MINIMALLY INVASIVE SURGICAL TECHNIQUE IN THE MANAGEMENT OF PERIANAL FISTULAS USING THE SURGISIS® AFP MATERIAL

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For centuries the treatment of anal fistulas was a major challenge, due to the diversified etiology, multitude of types, risk of postoperative sphincter insufficiency and significant recurrence rate. Already Hipokrates (430 p.n.e.) dealt with the problem of fistulas. Jan from Arden in 1376 elaborated a study: „Treatises of Fistula in Ano; Hemorrhoids, and Clysters” giving foundations to fistula canal probing, fistulotomy, and setonage. In the 17-th century, the king of France, Ludwig XIV was subject to anal fistula surgery, richly rewarding his physician Charles Felix. The turn of the 20-th century brought further discoveries in the field of pathophysiology and novel surgical techniques (Goodsall, Milligan and Morgan, Thompson), which with slight modifications survived to modern times.

The development of biotechnology, including molecular engineering created a real opportunity to introduce novel methods into the treatment of perianal fistulas with the simultaneous limitation of the invasiveness of the method and number of postoperative complications.

In most cases the anal fistula is a chronic phase of active inflammation of the perianal region. Due to infection of Herman glands located in the anal crypts one may observe the development of an abscess with pus compressing surrounding tissues and forming a canal with an external opening. Its walls are lined with granulation tissue creating a persistent fistula (cryptogenic theory) (1).

Canons of surgical management of perianal fistulas include the precise determination of the course of the anal canal and its position in relation to the sphincter system, drainage of all coexisting inflammatory foci, eradication of the fistula canal with special attention to the risk of recurrence and anal sphincter damage (2).

According to guidelines established by Goodsall and Miles (3), the location of the external and internal opening of the fistula, the course of the primary canal and its branches, as well as the presence of concomitant diseases, should be determined during the preoperative examination. Apart from typical diseases presented in tab. 1, one should also consider the possibility of sacro-coccygeal teratoma and perianal dermoid cysts in the differential diagnosis. In case of the latter, radical surgery is doubtful and often leads towards the development of a chronic sacro-coccygeal fistula (4).

Prior to the decision concerning the choice of the operative technique one should determine the location of the fistula canal, in relationship to the external anal sphincter (EAS). This is possible thanks to fistulography, ERUS

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<tr>
<td>Suppurative hidradenitis</td>
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<td>Bartholin's gland abscess</td>
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<td>Anal fissure</td>
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<td>Capillary cyst</td>
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Surgisis® AFP in the management of perianal fistulas

with hydrogen peroxide enhanced anal canal (5, 6), MRI with a fistulogram, and the perioperative examination. The obtained result enables to assign a given case to one of the IV anal fistula groups, according to Park’s classification (7). Type I – intersphincteric, type II – transsphincteric, type III – suprasphincteric, type IV – retrosphincteric – the internal opening is located above the serrate line (fig. 1 and 2).

Another practical division considers simple and complex fistulas. Complex fistulas connected with an increased postoperative incontinence rate include the following: high transsphincteric (comprising >1/3 of the EAS diameter), suprasphincteric, retrosphincteric, rectovaginal, and horseshoe fistulas, anterior fistulas in female patients, and fistulas coexisting with Leśniowski-Crohn’s or post-radiation diseases (9).

Fistulotomy (lay-open technique) and fistulectomy are the methods of choice in the treatment of submucous (not subject to Parks classification), intersphincteric and low transsphincteric fistulas (10). The simultaneous eradication depends on the amount of the EAS comprising the fistula canal, and should not exceed 1/3 of the lower perimeter (fig. 3). A properly performed procedure, results in a low recurrence rate (0-9%), and 0-33% damage to the anal sphincters (11-20). Particular attention should be paid to anterior fistulas, since lack of puborectal muscle protection (forming Park’s angle with the posterior and lateral rectal walls) and postnatal EAS weakening increase the risk of postoperative complications.

These rules may not apply to patients subject to perineal injuries, past perianal surgery or congenital anomalies of the distal segment of the gastrointestinal tract. The individual approach to the patient enables to estimate the risk of sphincter damage and change the surgical technique to less radical.

Durable and effective treatment of perianal fistulas, while reducing the risk of complications to a minimum is the main challenge of modern coloproctology. These conditions are difficult to achieve in case of complex fistulas, therefore, the multitude of proposed procedures.

The most popular invasive surgical methods dealing with complex perianal fistulas include the technique of gradual EAS cutting seton, and the simultaneous excision of the fistula and closure of the internal opening by means...
of the endorectal advancement flap (ERAF) (22).

Surgery with the use of a seton gained popularity, due to its simplicity and low recurrence rate. As a result of the ongoing healing process in the enucleated retrospincteric fragment of the fistula, one may observe the development of a scar, which fixes the EAS surface adhering to the lateral wall of the fistula. The sutures transverse the fistula successively intersecting the anterior wall, peripheral surface of the EAS, muscular layer, and medial surface, connecting the fundus of the fistula with the lumen of the anal canal. The intersecting strands direct the post-inflammatory scar development, preventing from EAS retraction by means of the increasing number of severed muscular fibers. Connective tissue synthesis, contraction and remodeling of collagen fibers determine the gradual cutting of the EAS, which should last between 2 and 6 weeks. The retrospincteric segment of the anal canal is connected with its lumen enabling fistula healing.

The endorectal advancement flap technique (ERAF) consists in the excision of the fistula canal to the level of the intersphincteric space (fig. 1 and 2). The resulting “tunnel” is left open for treatment. Using the approach from the lumen of the anal canal, preparing in the intersphincteric space, one should create a rectangular flap with the pedunculated base extending above the pectinate line. The flap covers the mucous and submucous membranes, and the internal anal sphincter (IAS). The creation of the flap is terminated by the shortening of the fragment comprising the internal opening of the fistula. The success of the operation depends on the size of the flap (the base twice the size of its height), tightness of the endorectal advancement flap placed at the site of the excised fistula, as well as the implantation of interrupted sutures enabling proper blood supply.

The above-mentioned surgical techniques are considered as sphincter-saving methods. However, their invasiveness may impair the proper functioning of the sphincteric system. The cutting seton operation is connected with frequent outpatient control visits, discomfort (23, 24, 25), anal canal deformation (“key-hole” type) manifested by soiling of underwear, low recurrence rate (0-8%), and incontinence symptoms (especially gas incontinence and underwear soiling) ranging between 2 and 63% (21, 24, 26-32).

ERAF is a safe, however, technically difficult method. The displacement of the flap below the serrate line may lead to the eversion of the mucous membrane of the anal canal and symptoms of the so-called “wet anus”, and the developing scar might hinder the possible re-operation. Recurrent fistulas are diagnosed in 2-45% of patients (33-43). Van der Hagen et al. demonstrated a 37% efficacy of the ERAF technique in 41 patients (high transspincteric, suprasphincteric, and retrosphincteric fistulas). The observation period was 72 weeks (43). Sphincter system insufficiency was observed in 35% of cases diagnosed with high transspincteric fistulas (33, 41, 43-47).

The high percentage of postoperative complications and frequent recurrence, as well as rapid desire to return to everyday activities are evidence of the need to develop novel, effective, and safe operative techniques. The implantation of the AFP Surgisis plug is one such method, gaining more and more recognition (Anal Fistula Plug) (fig. 4). Initial reports concerning the new minimally invasive perianal fistula treatment technique date back to 2004, when Robb et al. obtained a 65% efficacy of the method, considering 17 healthy volunteers (48).

Eradication of the fistula tract seems to be the key issue in the treatment of perianal fistulas with simultaneous sphincter system preservation. The cone-like shape of the biodegradable AFP material enables to tightly close the primary opening of the fistula. Further stages of healing are possible thanks to the presence of collagen type I fibers obtained during the process of porcine small intestinal submucosa lyophilization. The inactivation of living cells enables to obtain an acellular matrix, which becomes indifferent to the immunological system of the human being, and is the scaffold for angiogenesis. During the three

Fig. 4. Surgisis® AFP plug
month period the implanted material is completely replaced by native tissue leading towards the healing of the fistula (49-52).

After placing the patient in the lithotomic position and preparing the operative field, the Surgisis® AFP material should be submerged in physiological saline or Ringer’s solution for a period of 5 minutes. The “sine quo non” factor is the presence of the primary opening located by means of a sterile probe (fig. 5). The narrow end of the AFP plug is sutured to the bougie protruding from the internal opening. The probe-filum-plug system is dragged through the external opening of the fistula until the occurrence of resistance (closure of the primary opening by the wider end of the plug (fig. 6). Excess amount of the AFP plug is severed at the level of both openings.

After adjusting the AFP plug its end is pulled out several millimeters above the level of the intestinal wall. Using an absorbable suture the plug is pierced 3-4 mm below the edge of the wider end to a depth of 2-3 mm. A knot is created with the free end left intact – 5 cm (fig. 7 – point 2). The „plug” is drawn back into the fistula canal, through the primary opening, mucous and submucous membranes, and internal sphincter muscle. The needle is directed through the plug and protrudes from the other side of the opening (fig. 7 – point 3, 4, 5). The same is repeated on the opposite side creating a twisted suture (fig. 7 – point 6). As a result the proximal end of the plug is completely covered by the native tissue rendering impossible the dislocation of the AFP plug within the fistula canal and the penetration of the fecal content into its lumen (fig. 9). The tight closure of the fistula is the key moment of the procedure, enabling proper wound healing. The distal end of the AFP plug is sutured to the edge of the secondary fistula opening. This prevents from the accumulation of secretion, occurrence of inflammation and abscess development. The average implantation time of the Surgisis® AFP plug to the transsphincteric fistula canal was 25 minutes (ranging between 10 and 50 minutes) (21, 55).

According to the guidelines proposed by the manufacturer one should limit the risk of infecting the AFP material, performing abdominal enema before the operation, administering perioperative antibiotics, introducing the aseptic technique (avoid contact of AFP with latex gloves), and proper patient selection without features of massive inflammation including purulent discharge.
When planning postoperative antibiotic therapy one should avoid drugs inhibiting the neovascularization and infiltration of the implantable material, such as gentamycin (56), vancomycin (57), bacytracin (58, 59), polymyxin B (60), and iodopovidon (59).

Due to the numerous discrepancies considering the practical use of AFP a scientific conference took place in 2007 with members of leading Coloproctological Surgery Departments. During the meeting several issues were discussed including the efficacy of the AFP plug method, its limitations and patient safety. The type II perianal fistula (according to Parks’ classification) was considered as the main indication for AFP use. Enucleation and other fistula surgical debridement methods are not indicated, due to the broadening of the lumen of the fistula. Patients with active inflammation should not be directed for surgery, thus, if required, seton drainage should be used for a period of 6 to 12 weeks (tabl. 2).

Postoperative recommendations include conservative lifestyle for a period of two weeks, douching of the surgical field, and proper defecation.

The healing of the fistula during the 12 weeks after surgery is evidence of the efficacy of Surgisis® AFP implantation. The most common reasons of failure include wide fistula canal, active inflammation of the operated area, and improper AFP plug fixation (the suture covered the mucous membrane without the external anal sphincter) (61). Most failures may be diagnosed during the initial 50 days after the operation (62).

In most cases the day before the operation the patient is subject to an enema, receives perioperative antibiotics (parenteral metronidazol), while after the procedure receives for a period of 7 days oral ciprofloxacin and metronidazol (oral and ointment). In combination with a proper diet, lack of physical and sexual activity for a period of two weeks the risk of AFP material dislocation is low (63, 64, 65). This has important implications for the entire treatment process, since reoperations are characterized by reduced efficiency (65). Preliminary medical data describing the resistance of the SIS (small intestine submucosa) material to infection with the possibility of active inflammation contamination (66, 67, 68) were not confirmed by studies concerning the treatment of anal fistulas. Therefore, proper eradication and perianal abscess drainage are recommended, prior to AFP plug implantations (55, 65, 69).

Operative techniques presented in subsequent literature data often deviated from the above-mentioned guidelines, emphasizing the individual assessment of each patient. Systematization of the existing knowledge should facilitate the selection of patients, and enable to obtain a high recovery rate considering patients with perianal fistulas subject to AFP plug implantation.

The final success largely depends on the location and length of the fistula. The fixation of the AFP material is influenced by the proper closure of the internal opening of the fistula and mechanical compression of adjacent tissues. Hence, the displacement/expulsion of AFP were more frequently observed in case of short and superficial fistulas (63, 64). The authors suggested the suturing of the proximal
end of AFP using Vicryl 2-0 sutures, characterized by a sufficiently large mechanical strength.

Christoforidis et al. analysed 64 procedure results considering the treatment of perianal fistulas using the AFP material. They obtained an inversely proportional relationship between the amount of the sphincter complex covering the fistula canal and recovery rate (p<0.05): 65% (9/14) recovery considering fistulas comprising < 1/3 EAS, 26% (9/34) recovery considering fistulas comprising 1/3-2/3 EAS, and 13% (2/16) recovery in case of fistulas covering >2/3 EAS (70). This is contrary to the common belief about the role of compression of adjacent tissues to prevent the dislocation of the implanted material. Due to the fact that the surgical procedures were performed by 15 surgeons and lack of pre- and postoperative protocols, the reliability of the above-mentioned results was reduced. In other studies the authors excluded patients with low transsphincteric fistulas, according to AFP plug implantation guidelines.

Schwandner et al. considered the eradication of the anal canal and improper surgical technique, as factors influencing the outcome of the procedure (71). Five of the 18 patients required reoperation, due to AFP plug dislocation: 2 cases, and fistula canal secretion – 3 cases. A persistent fistula could be the result of leakage of the internal opening leading to the development of a residual abscess or lateral tract of the fistula in the intersphincteric space, as well as withdrawal from the enucleation of the fistula canal. The granulation tissue in the fistula canal served as a barrier for the migrating host cells.

Considering yet another study the large diameter of the fistula canal was responsible for the dislocation of the AFP plug. The authors proposed a modification to the surgical technique consisting in the implantation of two AFP plugs to the wide fistula canal (21). Another solution consists in the treatment of a wide fistula canal by placing a seton and local administration of a 10% solution of metronidazole. Six to eight weeks after the acute stage of inflammation is controlled, the risk of chronic inflammation is reduced, and fistula walls are covered by connective tissue, the patient is qualified for AFP plug implantation (63, 64). Seton presence facilitates the implantation of the AFP plug by means of the “pull-through” method without having to probe the fistula canal (63).

Despite numerous attempts an algorithm concerning treatment of complex fistulas or multiple fistulas using the AFP material has not been established. Multiple fistulas may be managed by means of AFP plug implantation to each canal with a primary opening (64, 65, 72). In case of complex fistulas closure of the primary opening should be pursued (63). Each canal of the horseshow fistula should be supplied by Surgisis® AFP material with tight closure of the primary opening (63, 73). Lawes et al. filled the fistula with the AFP material, and the primary opening was additionally covered by an endorectal advancement flap. Considering the three patients, recurrence was observed in one case (74). Ky et al. used collagen plugs in the treatment of anal fistulas (44 patients) with the recovery rate amounting to 54.6% (65). The procedure is technically difficult and prolongs surgery, and has no visible effect on the number of recovery cases.

Initial results demonstrated the higher efficacy of the AFP plug implantation method, as compared to previous techniques used in the treatment of perianal fistulas. However, the small number of investigated groups and lack of a uniform methodology render impossible the formulation of conclusions, considering management standards. Analysis of the benefits of minimally invasive techniques is a dynamic and time-consuming process, requiring multicenter involvement. Considering a study of 80 patients the implantation of AFP, as compared to ERAF was burdened with a lower percentage of symptomatic postoperative anal sphincter insufficiency. In case of the I group, 16% of patients presented with gas incontinence (0-3 points, according to CCF-FI), while in case of ERAF, one additionally observed stool incontinence or a change in lifestyle, due to frequent incontinence (3-12 points, according to CCF-FI). In two cases reoperation was required, due to bleeding after ERAF. The low effectiveness of recovery (32%) after AFP plug implantation was connected with the absence of antibiotic therapy, canal enucleation, lack of seton implantation in case of active inflammation, uncertain postoperative protocol, improper diet and perioperative

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1 Cleveland Clinic Florida Fecal Incontinence score
physical activity, as well as excessive enthusiasm for the use of AFP in case of complex and recurrent fistulas (75, 76, 77).

The two latter reasons were confirmed by Safar et al., who additionally observed the inaccurate treatment of the fistula canal from epithelial cells and faulty operative technique (69). In 2009, a study was published confirming the correlation between seton implantation and increase in the recovery rate (p=0.05) (62). The above-mentioned result should not be surprising, considering the etiology of perianal fistulas, inflammation as the main AFP plug implantation failure factor (62, 74), and efficacy of setonage during classical operative techniques in the treatment of fistulas (8, 78, 79).

Schwandner et al. analysed results from the largest group of patients operated using the AFP plug, and confirmed the negative influence of diabetes mellitus and smoking (p=0.002; p=0.005, respectively). The gender and length of the transphincteric fistula (length of the canal: 3-8 cm; median 5 cm) had no influence on the efficacy of treatment (55).

During the 2008 conference summarizing thus far obtained AFP plug treatment results, history of perianal fistula operation was not considered as a contraindication for surgery (80). Of the five studies dealing with the above-mentioned problem, three showed no dependency (21, 70, 81), while in case of two physicians turned their attention to such a possibility (74, 82). Unfortunately, studies performed on a larger patient group did not consider the above-mentioned factor. Thus, influence of previous operations on AFP plug implantation technique results remains an open issue.

The use of MRI, in order to determine the course of the fistula canal, compliance with the study protocol, antibiotic therapy, proper wound cleaning (H\textsubscript{2}O\textsubscript{2}, enucleation), surgical procedures performed by experienced surgeons, and qualification of patients previously non-operated, were considered as the main factors of high efficacy (83%) of anal fistula treatment using the AFP plug (72). In case of an abscess or active inflammation patients were subject to several weeks of seton drainage. Statistical analysis showed no influence of seton drainage on the recovery rate. However, thorough evaluation of the study methodology revealed some irregularities raising doubts about the credibility of the formulated conclusion. Lack of random selection of patients (active inflammation of the fistula qualified the patient to a two-staged operation with the use of a seton) contributed to the evaluation of AFP plug implantation results in case of an active vs. non-active inflammatory environment. No differences in the recovery rate of both groups (p=0.7) was evidence of the efficacy of fistula setonage in case of active inflammation (72).

Amongst the 60 simple transphincteric fistulas the efficacy of the AFP plug material amounted to 62% during the 12-month observation period. The Authors pointed to the too hasty qualification of the AFP plug implantation procedure as a failure (remodeling lasts up to 6 months) (83), negative influence of smoking (p=0.005), and improper patient selection. The lack of consistent assessment of the debridement of the anal canal impedes angiogenesis and AFP plug infiltration by host cells. Thus, it is important to remove the granulation tissue without opening the fistula canal (55, 84). A comparable efficacy of perianal fistula treatment was observed in other studies (60 – 80%) (tab. 3).

The qualification of patients with complex and recurrent fistulas for surgery and lack of experience considering the new operative technique (tab. 3; number of AFP material dislocations) affect the reduction of the recovery rate. Ky et al. compared the treatment efficacy of simple and complex fistulas receiv-

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<th>Indications</th>
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<td>transphincteric fistula</td>
<td>intersphincteric fistula</td>
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<tr>
<td>retrosphincteric fistula</td>
<td>rectovaginal fistula (short fistula canal)</td>
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<td>intersphincteric fistula (when classical fistulotomy is burdened with the risk of postoperative incontinence (intestinal inflammatory diseases, post - radiation)</td>
<td>active inflammation (purulent discharge, inflammatory infiltration, communication between the fistula lumen and site of the removed abscess)</td>
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<td>rectovaginal fistula (an alternative for surgery)</td>
<td>lack of the external and internal opening of the fistula</td>
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The presence of Crohn’s disease reduced the recovery rate from 66.7% to 28.6% (p=0.017) (65). The most common cause of failure is the presence of active inflammation, as an effect of the leakage of the internal opening of the fistula, improper wound debridement (enucleation of the fistula canal was absent), and closure of the external fistula opening (69). The treatment of AFP implantation as the method of last resort, and low number of cohorts renders impossible the full evaluation of its usefulness (tab. 3).

Surgisis® AFP is an example of a novel minimally invasive perianal fistula treatment method. Wang et al. suggested the higher effectiveness of the endorectal advancement flap technique in the management of recurrent fistulas (76). However, the actual usefulness of the AFP plug requires further investigations with strict adherence to perioperative protocols (MRI examinations, antibiotic therapy, and wound debridement). Analysis of treatment costs considering postoperative hospitalization showed the advantage of the AFP plug implantation method over ERAF (87). In light of previous results AFP plug implantation is an alternative to the treatment of simple, high cryptoglandular transsphincteric fistulas, and its advantage consists in the maintenance of the integrity of the sphincter system and short convalescence period. In addition to the reduction in the number of complications this is important for the surgeon in case of eventual reoperation. The ultimate success depends on the proper operative technique and active patient cooperation in complying with the perioperative protocol.
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