baysal University Faculty of Medicine Institutional Ethics Committee (approval number: 2014/06-57, date 25.02.14).

Informed Consent: Informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.Ş., Ö.A., D.Y., U.A., Concept: N.Ş., Ö.A., Design: N.Ş., Ö.A., Data Collection or Processing: N.Ş., Ö.A., D.Y., U.A., Analysis or Interpretation: N.Ş., Ö.A., Literature Search: N.Ş., Ö.A., Writing: N.Ş., Ö.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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DOI: 10.4274/tjcd.galenos.2022.2021-12-15
Turk J Colorectal Dis 2022;32:245-251

RESEARCH ARTICLE

Evaluation of Activity of Perianal Fistulas by Diffusion-Weighted Imaging

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ABSTRACT

Aim: The aim of this study was to evaluate the role of diffusion-weighted magnetic resonance imaging (MRI) in assessing the activity of perianal fistulae.

Method: This retrospective, cross-sectional study included 30 patients with perianal fistula. MRI with diffusion-weighted imaging (DWI) was performed with 1.5 T-scanner. The MRI findings were correlated with local clinical examination and or postoperative findings as reference.

Results: A total of 42 perianal fistulae in 30 patients were identified. The detection rate of perianal fistula by DWI was less than by T2-weighted (T2W) and combined DWI-T2W imaging. Thirty-three perianal fistulae (76.2%) were clearly diagnosed in 42 fistulae on DWI, 40 (88.1%) on T2W, and 41 fistulae (95.2%) on DWI-T2W images. The mean of apparent diffusion coefficient (ADC) values was significantly different between active fistulae at 0.919±0.165 $x10^{-3}$ mm^2/s and inactive fistulae at 1.235±0.220 $x10^{-3}$ mm^2/s ($p<0.0035$). A cut-off mean ADC value of 1.005 $x10^{-3}$ mm^2/s was used to differentiate active from inactive fistula with a sensitivity of 84% and a specificity of 71.5%.

Conclusion: These results showed that the ADCs measured from active and inactive perianal fistulae differ significantly in patients who were on an antibiotic treatment. Therefore, DWI may be used to evaluate the activity of a perianal fistula and identify patients with a higher likelihood of recurrence.

Keywords: Perianal fistulae, activity, diffusion-weighted MRI

Introduction

Perianal fistulae and abscesses have a prevalence of 1 per 10,000 of the population, with an underlying cause of anal glandular infection, Crohn's disease, radiotherapy, or secondary malignancy.[1,2] Perianal fistulae usually result from anal gland obstruction with subsequent infection, associated secondary abscess formation, and its complications. Once a fistula has formed healing may take considerable time and recurrences occur, often after apparent healing.[1,2] The therapeutic approach to the fistula largely depends on the presence of the activity of the fistula, so an accurate assessment of fistula activity is clinically important in deciding whether a medical or a surgical treatment will be more appropriate. Recurrence of fistula occurs in up to 25-30% of patients after surgery, usually due to an infection that went unnoticed during surgery and/or due to a poorly treated fistula.[3]

The presence, extent and activity of perianal fistulae are evaluated by various methods, including anal ultrasound, examination under anesthesia, computed tomography fistulography and magnetic resonance imaging (MRI). Evaluation of a fistula by anal ultrasound and (preoperative) examination under anesthesia can be done easily, however these methods can miss an abscess and the relationship of the fistula with the adjacent perianal muscle layers may not be established by these methods.[4] MRI, on the other hand, not only demonstrates the fistula tract and its course, but can also show an abscess in the vicinity of the fistula tract that lies beyond the reach of the digital exam.[5-8] Accurate preoperative evaluation of a fistula by MRI can therefore determine optimal surgical planning, may decrease the rate of recurrence and can have an impact on the surgical outcome.[5] The activity of a perianal fistula can also be evaluated by MRI. Active fistulae that are filled with pus and granulation tissue

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Received: 31.01.2022 **Accepted:** 22.06.2022

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Turkish Journal of Colorectal Disease published by Galenos Publishing House.

and have mural edema are detected by high signal on T2-weighted images (T2W).[5-8] On post-contrast T1-weighted imaging (T1W) mural granulation tissue of an active fistula will enhance against the hypointense fluid in the fistula lumen and any inflammation that extends to adjacent soft tissues will also enhance.[7,8]

Diffusion-weighted MRI (DWI) has also been suggested to aid in the evaluation of the activity of perianal fistulae, as hypercellularity seen in inflammatory processes and abscesses cause diffusion restriction.[9] Studies using DWI with higher b-value provided better contrast, more tissue diffusibility, and less T2 shine-through effect.[10] Some studies also suggested that the mean apparent diffusion coefficient (ADC) values compared between active and inactive fistulae differed significantly and thus could be used to differentiate between these entities.[11-14]

The purpose of this study was to assess the usefulness of DWI and ADC values to evaluate perianal fistula activity.

Materials and Methods

All procedures performed in studies involving human participants were in carried out in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Haydarpaşa Numune Training and Research Hospital Ethics Committee (approval number: E-62977267-771, date: 25.01.2022). Informed consent was obtained from all individual participants included in the study. We reviewed the MRI images of 37 patients who were referred to the radiology department for an MRI exam because of suspected clinical symptoms of a perianal fistula. Claustrophobic patients and patients with an implanted pacemaker (n=4) and patients with recurrent symptoms of a previously healed fistula (n=3) were excluded from the study, leaving 30 patients (18 men and 12 women, mean age, 39 years) to be included. Of these, 15 had anal glandular infection with no obvious underlying disease, 10 had Crohn's disease and 5 had ulcerative colitis. All 30 patients were put on antibiotic treatment for an average of 1 week before the MRI examination (range: 4-11 days).

MRI Examination

All patients were examined in a supine position with a 1.5-T MRI-unit (Optima 760w, GE Medical Systems, Milwaukee, WI, USA) using a pelvic phased-array coil. No anti-peristaltic agent or oral/rectal contrast agent was given before the exam. Non-contrast, T1W [repetition time/time to echo (TR/TE), 600/14 ms] and fat-suppressed T2W images (TR/TE 2863/90 ms) were obtained in the axial plane.

The MRI parameters were: 3 mm slice thickness, 1 mm inter-slice gap, Matrix size 330x265, and a field of view (FOV) of 35x35 cm.

DWI, which is a single-shot, spin-echo, echo-planar imaging, was acquired in the axial plane with the application of three gradients in three orthogonal planes. DWI parameters were: TR/TE of 4000/84 ms, Flip angle of 90°, slice thickness 5 mm, inter-slice gap 0.5 mm, Matrix size 256x256, FOV 40 cm and b-values of 0 and 800 s/mm^2.

0.2 mL/kg Gadoterate Meglumine was administered as intravenous contrast agent at a rate of 2 mL/s. Total scan time was approximately 25 minutes. The MR protocol is summarized in Table 1.

Analysis of MRI Images

The perianal fistula was evaluated using T1W, T2W, DWI and fat-suppressed post-contrast T1W sequences.

Table 1. MR protocol

Parameter	Oblique axial T1W TSE	Oblique coronal T2W TSE	Oblique axial T2W TSE	Axial DWI	Oblique axial 3D T1W GRE
TR/TE (ms)	600/14	2863/90	2863/90	4000/84	550/10
Bandwidth (Hz/pixel)	50	125	62.5	1628	520
Rectangular FOV (cm)	35	35	35	40	32
Slice thickness (mm)	3.5	3.5	3.5	5	2.6
Inter-slice Gap (mm)	1	1	1	0.5	1
ETL	3	28	30		4
NEX	1	1.5	1.5	4	2
Matrix	288x192	330x265	212x186	256x256	320x256
Phase encoding	AP	Transverse (RL)	Transverse (RL)	AP	S/I

MR: Magnetic resonance, T1W: T1-weighted imaging, DWI: Diffusion-weighted Imaging, GRE: Gradient-echo Imaging, TR/TE: Repetition time/time to echo, FOV: Field of view, ETL: Echo train length, NEX: Number of excitations

The images were reviewed by one radiologist with more than 17 years of experience in abdominal radiology and the following features were recorded: identification of the primary fistula tract with its internal opening; any secondary ramification(s); and any finding of inflammation or abscess. The appearance of a perianal fistula was defined as a linear or oval structure surrounded by an irregular area, hypointense to isointense on T1W and isointense to hyperintense on T2W images. An inflammation was defined as an area of increased signal intensity on T2W image and showing an ill-defined, diffuse post-contrast enhancement, whereas an abscess was identified as an area of diffusion restriction with irregular peripheral contrast enhancement (Figure 1A-E). Then the fistulas were classified according to the St. James's University Hospital.[15] The definition of fistulae according to St. James's University Hospital classification is: A grade 1 fistula is a simple linear intersphincteric fistula; a grade 2 fistula is a grade 1 fistula with a concomitant abscess or an additional fistulous tract; a grade 3 fistula traverses the external sphincter; a grade 4 fistula is a trans-sphincteric fistula with an abscess or an additional tract in the ischiorectal fossa; and a grade 5 fistula is a supralevator or translevator fistula.

An ADC map was generated automatically following the acquisition of DWI. The radiologist who was unaware of the clinical and post-surgical findings selected a slice which showed the most of the lesion compared to the other views and drew a circular region of interest (ROI) with a minimum area of 6 mm^2 on the ADC map (Figure 1B). Measured ADC values from the ADC map were recorded for each lesion. The positions of the ROIs were determined by reviewing both DW and fat-suppressed T2W images. If a patient had multiple lesions, all lesions were analyzed and the lowest ADC was recorded.

Reference Standards

Surgical findings were used as the gold standard for the assessment of active and inactive fistulae in 28 patients who underwent surgery. Fistulae were confirmed as active if pus was identified during surgery. Two patients who did not undergo surgery were evaluated based on findings of local clinical examination. When pus and or signs of inflammation (redness, pain, and swelling around the perianal fistula) were seen on local examination, the fistula was defined as active. Fistulae that did not reveal any of these signs or pus were defined as inactive.

At our institution a patient with signs and symptoms of a perianal fistula is routinely put on antibiotic treatment as a first-line therapeutic approach. If antibiotic therapy fails to be effective for healing, fistula surgery is contemplated. The decision for surgery (either open surgery or the use of setons) depends on the presence of several findings, including the presence of pus, clinical signs of active inflammation, elevated serum C-reactive protein levels (>2 mg/L), and no improvement of symptoms during medical treatment.

Definition of Active and Inactive Perianal Fistulae

Fistulae which needed surgical intervention within one week after the MRI examination, and which were confirmed to have inflammation during surgery, were defined as active. The time between surgery and MRI exam was constrained by a one-week interval to avoid inclusion of newly developed fistulae. Fistulae that did not need surgery within one week of the MRI examination, and lesions which were confirmed with an absence of inflammation during surgery, were defined as inactive.

The surgeon had access to MRI images and used MRI for the purpose of lesion localization only, rather than for the evaluation of disease activity.

Detection of Fistulae

The detection of a perianal fistula was evaluated on a 3-point scale from 0 to 2. Score 0: no visible fistula, 1: probable fistula, and 2: clearly visible fistula. To assess the diagnostic performance of DWI in the evaluation of a perianal fistula, the appearance of a fistula was scored on DWI, T2W, combined T2W-DWI images, and post-contrast T1W where the combined T2W-contrast enhanced MRI images were taken as reference for grading.[14,16]

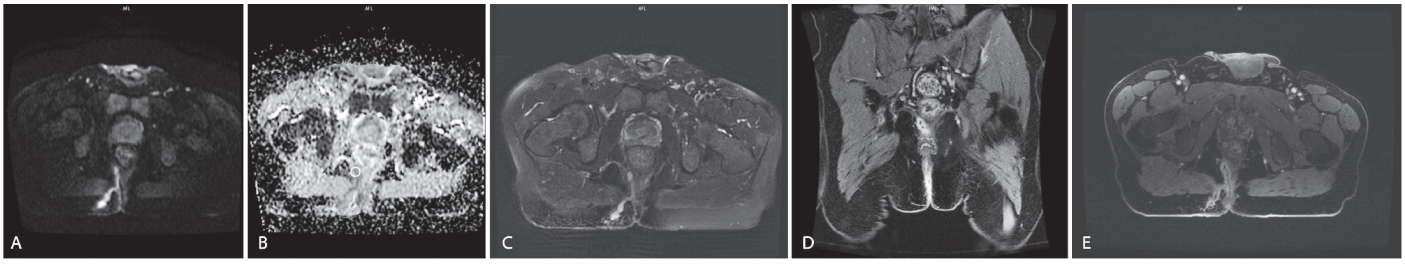

Figure 1. A) DWI of a grade 1 perianal fistula with increased signal along the fistula tract. B) ADC image of DWI showing decreased signal intensity within the fistula lumen, consistent with diffusion restriction and thus inflammatory pus. The circle denotes the position of the ROI, which measured a mean ADC of 0.910x10-3 mm2/s. The fistula was classified active. C) Fat-suppressed T2W of the same fistula with high signal of the fistula lumen against a background of low signal. D, E) Post-contrast coronal and axial T1W images showing intense mural contrast enhancement of the fistula tract
DWI: Diffusion-weighted imaging, ADC: Apparent diffusion coefficient, ROI: Region of interest, T2W: T2-weighted, T1W: T1-weighted

Statistical Analysis

Kolmogorov-Smirnov tests were used to test if the distribution of ADC values of two different groups (i.e. active and inactive) conformed to a normal pattern. ADCs of both groups were compared using an unpaired t-test. If a significant difference in ADCs between both groups was found, additional receiver operating characteristic (ROC) curve analysis was conducted to calculate the area under the curve and the optimal cut-off ADC with corresponding sensitivity, specificity, positive predictive value, and negative predictive value. A p values smaller than 0.05 were considered statistically significant. Statistical analyses were done using SPSS, version 25.0 (IBM Corp., Armonk, NY, USA).

Results

This retrospective, cross-sectional study included 30 patients, (18 men and 12 women). The mean ± standard deviation (SD) age was 35±1.4 years. Twelve (40%) out of 30 patients had more than one fistula with a total of 42 perianal fistulae in all patients. Twenty-one patients (70%) had 31 active fistulae and nine patients (30%) had 11 inactive fistulae. In 17 patients (56.7%) secondary branch-offs from the primary fistula tract were present. Horseshoe-appearing fistula was found in three patients (10%). Abscess formation adjacent to the perianal fistula was seen in 11 patients (36.7%). According to SJUH classification, there were 22 grade 1, 12 grade 2, and eight grade 3 fistulae. The patient characteristics of the study population are shown in Table 2.

Table 2. Patient characteristics of the study group

Mean ± SD age, (years)	35±1.4
Gender n (%)	
Female	12 (40)
Male	18 (60)
Fistulae	
Total	42
Inactive	11 (26.2%)
Active	31 (73.8%)
Secondary tracts	17 patients
Horse-shoe	3 patients (10%)
Abscess formation	11 patients (36.7%)
Fistula classification	
Grade 1	22 (52.4%)
Grade 2	12 (28.6%)
Grade 3	8 (19.0)

SD: Standard deviation

ADC Values of Perianal Fistulae

ROI placement within the perianal fistula is shown in Figure 1B for active and inactive fistulae. Mean size of ROIs used for ADC measurements was 10.3 mm^2 (range: 6-18.2 mm^2). The mean ± SD ADC value of active perianal fistulae was 0.919±0.165x10^{-3} mm^2/s and that of inactive fistulae was 1.235±0.220 x10^{-3} mm^2/s. Although the boxplot of mean ADC values of active and inactive fistulae shows some overlap between the two groups there was a statistically significant difference between them with a p-value of 0.0035 (Figure 2). The area under the ROC curve (AUC) was 0.725. A cut-off mean ADC value of 1.005x10^{-3} mm/s to differentiate an active fistula from an inactive one yielded a sensitivity of 84%, a specificity of 71.5%, a positive predictive value of 84.5%, a negative predictive value of 71.2%, and a diagnostic accuracy of 79.93% (Table 3, Figure 3).

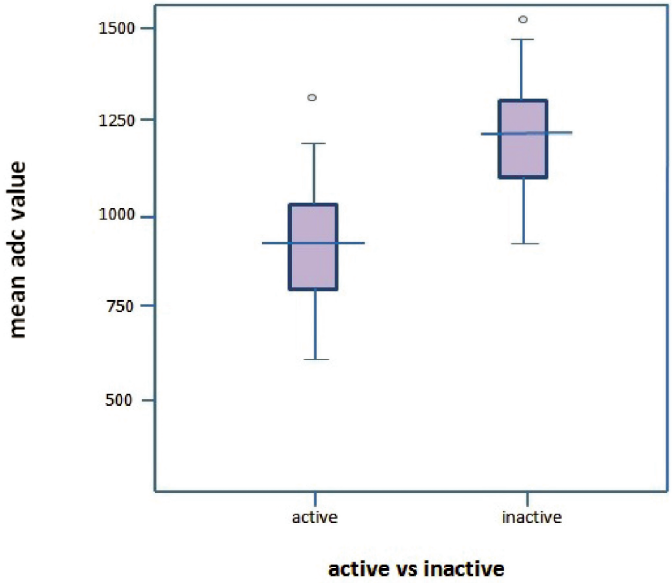

Figure 2. Boxplot showing the range of distribution of the mean ADC values of active and inactive perianal fistulae
ADC: Apparent diffusion coefficient

Detection of a an Active vs Inactive Perianal Fistula on DWI, T2W, and Post-Contrast MRI

Of 42 perianal fistulae in 30 patients, 33 perianal fistulae (76.2%) were clearly identified (score 2) on DWI, compared to 40 fistulae (88.1%) on T2W, 41 fistulae (95.2%) on combined DWI-T2W, and 41 fistulae (90.5%) on post-contrast MRI. In nine patients, a fistula was probably present (score 1) on DWI compared to two patients on T2W, one inactive fistula on post-contrast MR and one inactive fistula on combined DWI-T2W. The detection scores on DWI did not differ significantly from that of T2W (p=0.347) and both were less than the detection score of combined DWI-T2W. However, the detection scores of active perianal fistulae

on DWI were significantly different from that of inactive fistulas (p=0.0035) whereas the detection scores on T2W, contrast-enhanced MRI, and combined DWI-T2W did not show any statistically significant difference between the active and inactive fistulae (Table 4).

Discussion

Following antibiotic treatment, a perianal fistula may not heal completely and remain active exhibiting ongoing inflammation. In these cases surgical excision of fistulous tracts and drainage of any associated abscess with preservation of the anal sphincteric complex becomes the primary treatment.[16] Postoperative recurrence of a fistula is usually caused by failure to treat or detect an active (inflamed) fistula and/or abscess at the time of surgery.[17] Preoperative detection of an active fistula is therefore important to prevent this recurrence. Our study results showed that MRI using DWI can differentiate an active perianal fistula from an inactive one. In particular, ADC values measured from the fistula helped to identify an active fistula.

The detection rate of fistula by preoperative MRI has been reported to be around 86-88% when surgical findings are taken as reference.[7,18] T2W sequence, with and without fat-suppression, and contrast-enhanced T1W sequence are usually used for the initial evaluation of a perianal fistula. The added value of DWI in diagnosing perianal fistula was studied by Hori et al.[19] who found that the confidence scores of the combinations of DWI and TW sequence and of contrast-enhanced and T2W were statistically significantly greater than those with T2W images alone (p=0.0047 and p=0.014, respectively). Similarly, Mohsen and Osman[13] and Boruah et al.[14] reported higher detection rates of fistulae with the combined use of DWI-T2W images compared to T2W, DWI and post-contrast T1W images alone. However, Baik et al. [20] suggested that the performances between combined DWI-T2W images and contrast-enhanced MRI to detect a perianal fistula were comparable.

DWI depicts increased signal in areas with high cellular density, such as in abscess formation and inflammatory processes.[21] So the role of MRI has not only been investigated for the detection of fistulae, but also to evaluate the activity of the fistula owing to its ability to depict signal in areas.[22-24] Liu et al.[25], studied the role of preoperative DWI to predict the activity of perianal fistulae. They found that the ADC value of a perianal fistula was inversely proportional to the activity of the anal fistula. They concluded that the lower the ADC value of a preoperative fistula, the more likely the fistula will recur after surgery.[25] Similarly, the results of a study conducted by Boruah et al.[14] suggested preoperative

Table 3. Diagnostic performance of ADC cut-off values

Criteria (cut-off ADC value)	Sensitivity (%)	Specificity (%)
≤0.912	68	98
≤1.105	84	71.5
≤1.190	89	62

ADC: Apparent diffusion coefficient

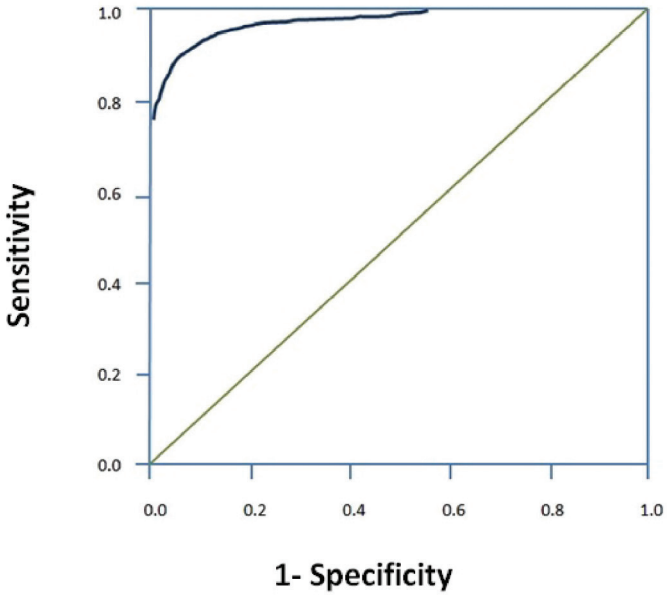

Figure 3. Receiver operating characteristic curve of the mean apparent diffusion coefficient values for perianal fistulae

Table 4. Distribution of detection scores according to MRI sequences

Sequence	Detection score	Total number (n=42)	Active fistula (n=30)	Inactive fistula (n=12)	p
Contrast-enhanced MR	Score 2	41	31	10	0.060
	Score 1	1	0	1	
	Score 0	0	0	0	
T2W	Score 2	40	28	13	0.390
	Score 1	2	1	1	
	Score 0	0	0	0	
T2W-DWI	Score 2	41	30	11	0.450
	Score 1	1	0	1	
	Score 0	0	0	0	
DWI	Score 2	33	27	6	0.0035
	Score 1	9	4	5	
	Score 0	0	0	0	

DWI: Diffusion-weighted imaging, T1W, T2W: T1-weighted, T2-weighted, MR: Magnetic resonance

DWI may predict the activity of a fistula as the ADC values obtained from patients with active fistulae in their study were significantly lower than the ADC values obtained from inactive fistulas. They also found an ADC cutoff of 1.105 $x10^{-3}$ mm^2/s which differentiated active from an inactive fistula with a sensitivity of 87.5% and specificity of 73.3%.[14] Yoshizako et al.[26] also showed that ADCs of active fistulae were significantly lower than those of the inactive group; however, they also reported that a significant overlap between the two groups existed. It has been suggested that the overlap between active and inactive fistulae may be caused by various factors, such as variable viscosities of the pus found within the inflammatory area of a fistula, which, in turn, affected the measured ADC value.[14] Furthermore, the viscosity of the fistula pus may change over time, as seen in abscesses elsewhere outside the perianal area.[27] Finally, fibrosis that develops over time at and around the fistula tract may also lower the measured ADC value, resulting in overlapping of ADC values of active and inactive fistulae. Nevertheless, our study results showed that a cutoff of 1.005 $x10^{-3}$ mm/s ADC can be used to differentiate between active and inactive fistulas, which is comparable to other studies.[14,26]

Baik et al. [20] suggested that the performance of combined DWI-T2W images and contrast-enhanced MRI to detect a perianal fistula were comparable. Moreover, considering the added ability of DWI to assess the activity of a fistula, it appears reasonable to use DWI in evaluating a perianal fistula, especially in patients with contraindication to contrast agents, as DWI obviates the use of contrast agents. DWI is also a widely available sequence in most MRI scanners with a short scan time (approx. 2 min 30 sec in our MR unit).

Study Limitations

Our study has some limitations. The retrospective nature of the study with its small number of subjects prevents generalization of the conclusion, so studies with larger number of subjects are needed. Second, the use of antibiotics before the MR examination may have affected the fistula activity in the intervening duration. So the results of this study may only be applicable to this particular patient population and may not be generalized. However, as all patients received antibiotics any patient selection bias was avoided. Third, only two b-values (0 and 800 s/mm^2) were used for ADC calculation. To increase the accuracy of the measured ADCs and the calculated ADC cut-off, studies implementing more b-values can be conducted in the future. Finally, the ADC measurements were performed by one radiologist. A study with more observers where a kappa value assessing inter-observer agreement can be calculated may increase the accuracy and reliability of the results.

Conclusion

The present study showed that the ADCs measured from active and inactive perianal fistulae differ significantly in patients who were all on antibiotic treatment. Therefore, DWI may be used to evaluate the activity of a perianal fistula and identify patients with a higher likelihood of recurrence.

Ethics

Ethics Committee Approval: This study was approved by the Haydarpaşa Numune Training and Research Hospital Ethics Committee (approval number: E-62977267-771, date: 25.01.2022).

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

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DOI: 10.4274/tjcd.galenos.2022.2022-9-3
Turk J Colorectal Dis 2022;32:252-257

RESEARCH ARTICLE

Comparison of Microbiological Profile of Drained Intra-Abdominal Abscess in Patients with Crohn's Disease and Colonic Diverticulitis

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ABSTRACT

Aim: To investigate the microbiological profile of intra-abdominal abscesses drained from patients with Crohn's disease (CD) compared to patients with complicated diverticulitis coli (cDC).

Method: This was a retrospective, cohort, pilot study. Inclusion criteria were adult patients who underwent percutaneous ultrasonographic/computed tomography (CT) guided drainage or aspiration of abscess. Cultures were performed for all patients and tested with Gram staining. Demographic data, pre-operative medications taken for CD, abscess size, antibiotic coverage after drainage, abscess recurrence, surgical resection, resection type and post-operative complications were investigated.

Results: A total 44 patients with CD (n=18) and cDC (n=26) were investigated in this pilot study. Cultures showed mostly mixed Gram-positive and negative bacteria in both CD and cDC, but Gram-negative culture was more prevalent in cDC (p=0.029). The most common bacteria was *Escherichia coli* in both groups. Anaerobic bacteria were the second most common flora in patients with cDC, while *Streptococcus*, *Enterococcus*, Extended spectrum Beta Lactamase-producing organisms, *Pseudomonas*, *Morganella* and *Proteus* were the second most common in patients with CD.

Conclusion: Mixed Gram-positive and negative bacteria with *Escherichia coli* were the most common bacteria in CD and cDC. Both groups also showed significant growth of *Enterococci*, *Streptococci*, and anaerobic bacteria in culture. *Klebsiella pneumoniae* was significantly more prevalent in patients with CD.

Keywords: Crohn's disease, diverticulitis, abscess, percutaneous drainage, bacteria

Introduction

Patients with Crohn's disease (CD) may develop intra-abdominal abscesses, which occur in 10% to 28% of patients.[1] At least 80% of abscesses contain multiple bacteria types, which are typically a mixture of aerobic and anaerobic flora. The most common aerobes are *Escherichia coli* and *Enterococcus* spp., and the most common anaerobes are Bacteroides fragilis and *Peptostreptococcus* species. Importantly, fungal infections including *Candida albicans* may be present in chronic abscesses, especially when patients are immune-suppressed, malnourished, or on protracted courses of antibiotic therapy.[1,2]

A recent study found bacterial isolates from CD-associated abscesses included *E. coli* (54%), *Bacteroides fragilis* (44%), *Enterococci* (41%), and *Viridans streptococci* (31%).[3] However, other studies also show an alarming increase in quinolone-resistant *E. coli*[4] intrinsic third-generation cephalosporin resistant *Enterococcus faecium*[5] and *Candida* spp.[6] Owing to a lack of prospective studies, current treatment concepts are based on retrospective data and case series, and favor a combination of broad-spectrum antibiotic therapy and percutaneous drainage, followed by delayed surgical therapy if necessary.[7,8]

Abscesses may also complicate up to 30% of cases with diverticulitis coli (cDC), due to non-contained perforations.[9] In cultures obtained from cDC patients anaerobic bacteria alone were present in 18%, aerobic bacteria alone in 5% and, more commonly, mixed aerobic and anaerobic flora in 77%. The predominant aerobic and facultative organisms

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Received: 13.09.2022 **Accepted:** 09.10.2022

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Turkish Journal of Colorectal Disease published by Galenos Publishing House.

were *E. coli* and *Streptococcus* spp. Poly-microbial flora were recovered in 86% of patients.[10] Therefore, broad-spectrum antibiotics are recommended. However, there is no consensus about antibiotic regimen in cDC.[11,12] There is little evidence to suggest that oral antibiotics are as effective as intravenous antibiotics.[13] The rate of relapse at 30 days following non-operative management of cDC was 18.9% and the rate of recurrence following non-operative management was 25.5% at a mean follow-up of 38 months.[14]

Few studies have compared the bacterial species identified in cultures from abscesses formed in patients with CD and cDC. The aim of this study was to investigate the microbiological profile in abscess fluids drained from patients with CD compared to intra-abdominal abscess fluid drained from patient with cDC.

Materials and Methods

This was a retrospective, cohort, pilot study. The cohort of patients had a diagnosis of CD or cDC and had undergone radiologically-guided, percutaneous drainage of intra-abdominal abscess in a single tertiary center (Aalborg University Hospital) in the period 2008-2019.

The primary objective was to investigate the microbiological profile of culture isolates obtained from intra-abdominal abscesses drained in patients with CD compared to those with cDC.

Patients

Adult patients who underwent radiologically-guided, percutaneous drainage, using either ultrasonography (US) or computed tomography (CT), as part of treatment were included. Aspiration of intra-abdominal abscesses was performed and samples from the drainage were cultured from patients in both the CD and cDC groups. Gram-staining was used to detect positive, negative and mixed species.

Data items included demographic data, pre-operative medications in the CD group, abscess size, antibiotic coverage after drainage, recurrence of abscess, surgical resection, type of resection and post-operative complications, Data items were collected and compared in the CD and cDC groups. Informed consent from individual patients was not deemed necessary because of the retrospective nature of the study. However, ethical approval to collect data was obtained from the Danish Agency (approval number: STPS 3-3013-3045/1).

Statistical Analysis

SPSS, version 27, was used for analysis of data (IBM Corp., Armonk, NY, USA). Continuous variables were reported using median and interquartile range (IQR). For univariate analysis, Pearson chi-square and Fisher's exact tests were used for categorical variables and Mann-Whitney U test for continuous variables. A two-sided p-value less than 0.05 was considered statistically significant.

Due to the pilot nature of this study multivariate analysis was not done.

Results

A total of 44 patients with CD (n=18) and cDC (n=26) were investigated in this pilot study. Of 18 patients with CD, 10 (55.6%) were females and median IQR age at time of diagnosis was 32 (24.25-47.75) years. Similarly, among the 26 patients with cDC, 18 (69.2%) were females and median (IQR) age at diagnosis was 55.5 (39.5-62.25) years (Table 1). All patients underwent percutaneous, radiologically-guided drainage of an intra-abdominal abscess. The specimens were then cultured for determination of microbiological profile in both groups of patients.

There was a significant difference in median largest diameter of abscess between the two groups (p=0.04). Abscesses were larger in cDC with a median (IQR) largest diameter of 65 (42.5-78.75) mm compared to 40 (33.75-70) mm in patients with CD (Table 1).

There was no significant difference in antibiotic coverage in the two groups, in that all patients with CD and cDC received broad spectrum antibiotics prior to abscess drainage. However, there was a significant difference in other pre-operative medications, including steroids, immunosuppressive agents and biologics, with predominance of those medications in patients with CD (p<0.001) (Table 1).

Cultures after drainage were performed and results showed mostly mixed Gram-positive and Gram-negative bacteria in both groups, but in patients with cDC, there was a significantly higher proportion of cultures of Gram-negative bacteria only (p=0.029) (Figure 1, 2).

The most common bacterial spp. in cultures was *E. coli* in both groups of patients. Anaerobic bacteria were the second most common spp. in cDC, while *Streptococcus*, *Enterococcus*, extended spectrum beta lactamase (ESBL)-producing organisms, *Pseudomonas*, *Morganella* and *Proteus* were the second most common in patients with CD (Figure 1, 2). Recurrence of abscess was reported in 33.3% of patients with CD after radiologically guided percutaneous drainage compared to cDC patients who reported no abscess recurrence after drainage (p=0.019) (Table 2).

In patients with CD who underwent surgical resection, abscess was present at the time of surgery (50%), compared to 15.4% of cDC patients with abscess at time of surgery. Fistula was the most common post-operative complication

Table 1. Baseline demographic and medical characteristics of the patients in the Crohn's disease and diverticulitis coli groups prior to abscess drainage

	Crohn's disease, n=18/44 (40.9%)	Diverticulitis coli, n=26/44 (59.1%)	Univariate analysis, (p)
Demographics*			
Age, median (IQR), years	32 (24.25-47.75)	55.5 (39.5-62.25)	0.006
Gender (female)	10 (55.6%)	18 (69.2%)	ns
BMI, median (IQR), (kg/m^2)	21.95 (18.7-28.0)	26.2 (23.05-31.1)	0.02
DM, any type	1 (5.6)	2 (7.7)	ns
Insulin-dependent DM	0 (0)	1 (3.8)	ns
Non-insulin dependent DM	1 (5.6)	1 (3.8)	ns
Smoking, at any time	9 (50)	8 (30.8)	ns
Current smoker	8 (44.4)	5 (19.2)	ns
Ex-smoker	1 (5.6)	3 (11.5)	ns
Median (IQR) abscess size (mm)	40 (33.75-7)	65 (42.5-78.75)	0.046
Medical treatment before drainage			
Antibiotics	16 (88.9)	25 (96.2)	ns
Steroids	13 (72.2)	0 (0)	<0.001
Immunosuppressive therapy	9 (50)	0 (0)	<0.001
Biologics therapy	6 (33.3)	1 (3.8)	0.009

*All results are given as n (%) unless otherwise stated. IQR: Interquartile range, ns: Not significant, BMI: Body mass index, DM: Diabetes mellitus

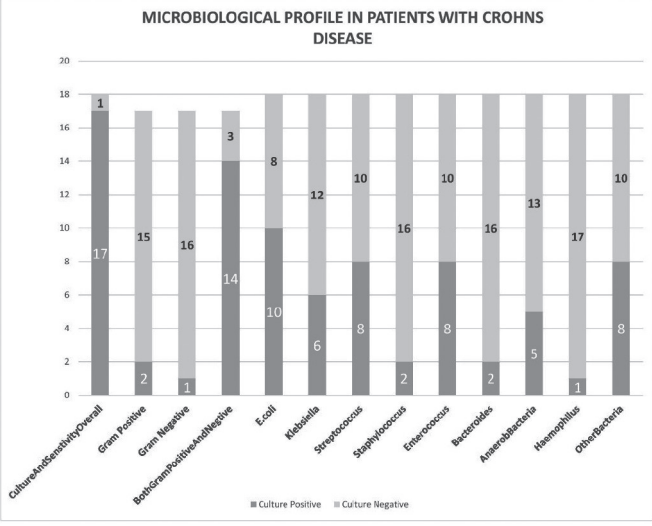

Figure 1. Microbiological profile in cohort of Crohn's patients who underwent radiologically guided percutaneous abscess drainage

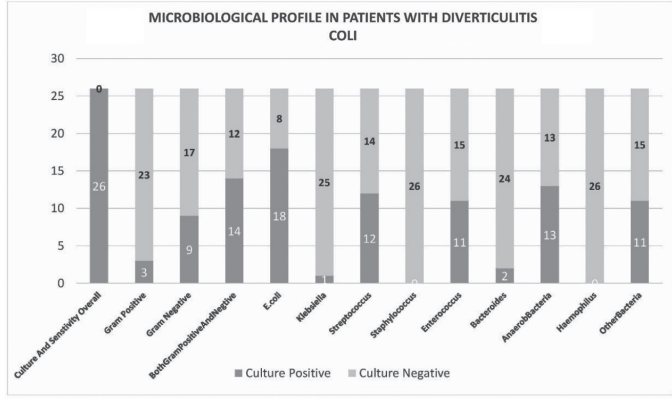

Figure 2. Microbiological profile in cohort of diverticulitis patients who underwent radiologically guided percutaneous abscess drainage

reported for both groups. In the CD group, the second most common post-operative complication was ileus (commonly grade 2 ileus) and sepsis (commonly grade 2 sepsis) (21.4%). However, the second most common post-operative complications were superficial surgical site infection SSI (7.7%) in the cDC group (Table 3).

Discussion

This study demonstrated predominantly mixed Gram-positive and negative bacteria and *E. coli* in cultures recovered from abscesses in both CD and cDC patients. Both groups showed significant growth of *Enterococci*, *Streptococci* and anaerobic bacteria in culture from drained intra-abdominal abscesses.

These data confirm previous studies on types and species of bacteria in intra-abdominal abscesses in CD and cDC, in which *E. coli*, *Enterococci*, *Streptococci* and anaerobic

Table 2. Comparison of the Crohn's disease and diverticulitis coli groups after abscess drainage and microbiological profile of isolates following culture

	Crohn's disease, n=18/44 (40.9%)	Diverticulitis coli, n=26/44 (59.1%)	Univariate analysis, (p)
After drainage*			
Culture and sensitivity performed	17 (94.4)	26 (100)	ns
Gram-positive only	2/17 (11.8)	3 (11.5)	ns
Gram-negative only	1/17 (5.9)	9 (34.6)	0.029
Mixed Gram-positive and negative	14/17 (82.4)	14 (53.8)	ns
E. coli	10 (55.6)	18 (69.2)	ns
Klebsiella pneumoniae	6 (33.3)	1 (3.8)	0.009
Streptococcus	8 (44.4)	12 (46.2)	ns
Staphylococcus	2 (11.1)	0 (0)	ns
Enterococcus	8 (44.4)	11 (42.3)	ns
Bacteroides	2 (11.1)	2 (7.7)	ns
Anaerobic bacteria	5 (27.8)	13 (50)	ns
Haemophilus	1 (5.6)	0 (0)	ns
Other bacteria	8 (44.4)	11 (42.3)	ns
Hemoglobin level, median (IQR), (g/dL)	7.1 (6.4-8.5)	7.05 (6.275-7.65)	ns
Albumin level, median (IQR),	29 (27-37.5)	27 (23.5-30.5)	ns
Antibiotics coverage after drainage	17 (94.4)	26 (100)	ns
Recurrence of abscess	6 (33.3)	0 (0)	0.019

*All results are given as n (%) unless otherwise stated. IQR: Interquartile range, ns: Not significant

bacteria were reported to be the predominant pathogens.[1,10] These findings were not surprising, as the origin of all these infections are the gastrointestinal flora. In addition, both groups of patients showed significant number of positive cultures for ESBL-producing organisms. probably due to bacterial resistance as a result of wide antibiotic coverage used in the treatment regimen for both conditions.[15] However, patients with CD and using immunosuppressants were more likely to have an intra-abdominal infection caused by ESBL-producing bacteria.[5] Immunosuppressive therapy was also associated with a markedly increased risk for development of intra-abdominal abscess in patients with CD.[16]

There was a significant difference in microbiological profile between the groups of patients in terms of *Klebsiella pneumoniae* culture, which was significantly more prevalent in the CD group. There is a general consensus that CD develops as the result of immune-mediated tissue damage triggered by infections with intestinal microbial agents. Based on the results of existing microbiological, molecular, and immunological studies, *Klebsiella pneumoniae* seems to have a key role in the initiation and perpetuation of the pathological damage involving the gut and joint tissues in patients with CD.[17] Abscess recurrence after drainage was also more commonly reported in CD, which again is expected due to the chronic inflammatory nature of CD in comparison to cDC.

Use of broad-spectrum antibiotics with coverage for Gram-positive, Gram-negative and anaerobic bacteria is mandatory for the treatment of cDC, that is diverticulitis with perforation and/or abscess. This type of antibiotherapy may be part of management in patients with CD, but our results suggest anti-*Klebsiella pneumoniae* antimicrobial agents, such as rifampicin, might be added to the treatment regimen.[17]

The primary limitation of this study was that it involved data from a single tertiary center, which may introduce referral bias and raises concerns of generalizability. Patients from referral centers often have more severe disease resulting in more frequent health care encounters, hospitalizations, surgeries, and use of immunosuppressive drugs and antibiotics, all factors which may affect the types of bacteria implicated in abscesses formed in these patients. Another important limitation was the small sample size and lack of

Table 3. Comparison of surgery and post-operative complications in the Crohn's disease and diverticulitis coli groups

	Crohn's disease n=18 (40.9)	Diverticulitis coli, n=26 (59.1)	Univariate analysis, (p)
After surgery			
Urgency (elective)	9/14 (64.3)	4/5 (80%)	ns
Resection	14/14 (100)	4 (15.4)	<0.001
Resection (small bowel)	1/14 (7.1)	0 (0)	ns
Resection (ileo-colic)	5/14 (35.7)	1 (3.8)	0.007
Resection (colectomy)	1/14 (7.1)	3 (11.5)	ns
Resection (sigmoid)	0/14 (0)	1 (3.8)	ns
Resection (combination)	7/14 (50)	0 (0)	ns
Abscess at time of surgery	7/14 (50)	4 (15.4)	0.019
Fistula	10/14 (71.4)	2 (7.7)	<0.001
Ileus, all	3/14 (21.4)	1 (3.8)	ns
Post-op ileus grade 1	1/14 (7.1)	1 (3.8)	ns
Post-op ileus grade 2	2/14 (14.3)	0 (0)	0.048
Post-op ileus grade 3b	0/14 (0)	1 (3.8)	ns
IASC, all	4/14 (28.6)	1 (3.8)	0.024
IASC grade 1	1/14 (7.1)	0 (0)	ns
IASC grade 2	1/14 (7.1)	0 (0)	ns
IASC grade 3a	1/14 (7.1)	0 (0)	ns
IASC grade 3b	1/14 (7.1)	1 (3.8)	ns
Deep SSI overall	0/14 (0)	1 (3.8)	ns
Deep SSI grade 3b	0/14 (0)	1 (3.8)	ns
SSI, all	0/14 (0)	2 (7.7)	ns
SSI grade 1	0/14 (0)	1 (3.8)	ns
SSI grade 3b	0/14 (0)	1 (3.8)	ns
Sepsis, all	3/14 (21.4)	1 (3.8)	ns
Sepsis grade 1	1/14 (7.1)	0 (0)	ns
Sepsis grade 2	2/14 (14.3)	0 (0)	0.048
Sepsis grade 3b	0/14 (0)	1 (3.8)	ns
Stoma, all	4/18 (22.2)	2 (7.7)	ns
End ileo-stomi	2/18 (11.1)	1 (3.8)	ns
End colostomi	2/18 (11.1)	1 (3.8)	ns
Complication rate	4/14 (28.6)	4 (15.4)	ns
LOS binary (<8 days)	11/18 (61.1)	25 (96.2)	0.003
Post-op re-admission	4/18 (22.2)	3 (11.5)	ns
Re-operation	4/18 (28.6)	2 (7.7)	ns

All results are given as n (%). ns: Not significant, SSI: Surgical site infection

information regarding other types of bacteria, fungi and antibiotic sensitivity and resistance. Future large prospective studies are needed to explore the microbiological profile of abscess-dwelling organisms in CD and cDC patients.

Conclusion

Mixed Gram-positive and negative bacteria with *Escherichia coli* predominance were the most common bacteria culture in both groups. One notable finding was that *Klebsiella pneumoniae* was more commonly found in cultures from intra-abdominal abscesses drained from patients with CD compared to cultures of intra-abdominal abscess in patients with cDC. This suggests that a trial of adding a *Klebsiella*-specific antimicrobial agent to the antibiotic regimen used in these patients may be worthwhile.

Ethics

Ethics Committee Approval: However, ethical approval to collect data was obtained from the Danish Agency (approval number: STPS 3-3013-3045/1).

Informed Consent: Informed consent from individual patients was not deemed necessary because of the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.F.A.R., H.A., A.E.H., Concept: R.F.A.R., H.A., A.E.H., Design: R.F.A.R., H.A., A.E.H., Data Collection or Processing: R.F.A.R., H.A., A.E.H., Analysis or Interpretation: R.F.A.R., H.A., A.E.H., Literature Search: R.F.A.R., H.A., A.E.H., Writing: R.F.A.R., H.A., A.E.H., OpenSourceResearch is an international organization with a special focus on implementing information technologies and artificial intelligence in clinical research. The manuscript will be background material for other studies that the organization is planning to conduct, as shown on its website: https://www.osrc.network.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support

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DOI: 10.4274/tjcd.galenos.2022.2022-4-1
Turk J Colorectal Dis 2022;32:258-259

LETTER TO THE EDITOR

Can Artificial Intelligence be as Effective in the Treatment of Anal Fistula as in Colorectal Surgery?

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Keywords: Artificial Intelligence, proctology, surgery

Dear Editor,

I read with interest the study entitled "Artificial Intelligence in Pre-operative Assessment of Patients in Colorectal Surgery" by Ng et al.[1] The number of artificial intelligence-based studies in the field of colorectal surgery has been increasing in recent years. The size, number, location of polyps detected in preoperative colonoscopic examinations, laboratory findings of the patient and abdominal imaging were evaluated together with the effect of artificial intelligence (AI).[2] With these data, studies have been conducted to predict whether postoperative complications (surgical site infection, anastomotic leakage, etc.), local recurrence or metastasis will develop in patients, and the length of disease-free survival in patients.[2,3] However, AI-based studies are very limited in terms of anal fistula (AF) surgery. AF is defined as a pathological epithelial pathway that connects the perianal surface with the anal canal or rectum.[4] AF, which is often considered the chronic stage of a perianal abscess, is a disease that may reduce the quality of life of affected patients.[5] Fistulectomy, seton or hybrid seton placement, fistulotomy, use of bioabsorbable materials such as an AF plug, platelet-rich plasma or fibrin glue, flap surgery, ligation of intersphincteric fistula, video-assisted AF treatment, and AF laser closure are the different methods which are generally used in the treatment of AF.[6-8] Despite improvements in imaging and technological methods, there is no definitive treatment method for this chronic disease, which can recur. Previous studies have shown that multiple fistula tract, fistula type (such as high transsphincteric or horseshoe fistula), poor drainage, incorrect seton application, incorrect preoperative fistula mapping, gender, obesity, smoking, and diabetes mellitus play a role in the recurrence of AF.[9,10] There are imaging-weighted, studies including modalities such as magnetic resonance imaging 3D modeling, endoanal ultrasonography, and three-dimensional endoanal ultrasound which have investigated the utility of these modalities in the correct preoperative diagnosis of AF.[3,5] However, there is no effective laboratory, imaging, or predictive tool or method to predict which patients will develop postoperative complications (surgical site infection, perineal sepsis, fecal incontinence) and relapse during follow-up in patients operated for AF.[9,10] An AI-based study, combining preoperative imaging, laboratory and patient risk factors in those who will undergo surgery for AF, with the pre-operative modeling to be created, have the potential to provide a predictor of postoperative complications, an estimated recurrence, and surgical recovery rate, as in the AI-based studies in colorectal surgery. By specifying an estimated surgical cure rate according to these preoperative prediction models and risk classification, patients can be informed about treatment by the surgeon. By analyzing these determined rates and the modifiable risk factors for known complications and recurrence for the patient groups in the postoperative or follow-up period, it would be possible to provide high-volume treatment of patients in centers experienced in the field of proctology. This may lead to a decrease in the complication and recurrence rate, with an attendant improvement in the quality of life of the patients and an increased chance of successful treatment.

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Received: 02.04.2022 **Accepted:** 10.05.2022

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Turkish Journal of Colorectal Disease published by Galenos Publishing House.

Peer-review: Internally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

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