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Chapter

Ambulatory Surgery for Perianal Disease

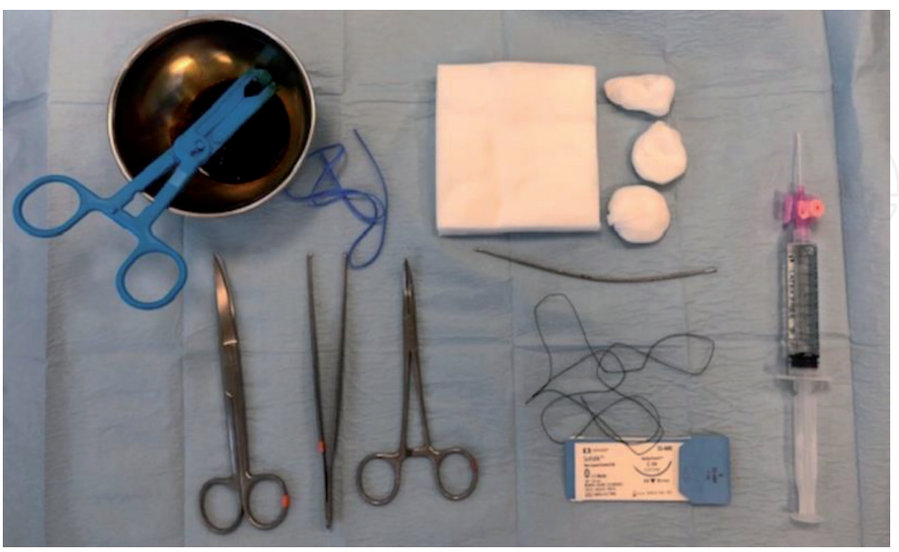
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Abstract

The gold standard in the diagnosis and treatment of proctological diseases is the exploration of the anal canal and distal rectum under anaesthesia (EUA), routinely performed as day case surgery. In selected cases it can be conducted as an outpatient exploration (OE) during a specialist surgical consultation. In the outpatient setting it is possible and safe to perform rubber band ligation, sclerotherapy and infrared coagulation for the treatment of haemorrhoidal disease, excision and incision of thrombosed external haemorrhoids, abscess drainage, setonage and fistulotomy also in case of perianal Crohn's disease, anal warts and skin tags removal. In terms of patients' satisfaction and success rate OE is comparable to EUA. All procedures can be performed under local anaesthesia. Pain control after the procedure is provided by oral pain killers.

Keywords: outpatients exploration, haemorrhoids, abscess and anal fistula, skin tags, anal warts, perianal Crohn's disease

1. Introduction



In the last decades, efforts and resources have been focused on developing health care services, resulting in newer facilities, greater resources of equipment and improved staffing, so that nowadays, surgical procedures can be carried out in large hospitals, providing both surgeons and patients safety and comfort. Consequently, not only major surgical interventions, but also minor procedures not requiring

preoperative preparation, special equipment, nor hospital stay, are performed in these hospitals, thus tremendously increasing both the costs of medical treatment and the length of waiting lists for hospitalisation [1].

Recently, attention has shifted to outpatient care aiming to ensure safe surgical and medical assistance at reduced costs, spared resources and in shorter waiting times, through both office-based procedures, which include minor operation performed under local anaesthesia, requiring a short time to discharge (ranging from minutes to hours after the procedure) and day-surgery interventions, encompassing surgical operations more complex than office-based procedures, but easier than major surgery requiring at least an overnight stay [1, 2].

During the last 30 years, government with the support of health insurance companies, medical groups and hospital associations focused their concerted efforts on the development of proctologic office-based procedures in order to reduce hospital costs and release beds for major surgeries. While almost 30–50% of all surgeries can be safely realised in outpatient sectors, this rate raises to 90% in anorectal operations [1]. In fact, even if complications rate following anorectal office-based procedures are extremely variable, the majority of them are minor complications and do not require hospitalisation, nor further surgical intervention.

Factors appealing to physicians include significant costs saving achieved avoiding the cost of admission, use of ward-based supplies, respiratory therapy, increased medication costs, and laboratory charges. Other advantages include lack of need to perform trichotomy, prophylactic antibiotic treatment, and enema administration. Moreover, also patients' satisfaction degree is increased thanks to the ease of scheduling cases, the advantage of avoiding a hospital stay and the early return home [1, 3].

However, to perform ambulatory anorectal surgery, a proper patient selection is necessary. Patient comorbidities as well as functional limitations should be assessed. The type and extent of surgery should be considered since not all anorectal procedures are minor [3].

2. Patient position

Patient positioning during proctologic assessment is important for patients and doctors. Patients undergoing both proctologic examination and ambulatory procedures are usually embarrassed because they lay naked on uncomfortable position, that can be:

- Sims' position, or left lateral position
- Lithotomy position with lifted legs, or gynaecological position
- Knee–chest position
- Knee–chest position with patients body bent forward, or jack-knife position

Even though the majority of individuals would favour Sims' position if they had the choice, they do not feel less embarrassed, thus preferring to let doctors free to choose the most suitable position to get reliable diagnoses of anal complaints [4]. The most performed positions are left lateral Sims' position and jack-knife position. The former is more comfortable for the patients and is easily and quickly achieved by the patient itself, allowing doctors to save time. This position is the most suitable to analyse haemorrhoids, but can be adapted to each proctologic disease. The

jack-knife position, on the contrary, requires a scissoring table able to lift the hip, letting head and legs down and takes more time to be obtained. The sloping position of the patient makes it difficult to analyse haemorrhoids, however as the buttocks fall to each side, and finger tips of both hands of the investigator are free, it provides a better field of view on anal and perianal surface in good lighting. Since sensitivity, specificity, and the predictive value of anal diagnoses in different proctological positions are unknown, and considering that none of different proctological positionings are most embarrassing to patients, doctors choice usually depends on their own customs and preferences.

3. Anaesthesia

Ambulatory anaesthesia has to provide a rapid onset analgesic effect, ensuring pain control and allowing an early discharge after the treatment is performed. The choice of the intra-operative anaesthetic management should consider patient's related factors, such as age, clinical condition and preference, surgeons' preference and procedural related factors, such as the kind of treatment and its length [5]. Anaesthesia for ambulatory procedures ranges from local to loco-regional anaesthesia, including pudendal nerve block and posterior perineal block; however, the easiest and shortest therapeutic sessions could even be performed without any anaesthesia, paying attention to the post-operative management, especially in terms of post-operative pain control.

Local anaesthesia is obtained through subcutaneous, intradermal or submucosal 1% lidocaine injections. Complications rate following local anaesthesia are extremely low, thus allowing to safely perform it in an outpatient setting. They include pain, which is usually due to the injected anaesthetic volume causing tissue distension, allergic reactions, and infections. Cardiovascular collapse is a rare but potentially life-threatening complication, requiring promptly intubation and vosoactive substances, steroids and myorelaxant drugs administration. Local anaesthesia is a quick and easy to perform anaesthesia, that allows performing minor ambulatory procedures, keeping pain under control.

Loco-regional anaesthesia includes pudendal nerve block and posterior perineal block. Pudendal nerve block, firstly described by Mueller in 1908, is performed with the patient in gynaecological position and is usually preceded by local anaesthesia administration if carried out in an ambulatory setting to an awake patient. After identifying the ischial spine, the needle punctures the skin transperineally, medial to the ischial tuberosity, 2–3 centimetres away from the anal margin. The needle is advanced in the posterolateral direction until the ischial spine and then rotated in the medial inferior direction to the ischial spine, passing through the sacrospinous ligament. After negative aspiration, the local anaesthetic, usually ropivacaina, is injected. Posterior perineal block, also known as Marti's technique, is performed with the patient in gynaecological or lithotomic position and preceded –in case of outpatient setting, by local anaesthesia administration, just as for pudendal nerve block. It involves infiltration of the inferior hemorrhoidal nerves, the posterior branch of the internal pudendal nerves, and the anococcygeal nerves and block of the inferior gluteal nerves and of perineal branches of minor nerves from the sacral plexus. It is achieved injecting ropivacaina or lidocaine 2 cm from the anal verge in the posterior commissure, 8 to 10 centimetres deeply into each ischiorectal fossa and superficially in the anterior commissure to achieve a complete infiltration of the perineal skin. Loco-regional anaesthesia is usually suitable to perform exploration under anaesthesia (EUA) of the anal canal in operative theatre and is associated to general anaesthesia to reach a complete multimodal pain control. In the ambulatory setting loco-regional techniques are unfrequently used, but

sometimes may be required to perform more invasive treatments. Complications are the same as for local anaesthesia, thus even if more invasive than local anaesthesia, these techniques may be safely performed for outpatient treatment.

4. Postoperative management

Postoperative management after proctologic office-based procedures mostly focuses on post-procedural pain control. It starts with anaesthesia performed during the procedure, so that the dose of analgesic drugs thereafter required is reduced and recovery time and return to daily living activities are shortened. After office-based procedures the pain can be controlled with oral pain killers administration. While the use of non-steroidal anti-inflammatory drugs (NSAIDs) alone is poorly effective to control severe pain and the use of narcotics alone may cause various side effects such as nausea, vomiting, dizziness and constipation (thus ultimately exacerbating pain symptoms), multimodal or balanced analgesia is the most effective treatment. It consists of administering in addition to narcotics, drugs with different mechanisms of actions and target pathways, including NSAIDs, acetaminophen, gabapentinoids, dexamethasone, alpha 2 agonists, NMDA receptor antagonists, and duloxetine. Acetaminophen and NSAIDs such as ketorolac and ibunoprofen successfully manage pain, resulting in an effective narcotic-sparing approach. The administration of pain killers drugs belonging to different classes results in increased analgesic effect and reduced drugs-induced side effects [5–7].

Analgesia may be provided by lidocaine and prilocaine ointment, too, ensuring supplemental pain relief and furtherly sparing narcotics.

Besides oral pain killers administration and local analgesic ointments application, anal burning and patient satisfaction may be improved by warn sitz baths. They are considered a worthwhile potential adjunct with little associated risk even if do not significantly reduce actual pain. Sitz baths or showers starting within 24 hours of the operation should be performed three times per day and after bowel movements for comfort and cleanliness [8].

Finally, to ensure pain control, it is fundamental to avoid constipation. Usually increased dietary fibre and fluid intake is sufficient to reduce postoperative constipation and pain upon defecation. However, even if dietary modification could guarantee stool softening, some physicians feel more comfortable recommending stimulant laxatives and stool softeners [5].

Postoperative management includes also follow-up instructions and written discharge instructions, improving patient satisfaction and decreasing the need for patients to seek additional medical attention, thus even reducing costs.

5. Haemorrhoids

Haemorrhoids are arteriovenous sinusoids, located in the sub-epithelial space, embedded in connective tissue and smooth muscle fibres, participating to 15–20% of the anal continence [9–12]. Haemorrhoidal disease (HD) is characterised by abnormally congested and downward displaced haemorrhoids [11–13].

HD is one of the most frequent medical and surgical diseases and the commonest proctologic disease, experienced by more than 50% of the population over 50 years old in various degree. Reports on HD prevalence rate widely varies (4,4–39%) [9, 14–16] because clinical manifestations may overlap with those of others anorectal diseases and may be wrongly attributed to other proctologic conditions; moreover many patients are asymptomatic, not requiring any treatment, while others self-diagnose and self-manage without referring to a specialist.

Increased intraabdominal pressure due to constipation and prolonged straining are the commonest conditions leading to haemorrhoidal disease because of obstruction of venous return, resulting in engorgement of the haemorrhoidal plexus [17]. Moreover, defecation of hard faecal material increases shearing force on the anal cushions.

Painless rectal bleeding is the commonest onset of haemorrhoidal disease, which may present as minimal bright red bleeding per rectum or hematochezia after bowel movements [18–20], or even severe acute lower gastrointestinal bleeding requiring hospitalisation and blood transfusion in the most severe cases [17, 19]. Although rectal bleeding is the commonest sign of HD, less frequent presentations may be prolapse (even determining difficult defecation), mucous discharge, swelling, soiling, perianal skin irritation, itching, feeling of a lump, and discomfort. Acute anal pain is rarely a presentation symptoms, appearing only in case of thrombosed external haemorrhoids.

Despite such a variable clinical onset, HD diagnosis is easily achieved collecting the medical history and performing a physical examination including abdominal examination, and a local examination with the patient on a left lateral position, including inspection of the perianal tissues, anorectal digital examination, and anoscopy. However, even if haemorrhoids are easily recognised, it is necessary to perform an endoscopic examination to exclude more severe colorectal conditions [17].

Once HD has been diagnosed, the chosen treatment depends on haemorrhoids location, on the severity of the disease and on an eventual previously administered treatment. Haemorrhoids location refers to the dentate line, allowing a distinction between internal (above the dentate line and covered with mucosa) and external haemorrhoids (below the dentate line and coated with squamous epithelium), which differ not only for their position, but also blood supply, drainage, epithelization and innervations [20]. In particular, internal haemorrhoids receive visceral innervations and are less sensitive to pain, thus amenable to office-based treatment performed without or with minimal anaesthesia. On the contrary, external haemorrhoids are more sensitive to pain receiving somatic innervations and, therefore, require surgical treatment performed under anaesthesia, thrombosed external haemorrhoids being the only exception.

Regarding to haemorrhoids severity, while no widely accepted classification exists for external haemorrhoids, the extent of internal haemorrhoids is usually assessed with the Goligher classification [10, 17, 21], depending on the degree to which they prolapse from the anal canal, so that bleeding without prolapse stands for grade I, haemorrhoidal piles prolapsing during straining correspond to grade II and III if they respectively reduce spontaneously or manually, and non reducible haemorrhoids are classified as grade IV. As the grade becomes worse, office-based procedures or surgery are required. In particular grade I treatment is usually conservative, grade II and III are amenable of office-based procedures, and grade IV haemorrhoids require surgery.

However, even if the chosen treatment depends on both haemorrhoids location and severity degree, usually the first therapeutic step is conservative and consists on dietary and lifestyle modifications, if necessary associated to topical or oral medication. Conservative treatment is successful for the majority of patients and could be periodically administered for as long as the patient wishes. If conservative treatment fails or the patient chooses a more invasive approach, office-based procedures or surgery are indicated [12, 14, 22].

5.1 Outpatient treatment

Outpatient treatment is recommended for symptomatic patients affected by grade I, II or III haemorrhoidal disease refractory to conservative treatment [12, 14, 22]. It encompasses rubber band ligation, sclerotherapy, infrared coagulation, excision of

thrombosed external haemorrhoids and few other techniques, not frequently used, such as electrotherapy, HET bipolar system, YAG or carbon dioxide laser and cryosurgery [23]. Their common aim is to slough haemorrhoidal tissue and generate a scar so that residual tissue is fixated to the underlying sub-mucosal tissue and anorectal muscular ring. Each procedure is adopted in specific circumstances, being rubber band ligation the most frequently performed with a wider therapeutic range. Even if they differ for technical features and indications, all the office-based procedures are characterised by faster recovery and less pain than surgical treatment [24]. Moreover, complication rate following outpatient treatment is extremely low, varying between post-procedural pain –usually easy-controlled by oral painkillers, to perineal sepsis –the most severe and life threatening condition, which is extremely rare.

Ambulatory procedures may require more than one treatment session and can be repeated until a complete response, if the patient agrees. In fact, since haemorrhoidal disease is not a severe clinical condition, it is up to the patient whether to manage them with a conservative approach or surgery. Choice of the outpatient treatment should take into consideration patient preferences, availability of procedures and fitness for further procedures. Only in case of coexisting internal haemorrhoids and additional anorectal pathologies surgery should be suggested as first line treatment [12, 14, 22].

5.2 Rubber band ligation

Rubber band ligation (RBL) is the most commonly performed office-based treatment, having the widest therapeutic range and the highest success rate. This procedure is recommended to treat almost all patients affected by symptomatic internal haemorrhoids refractory to conservative treatment, being contraindicated only in few cases:

- Grade IV internal haemorrhoids, since symptoms improvement is registered in less than 50% of cases
- Thrombosed haemorrhoids, characterised by excruciating pain that makes the procedure impossible to be performed
- Anticoagulant therapy or coagulation disorders, because of the increased risk of delayed haemorrhage [25]
- Immunodeficiency and diabetes mellitus, because of the increased risk of infection and sepsis [26]
- Concomitant anorectal diseases, for which surgery should be the first line treatment
- Pregnancy, usually determining a transient condition, requiring a conservative treatment

During the procedure, patients lay on left lateral position or semi-inverted jackknife position, being the former more comfortable for the patient. The anoscope is essential to perform the procedure, consisting on the positioning of a rubber band on the base of the haemorrhoid, at least 5 mm above the dentate line. The application of the elastic band causes immediate ischemic damage and 3 to 5 days delayed necrosis, leading to a localised sub-mucosal scarring that secures the mucosal layers to the underlying tissues. Rubber band application may be performed using both

forceps or suction devices [27, 28]. The former represents the traditional technique but requires two people to be performed: the operator and the assistance, whose role is to hold the anoscope. The latter includes both endoscopic suction devices and vacuum suction devices, which allow the operator to hold both the ligator and the anoscope, performing the procedure without any assistant.

Usually just one pile per session is treated, in order to reduce procedure-related risks. Multiple sessions should be performed in 4-week intervals, to allow a complete recovery from the previous treatment [29].

If the procedure is correctly performed, with the rubber band placed at least 5 mm above the dentate line, the patient has no pain, thus the procedure can safely be performed without any anaesthesia. Whenever the patient experiences pain, the band is wrongly placed below the dentate line, onto somatically innervated tissue, and should promptly be removed. Beside pain, that occurs in almost 8% of the procedures and is most frequently due to band misplacement [30], other extremely rare complications include [31–34]:

- Bleeding
- Thrombosis
- Skin tags
- Localised infection
- Liver abscesses
- Endocarditis
- Perineal sepsis
- Death

RBL is the most effective office-based procedures, improving symptoms in 93–100% of patients having grade II haemorrhoids and 78–84% of those having grade III haemorrhoids and reducing bleeding in up to 90% of patients [30, 35]. When compared to haemorrhoid artery ligation (HAL), it shows lower rates of bleeding, intra- and post-procedural pain, but higher risk of recurrences. The same has to be said comparing RBL to surgery: the former has a reduced complication risk compared to surgery, while the latter has lower recurrence rates [36].

5.3 Sclerotherapy

Sclerotherapy is the second most frequently performed outpatient procedure for haemorrhoidal disease. Since bleeding and infection risk is lower than after rubber band ligation, this procedure finds application whenever RBL cannot be performed, thus it is recommended for patients on anticoagulant therapy or coagulation disorders and in case of immunodeficiency or other pathological conditions increasing infective risks [35].

As for RBL, the procedure is performed through an anoscope, with the patient laying on left lateral position. Sclerosing solutions are injected into the submucosa plane above the dentate line, so that the treatment does not require any anaesthesia, and determine an intense inflammatory reaction that leads to scarring and adhesion of haemorrhoids to the underlying tissue just like after ligation with elastic bands.

The most frequently used solutions are aluminium potassium sulphate and tannic acid (ALTA, which seems to be the most effective) [37–39], 5% phenol in vegetable oil and 50% dextrose water.

Complications following sclerotherapy are even rarer than after RBL, considering patients major complain is painful intra-procedural injection, reported in almost 90% of cases, while post-procedural pain is experienced only by 25–50% of patients. Bleeding is uncommon and in the majority of cases is a self-limited condition following injection. The most frequent post-operative complication is mucosal necrosis, which is reported in less than 4% of patients and is usually caused by too superficial injections (not reaching the submucosal layer). Rare but major complications include impotence, fatal necrotising fasciitis, rectourethral fistulas, and rectal perforations, that are mostly ascribed to misplaced injections –both in non haemorrhoidal tissue or in the vascular system [40].

Sclerotherapy successfully manage haemorrhoidal bleeding, leading to an improvement in 100% of patients with second and third degree haemorrhoids [35, 39]. Moreover it leads to a complete resolution of symptoms in 88% of I degree haemorrhoids and 52% III degree haemorrhoids. However, even if much safer than RBL and despite its high success rate, recurrences are more frequent in patients undergoing sclerotherapy than ligation with elastic bands, thus the latter resulting as the preferred choice for both surgeons and patients whenever not contraindicated [41].

5.4 Infrared coagulation

Infrared coagulation (IC) is an outpatient procedure indicated for the treatment of refractory to conservative treatment grade I, II and III haemorrhoidal disease [12, 14]. In literature, data regarding IC treatment are extremely variable, ranging from studies showing similar results as for sclerotherapy, to papers underlying higher recurrence rates with fewer post-procedural complications and less intra-procedural discomfort. Thus, whether to use infrared coagulation or sclerotherapy depends on availability of procedures and surgeon preferences.

Infrared coagulation is also performed through an anoscope, with the patient laying in the same position as for the previous procedures. It consists of infrared light waves application on the haemorrhoidal tissue above the dentate line, which are converted into heat determining an immediate protein coagulation and necrosis, visible as 3 mm wide and 3 mm deep white spot on the mucosa. The treatment of each haemorrhoid cushion may require from three to five applications. As for the other office-based procedures, IC causes a scar fixating the redundant haemorrhoidal mucosa to the underlying tissues.

Complications following infrared coagulation include pain, which is the most frequent occurring in 16–100% of patients and bleeding, which ranges from 15 to 45% of cases [42, 43]. Moreover, many studies report high frequency of persistency and recurrence after the treatment: recurrence rate is estimated to be about 15% at three months.

Success rates reported by a recent meta-analysis widely range from 22 to 51 and 78%, when considering respectively grade III, II and I haemorrhoidal disease [35, 43].

5.5 Excision and incision of thrombosed external haemorrhoids

Haemorrhoidal excision is a procedure that can be performed both in an office-based setting and in the operating theatre. It is the only office-based procedure

suitable for the treatment of external haemorrhoids, which are localised below the dentate line, have somatic innervation and thus are more sensitive to pain, making surgery performed in the operating theatre the best therapeutic option.

Thrombosed external haemorrhoids belong to the so called anorectal emergencies. They occur with an acutely painful purplish or blue mass in the perianal area that gradually reduces after the first couple of days; bleeding may present in case the high pressure within the thrombus causes overlying skin erosion. It is important to differentiate this pathologic condition from complicated internal haemorrhoids and anal pigmented melanoma, whose onset in similar being characterised by perianal pain. External haemorrhoids are covered with anoderm and usually suddenly appear, while internal haemorrhoids are covered with mucosa and anal pigmented melanoma has a long story of pigmented skin lesion [44].

Excision of the thrombosed external haemorrhoids is indicated for patients experiencing persistent pain from 72 hours or less, providing immediate relief [45]. After 48 to 72 hours, the thrombus organises and contracts, diminishing symptoms so that a conservative management can be proposed, obviating the need for surgical management. Surgical treatment for thrombosed external haemorrhoids may be required also in case of residual skin tags resulting from the healing process of a small ulcer following a spontaneous evacuation of a thrombosed haemorrhoid. However, residual skin tags rarely cause enough symptoms to warrant its removal; only in case of large skin tags determining skin irritation, itching, pain, or inability to keep proper hygiene, excision can be beneficial.

The office-based procedure to treat thrombosed external haemorrhoids include excision and incision. The former can be performed in the operating room as well as in an appropriately equipped office. After the administration of both local anaesthesia and anal block, the excision of a thrombosed haemorrhoid is performed by making an elliptical incision in the overlying skin. A careful dissection of the haemorrhoid from the superficial fibres of the anal sphincter is carried out, trying to avoid injury. Thereafter skin edges can be left open allowing drainage or reapproximated with absorbable sutures [46]. Topical antibiotic ointments are not routinely applied as infections are rare in this well-vascularized sites.

Inexperienced physicians, unable to perform haemorrhoids excision, can manage this anorectal emergency with a simple incision of the overlying skin, allowing evacuation of thrombus, thus producing immediate relief of pain.

However, incision and evacuation of the clot is associated with a 30% risk of reaccumulation and thrombosis, which may disseminate to adjacent hemorrhoidal columns [47], thus this technique is not recommended and whenever performed requires a follow-up within the next 24 to 48 hours for surgical evaluation. On the contrary, recurrence rate for a completely excised thrombosed hemorrhoid is lower (5–19%) [48, 49].

If surgery is not feasible, conservative management would be offered including anti-inflammatory analgesics, warm sitz bath, reducing activity and avoiding constipation. Education and reassurance about this condition and its benign nature would be beneficial to the patient.

6. Abscess and anal fistula

Abscesses and anal fistulas are common anorectal problems, representing two different phases of the same infectious process. Perianal and perirectal abscesses

are acute infections, resulting in pus collection, mostly due to non-specific cryptoglandular obstruction [50]. Anorectal fistulas represent the chronic evolution of a suppurative process, characterised by an epithelised tract connecting two epithelised surfaces, in particular anal or rectal mucosa to the perianal skin or perineum [51, 52].

Estimated anal abscess incidence is about 2 cases per 10,000 population per year [53, 54], leading to fistula formation in about 25% of patients. Fistulas may present de novo, but in about 30–50% of patients, they follow a previous anorectal abscess. Both anal abscesses and fistulas affect men twice more than women, having a mean age of presentation of 40 years (ranging from 20 to 60 years). However, since most patients attribute proctologic symptoms to haemorrhoidal disease without referring to a specialist, abscesses and fistulas real incidence is unknown.

As previously said, both anal abscesses and fistulas usually originate from obstructed anal crypt glands. Less frequently they can be caused by inflammatory bowel disease (mainly Crohn's disease), infection such as actinomycosis, tuberculosis and lymphogranuloma venereum, human immunodeficiency virus, trauma (both in case of iatrogenic injuries and foreign rectal bodies), surgery, malignancy and irradiation [50, 55].

The commonest onset of a perianal abscess is constant severe pain, usually not related to bowel movements, that can be associated to general symptoms such as fever or generalised malaise [52]. On the contrary, intermittent perianal pain exacerbated by bowel movements and chronic purulent drainage are typical manifestations of fistulas [56].

On physical examination, abscesses present as erythematous, tender and fluctuant masses; purulent drainage, either from the overlying skin or from the rectum, can be present if the abscess has begun to spontaneously drain [52]. On the contrary, the presence of an external opening draining pus and a palpable cord leading from the detected external orifice to an internal orifice, are the most common findings in case of anal fistula [56].

Although collecting the medical history and performing a physical examination allow to detect the majority of abscesses and fistulas, sometimes patients may not have any physical finding on examination, and further instrumental exams may be required. Local examination may result difficult in case of deep abscesses, not appreciable on external examination nor by digitorectal examination, and in case of incomplete or blind-ended fistulas, lacking of the external orifice. Moreover, symptoms of both conditions may overlap with the clinical manifestations of other proctologic diseases. In these cases and in case of complex or recurrent fistulas, imaging is necessary [57, 58]. The most commonly performed imaging studies are magnetic resonance imaging (MRI), which is the gold standard imaging technique, and endosonography (EUS), having a specificity of 69% and 43% respectively, and the same sensitivity of 87% [58–60]. Instrumental investigation gives important information about abscess localisation, fistula anatomy and integrity of the sphincter muscles, allowing to establish the proper treatment.

In case of anal abscesses, the required treatment is always a prompt drainage, considering that all undrained abscess can expand toward adjacent spaces or progress to a systemic infection [56, 57]. Surgical approach may vary depending on imaging findings, that allow to classify an abscess as follow:

- Simple anorectal abscess, or perianal abscess
- Complex anorectal abscess, including:

- Ischiorectal abscess, which extended through the external anal sphincter into the ischiorectal space
- Intersphincteric abscess, located in the intersphincteric groove
- Supraelevator abscess, reaching the supralevator space and originating from cryptoglandular infection or pelvic inflammatory processes
- Horseshoe abscess, rising posteriorly to the anal canal and extending to the ischiorectal space

According to this classification, perianal abscesses treatment can be safely performed in an outpatient setting, while in case of complex, large or deep abscesses, drainage should be performed in the operating room, under general anaesthesia, sedation or local anaesthesia [61].

Anorectal fistula management is quite more difficult, considering the chosen surgical treatment depends on the relation between the fistula tract and the external anal sphincter, and on the amount of the sphincter complex involved with the fistulous tract. According to Parks' classification, firstly described in 1976, four different types of anal fistula can be identified based on the relationship between the primary track and the sphincter [62]:

- Parks type 1, intersphincteric fistula (45%), which extend between internal and external sphincter
- Parks type 2, transsphinteric fistula (30%), passing through internal and external sphincter, reaching perineum
- Parks type 3, sovrasphincteric fistula (20%), which encircles both internal and external sphincters, reaching the ischiorectal fossa
- Parks type 4, extrasphincteric fistula (3%), which encompasses the entire sphincter apparatus, including the levators, reaching the skin overlying the buttock; this fistula usually does not come from a cryptoglandular abscess
- Superficial, not involving any sphincter muscle (not included in the original Parks classification)

A fistula can also be categorised as simple or complex. The former includes those with an intersphincteric or low transsphincteric track that involves less than 30% of the sphincter complex. A fistula in the presence of inflammatory bowel disease, malignancy, incontinence, chronic diarrhoea or previous irradiation should be considered complex as well as those with an anterior track in a female patient [63]. In some complex cases, a staged surgical procedure will be required.

Since perianal infection sequelae range from minor pain and social embarrassment due to smelly purulent drainage, to life-threatening sepsis, once a diagnosis is established, surgery is the mainstay of the treatment, aiming to resolve local infection, remove fistulous tracts, avoid recurrences and preserve sphincteric function.

6.1 Abscess drainage



Abscess incision and drainage is a procedure that can be performed either under local anaesthesia, in an ambulatory setting, whenever the pus collection is small and superficial, either under general anaesthesia, sedation or local anaesthesia in the operating room, in case of more complex, larger or deeper abscesses [56, 57]. In these cases an office-based treatment can be performed only in referral centres if carried out by expert surgeons.

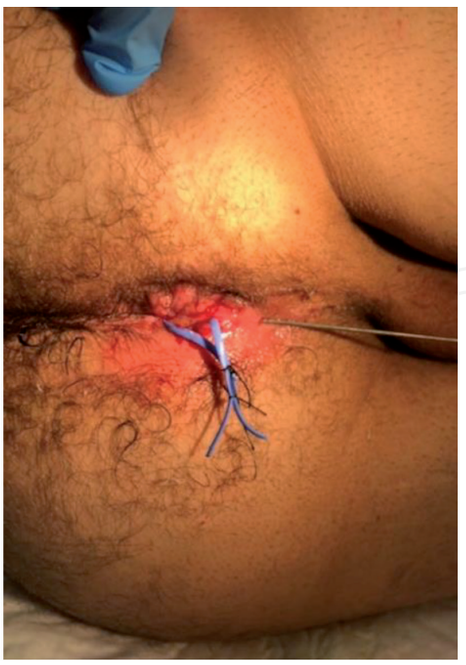
Incision should be performed as close as possible to the anal verge minimising the length of a potential fistula while still providing adequate drainage of the collection. As 30–70% of abscesses present with a concomitant fistula, surgeons question whether to perform or not a primary fistulotomy with the abscess drainage [64–67]. Data regarding this argument show primary fistulotomy reduces the risk of recurrence and persistence of the disease, but increase sphincter damage risk even leading to faecal incontinence [56, 57, 68]. Thus, primary fistulotomy is recommended only in case of simple anal fistula or high recurrence risk.

While perianal abscesses (simple abscesses) may be treated in an ambulatory setting, complex abscesses usually require an operating theatre, except for small intersphincteric abscesses, that can be managed without requiring an exploration under anaesthesia (EUA).

Regardless of the surgical setting, a course of empiric antibiotics is strongly recommended for all patients who went through incision and drainage of an anorectal abscess, in order to reduce the rate of fistula formation. Recommended drugs are amoxicillin-clavulanate or a combination of ciprofloxacin and metronidazole, administered for a four- to five-day course [69]. However, even if this treatment reduces fistula recurrence rate, it does not affect abscess recurrence rate [70].

6.2 Setonage and fistulotomy





Setonage and fistulotomy represent the gold standard for the treatment of anorectal fistulas and can be performed both in an outpatient setting and in an operating room, depending on fistula anatomical features. The placement of a seton can be considered when the internal opening is identifiable. Fistulotomy can be carried out with a simultaneous drainage of the abscess in case of a simple fistula, or can be performed as a second stage procedure 4–8 weeks after drainage [56, 57].

Fistulotomy is performed with the patient laying on a left lateral position. After a probe is inserted into the external opening and gently passed along the fistula tract to the internal opening, an incision is made over the entire length of the fistula using the probe as a guide. The tract is then gently curetted and is left opened to heal for second-intention healing or marsupialised to promote healing, depending on surgeons preference. The most critical step in this procedure is to identify and curette the internal opening to reduce the risk of recurrence, since concomitant induration due to inflammation may obscure the internal opening. Hydrogen peroxide injected through the external orifice may help to identify the internal opening [66], while overzealous attempts with a fistula probe should be discouraged as they can cause iatrogenic damage [71].

The most concerning potential complication of a fistulotomy is incontinence (either to solid faeces or liquid faeces or gas) from procedure-related damageto the external anal sphincter. The reported rates of incontinence are highly variable, ranging from 0 to 82% [72, 73], with an increased risk if the fistulotomy is performed at the time of the drainage of an acute abscess [74]. Nevertheless, when fistulotomy is used forsimple anal fistulas in properly selected patients, the risk of faecal incontinence is minimal or none [75, 76].

This treatment is indicated to manage simple fistulas, thus superficial fistulas, intersphincteric fistulas and low transsphincteric fistulas, involving less than 30% of the sphincter complex. For these fistula it is an effective treatment with a high success rate ranging from 79 to 100% [77–79] and low recurrence rates [66, 72, 80, 81].

In females and in patients with preoperative impairment of continence, a high or recurrent fistula, previous fistula surgery or Crohn's disease, any division of the

sphincter should be undertaken with caution and by an experienced surgeon [82]. The location of the internal opening per se, whether high or low in the anal canal, should not be used as a guide to "safe fistulotomy".

As fistulotomy, also the insertion of a seton through the fistula track is performed with the patient laying on a left lateral position and requires fistula track probing. Once the seton lays through the fistula track it can be used in different ways. A loose seton purpose is to facilitate drainage preventing an acute exacerbation of abscess formation and to allow healing of any secondary tracts, allowing local assessment some weeks later [57, 83]. A cutting seton purpose is to allow a gradual division of the sphincter, thank to a progressive tightening [57, 84]. Recently reported data of patients undergoing fistulotomy with a cutting seton tightened every 6–8 weeks, reported healing rates over 90% with only minor disturbances in anal sphincter function in 4% of patients [85–87].

Complex fistula treatment, including ligation of intersphincteric fistula tract (LIFT) [88, 89], advancement flap [90, 91], diversion, proctectomy and modified Haley procedure, cannot be performed in an office-based setting.

7. Perianal Crohn's disease

Crohn's disease (CD) is an idiopathic, incurable chronic inflammatory disease of the GI tract [92–95], associated in more than 30% of cases to symptoms of perianal disease (PAD) [96–98]. The risk of developing PAD is consistent with the time from the diagnosis of CD, from 20% after ten years and up to 30% after twenty years. However, PAD is far more common in patients with colon (41%) and rectum (90%) localization and less in patients with ileal disease (12%) [99–102]. Early diagnosis and correct treatment are crucial to allow patients to promptly start medical treatments with antitumor necrosis factor (tnf) which is considered the cornerstone of treatment, offering the best long-term control of PAD [103–116].

The gold standard to assess symptomatic perianal disease (PAD) in CD patients is the exploration of the anal canal and distal rectum under anaesthesia (EUA) [117–122]. EUA usually allows a correct diagnosis of fistulous tracts, a classification of the fistula, and an appropriate treatment of the PAD at the same time. In tertiary centres, PAD treatment can be performed also in an outpatient setting by expert surgeons. Whether to perform an EUA or an outpatient exploration (OE) depends on the anatomy, the type of fistula, and finally, the surgeon's expertise [123–129]. Moreover, active proctitis control must be achieved whenever possible prior to any surgical treatment. Treatment strategy and procedures are different in an acute or in an elective setting; in acute management, the main aim is sepsis control: incision and drainage of every abscess are strongly advised, while placement of a loose seton should be considered only if the fistulous tract can be promptly and easily identified [120]. In an elective setting, an exploration of the anal canal and distal rectum under anaesthesia is recommended and, in case of complex fistula, even in the presence of proctitis, a loose, draining seton could be passed if the internal and external orifices of the fistulous tract are found. A fistulotomy or fistulectomy can be safely considered for simple posterior fistulas [133].

Perianal fistulas in CD may be simple or complex according to the American Gastroenterological Association (AGA) [130–133]. Simple fistulas have a high healing rate, while complex fistulas are difficult to treat and show a poor healing rate and increased rate of relapse.

The aim of the surgical treatment of PAD in CD patients should be symptoms or complication control, allowing patients to pursue a timely medical therapy, in a multidisciplinary management. In the presence of a symptomatic perianal fistula, an optimal result can be considered to avoid sepsis, allowing for a good drainage

before thinking to the complete healing of the fistula and finally preventing the recurrence and preserving the continence of the anal sphincter. It is essential to ensure timely treatment, because perianal fistulas significantly impair the quality of life of the patients, to avoid the potentially disastrous consequences such as those of an undrained sepsis or ramification of the fistulous tracts [134–139]. Only the patients with symptomatic Crohn's anal fistula should undergo a surgical treatment. The gold standard treatment for symptomatic perianal disease in CD patients is conducted during the EUA. Most of the series available in literature refer to day surgery or overnight admission. Unfortunately, a timely treatment is not always possible and this, as said, may well represent a relevant clinical issue.

According to the Association of Coloproctology of Great Britain and Ireland consensus conference on surgical management of fistulating perianal Crohn's disease, experienced surgeons should always try to place a seton when the fistulous tract is readily identifiable and this should be possible most of the times in "skilled hands". Compliance of patients to the procedure was high and, from a surgical point of view, the OE was nice to perform without difficulties or trouble in all cases.

This procedure should be offered in a high-volume center in which a multidisciplinary dedicated team is available. In selected cases, OE may be offered as a "bridge to surgery," able to faster solve critical clinical issues or palliate disabling symptoms with low morbidity and discomfort, also allowing patients to continue medical therapy. OE can be repeated, if necessary, in different occasion. From an economical point of view, the OE can definitively save logistics and money. The OE surely is a minimally invasive approach, with low morbidity and very low patient stress. OE could be a safe and effective procedure that can be proposed to the vast majority of patients with Crohn's fistulas. It is not recommended in nonexperienced hands and in high complex or rectovaginal fistulas (Hughes classification 1b, 1d or 2d, and 2e).

8. Anal warts



Anal warts, also known as condyloma acuminata, are growths of tissue localised in the area around and inside the anus, usually caused by human papillomavirus (HPV).

The Human Papilloma Virus (HPV) used to be thought as one of the most common sexually transmitted diseases (STds) [140]. The estimated incidence of HPV infection is high, with 14 million persons infected annually and 79 million persons with prevalent infection [141]. Its family (Papillomaviridae) consists of more than 120 viruses presenting a tropism toward either the cutaneous or mucosa epithelium, however the vast majority (90%) of anal warts are caused only by two low-risk HPV subtypes: 6 and 11 [142]. Further HPV-associated diseases include other mucocutaneous warts as well as cervical, anal, vaginal, vulvar, penile, and oropharyn-geal cancers.

Anogenital warts (AGWs) diagnosis is most often based on their clinical appearance, and tests for the presence of HPV are not recommended for their diagnosis. They firstly appear as tiny spots or growths, whose dimensions may rapidly increase even covering the anal area. Usually, they do not cause any pain or discomfort. Some patients may experience itching, bleeding, mucus discharge, or a feeling of a lump or mass in the area. Histologic examination of biopsy specimens can be performed to rule out intraepithelial or invasive squamous cell carcinomas (SCCs), which can coexist with or appear similar to AGWs.

Therapeutic options for the treatment of anal warts range from topical medical therapies to surgery. Many treatment modalities for anal warts are primarily focused on destroying or removing the warts locally rather than eliminating the infection [143]. There are several factors that influence the choice of treatment modality, such as location of the warts (all intra-anal or rectal warts should be managed by a specialist), number of lesions, patient's ability to apply prescribed creams or gels, patient's preference, cost of the treatment and patient's immunosuppression status.

Treatment plans can be classified either as patient self-administered modalities (for warts locat-ed on the perianal skin only) or treatment administered by a professional (for lesions in an intra-anal or rectal mucosa location).

Patient-applied treatment consists of topical medications includig podophyllin, trichloroacetic acid, bichloroacetic acid, sintecatechins and imiquimod or 5-fluorouracil that can be safely applied at home. Recurrence rates after topical medications widely range from 6.5–55%, being sinecatechins the most effective treatment with eradication rate similar to other topically applied treatments, but the lowest recurrence rate [144–146]. Moreover, patient-applied treatment side effects, which are similar for all the ointments and include redness, irritation or a burning sensation, are reported by only 1 out of 3 treated patients.

Following the center for disease control and prevention recommendations, treatments administered by a medical provider include 80–90% trichloroacetic acid (TCA) application, cryotherapy with liquid nitrogen or surgery/electrosurgery [147]. Just as for haemorrhoids, all of the procedures can be offered in an outpatient setting only to patients having small perianal warts, once the conservative treatment fails. Larger lesions require surgery performed in an operating theatre.

TCA has an erosive and chemically destructive activity; its application on AGWs burns and cauterises skin lesions. Its destructive activity may extend to nearby healthy skin, thus care must be taken during application. It is not recommended for intra-anal use. Success rates are satisfactory, ranging from 70 to 81% [148, 149], but recurrence rate is high: 36% [149].

Cryotherapy seems to be the best therapeutic. The treatment consist of freezing lesions using a liquid nitrogen cooling probe, which results in necrosis and further clearance of destroyed tissue. Complications can include the destruction of healthy skin, and ulcers or scar formation. Even if eradication and recurrence rates are similar to TCA (86% and 39% respectively) [148, 149], cryotherapy is usually preferred because it is cost effective, minimally invasive, painless and can be applied to intra-anal warts.

Surgical excision is the oldest approach, but for patients suffering from a giant condyloma (Buschke-Loewenstein tumour) it may be the treatment of choice [150, 151]. A more contemporary surgical approach, electrosurgery, is a very effective technique with a clearance rate of 94% [152] but can be painful and requires local or intravenous anaesthesia, thus cannot be performed in an ambulatory setting.

Whether specialist–applied treatment is performed in the operating room or in an ambulatory setting, it usually has satisfactory eradication rates, but also high recurrence rate, ranging from 25 to 40% [152] discouraging clinical use. Actually, all of these modalities are targeted to remove warts locally and do not destroy all the very small or subclinical lesions in the surrounding healthy-looking skin, thus increasing the risk of recurrence.

9. Skin tags



Anal skin tags are perianal skin excesses, resulting from repeated scarring, just as in case of healing from anal fissure or thrombosed external haemorrhoids, exacerbated by excess cleaning or rubbing. Affected patients are bothered by the skin excess, but usually do not complain about pain or bleeding.

Treatment includes the management of both the underlying cause and the skin lesion. The latter consists of skin tags excision easily performed as an office-based treatment, that should always follow the resolution of the underlying ano-rectal disease, to minimise the risk of recurrence.

Conflict of interest

The authors declare no conflict of interest.

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References

[1] Sobrado CW. Outpatient surgical proctology--past, present and future. Arq Gastroenterol. 2005;42(3):133-135. doi: 10.1590/s0004-28032005000300001

[2] Sibio S, Di Giorgio A, Campanelli M, Di Carlo S, Divizia A, Fiorani C, Scaramuzzo R, Arcudi C, Del Vecchio Blanco G, Biancone L, Sica G. Ambulatory Surgery for Perianal Crohn's Disease: Study of Feasibility. Gastroenterol Res Pract. 2018:5249087. doi: 10.1155/2018/5249087

[3] Ternent CA, Fleming F, Welton ML, Buie WD, Steele S, Rafferty J; American Society of Colon and Rectal Surgeons. Clinical Practice Guideline for Ambulatory Anorectal Surgery. Dis *Colon rectum*. 2015;58(10):915-922. doi: 10.1097/DCR.0000000000000451

[4] Gebbensleben O, Hilger Y, Rohde H. Patients' views of medical positioning for proctologic examination. Clin Exp Gastroenterol. 2009;2:133-138. doi: 10.2147/ceg.s8429

[5] Lee JH. Anesthesia for ambulatory surgery. Korean J Anesthesiol. 2017; 70(4):398-406. doi: 10.4097/kjae.2017.70.4.398

[6] Kehlet H. Postoperative opioid sparing to hasten recovery: what are the issues? Anesthesiology. 2005;102(6):1083-1085. doi: 10.1097/00000542-200506000-00004

[7] White PF. The changing role of non-opioid analgesic techniques in the management of postoperative pain. Anesth Analg. 2005;101(5 Suppl):S5-22. doi: 10.1213/01.ane.0000177099.28914.a7

[8] Tejirian T, Abbas MA. Sitz bath: where is the evidence? Scientific basis of a common practice. Dis *Colon rectum*. 2005;48(12):2336-2340. doi: 10.1007/s10350-005-0085-x

[9] Lohsiriwat V. Treatment of hemorrhoids: A coloproctologist's view. World J Gastroenterol. 2015;21(31):9245-9252. doi: 10.3748/wjg.v21.i31.9245

[10] Jacobs D. Clinical practice. Hemorrhoids. N Engl J Med. 2014;371(10):944-951. doi: 10.1056/NEJMcp1204188

[11] van Tol RR, Kimman ML, Melenhorst J, Stassen LPS, Dirksen CD, Breukink SO; Members of the Steering Group. European Society of Coloproctology Core Outcome Set for haemorrhoidal disease: an international Delphi study among healthcare professionals. Colorectal Dis. 2019;21(5):570-580. doi: 10.1111/codi.14553

[12] van Tol RR, Kleijnen J, Watson AJM, Jongen J, Altomare DF, Qvist N, Higuero T, Muris JWM, Breukink SO. European Society of ColoProctology: guideline for haemorrhoidal disease. Colorectal Dis. 2020;22(6):650-662. doi: 10.1111/codi.14975

[13] Rho M, Guida AM, Materazzo M, Don CP, Gazia C, Ivanikhin AM, Tognoni V, Venditti D. Ligasure Hemorrhoidectomy: Updates on Complications after an 18-Year Experience. Rev Recent Clin Trials. 2020. doi: 10.2174/1574887115999201006201926

[14] Gallo G, Martellucci J, Sturiale A, Clerico G, Milito G, Marino F, Cocorullo G, Giordano P, Mistrangelo M, Trompetto M. Consensus statement of the Italian society of colorectal surgery (SICCR): management and treatment of hemorrhoidal disease. Tech Coloproctol. 2020;24(2):145-164. doi: 10.1007/s10151-020-02149-1

[15] Gallo G., Sacco R., Sammarco G. (2018) Epidemiology of Hemorrhoidal Disease. In: Ratto C., Parello A., Litta F. (eds) Hemorrhoids. Coloproctology,

2020;22(6):650-662. doi: 10.1111/codi.14975

[16] Riss S, Weiser FA, Schwameis K, Riss T, Mittlböck M, Steiner G, Stift A. The prevalence of hemorrhoids in adults. Int J Colorectal Dis. 2012; 27(2):215-220. doi: 10.1007/s00384-011-1316-3

[17] Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. World J Gastroenterol. 2012;18(17):2009-17. doi: 10.3748/wjg.v18.i17.2009

[18] Trompetto M, Clerico G, Cocorullo GF, Giordano P, Marino F, Martellucci J, Milito G, Mistrangelo M, Ratto C. Evaluation and management of hemorrhoids: Italian society of colorectal surgery (SICCR) consensus statement. Tech Coloproctol. 2015;19(10):567-575. doi: 10.1007/s10151-015-1371-9

[19] Gralnek IM, Ron-Tal Fisher O, Holub JL, Eisen GM. The role of colonoscopy in evaluating hematochezia: a population-based study in a large consortium of endoscopy practices. Gastrointest Endosc. 2013;77(3):410-418. doi: 10.1016/j.gie.2012.10.025

[20] Newman J, Fitzgerald JE, Gupta S, von Roon AC, Sigurdsson HH, Allen-Mersh TG. Outcome predictors in acute surgical admissions for lower gastrointestinal bleeding. Colorectal Dis. 2012;14(8):1020-1026. doi: 10.1111/j.1463-1318.2011.02824.x

[21] Goligher JC, Leacock AG, Brossy JJ. The surgical anatomy of the anal canal. Br J Surg. 1955;43(177):51-61. doi: 10.1002/bjs.18004317707

[22] Davis BR, Lee-Kong SA, Migaly J, Feingold DL, Steele SR. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Hemorrhoids. Dis *Colon rectum*. 2018;61(3):284-292. doi: 10.1097/DCR.0000000000001030

[23] Marques CF, Nahas SC, Nahas CS, Sobrado CW Jr, Habr-Gama A, Kiss DR. Early results of the treatment of internal hemorrhoid disease by infrared coagulation and elastic banding: a prospective randomized cross-over trial. Tech Coloproctol. 2006;10(4):312-317. doi: 10.1007/s10151-006-0299-5

[24] Shanmugam V, Thaha MA, Rabindranath KS, Campbell KL, Steele RJ, Loudon MA. Rubber band ligation versus excisional haemorrhoidectomy for haemorrhoids. Cochrane Database Syst Rev. 2005;(3):CD005034. doi: 10.1002/14651858.CD005034

[25] Nelson RS, Ewing BM, Ternent C, Shashidharan M, Blatchford GJ, Thorson AG. Risk of late bleeding following hemorrhoidal banding in patients on antithrombotic prophylaxis. Am J Surg. 2008;196(6): 994-999; discussion 999. doi: 10.1016/j.amjsurg.2008.07.036

[26] Buchmann P, Seefeld U. Rubber band ligation for piles can be disastrous in HIV-positive patients. Int J Colorectal Dis. 1989;4(1):57-58. doi: 10.1007/BF01648552

[27] Wehrmann T, Riphaus A, Feinstein J, Stergiou N. Hemorrhoidal elastic band ligation with flexible videoendoscopes: a prospective, randomized comparison with the conventional technique that uses rigid proctoscopes. Gastrointest Endosc. 2004;60(2):191-195. doi: 10.1016/s0016-5107(04)01551-2

[28] Ramzisham AR, Sagap I, Nadeson S, Ali IM, Hasni MJ. Prospective randomized clinical trial on suction elastic band ligator versus forceps ligator in the treatment of haemorrhoids. Asian J Surg. 2005;28(4):241-245. doi: 10.1016/S1015-9584(09)60353-5

[29] Khubchandani IT. A randomized comparison of single and multiple rubber band ligations. Dis *Colon rectum*.

1983;26(11):705-708. doi: 10.1007/BF02554977

[30] Iyer VS, Shrier I, Gordon PH. Long-term outcome of rubber band ligation for symptomatic primary and recurrent internal hemorrhoids. Dis *Colon rectum*. 2004;47(8):1364-1370. doi: 10.1007/s10350-004-0591-2

[31] Beattie GC, Rao MM, Campbell WJ. Secondary haemorrhage after rubber band ligation of haemorrhoids in patients taking clopidogrel--a cautionary note. Ulster Med J. 2004;73(2):139-41. PMCID: PMC2475464

[32] Chau NG, Bhatia S, Raman M. Pylephlebitis and pyogenic liver abscesses: a complication of hemorrhoidal banding. Can J Gastroenterol. 2007;21(9):601-603. doi: 10.1155/2007/106946

[33] Tejirian T, Abbas MA. Bacterial endocarditis following rubber band ligation in a patient with a ventricular septal defect: report of a case and guideline analysis. Dis *Colon rectum*. 2006;49(12):1931-1933. doi: 10.1007/s10350-006-0769-x

[34] McCloud JM, Jameson JS, Scott AN. Life-threatening sepsis following treatment for haemorrhoids: a systematic review. Colorectal Dis. 2006;8(9):748-755. doi: 10.1111/j.1463-1318.2006.01028.x

[35] Cocorullo G, Tutino R, Falco N, Licari L, Orlando G, Fontana T, Raspanti C, Salamone G, Scerrino G, Gallo G, Trompetto M, Gulotta G. The non-surgical management for hemorrhoidal disease. A systematic review. G Chir. 2017;38(1):5-14. doi: 10.11138/gchir/2017.38.1.005

[36] Brown SR, Tiernan JP, Watson AJM, Biggs K, Shephard N, Wailoo AJ, Bradburn M, Alshreef A, Hind D; HubBLe Study team. Haemorrhoidal artery ligation versus rubber band ligation for the management of symptomatic second-degree and third-degree haemorrhoids (HubBLe): a multicentre, open-label, randomised controlled trial. Lancet. 2016;388(10042):356-364. doi: 10.1016/S0140-6736(16)30584-0

[37] Moser KH, Mosch C, Walgenbach M, Bussen DG, Kirsch J, Joos AK, Gliem P, Sauerland S. Efficacy and safety of sclerotherapy with polidocanol foam in comparison with fluid sclerosant in the treatment of first-grade haemorrhoidal disease: a randomised, controlled, single-blind, multicentre trial. Int J Colorectal Dis. 2013;28(10):1439-1447. doi: 10.1007/s00384-013-1729-2

[38] Yano T, Asano M, Tanaka S, Oda N, Matsuda Y. Prospective study comparing the new sclerotherapy and hemorrhoidectomy in terms of therapeutic outcomes at 4 years after the treatment. Surg Today. 2014;44(3):449-453. doi: 10.1007/s00595-013-0564-y

[39] Tsunoda A, Nakagi M, Kano N, Mizutani M, Yamaguchi K. Serum aluminum levels in dialysis patients after sclerotherapy of internal hemorrhoids with aluminum potassium sulfate and tannic acid. Surg Today. 2014;44(12):2314-2317. doi: 10.1007/s00595-014-0914-4

[40] Schulte T, Fändrich F, Kahlke V. Life-threatening rectal necrosis after injection sclerotherapy for haemorrhoids. Int J Colorectal Dis. 2008;23(7):725-726. doi: 10.1007/s00384-007-0402-z

[41] MacRae HM, McLeod RS. Comparison of hemorrhoidal treatments: a meta-analysis. Can J Surg. 1997;40(1):14-17. doi: 10.1007/BF02048023

[42] Gupta PJ. Infrared coagulation versus rubber band ligation in early stage hemorrhoids. Braz J Med Biol Res. 2003;36(10):1433-1439. doi: 10.1590/s0100-879x2003001000022

[43] Dimitroulopoulos D, Tsamakidis K, Xinopoulos D, Karaitianos I, Fotopoulou A, Paraskevas E. Prospective, randomized, controlled, observer-blinded trial of combined infrared photocoagulation and micronized purified flavonoid fraction versus each alone for the treatment of hemorrhoidal disease. Clin Ther. 2005;27(6):746-754. doi: 10.1016/j.clinthera.2005.06.016

[44] Lohsiriwat V. Anorectal emergencies. World J Gastroenterol. 2016;22(26):5867-5878. doi: 10.3748/wjg.v22.i26.5867

[45] Aigner F, Gruber H, Conrad F, Eder J, Wedel T, Zelger B, Engelhardt V, Lametschwandtner A, Wienert V, Böhler U, Margreiter R, Fritsch H. Revised morphology and hemodynamics of the anorectal vascular plexus: impact on the course of hemorrhoidal disease. Int J Colorectal Dis. 2009;24(1):105-113. doi: 10.1007/s00384-008-0572-3

[46] Grosz CR. A surgical treatment of thrombosed external hemorrhoids. Dis *Colon rectum*. 1990;33(3):249-250. doi: 10.1007/BF02134191

[47] Rivadeneira DE, Steele SR, Ternent C, Chalasani S, Buie WD, Rafferty JL; Standards Practice Task Force of The American Society of Colon and Rectal Surgeons. Practice parameters for the management of hemorrhoids (revised 2010). Dis *Colon rectum*. 2011;54(9):1059-1064. doi: 10.1097/DCR.0b013e318225513d

[48] Greenspon J, Williams SB, Young HA, Orkin BA. Thrombosed external hemorrhoids: outcome after conservative or surgical management. Dis *Colon rectum*. 2004;47(9):1493-1498. doi: 10.1007/s10350-004-0607-y.

[49] Jongen J, Bach S, Stübinger SH, Bock JU. Excision of thrombosed external hemorrhoid under local anesthesia: a retrospective evaluation of 340 patients. Dis *Colon rectum*. 2003;46(9):1226-1231. doi: 10.1007/s10350-004-6719-6

[50] PARKS AG. Pathogenesis and treatment of fistuila-in-ano. Br Med J. 1961;1(5224):463-469. doi: 10.1136/bmj.1.5224.463

[51] Gosselink MP, van Onkelen RS, Schouten WR. The cryptoglandular theory revisited. Colorectal Dis. 2015;17(12):1041-1043. doi: 10.1111/codi.13161

[52] Abcarian H. Anorectal infection: abscess-fistula. Clin Colon Rectal Surg. 2011;24(1):14-21. doi: 10.1055/s-0031-1272819

[53] Sneider EB, Maykel JA. Anal abscess and fistula. Gastroenterol Clin North Am. 2013;42(4):773-784. doi: 10.1016/j.gtc.2013.08.003

[54] Zanotti C, Martinez-Puente C, Pascual I, Pascual M, Herreros D, García-Olmo D. An assessment of the incidence of fistula-in-ano in four countries of the European Union. Int J Colorectal Dis. 2007;22(12):1459-1462. doi: 10.1007/s00384-007-0334-7

[55] Parés D. Pathogenesis and treatment of fistula in ano. Br J Surg. 2011;98(1):2-3. doi: 10.1002/bjs.7341

[56] Vogel JD, Johnson EK, Morris AM, Paquette IM, Saclarides TJ, Feingold DL, Steele SR. Clinical Practice Guideline for the Management of Anorectal Abscess, Fistula-in-Ano, and Rectovaginal Fistula. Dis *Colon rectum*. 2016;59(12):1117-1133. doi: 10.1097/DCR.0000000000000733.

[57] Amato A, Bottini C, De Nardi P, Giamundo P, Lauretta A, Realis Luc A, Tegon G, Nicholls RJ; Italian society of colorectal surgery. Evaluation and management of perianal abscess and anal fistula: a consensus statement developed by the Italian Society of Colorectal Surgery (SICCR). Tech

Coloproctol. 2015;19(10):595-606. doi: 10.1007/s10151-015-1365-7

[58] Siddiqui MR, Ashrafian H, Tozer P, Daulatzai N, Burling D, Hart A, Athanasiou T, Phillips RK. A diagnostic accuracy meta-analysis of endoanal ultrasound and MRI for perianal fistula assessment. Dis *Colon rectum*. 2012;55(5):576-585. doi: 10.1097/DCR.0b013e318249d26c

[59] Buchanan GN, Halligan S, Bartram CI, Williams AB, Tarroni D, Cohen CR. Clinical examination, endosonography, and MR imaging in preoperative assessment of fistula in ano: comparison with outcome-based reference standard. Radiology. 2004;233(3):674-681. doi: 10.1148/radiol.2333031724

[60] Pomerri F, Dodi G, Pintacuda G, Amadio L, Muzzio PC. Anal endosonography and fistulography for fistula-in-ano. Radiol Med. 2010;115(5):771-783. doi: 10.1007/s11547-010-0524-1

[61] Rizzo JA, Naig AL, Johnson EK. Anorectal abscess and fistula-in-ano: evidence-based management. Surg Clin North Am. 2010;90(1):45-68, Table of Contents. doi: 10.1016/j.suc.2009.10.001

[62] Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. Br J Surg. 1976;63(1):1-12. doi: 10.1002/bjs.1800630102

[63] Fazio VW. Complex anal fistulae. Gastroenterol Clin North Am. 1987;16(1):93-114. PMID: 3298058

[64] Schouten WR, van Vroonhoven TJ. Treatment of anorectal abscess with or without primary fistulectomy. Results of a prospective randomized trial. Dis *Colon rectum*. 1991;34(1):60-63. doi: 10.1007/BF02050209

[65] Tang CL, Chew SP, Seow-Choen F. Prospective randomized trial of drainage alone vs. drainage and fistulotomy for acute perianal abscesses with proven internal opening. Dis *Colon rectum*. 1996;39(12):1415-1417. doi: 10.1007/BF02054531

[66] Ho YH, Tan M, Chui CH, Leong A, Eu KW, Seow-Choen F. Randomized controlled trial of primary fistulotomy with drainage alone for perianal abscesses. Dis *Colon rectum*. 1997;40(12):1435-1438. doi: 10.1007/BF02070708

[67] Oliver I, Lacueva FJ, Pérez Vicente F, Arroyo A, Ferrer R, Cansado P, Candela F, Calpena R. Randomized clinical trial comparing simple drainage of anorectal abscess with and without fistula track treatment. Int J Colorectal Dis. 2003;18(2):107-110. doi: 10.1007/s00384-002-0429-0

[68] Malik AI, Nelson RL, Tou S. Incision and drainage of perianal abscess with or without treatment of anal fistula. Cochrane Database Syst Rev. 2010;(7):CD006827. doi: 10.1002/14651858.CD006827.pub2

[69] Sawyer RG, Claridge JA, Nathens AB, Rotstein OD, Duane TM, Evans HL, Cook CH, O'Neill PJ, Mazuski JE, Askari R, Wilson MA, Napolitano LM, Namias N, Miller PR, Dellinger EP, Watson CM, Coimbra R, Dent DL, Lowry SF, Cocanour CS, West MA, Banton KL, Cheadle WG, Lipsett PA, Guidry CA, Popovsky K; STOP-IT Trial Investigators. Trial of short-course antimicrobial therapy for intraabdominal infection. N Engl J Med. 2015;372(21):1996-2005. doi: 10.1056/NEJMoa1411162

[70] Mocanu V, Dang JT, Ladak F, Tian C, Wang H, Birch DW, Karmali S. Antibiotic use in prevention of anal fistulas following incision and drainage of anorectal abscesses: A systematic review and meta-analysis. Am J Surg. 2019;217(5):910-917. doi: 10.1016/j.amjsurg.2019.01.015

[71] de Groof EJ, Cabral VN, Buskens CJ, Morton DG, Hahnloser D, Bemelman WA; research committee of the European Society of Coloproctology. Systematic review of evidence and consensus on perianal fistula: an analysis of national and international guidelines. Colorectal Dis. 2016;18(4):O119–O134. doi: 10.1111/codi.13286

[72] Hammond TM, Knowles CH, Porrett T, Lunniss PJ. The Snug Seton: short and medium term results of slow fistulotomy for idiopathic anal fistulae. Colorectal Dis. 2006;8(4):328-337. doi: 10.1111/j.1463-1318.2005.00926.x

[73] Dziki A, Bartos M. Seton treatment of anal fistula: experience with a new modification. Eur J Surg. 1998;164(7):543-548. doi: 10.1080/110241598750005930

[74] Quah HM, Tang CL, Eu KW, Chan SY, Samuel M. Meta-analysis of randomized clinical trials comparing drainage alone vs primary sphincter-cutting procedures for anorectal abscess-fistula. Int J Colorectal Dis. 2006;21(6):602-609. doi: 10.1007/s00384-005-0060-y

[75] Hall JF, Bordeianou L, Hyman N, Read T, Bartus C, Schoetz D, Marcello PW. Outcomes after operations for anal fistula: results of a prospective, multicenter, regional study. Dis *Colon rectum*. 2014;57(11):1304-1308. doi: 10.1097/DCR.0000000000000216

[76] Abramowitz L, Soudan D, Souffran M, Bouchard D, Castinel A, Suduca JM, Staumont G, Devulder F, Pigot F, Ganansia R, Varastet M; Groupe de Recherche en Proctologie de la Société Nationale Française de Colo-Proctologie and the Club de Réflexion des Cabinets et Groupe d'Hépato-Gastroentérologie. The outcome of fistulotomy for anal fistula at 1 year: a prospective multicentre French study. Colorectal Dis. 2016;18(3):279-285. doi: 10.1111/codi.13121

[77] Davies M, Harris D, Lohana P, Chandra Sekaran TV, Morgan AR, Beynon J, Carr ND. The surgical management of fistula-in-ano in a specialist colorectal unit. Int J Colorectal Dis. 2008;23(9):833-838. doi: 10.1007/s00384-008-0444-x

[78] Westerterp M, Volkers NA, Poolman RW, van Tets WF. Anal fistulotomy between Skylla and Charybdis. Colorectal Dis. 2003;5(6):549-551. doi: 10.1046/j.1463-1318.2003.00459.x

[79] Ho KS, Tsang C, Seow-Choen F, Ho YH, Tang CL, Heah SM, Eu KW. Prospective randomised trial comparing ayurvedic cutting seton and fistulotomy for low fistula-in-ano. Tech Coloproctol. 2001;5(3):137-141. doi: 10.1007/s101510100015

[80] Christensen A, Nilas L, Christiansen J. Treatment of trans-sphincteric anal fistulas by the seton technique. Dis *Colon rectum*. 1986;29(7):454-455. doi: 10.1007/BF02561583

[81] van Koperen PJ, Wind J, Bemelman WA, Bakx R, Reitsma JB, Slors JF. Long-term functional outcome and risk factors for recurrence after surgical treatment for low and high perianal fistulas of cryptoglandular origin. Dis *Colon rectum*. 2008;51(10):1475-1481. doi: 10.1007/s10350-008-9354-9

[82] Jordán J, Roig JV, García-Armengol J, García-Granero E, Solana A, Lledó S. Risk factors for recurrence and incontinence after anal fistula surgery. Colorectal Dis. 2010;12(3):254-260. doi: 10.1111/j.1463-1318.2009.01806.x

[83] Kelly ME, Heneghan HM, McDermott FD, Nason GJ, Freeman C, Martin ST, Winter DC. The role of loose seton in the management of anal fistula: a multicenter study of 200 patients. Tech Coloproctol. 2014;18(10):915-919. doi: 10.1007/s10151-014-1186-0

[84] Williams JG, MacLeod CA, Rothenberger DA, Goldberg SM. Seton treatment of high anal fistulae. Br J Surg. 1991;78(10):1159-1161. doi: 10.1002/bjs.1800781004

[85] Patton V, Chen CM, Lubowski D. Long-term results of the cutting seton for high anal fistula. ANZ J Surg. 2015;85(10):720-727. doi: 10.1111/ans.13156

[86] Rosen DR, Kaiser AM. Definitive seton management for transsphincteric fistula-in-ano: harm or charm? Colorectal Dis. 2016;18(5):488-495. doi: 10.1111/codi.13120

[87] Ritchie RD, Sackier JM, Hodde JP. Incontinence rates after cutting seton treatment for anal fistula. Colorectal Dis. 2009;11(6):564-571. doi: 10.1111/j.1463-1318.2008.01713.x

[88] Rojanasakul A, Pattanaarun J, Sahakitrungruang C, Tantiphlachiva K. Total anal sphincter saving technique for fistula-in-ano; the ligation of intersphincteric fistula tract. J Med Assoc Thai. 2007;90(3):581-586

[89] Shanwani A, Nor AM, Amri N. Ligation of the intersphincteric fistula tract (LIFT): a sphincter-saving technique for fistula-in-ano. Dis *Colon rectum*. 2010;53(1):39-42. doi: 10.1007/DCR.0b013e3181c160c4

[90] Yellinek S, Krizzuk D, Moreno Djadou T, Lavy D, Wexner SD. Endorectal advancement flap for complex anal fistula: does flap configuration matter? Colorectal Dis. 2019;21(5):581-587. doi: 10.1111/codi.14564

[91] Podetta M, Scarpa CR, Zufferey G, Skala K, Ris F, Roche B, Buchs NC. Mucosal advancement flap for recurrent complex anal fistula: a repeatable procedure. Int J Colorectal Dis. 2019;34(1):197-200. doi: 10.1007/s00384-018-3155-y

[92] Lightner AL, Vogel JD, Carmichael JC, Keller DS, Shah SA, Mahadevan U, Kane SV, Paquette IM, Steele SR, Feingold DL. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surgical Management of Crohn's Disease. Dis *Colon rectum*. 2020;63(8):1028-1052. doi: 10.1097/DCR.0000000000001716

[93] Strong SA, Koltun WA, Hyman NH, Buie WD; Standards Practice Task Force of The American Society of Colon and Rectal Surgeons. Practice parameters for the surgical management of Crohn's disease. Dis *Colon rectum*. 2007;50(11):1735-1746. doi: 10.1007/s10350-007-9012-7

[94] Strong S, Steele SR, Boutrous M, Bordineau L, Chun J, Stewart DB, Vogel J, Rafferty JF; Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. Clinical Practice Guideline for the Surgical Management of Crohn's Disease. Dis *Colon rectum*. 2015;58(11):1021-1036. doi: 10.1097/DCR.0000000000000450

[95] Petagna L, Antonelli A, Ganini C, Bellato V, Campanelli M, Divizia A, Efrati C, Franceschilli M, Guida AM, Ingallinella S, Montagnese F, Sensi B, Siragusa L, Sica GS. Pathophysiology of Crohn's disease inflammation and recurrence. Biol Direct. 2020;15(1):23. doi: 10.1186/s13062-020-00280-5.

[96] Schwartz DA, Loftus EV Jr, TremaineWJ, PanaccioneR, HarmsenWS, Zinsmeister AR, Sandborn WJ. The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. Gastroenterology. 2002;122(4):875-880. doi: 10.1053/gast.2002.32362

[97] Sica GS, Di Carlo S, Tema G, Montagnese F, Del Vecchio Blanco G, Fiaschetti V, Maggi G, Biancone L. Treatment of peri-anal fistula in Crohn's disease. World J Gastroenterol.

2014;20(37):13205-13210. doi: 10.3748/wjg.v20.i37.13205

[98] Singh B, McC Mortensen NJ, Jewell DP, George B. Perianal Crohn's disease. Br J Surg. 2004;91(7):801-814. doi: 10.1002/bjs.4613

[99] van der Hagen SJ, Baeten CG, Soeters PB, van Gemert WG. Long-term outcome following mucosal advancement flap for high perianal fistulas and fistulotomy for low perianal fistulas: recurrent perianal fistulas: failure of treatment or recurrent patient disease? Int J Colorectal Dis. 2006;21(8):784-790. doi: 10.1007/s00384-005-0072-7

[100] A. M. Scanu, Fistole perianali nella malattia di Crohn iter formativo in coloproctologia corso avanzato e update in colo proctologia. [Internet] Vercelli, 2008. Available from: https://www.siccr.org/wp-content/uploads/2015/08/scanu_doc.pdf [Accessed: 2008-12-15/17]

[101] Ingallinella S, Campanelli M, Antonelli A, Arcudi C, Bellato V, Divizia A, Franceschilli M, Petagna L, Sensi B, Sibio S, Siragusa L, Sica GS. The Role of Active Inflammation and Surgical Therapy in Crohn's Disease Recurrence. Gastroenterol Res Pract. 2020;2020:2845407. doi: 10.1155/2020/2845407

[102] L. Biancone, S. Onali, E. Calabrese, C. Petruzziello, F. Zorzi, G. Condino, G.S. Sica, F. Pallone. Non-invasive techniques for assessing postoperative recurrence in Crohn's disease. Dig Liver Dis. 2008;40,(2):265-270. doi: 10.1016/S1590-8658(08)60536-8

[103] Lee MJ, Freer C, Adegbola S, Elkady S, Parkes M, Hart A, Fearnhead NS, Lobo AJ, Brown SR. Patients with perianal Crohn's fistulas experience delays in accessing anti-TNF therapy due to slow recognition, diagnosis and integration of specialist services: lessons learned from three referral centres. Colorectal Dis. 2018;20(9):797-803. doi: 10.1111/codi.14102

[104] Gold SL, Cohen-Mekelburg S, Schneider Y, Steinlauf A. Perianal Fistulas in Patients With Crohn's Disease, Part 1: Current Medical Management. Gastroenterol Hepatol (N Y). 2018;14(8):470-481. PMID: 30302062

[105] Sica GS, Biancone L. Surgery for inflammatory bowel disease in the era of laparoscopy. World J Gastroenterol. 2013;19(16):2445-2448. doi: 10.3748/wjg.v19.i16.2445

[106] Comparative study of laparoscopic vs open gastrectomy in gastric cancer management Sica, G.S., Iaculli, E., Biancone, L., di Carlo, S., Scaramuzzo, R., Fiorani, C., Gentileschi, P., Gaspari, A.L. World Journal of Gastroenterology. 2011;17(41):4602-4606. doi: 10.3748/wjg.v17.i41.4602

[107] EuroSurg Collaborative. EuroSurg: a new European student-driven research network in surgery. Colorectal Dis. 2016 Feb;18(2):214-215. doi:10.1111/codi.13260

[108] D'Ugo S, Romano F, Sibio S, Bagaglini G, Sensi B, Biancone L, Monteleone G, Sica GS. Impact of surgery on quality of life in Crohn's disease: short- and mid-term follow-up. Updates Surg. 2020;72(3):773-780. doi: 10.1007/s13304-020-00738-1

[109] Divizia A, Sensi B, Sica GS. Ambulatory management of perianal Crohn's disease during the COVID-19 pandemic. Colorectal Dis. 2020;22(6):645-646. doi: 10.1111/codi.15104

[110] Torres J, Bonovas S, Doherty G, Kucharzik T, Gisbert JP, Raine T, Adamina M, Armuzzi A, Bachmann O, Bager P, Biancone L, BokemeyerB,BossuytP,BurischJ,CollinsP, El-Hussuna A, Ellul P, Frei-Lanter C, Furfaro F, Gingert C, Gionchetti P,

Gomollon F, González-Lorenzo M, Gordon H, Hlavaty T, Juillerat P, Katsanos K, Kopylov U, Krustins E, Lytras T, Maaser C, Magro F, Marshall JK, Myrelid P, Pellino G, Rosa I, Sabino J, Savarino E, Spinelli A, Stassen L, Uzzan M, Vavricka S, Verstockt B, Warusavitarne J, Zmora O, Fiorino G. ECCO Guidelines on Therapeutics in Crohn's Disease: Medical Treatment. J Crohns Colitis. 2020;14(1):4-22. doi: 10.1093/ecco-jcc/jjz180

[111] Franzè E, Monteleone I, Laudisi F, Rizzo A, Dinallo V, Di Fusco D, Colantoni A, Ortenzi A, Giuffrida P, Di Carlo S, Sica GS, Di Sabatino A, Monteleone G. Cadherin-11 Is a Regulator of Intestinal Fibrosis. J Crohns Colitis. 2020;14(3):406-417. doi: 10.1093/ecco-jcc/jjz147

[112] Franzè E, Dinallo V, Laudisi F, Di Grazia A, Di Fusco D, Colantoni A, Ortenzi A, Giuffrida P, Di Carlo S, Sica GS, Di Sabatino A, Monteleone G. Interleukin-34 Stimulates Gut Fibroblasts to Produce Collagen Synthesis. J Crohns Colitis. 2020;14(10):1436-1445. doi: 10.1093/ecco-jcc/jjaa073

[113] Franzè E, Di Grazia A, Sica GS, Biancone L, Laudisi F, Monteleone G. Interleukin-34 Enhances the Tumor Promoting Function of Colorectal Cancer-Associated Fibroblasts. Cancers (Basel). 2020;12(12):3537. doi: 10.3390/cancers12123537

[114] Franzè, E., Dinallo, V., Rizzo, A., Di Giovangiulio, M., Bevivino, G., Stolfi, C., Caprioli, F., Colantoni, A., Ortenzi, A., Di Grazia, A., Sica, G., Sileri, P., Rossi, P., Monteleone, G. Interleukin-34 sustains pro-tumorigenic signals in colon cancer tissue. Oncotarget. 2018;9(3):3432-3445

[115] Interleukin-34 Induces Cc-chemokine Ligand 20 in Gut Epithelial Cells. Franzè E, Marafini I, De Simone V, Monteleone I, Caprioli F, Colantoni A,Ortenzi A, Crescenzi F, Izzo R, Sica G, Sileri P, Rossi P, Pallone F, MonteleoneG.J.CrohnsColitis.2016;10(1):87-94. doi: 10.1093/ecco-jcc/jjv181

[116] Interleukin-25 production is differently regulated by TNF-alpha and TGF-beta 1 in the human gut. Fina D, Franze E, Rovedatti L, Corazza GR, Biancone L, Sileri PP, Sica G, MacDonald TT, Pallone F, Di Sabatino A, Monteleone G. Mucosal Immunology, 2011;4(2):239-44 doi: 10.1038/mi.2010.68

[117] Haggett PJ, Moore NR, Shearman JD, Travis SP, Jewell DP, Mortensen NJ. Pelvic and perineal complications of Crohn's disease: assessment using magnetic resonance imaging. Gut. 1995;36(3):407-410. doi: 10.1136/gut.36.3.407

[118] BuchananGN,HalliganS,BartramCI, Williams AB, Tarroni D, Cohen CR. Clinical examination, endosonography, and MR imaging in preoperative assessment of fistula in ano: comparison with outcome-based reference standard. Radiology. 2004;233(3):674-681. doi: 10.1148/radiol.2333031724

[119] Sloots CE, Felt-Bersma RJ, Poen AC, Cuesta MA, Meuwissen SG. Assessment and classification of fistula-in-ano in patients with Crohn's disease by hydrogen peroxide enhanced transanal ultrasound. Int J Colorectal Dis. 2001;16(5):292-297. doi: 10.1007/s003840100308

[120] Lee MJ, Heywood N, Sagar PM, Brown SR, Fearnhead NS; ACPGBI Perianal Crohn's Disease Group. Association of Coloproctology of Great Britain and Ireland consensus exercise on surgical management of fistulating perianal Crohn's disease. Colorectal Dis. 2017;19(5):418-429. doi: 10.1111/codi.13672

[121] Onali S, Calabrese E, Petruzziello C, Zorzi F, Sica GS, Lolli E, Ascolani M, Condino G, Pallone F, Biancone L. Endoscopic vs ultrasonographic findings related to Crohn's disease recurrence: a

prospective longitudinal study at 3 years. J Crohns Colitis. 2010;4(3):319-328. doi: 10.1016/j.crohns.2009.12.010

[122] Al-Khawari HA, Gupta R, Sinan TS, Prakash B, Al-Amer A, Al-Bolushi S. Role of magnetic resonance imaging in the assessment of perianal fistulas. Med Princ Pract. 2005;14(1):46-52. doi: 10.1159/000081923

[123] Sandborn WJ, Fazio VW, Feagan BG, Hanauer SB; American Gastroenterological Association Clinical Practice Committee. AGA technical review on perianal Crohn's disease. Gastroenterology. 2003;125(5):1508-1530. doi: 10.1016/j.gastro.2003.08.025

[124] Gecse KB, Bemelman W, Kamm MA, Stoker J, Khanna R, Ng SC, Panés J, van Assche G, Liu Z, Hart A, Levesque BG, D'Haens G; World Gastroenterology Organization, International Organisation for Inflammatory Bowel Diseases IOIBD, European Society of Coloproctology and Robarts Clinical Trials; World Gastroenterology Organization International Organisation for Inflammatory Bowel Diseases IOIBD European Society of Coloproctology and Robarts Clinical Trials. A global consensus on the classification, diagnosis and multidisciplinary treatment of perianal fistulising Crohn's disease. Gut. 2014;63(9):1381-92. doi: 10.1136/gutjnl-2013-306709

[125] Kotze PG, Shen B, Lightner A, Yamamoto T, Spinelli A, Ghosh S, Panaccione R. Modern management of perianal fistulas in Crohn's disease: future directions. Gut. 2018;67(6):1181-1194. doi: 10.1136/gutjnl-2017-314918

[126] Pellino G, Keller DS, Sampietro GM, Angriman I, Carvello M, Celentano V, Colombo F, Di Candido F, Laureti S, Luglio G, Poggioli G, Rottoli M, Scaringi S, Sciaudone G, Sica G, Sofo L, Leone S, Danese S, Spinelli A, Delaini G, Selvaggi F; Italian Society of Colorectal Surgery SICCR. Inflammatory bowel disease position statement of the Italian Society of Colorectal Surgery (SICCR): Crohn's disease. Tech Coloproctol. 2020;24(5):421-448. doi: 10.1007/s10151-020-02183-z

[127] Pellino G, Selvaggi F, Ghezzi G, Corona D, Riegler G, Delaini GG. A think tank of the Italian society of colorectal surgery (SICCR) on the surgical treatment of inflammatory bowel disease using the Delphi method: Crohn's disease. Tech Coloproctol. 2015;19(10):639-651. doi: 10.1007/s10151-015-1368-4

[128] Adamina M, Bonovas S, Raine T, Spinelli A, Warusavitarne J, Armuzzi A, Bachmann O, Bager P, Biancone L, Bokemeyer B, Bossuyt P, Burisch J, Collins P, Doherty G, El-Hussuna A, Ellul P, Fiorino G, Frei-Lanter C, Furfaro F, Gingert C, Gionchetti P, Gisbert JP, Gomollon F, González Lorenzo M, Gordon H, Hlavaty T, Juillerat P, Katsanos K, Kopylov U, Krustins E, Kucharzik T, Lytras T, Maaser C, Magro F, Marshall JK, Myrelid P, Pellino G, Rosa I, Sabino J, Savarino E, Stassen L, Torres J, Uzzan M, Vavricka S, Verstockt B, Zmora O. ECCO Guidelines on Therapeutics in Crohn's Disease: Surgical Treatment. J Crohns Colitis. 2020;14(2):155-168. doi: 10.1093/ecco-jcc/jjz187

[129] Ommer A, Herold A, Berg E, Fürst A, Post S, Ruppert R, Schiedeck T, Schwandner O, Strittmatter B. German S3 guidelines: anal abscess and fistula (second revised version). Langenbecks Arch Surg. 2017;402(2):191-201. doi: 10.1007/s00423-017-1563-z

[130] Koelbel G, Schmiedl U, Majer MC, Weber P, Jenss H, Kueper K, Hess CF. Diagnosis of fistulae and sinus tracts in patients with Crohn disease: value of MR imaging. AJR Am J Roentgenol. 1989;152(5):999-1003. doi: 10.2214/ajr.152.5.999

[131] Bouchard D, Abramowitz L, Bouguen G, Brochard C, Dabadie A,

de Parades V, Eléouet-Kaplan M, Fathallah N, Faucheron JL, Maggiori L, Panis Y, Pigot F, Rouméguère P, Sénéjoux A, Siproudhis L, Staumont G, Suduca JM, Vinson-Bonnet B, Zeitoun JD. Anoperineal lesions in Crohn's disease: French recommendations for clinical practice. Tech Coloproctol. 2017;21(9):683-691. doi: 10.1007/s10151-017-1684-y

[132] Orsoni P, Barthet M, Portier F, Panuel M, Desjeux A, Grimaud JC. Prospective comparison of endosonography, magnetic resonance imaging and surgical findings in anorectal fistula and abscess complicating Crohn's disease. Br J Surg. 1999;86(3):360-364. doi: 10.1046/j.1365-2168.1999.01020.x

[133] Bemelman WA, Warusavitarne J, Sampietro GM, Serclova Z, Zmora O, Luglio G, de Buck van Overstraeten A, Burke JP, Buskens CJ, Colombo F, Dias JA, Eliakim R, Elosua T, Gecim IE, Kolacek S, Kierkus J, Kolho KL, Lefevre JH, Millan M, Panis Y, Pinkney T, Russell RK, Shwaartz C, Vaizey C, Yassin N, D'Hoore A. ECCO-ESCP Consensus on Surgery for Crohn's Disease. J Crohns Colitis. 2018;12(1):1-16. doi: 10.1093/ecco-jcc/jjx061

[134] Sibio S, Di Giorgio A, Campanelli M, Di Carlo S, Divizia A, Fiorani C, Scaramuzzo R, Arcudi C, Del Vecchio Blanco G, Biancone L, Sica G. Ambulatory Surgery for Perianal Crohn's Disease: Study of Feasibility. Gastroenterol Res Pract. 2018;5249087. doi: 10.1155/2018/5249087

[135] An Y, Bellato V, Konishi T, Pellino G, Sensi B, Siragusa L, Franceschilli M, Sica GS; S-COVID Collaborative Group. Surgeons' fear of getting infected by COVID19: A global survey. Br J Surg. 2020;107(11):e543-e544. doi: 10.1002/bjs.11833

[136] Bellato V, Konishi T, Pellino G, An Y, Piciocchi A, Sensi B, Siragusa L, Khanna K, Pirozzi BM, Franceschilli M, Campanelli M, Efetov S, Sica GS; S-COVID Collaborative Group. Impact of asymptomatic COVID-19 patients in global surgical practice during the COVID-19 pandemic. Br J Surg. 2020;107(10):e364-e365. doi: 10.1002/bjs.11800

[137] Sensi B, Siragusa L, Efrati C, Petagna L, Franceschilli M, Bellato V, Antonelli A, Arcudi C, Campanelli M, Ingallinella S, Guida AM, Divizia A. The Role of Inflammation in Crohn's Disease Recurrence after Surgical Treatment. J Immunol Res. 2020;2020:8846982. doi: 10.1155/2020/8846982

[138] Sileri P, Sica G, Gentileschi P, Venza M, Manzelli A, Palmieri G, Spagnoli LG, Testa G, Benedetti E, Gaspari AL. Ischemic preconditioning protects intestine from prolonged ischemia. Transplant Proc. 2004;36(2):283-285. doi: 10.1016/j.transproceed.2004.01.078

[139] Sica, G.S., Djapardy, V., Westaby, S., Maynard, N.D. Diagnosis and management of aortoesophageal fistula caused by a foreign body. Annals of Thoracic Surgery. 2004;77(6):2217-2218 doi: 10.1016/j.athoracsur.2003.06.031

[140] Baseman JG, Koutsky LA. The epidemiology of human papillomavirus infections. J Clin Virol. 2005;32 Suppl 1:S16–S24. doi: 10.1016/j.jcv.2004.12.008

[141] Kreisel KM, Spicknall IH, Gargano JW, Lewis FM, Lewis RM, Markowitz LE, Roberts H, Satcher Johnson A, Song R, St Cyr SB, Weston EJ, Torrone EA, Weinstock HS. Sexually Transmitted Infections Among US Women and Men: Prevalence and Incidence Estimates, 2018. Sex Transm Dis. 2021. doi: 10.1097/OLQ.0000000000001355.

[142] Sturegard E, Johansson H, Ekstrom J, Hasson BG, Johnsson A, Gustafsson E, Dillner J, Forslund O.

Human papillomavirus typing in reporting condyloma. Sex Transm dis 2013;40:123-129. doi: 10.1097/OLQ.0b013e31827aa9b3.

[143] Lee PK, Bas Wilkins K. Condyloma and other infections including human immunodeficiency virus. Surg clin N am 2010;90:99-112. doi: 10.1016/j.suc.2009.09.005.

[144] Lacey CJN, Goodall RL, Rangarson Tennvall G, Maw R, Kinghorn GR, Fisk PG, Barton S, Byren I. Randomised controlled trial and economic evaluation of podophyllotoxin solution, podophyllotoxin cream, and podophyllin in the treatment of genital warts. Sex Transm Infect 2003;79:270-275. doi: 10.1136/sti.79.4.270.

[145] Edwards A, Atma-Ram A, Thin RN. Podophyllotoxin 0.5% v. podophyllin 20% to treat penile warts. Genitourin Med 1988;64:263-265. doi: 10.1136/sti.64.4.263.

[146] Tatti S, Stockfleth E, Beutner KR, Tawfik K, Elsasser U, Weyrauch P, Mescheder A. Polyphenon E: a new treat-ment for external anogenital warts. Br J dermatol 2010;162:176-184.

[147] STd Treatment Guidelines [Internet]. Available from: www.cdc.gov/std/treatment/2010/genital-warts.htm

[148] Abdullah AN, Walzman M, Wade A. Treatment of external genital warts comparing cryotherapy (liquid nitro-gen) and trichloroacetic acid. Sex Transm dis 1993;20:344-345. PMID: 8108758

[149] Godley MJ, Bradbeer CS, Gellan M, Thin RN. Cryotherapy compared with tricholoroacetic acid in treating geni-tal warts. Genitourin Med 1987;63:390-392. doi: 10.1136/sti.63.6.390.

[150] Balik E, Eren T, Bugra D. A surgical approach to anogenital buschke-Loewenstein tumours (giant condyloma acuminate). Acta chir belgica 2009;109:612-616. doi: 10.1080/00015458.2009.11680497.

[151] Paraskevas KI, Kyriakos E, Poulios V, Stathopoulos A, Tzovaras A, Briana DD. Surgical management of giant condyloma acuminatum (Suschke-Loewenstein tumor) of the perianal region. Dermatol Surg 2007;33:638-644. doi: 10.1111/j.1524-4725.2007.33125.x.

[152] Stone KM, Becker TM, Hadgu A, Kraus SJ. Treatment of external genital warts: a randomised clinical trial comparing podophyllin, cryotherapy, and electrodesiccation. Genitourin Med. 1990;66(1):16-19. doi: 10.1136/sti.66.1.16.