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Review

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Recent advances in the diagnosis and treatment of complex anal fistula

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Anal fistula can be a challenging condition to manage, with complex fistulas presenting even greater difficulties. The primary concerns in treating this condition are a risk of damage to the anal sphincters, which can compromise fecal continence, and refractoriness to treatment, as evidenced by a high recurrence rate. Furthermore, the treatment of complex anal fistula involves several additional challenges. Satisfactory solutions to many of these obstacles remain elusive, and no consensus has been established regarding the available treatment options. In summary, complex anal fistula has no established gold-standard treatment, and the quest for effective therapies continues. This review discusses and highlights groundbreaking advances in the management of complex anal fistula over the past decade.

Keywords: Rectal fistula; Fistula; Wound healing; Magnetic resonance imaging; Stem cell

INTRODUCTION

Anal fistula is a complex surgical condition that presents a unique challenge due to its intricate anatomy and high recurrence rate, with various management modalities and no standardized protocols. The aim of the surgical treatment of anal fistula is to achieve definitive healing through closure, obliteration, or excision of the fistula tract while avoiding fecal incontinence (FI). Historical texts and contexts suggest that the French king's fistula, a central plot device in Shakespeare's play *All's Well That Ends Well*, was an anal fistula or fistula in ano [1]. The medieval *Treatises of Fistulae* by John of Ardene (1307–1392) details the use of sutures, specifically setons, for treating complex fistulas. The earliest known management of anal fistula with setons is attributed to Hippocrates (460–356 BC), but the innovation of setons is derived from the *Kshara Sutra* approach, which has been used to treat the disease known as "*bhagandara*" since the time of Sushruta in 800 BC. Abul Qasim Al-Zahrawi (936–1013 AD) described the use of cautery and curettage for treating perianal fistula in his seminal work *Al-Tasrif* [2]. The distinction of popularizing fistula surgery and elevating its acceptance belongs to the French surgeon Charles-François Felix (1635–1703). His successful operation on King Louis XIV of France in 1686 not only raised the status of surgeons above that of barbers, bringing them closer to physicians, but also garnered royal endorsement and respect for the profession. This pivotal surgical procedure performed on the king laid the groundwork for the modern management of fistula in ano.

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UPDATE ON CRYPTOGLANDULAR ANAL FISTULA OVER THE PAST DECADE

The broad field of anal fistulas has seen noteworthy updates and advancements over the past decade, which are detailed in this article.

ANATOMY

Two major anatomical contributions include the discovery of the outersphincteric space and the elucidation of the roof of ischiorectal fossa inside levator ani muscle (RIFIL) fistula.

The space between the external anal sphincter (EAS) and its surrounding lateral fascia, known as the Garg fascia, has been recognized as a key anatomical site in the context of complex anal fistula [3]. This area is referred to as the outersphincteric space [3, 4]. While it may appear part of the conventional intersphincteric space on radiological images, it is in fact distinct. The outersphincteric space potentially exists lateral to the EAS, situated between the EAS and the Garg fascia, and is of surgical relevance in cases of abscess [3, 4]. When a fistula or its associated pus breaches the EAS but is prevented from entering the ischiorectal fossa by the resistance of the Garg fascia, the pus is likely to disseminate along the Garg fascia within the outersphincteric space. Preoperative analysis of these anatomical spaces can provide colorectal surgeons with insights that aid in surgical planning and execution.

The other key anatomical advancement in the context of fistula management is the identification of RIFIL fistula (Fig. 1) [5]. When pus from the outersphincteric space ascends along the lateral border of the EAS and puborectalis, and then along the inferior border of the levator ani muscle, it is classified as a RIFIL fistula. These fistulas can extend to the lateral pelvic wall. Since RIFIL fistulas are formed by the superior movement of pus in the outersphincteric space, they do not penetrate the ischiorectal fossa and appear adherent to the inferolateral surface of the puborectalis and levator ani muscles (Figs. 1–3) [5].

Magnetic resonance imaging (MRI) is the preferred method for the evaluation of a fistula's trajectory, its relationship to the sphincter complex, and the presence of any secondary tracts or abscesses, which is essential for preoperative planning in cases of RIFIL fistula [5]. Due to their challenging location, RIFIL fistulas are more difficult to treat than other complex fistulas. The enclosed nature of RIFIL fistulas complicates access and treatment, conferring a higher likelihood of recurrence if not managed adequately [6]. In a large study involving 419 patients with anal fistula, RIFIL fistulas were identified in 10% of cases. Complex fistulas were significantly more common in RIFIL than non-RIFIL fistulas (85.7% vs. 38.5%, $P < 0.00001$), and the rate of surgical failure was also significantly higher in the RIFIL group (30.6%) compared to the non-RIFIL group (7.2%, $P = 0.0001$) [5]. Consequently, accurate diagnosis and proper management of RIFIL fistulas are crucial to prevent recurrence [5–7].

PATHOLOGY

In countries where tuberculosis (TB) is endemic, it can be associated with anal fistulas. This association might be causative, concurrent, or merely coincidental. A major challenge lies in the detection and diagnosis of TB in anal fistulas. Traditionally, histopathological examination of the fistula tract has been the method of choice for TB detection. However, recent studies have indicated that the detection rate using histopathology is relatively low. Real-time polymerase chain reaction (RT-PCR) appears to be significantly more accurate than both histopathology and GeneXpert

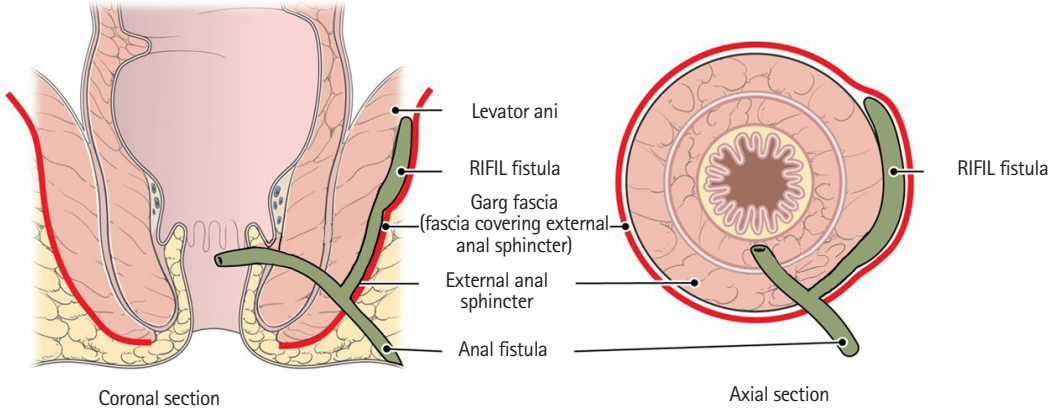

Fig. 1. Schematic diagram illustrating the outersphincteric space and roof of ischiorectal fossa inside levator ani muscle (RIFIL) fistula. Adapted from Garg et al. [5], with permission from Springer.

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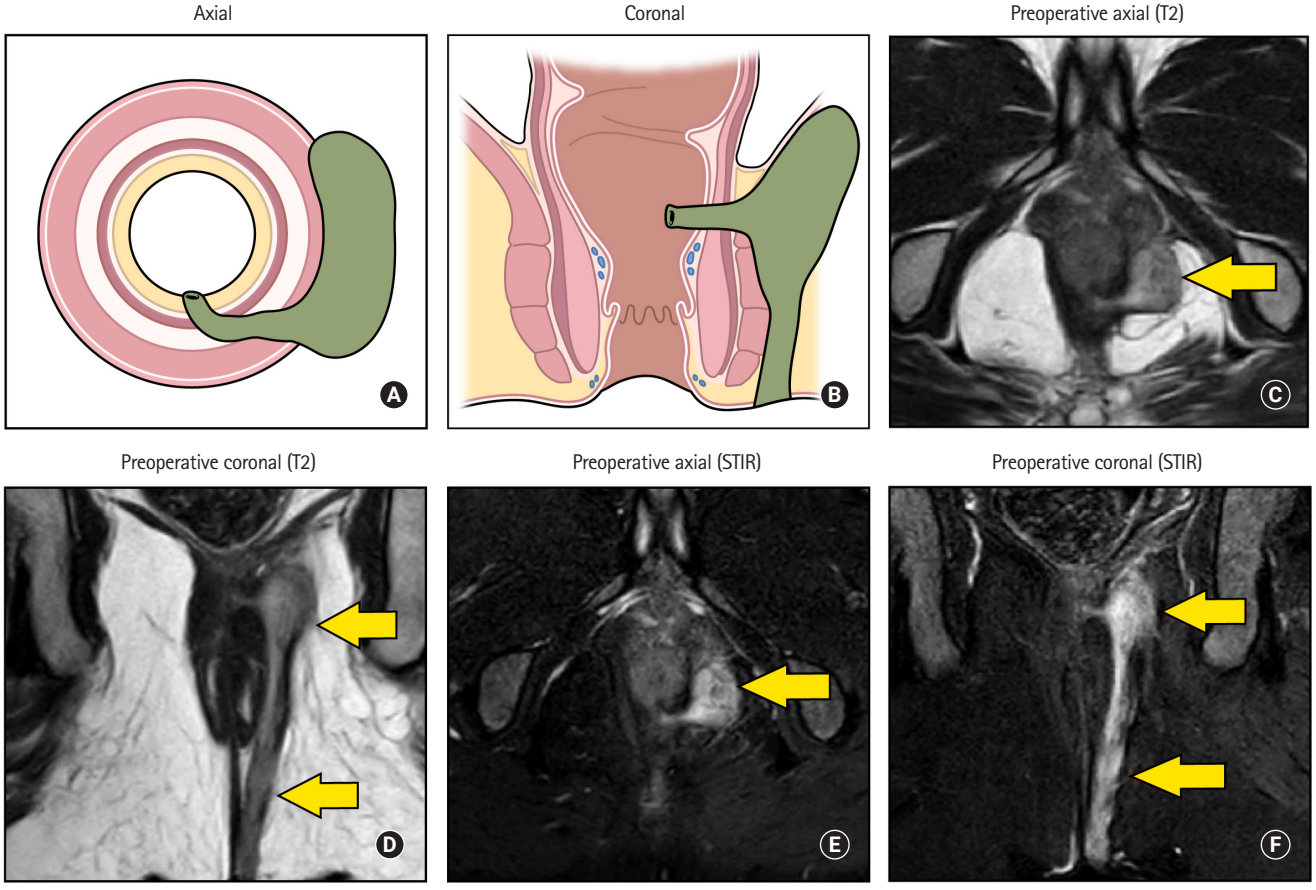

Fig. 2. A 42-year-old man presented with a left high transsphincteric fistula extending into the left roof of ischiorectal fossa inside levator ani muscle (RIFIL) space. (A) Schematic diagram of the axial section, revealing a fistula in the left outersphincteric space. (B) Schematic diagram of the coronal section, illustrating a left high transsphincteric fistula extending into the left RIFIL space. (C) On preoperative magnetic resonance imaging (MRI), the axial T2-weighted image reveals a fistula in the left outersphincteric space. (D) On preoperative MRI, the coronal T2-weighted image demonstrates a left high transsphincteric fistula extending into the left RIFIL space. (E) On preoperative MRI, the axial short-tau inversion recovery (STIR) image reveals a fistula in the left outersphincteric space. (F) On preoperative MRI, the coronal STIR image shows a left high transsphincteric fistula extending into the left RIFIL space. Arrows indicate the fistula.

for detecting TB [8, 9]. Additionally, RT-PCR analysis of pus has yielded higher detection rates compared to RT-PCR of fistula tissue [8, 9]. In a large study involving 1,336 samples from 776 patients, TB was identified in 133 samples (122 patients). Specifically, TB was detected in 77 of 331 pus samples (23.2%) tested with PCR, 52 of 703 tissue samples (7.4%) tested with PCR, 3 of 197 tissue samples (1.5%) tested with histopathological examination (HPE), and 1 of 105 samples (0.9%) tested with GeneXpert. PCR tissue testing was significantly more effective than HPE tissue analysis for detecting TB (7.4% vs. 1.5%, $P=0.0012$). Furthermore, complex fistulas were more common among TB-related fistulas than nontuberculous fistulas (69% vs. 44.3%, $P<0.00001$) [8]. Research also suggests that initiating anti-TB treatment either preoperatively or within 6 weeks postoperatively is preferable for optimal outcomes [8, 9]. In conclusion, while PCR represents the leading diagnostic method for TB in anal fistulas, the results must be interpreted in conjunction with clinical findings.

RADIOLOGY

Magnetic resonance imaging

MRI in the preoperative management of fistulas

The indications for MRI in patients with fistulas are subject to debate. The most widely accepted indication is for recurrent fistula. MRI is also indicated for complex fistulas, although the definition of this condition has not yet been standardized. A large study involving 229 patients produced noteworthy results [10]. This study correlated preoperative clinical assessments and MRI data with intraoperative findings. The results showed that 34.6% of fistulas that appeared simple upon clinical examination were actually

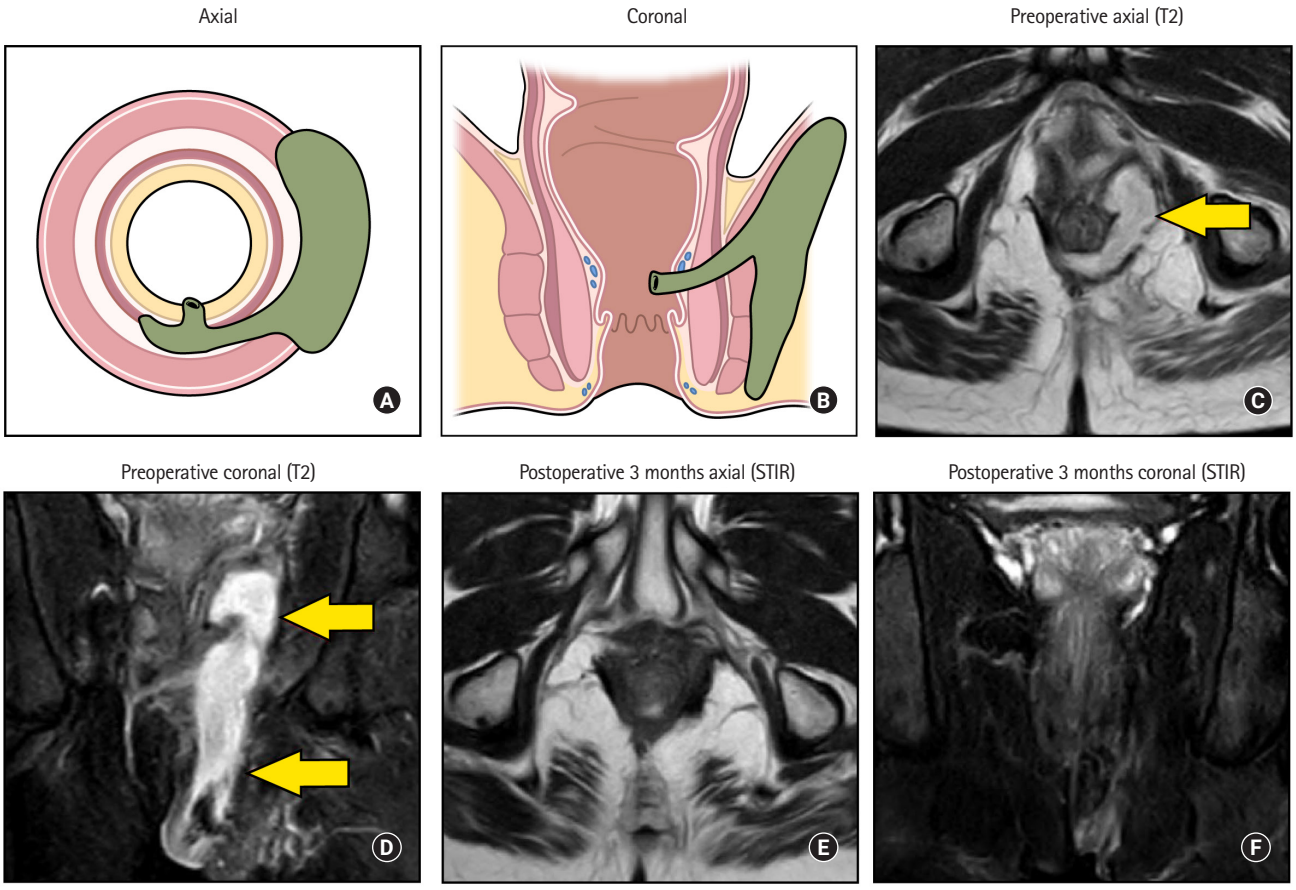

Fig. 3. A 51-year-old man with recurrent left high intersphincteric horseshoe abscess and fistula extending into the left roof of ischiorectal fossa inside levator ani muscle (RIFIL) space. He underwent successful management with the transanal opening of intersphincteric space (TROPIS) procedure, and postoperative magnetic resonance imaging (MRI) at 3 months confirmed complete healing of the fistula. (A) Schematic diagram of the axial section. (B) Schematic diagram of the coronal section, illustrating a left high intersphincteric abscess and fistula extending into the left RIFIL space. (C) On preoperative MRI, the axial T2-weighted image demonstrates a left-sided horseshoe intersphincteric abscess. The arrow indicates the fistula. (D) On preoperative MRI, the coronal short-tau inversion recovery (STIR) image reveals a left high intersphincteric horseshoe abscess and fistula extending into the left RIFIL space (arrows). (E) MRI axial T2-weighted image, taken 3 months postoperatively, demonstrating complete healing of the fistula and closure of the internal opening. (F) MRI coronal STIR image, taken 3 months postoperatively, demonstrating complete healing of the fistula and closure of the internal opening.

complex according to MRI analysis. Among fistulas that seemed complex based on clinical features, MRI provided information that influenced surgical decision-making in 52.5% of cases. The diagnostic accuracy of MRI was reported to be 98.6% for detecting fistula tracts and 97.7% for identifying internal openings. These results strongly support the routine use of MRI, even for fistulas that appear simple, as it impacted surgical decisions in approximately 1/3 of these cases and in about half of cases that appeared complex upon clinical examination. Consequently, regular MRI use could improve surgical outcomes and reduce the rate of recurrence. However, the cost of MRI remains a limiting factor. Therefore, the decision to use MRI for simpler fistulas should be carefully weighed, considering the cost of the imaging procedure, the risk of recurrence, and the potential consequences of recurrence.

Another study revealed that over half of the patients with recurrent fistula in ano exhibited anal sphincter defects or scarring, detected via MRI using an external phased-array coil [11]. Employing a combination of diffusion-weighted imaging (DWI) and T2-weighted (T2W) evaluation has demonstrated better performance in detecting fistulas than using either DWI or T2W imaging alone [12]. Additionally, DWI with the calculation of the mean apparent diffusion coefficient appears particularly effective in distinguishing between active and inactive fistulas, thus providing valuable information for treatment planning [13]. When not contraindicated, the administration of contrast is recommended to differentiate between abscesses and active inflammation [11].

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MRI reporting templates

Many in the field recognize the need to standardize the reporting of MRI and transrectal ultrasound by radiologists. Standardization would not only harmonize reporting practices worldwide but also make the task simpler and more objective for radiologists. Consistent reporting would ensure that all relevant information is included, thereby minimizing the loss of critical data during the transfer of information from the radiologist to the operating surgeon. In recent years, several templates have been developed to address this issue [14–16]. The most comprehensive effort to date is the creation of the Structured MRI and Endoanal Ultrasound Anal Fistula Reporting Template (SMART) [17]. This template was developed through a consensus-based Delphi study involving 96 experts, including 69 colorectal surgeons, 23 radiologists, 2 anatomists, and 1 gastroenterologist, from around the world. It has also received endorsements from 11 scientific societies, comprising 3 radiological and 8 surgical organizations.

Anal fistula is a 3-dimensional (3D) pathology characterized by complex networks of fistula tracts and the sphincter complex. To minimize information loss when reporting fistula findings on MRI and endoanal ultrasound (EAUS), various strategies are being developed. One such strategy is the 3D printing of MRI images [18]. The advent of 3D-EAUS has made this possible. Availability of a rotatable 3D model before surgery enables more precise detection of the location and extent of perianal disease. Additionally, it may reduce the interobserver variability associated with interpreting complex MRI scans prior to surgery [18]. Another recommendation is to supplement the written report with a video in which the radiologist explains and describes the characteristics of the fistula [16]. This approach not only conveys visual information alongside the written report but also supports the surgeons' learning process, while eliminating the need for the surgeon to be present in the MRI room.

Another excellent recommendation was to include a new parameter, height of penetration of the EAS (HOPE) by the anal fistula, in the reporting template. Typically, the extent of EAS involvement by the anal fistula is not detailed in the MRI report. However, this variable can be assessed by measuring HOPE on an MRI. The EAS is crucial for maintaining continence, and understanding the degree of its involvement by the fistula is essential to avoid damaging it during surgery. Notably, HOPE is distinct from the height of the internal or primary opening, which radiologists commonly report. HOPE and the height of the internal opening may differ in certain patients because a fistula can penetrate a substantial portion of the EAS before curving downward to open at a lower point, such as at the dentate line, as evident in suprasphincteric fistulas. In such scenarios, the HOPE parameter is of greater relevance to the surgeon than the height of the internal opening [16].

Role of MRI in the postoperative management of fistulas

Apart from preoperative assessment, the postoperative role of MRI in evaluating the healing of fistulas, particularly complex ones, has become increasingly important. MRI is particularly effective in assessing and confirming the complete healing of the internal opening and the intersphincteric portion of the fistula tract, with an accuracy rate exceeding 99.2% [19]. Furthermore, the radiological healing of the fistula as seen on MRI is highly correlated with the long-term healing of complex fistula in ano [19]. Clinically confirming the healing of these fistula components can be challenging [19]. However, radiological healing of fistulas typically trails behind clinical healing. During the early postoperative period (6–10 weeks), it can be difficult to distinguish healing (marked by granulation tissue) and inflammation from an active fistula tract or pus [20]. Consequently, postoperative MRI to assess fistula healing should be delayed until at least 12 weeks following surgery [20, 21].

MRI-based scoring system to predict long-term fistula healing

Anal fistula is notorious for its potential to recur, sometimes months or even years after surgical intervention. This possibility of recurrence causes considerable anxiety for both patients and surgeons, as the fear of the condition returning lingers even after clinical healing has been achieved. To mitigate this issue, various nomograms and scoring systems have been developed [22–24].

The Garg scoring system, detailed in Table 1, is recognized as the most accurate and user-friendly [23, 24]. Developed from a long-term follow-up study that analyzed 283 MRI scans from 183 patients, this scoring system incorporates 6 parameters —4 based on MRI findings and 2 on clinical examination—and assigns them differential weights based on a robust statistical methodology. Scores are calculated 3 months postoperatively and serve as predictors for the long-term outcomes of fistula healing. A total weighted score below 8 indicates that the fistula has healed and is unlikely to recur, while a score of 8 or above suggests that the fistula has not healed or is prone to recurrence (Table 1) [23, 24]. The Garg scoring system has demonstrated a very high positive predictive value (98.2%) and a moderately high negative predictive value (83.7%) [23], suggesting that a fistula deemed healed according to this system at 3 months postsurgery has an extremely low chance of recurrence (less than 1.8%). Further validation of the Garg scoring system in a prospective cohort of 57 patients revealed a positive predictive value of 100% [24].

Table 1. Garg scoring system for the prediction of long-term anal fistula healing [23, 24]

Parameter	Scoring	Weight	Possible weighted score	
			Minimum	Maximum
MRI assessment 3 mo after surgery				
1. Nonhealing of internal (primary) opening	Healed, 0 Not healed, 1	4	0	4
2. Nonhealing of fistula tract in the intersphincteric space	Healed, 0 Not healed, 1	4	0	4
3. Nonhealing of external tracts in the ischiorectal fossa	Healed, 0 Not healed, 1	1	0	1
4. Development of a new abscess in the intersphincteric space during the postoperative period	No, 0 Yes, 1	4	0	4
Clinical assessment 3 mo after surgery			0	
5. Flatus passage from any of the external openings (even occasionally)	No, 0 Yes, 1	4	0	4
6. Discharge from any external opening or anus	No, 0 Serous, 1 Purulent (lower amount, < 50% of preoperative quantity), 2 Purulent (higher amount, > 50% of preoperative quantity), 3	1	0	3
Total	-	-	0	20

A total weighted score < 8 indicates healing; a total weighted score ≥ 8 indicates nonhealing.
MRI, magnetic resonance imaging.

Artificial intelligence in MRI

The integration of artificial intelligence into coloproctology has included the application of artificial intelligence-assisted compressed sensing MRI for anal fistula. This approach has yielded superior subjective image perceptions and improved image quality, characterized by increased signal to noise and contrast to noise ratios. It also provides clear parameters for evaluating the accuracy of imaging information regarding the location of fistulas and the involved pelvic structures. Moreover, a 50% reduction in acquisition time has facilitated preoperative diagnosis and postoperative assessment, proving particularly beneficial for uncooperative patients who are prone to motion artifacts that can severely impact image quality [25].

Ultrasound in anal fistula

EAUS, whether transrectal or transperineal, is a valuable tool for evaluating anal fistula. The advent of 3D-EAUS has augmented the diagnostic process by providing detailed multiplanar reconstructions of the anal canal. This technology offers superior accuracy in delineating the relationship between the anal sphincter and the fistula tract. Additionally, it improves the detection of fistula tracts, internal openings, and defects in the anal sphincter, which are crucial considerations in surgical planning to preserve the integrity of the anal sphincter complex [26]. EAUS is favored for its cost-effectiveness, accessibility, and ease of follow-up. However, unlike MRI, EAUS is operator-dependent, and the images it produces cannot be reinterpreted by another radiologist or surgeon. In terms of accuracy, EAUS is comparable to, or slightly less accurate than, MRI. Thus, MRI is regarded as the gold standard for investigating anal fistula.

Various comparative studies have been conducted in recent years. EAUS was found to be slightly superior to MRI in pinpointing the internal opening; however, MRI was favored over EAUS for evaluating extrasphincteric fistulas and characterizing fibrotic tracts [27]. Another study indicated that EAUS was more accurate than MRI in detecting transsphincteric and intersphincteric fistulas, whereas MRI proved to be more effective in identifying suprasphincteric fistulas compared to EAUS [28]. A study published in 2024 comparing 3D-EAUS with external phased-array MRI found that the modalities were comparable in detecting internal anal sphincter lesions, but MRI detected more external sphincteric lesions than EAUS [29].

Cost-effectiveness of diagnostic tests for anal fistulas

Both MRI and EAUS are valuable diagnostic tools that aid in the detailed evaluation of fistula characteristics, planning of surgical management, and confirmation of fistula healing in the postoperative period. However, economic considerations must be addressed. The cost of these imaging modalities varies around the world. For instance, an MRI examination can cost between US

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$1,000 to $7,000 in the United States and Europe, while in India, the price ranges from approximately US $75 to $125. Similarly, EAUS may cost between US $300 and $3,000 in the United States and Europe, compared to US $25 to $75 in India. This cost disparity imposes a considerable financial burden on patients in higher cost regions. To alleviate these financial challenges, various policies could be implemented. These might include subsidizing the cost of MRI and EAUS, incorporating these tests into insurance coverage, and fostering public-private partnerships to increase the affordability and accessibility of these services. One benefit of EAUS is that it can be performed by the operating surgeon in an outpatient setting. This not only reduces the cost but also improves the utility and accessibility of EAUS, allowing for more frequent monitoring of postoperative recovery. Surgeons should also be proficient in interpreting MRI scans. Unlike EAUS, MRI is not operator-dependent, meaning that scans performed at a certain location can be interpreted by surgeons elsewhere. This capability can reduce the need for repeated MRIs in cases of complex fistula, ultimately helping to lower costs. In complex fistula cases, a practical approach might be to perform an MRI preoperatively and then use EAUS for follow-up assessments as needed, conducted at the operating surgeon's office. In summary, both MRI and EAUS are beneficial diagnostic modalities. Optimizing their application and cost is essential to maximize their utility and cost-effectiveness.

ANAL FISTULA MANAGEMENT

Fistula classification

The Parks classification was introduced in 1976, at a time when neither MRI nor EAUS were utilized for fistula assessment. This system categorized fistulas based on the anatomical pathway of the primary tract, distinguishing between intersphincteric and transsphincteric types (Table 2) [30]. The St. James University Hospital (SJUH) MRI-based classification, proposed by Morris et al. [31] in 2000, was highly similar to the Parks classification, with Parks grades I and II each being further divided into 2 subgroups (Table 2). However, a major shortcoming of both the Parks and SJUH classifications was that they were neither based on nor validated by patient data, and consequently, they did not classify fistulas according to their severity. Additionally, these classifications offered no guidance to surgeons on disease management. The Garg classification, introduced in 2017, classifies fistulas based on the extent of sphincter involvement rather than the anatomical

Table 2. Anal fistula classifications

Grade	Parks classification	St. James University Hospital classification	Garg classification
I	Intersphincteric	Intersphincteric linear	Low transsphincteric/low or high intersphincteric: single tract
II	Transsphincteric	Intersphincteric with extension(s) or associated abscess	Low transsphincteric/low or high intersphincteric: multiple tracts horseshoe or associated abscess
III	Suprasphincteric	Transsphincteric linear	IIIA: high transsphincteric (single tract)
			IIIB: anterior fistula in a female patient or any lower grade fistula with associated comorbidities[a]
IV	Extrasphincteric	Transsphincteric with extension(s) or associated abscess	High transsphincteric: multiple tract horseshoe or associated abscess
V	-	Supralevator and translevator extension	Suprasphincteric or supralevator orextrasphincteric or RIFIL fistula

Low fistula involves no more than 1/3, while high fistula involves more than 1/3, of the sphincter.
RIFIL, roof of ischiorectal fossa inside levator ani muscle.
[a]Comorbidities include Crohn disease, existing sphincter injury/weakness, and history of radiation.

Table 3. Garg classification [32, 33, 35]

Grade	Fistula description	Severity[a]
I	Low (single tract; intersphincteric or transsphincteric)	Simple
II	Low (multiple tracts or associated abscess or horseshoe tract; intersphincteric or transsphincteric)	Simple
III	High (single tract; intersphincteric or transsphincteric), anterior fistula in a female patient, or associated comorbidities[b]	Complex
IV	High (multiple tracts or associated abscess or horseshoe tract; intersphincteric or transsphincteric)	Complex
V	Suprasphincteric, supralevator, extrasphincteric, or RIFIL	Complex

"Low" fistula involves no more than 1/3 of the external sphincter, while "high" involves more than 1/3 of the sphincter.
RIFIL, roof of ischiorectal fossa inside levator ani muscle.
[a]Simple, fistulotomy can be performed safely; complex, fistulotomy can be avoided and a sphincter-saving procedure performed. [b]Associated comorbidities include already damaged/weakened sphincter, history of radiotherapy, and Crohn disease.

plane (Tables 2, 3) [32–34]. Developed through a study of 440 patients, the Garg classification represents the only system that has been established and later validated in a large cohort (848 patients) [35]. Notably, it is the first classification to grade the severity of the disease and provide surgeons with management guidance (Table 3) [35].

According to this classification, Garg grades I and II represent low fistulas, involving no more than 1/3 of the EAS, and are categorized as simple fistulas. Grades III and V are high fistulas, involving more than 1/3 of the EAS, and are of increasing complexity, thus classified as complex fistulas (Table 3) [32, 33, 35]. This distinction between low and high fistulas is the most critical factor for the operating surgeon. Unlike previous systems, the Garg classification provides clear guidance on the feasibility of performing fistulotomy—the most common and simplest procedure for anal fistulas worldwide. If a fistula is classified as simple (low, Garg grade I–II), fistulotomy can be safely performed. Conversely, if a fistula is complex (high, Garg grade III– V), fistulotomy is contraindicated, and a sphincter-sparing procedure is recommended [35].

Fistulotomy has the highest cure rate among all known procedures, with an impressive 96% to99% success rate. However, it remains highly underutilized due to surgeons' concerns about incontinence [36]. The Garg classification effectively addresses this concern. Additionally, fistulotomy is a technically straightforward procedure and is widely performed by general surgeons around the world, especially in developing countries [36]. With the inclusion of the Garg classification in MRI/EAUS reports, general surgeons can determine with greater precision when to perform fistulotomy and when to refer the patient to a specialized fistula or colorectal surgeon.

Garg cardinal principles for the management of complex fistulas

The 3 principles of management for complex fistula in ano, as devised by Garg [37], are as follows: (1) intersphincteric tract is like an abscess in a closed space (ISTAC); (2) drain all pus and ensure continuous drainage (DRAPED) postoperatively until complete healing occurs; and (3) healing occurs progressively until it is interrupted irreversibly by a collection (HOPTIC). More specifically, ISTAC suggests that a fistula tract in the intersphincteric space functions similarly to an abscess in a confined space and should be drained accordingly. DRAPED underscores the importance of evacuating the pus and maintaining effective drainage throughout the postoperative period until healing is complete. HOPTIC posits that the healing process is ongoing unless it is halted or permanently obstructed by an accumulation of pus or serous fluid. Surgical procedures should align with these principles to achieve optimal results. For instance, procedures such as transanal opening of the intersphincteric space (TROPIS) [38–40] and fistulectomy with primary reconstruction (FPR), which are based on the tenets of ISTAC and DRAPED, often result in better outcomes compared to the ligation of the intersphincteric fistula tract (LIFT) method. The LIFT technique, which primarily focuses on ISTAC and neglects DRAPED (since the opened intersphincteric space is not maintained postoperatively), has yielded moderate success rates.

Management of additional supralevator opening in complex fistula

Supralevator fistula in ano presents considerable management challenges, particularly when the fistula has an additional supralevator rectal opening (ASRO) beyond the primary internal opening at the dentate line. Prior to recent research, no guidelines or literature were available on the management of ASROs. The first study to address this issue was conducted by Garg et al. [41] in 2021. In that comparative study, the ASRO was managed in 3 distinct ways: (1) the ASRO was laid open into the rectum in continuity with the primary opening at the dentate line; (2) the mucosa around the ASRO was cauterized; or (3) the ASRO was left untreated. The findings suggested that the ASRO healed well regardless of the option employed. This result underscores the importance of properly managing the primary opening at the dentate line, as it appears to be the key factor in fistula healing. The study also provides reassuring evidence that leaving the ASRO untreated does not compromise the ultimate outcome of the fistula.

Management of fistulas with nonlocatable internal openings

In 10% to 25% of anal fistula cases, the internal or primary opening cannot be identified, even after thorough examination and assessment using MRI or transrectal ultrasound. A nonlocatable internal opening is associated with a particularly high risk of recurrence, up to 22 times higher than cases in which the opening can be located [42]. To address the issue, the Garg protocol was developed and has been demonstrated highly effective in managing fistulas with nonlocatable internal openings.

Garg protocol

In this protocol, MRI or EAUS is reevaluated to identify the site where the fistula is closest to the internal sphincter. It is presumed that the internal opening is situated at this location, and treatment is planned accordingly. For horseshoe anal fistulas lacking a visible internal opening, the protocol posits that the internal opening

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is likely to be in the midline— specifically, the posterior midline for posterior horseshoe fistulas and the anterior midline for anterior horseshoe fistulas (Fig. 4) [42].

New scoring system for the clinical assessment of FI

Several prevalent scoring systems exist for the evaluation of FI, with the most frequently used being the Cleveland Clinic scoring system, also known as the Wexner score, and the St. Mark's Hospital or Vaizey scores [43, 44]. However, these systems have serious shortcomings, rendering them neither accurate nor comprehensive. They are not derived from patient data, attribute equal weights to all types of FI (for instance, treating solid incontinence the same as flatus incontinence), are based on surgeons' perceptions, lack comprehensiveness, and introduce confounding bias, as symptoms secondary to FI are also assigned points. These issues have been addressed in the recently developed Garg Incontinence Scores (GIS), detailed in Table 4 [45–47]. The GIS assign different weights to various types of FI using a robust statistical methodology. They display superior comprehensiveness, incorporating all types of FI, including urge, stress, and mucus FI, which were previously omitted. Additionally, the GIS prioritized patient perspectives over physician perceptions in the development of the scoring system. Therefore, the GIS represent a paradigm shift in the evaluation of FI (Table 5) [45–47].

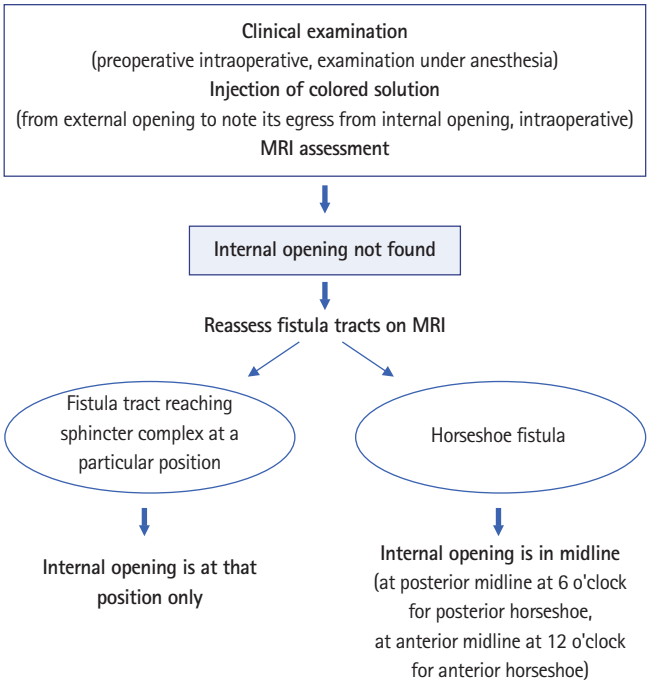

Fig. 4. The Garg protocol for the management of fistula with nonlocatable internal opening. MRI, magnetic resonance imaging.

UPDATE ON SURGICAL PROCEDURES FOR THE MANAGEMENT OF ANAL FISTULAS: FISTULOTOMY

Fistulotomy remains the gold standard for treating low fistulas [36]. However, this procedure is highly underutilized due to concerns about incontinence. This underutilization is regrettable, considering that fistulotomy is associated with the highest success rates, ranging from 95% to 100%. Consequently, when low fistulas suitable for fistulotomy are subjected to alternative treatments with lower success rates, unnecessary recurrences may result. The Garg classification plays a key role in this context, as it helps surgeons determine which fistulas can safely undergo fistulotomy (Garg grades I–II) and which should not (Garg grades III–V), as shown in Table 2 [32, 33, 35].

Recent attempts at sphincter closure after fistulotomy have yielded promising outcomes. A study assessing the safety and long-term efficacy of fistulotomy with primary sphincteroplasty (FIPS) concluded that FIPS should be considered a viable treatment option for selected simple anal fistulas, specifically intersphincteric and low transsphincteric types [48]. Compared to fistulectomy, fistulotomy offers several advantages: shorter operating time, reduced length of postoperative hospital stay, faster wound

Table 4. Garg Incontinence Scores [45–47]

Incontinence type	Weight	Frequency (point)			Maximum score
		Never	Occasional (≤1 episode/week)	Common (>1 episode/wk)	
Solid	8	0	1	2	16
Liquid	8	0	1	2	16
Urge	7	0	1	2	14
Flatus	6	0	1	2	12
Mucus	6	0	1	2	12
Stress	5	0	1	2	10
Total	-	-	-	-	80

Score in a cell = (weight for that incontinence type) × (frequency points). For example, a person with occasional liquid incontinence would have a score of 8 × 1 = 8. The maximum possible score is 80 (indicating total incontinence), while the minimum score is 0 (indicating no incontinence).

Table 5. Comparison of existing scoring systems for the clinical assessment of FI [45, 47]

Variable	Wexner score	Vaizey score	FISI	GIS
Comprehensive	No	No	No	Yes
FI type included				
Urge FI	No	Yes	No	Yes
Mucous FI	No	No	Yes	Yes
Presence of confounding parameters like "need to wear a pad," "need to take constipation-causing medicine," and "alteration of lifestyle"	Yes	Yes	No	No
Assignment of weights to each FI by an objective method	No	No	No	Yes
Inclusion of patient perceptions (n)	0	0	34	50
Inclusion of laypersons' perceptions (n)	0	0	0	50
Simple and easy to use	+++++	+++++	+	+++++
Detailed structured definitions	No	No	No	Yes
In-depth disability scores based on an objective description system	No	No	No	4D3L

FI, fecal incontinence; FISI, Fecal Incontinence Severity Index; GIS, Garg Incontinence Scores; 4D3L, 4 dimensions and 3 levels (modifed EQ-5D [EuroQol] description system).

healing, less postoperative pain, and lower incidence of postoperative complications [49]. Due to these benefits, fistulotomy has outperformed fistulectomy and remains the preferred treatment for patients with simple low-lying fistula in ano [49].

Fistulectomy with primary reconstruction

Fistulectomy for low fistulas is slightly less effective than fistulotomy, while fistulectomy for high fistulas carries a high risk of failure. Consequently, FPR, which includes primary sphincter repair, has garnered considerable interest. FPR has a high success rate (90%–95%) and is associated with minimal impact on continence [50, 51]. However, FPR is a technically challenging procedure and is generally not recommended for high transsphincteric fistulas (those involving more than 2/3 of the EAS) and suprasphincteric fistulas [50, 51].

Transanal opening of the intersphincteric space

The TROPIS procedure, a recently developed sphincter-preserving technique, stands out as the most promising of these approaches for managing complex anal fistulas (Fig. 5) [38–40]. This procedure is grounded in the ISTAC and DRAPED principles [37]. TROPIS represents a meaningful advancement in the treatment of complex fistula for 2 main reasons. First, it effectively addresses the intersphincteric part of the fistula tract by deroofing it into the anal canal via a transanal approach. Second, it promotes healing of the internal opening and the deroofed intersphincteric tract through secondary intention (Fig. 3).

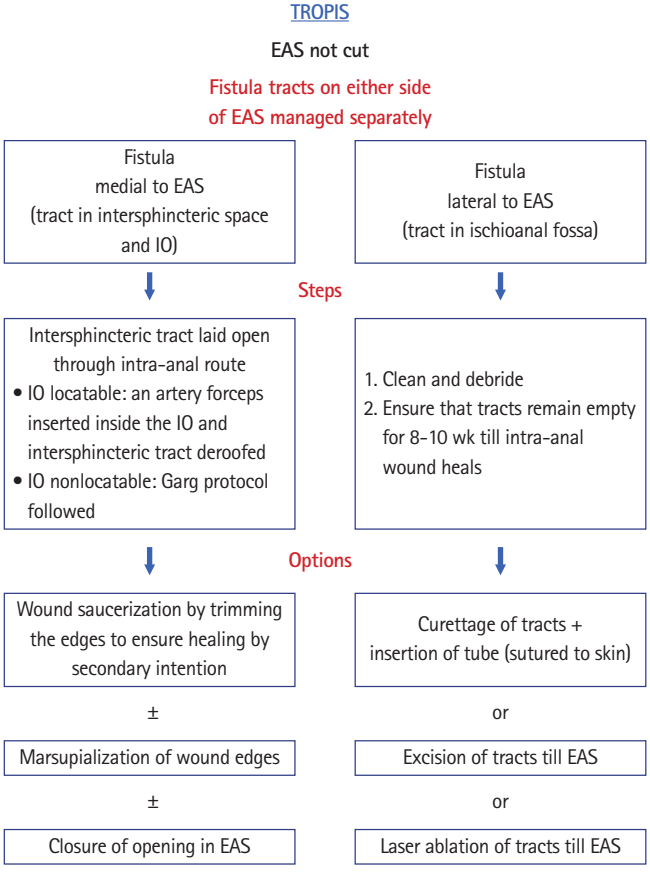

Fig. 5. Overview of transanal opening of the intersphincteric space (TROPIS). EAS, external anal sphincter; IO, internal opening.

In the TROPIS procedure, artery forceps are inserted transanally into the internal opening to access the fistula tract within the intersphincteric space. The mucosa and internal sphincter above the artery forceps are incised, and the edges are trimmed using electrocautery. Subsequently, the fistula tract in the intersphincteric space is laid open into the anal canal. This wound is left open to heal by secondary intention. Thus, the underlying principle of TROPIS is that healing in the presence of sepsis is more effective and reliable by secondary intention than by primary intention, which would involve attempting to close the internal opening

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with sutures. Fistula tracts lateral (or external) to the EAS can be managed using any method the surgeon finds convenient, such as excision or curettage with the insertion of a drainage tube or laser ablation (Fig. 5). A recent meta-analysis demonstrated that the TROPIS procedure has a success rate of 86%–93% (with a weighted healing rate of 89%) for treating complex high fistulas [52], as evidenced by long-term follow-up studies conducted around the world (Fig. 3) [38–40]. Another meta-analysis focusing on sphincter-sparing surgical procedures for complex anal fistula found that TROPIS has the highest cure rate among all reviewed procedures [53]. An additional benefit of TROPIS is its high success rate as a definitive primary single-stage procedure for fistulas associated with abscesses [54].

Ligation of the intersphincteric fistula tract

The LIFT procedure has been popular for over a decade as a sphincter-sparing procedure for the treatment of complex fistula. Numerous studies have reported high success rates, and a recent meta-analysis indicated pooled success and complication rates for LIFT of approximately 76% and 14%, respectively [55]. However, a prospective randomized controlled trial comparing LIFT with other surgical techniques found a lower success rate for LIFT, at about 42% [56]. This discrepancy may be due to the procedure's substantial reliance on the skill of the operator. Modifications to LIFT, such as the incorporation of a bioprosthetic graft (BioLIFT), have yielded improved surgical outcomes [57]. Additionally, the use of bone marrow mononuclear cells was found to accelerate healing, although this did not translate into improved healing success rates [58].

Device-based sphincter-sparing procedures

In the last decade, a number of device-based procedures have been developed and studied, including fibrin glue [59], anal fistula plug [60], over-the-scop clip (OTSC) [61], video-assisted anal fistula treatment [62], laser treatment for fistula in ano (Fistula-tract Laser Closure [FiLaC] or laser ablation of fistula tract [LAFT]) [63, 64], and FiXcision [65]. These device-based procedures initially demonstrated an encouraging success rate of 70% to 90%. However, over time, the success rate has markedly declined to 20% to 55%. These procedures were primarily developed to preserve continence in highly complex fistulas and appear effective for that purpose. However, almost all studies of these procedures have been conducted on simpler fistulas rather than an exclusive cohort of complex fistulas. In these studies, a success rate of 30% to 60% has been reported, predominantly in simple fistulas. For simple fistulas, the success rate of fistulotomy is between 95% and 100%, with no deterioration in continence observed. Although these device-based methods were originally designed for highly complex fistulas, the lack of data in this specific subset (that is, high complex fistulas exclusively) raises questions about their utility. Nonetheless, these procedures may be offered to patients who prefer sphincter-sparing options, provided they are fully informed about the high risk of recurrence.

Importantly, these device-based procedures primarily aim to manage the external aspects of fistula tracts without addressing the intersphincteric portion. Consequently, these procedures tend to have moderate success in treating simple low fistulas, which typically have minimal or no intersphincteric involvement, while they exhibit a lower success rate in managing complex high fistulas, which typically include a segment of the fistula tract within the intersphincteric plane.

Seton management of fistula in ano

The loose draining seton continues to play a role in the management of anal fistulas, serving as an adjunct to other procedures, and in the treatment of acute abscesses. However, the cutting seton also remains in use in many regions globally [66]. For low fistulas, the cutting seton demonstrates a high success rate; however, it is associated with greater morbidity and pain compared to fistulotomy, making it a less favorable option [67]. In the context of high fistulas, cutting seton use has been linked to a decline in continence, although the current data are insufficient to draw definitive conclusions.

Another novel technique is the "tube in tract" method, which serves as an alternative to the draining seton [68]. In this approach, a draining tube of an appropriate size is inserted into the external tract, positioned in the ischiorectal fossa but not traversing the EAS. The tube is then sutured to the skin. This method offers several advantages over a loose draining seton. Since it does not pass through the EAS or the internal opening, the likelihood of fistula closure is greater compared to a draining seton, which extends through the internal opening and keeps it patent. Occasionally, the sling may adhere or close around the seton, halting drainage; this issue does not occur with a draining tube. Additionally, the size of the tube can be adjusted to accommodate the volume of drainage needed. The underlying principle is that the skin at the external opening is problematic, as it tends to close prematurely, leading to the accumulation of pus. By ensuring that the skin at the opening remains patent with the use of a draining tube, the issue is addressed more effectively.

PRP in fistula treatment

Platelet-rich plasma (PRP) has shown positive results when used as an adjunct to other procedures. A meta-analysis revealed that

combining LIFT with PRP led to lower failure and complication rates in the management of complex anal fistula compared to other tested methods [69]. Another meta-analysis reported that the success rate of PRP in conjunction with other procedures was approximately 72.11%, whereas the cure rate for PRP alone stood at 62.39% [70]. However, long-term results are still anticipated.

Stem cell therapy in fistula treatment

Though still in the initial phase, mesenchymal stem cell therapy could represent a novel therapeutic approach for complex perianal fistulas, demonstrating high efficacy in the short term [71]. Autologous adipose-derived stem cells have also yielded promising results, with healing rates of up to 50% [72]. The primary appeal of stem cell therapy lies in its safety profile; however, its use is frequently limited due to high costs.

CONCLUSION

Anal fistulas, particularly complex ones, continue to pose a therapeutic challenge. With advances in diagnostic modalities, such as MRI and EAUS, these techniques have become crucial in diagnosis, disease assessment, and management planning. MRI has also facilitated the development of a new and improved classification system—the Garg classification—which enables surgeons to distinguish between simple and complex fistulas. MRI has been instrumental in identifying previously unrecognized anatomical spaces, such as the outersphincteric space, and pathways of fistula spread, exemplified by the RIFIL fistula. Furthermore, MRI is crucial for assessing and confirming the postoperative healing of fistulas. The role of properly addressing the intersphincteric portion of the fistula tract is now better understood, contributing to improved cure rates. Although several new device-based procedures have been introduced over the past decade, none has yet demonstrated substantial promise. While considerable progress has been made in the field of anal fistulas, much remains to be achieved.

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Conflict of interest

No potential conflict of interest relevant to this article was reported.

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REFERENCES

1. Cosman BC. All's Well That Ends Well: Shakespeare's treatment of anal fistula. Dis Colon Rectum 1998;41:914–24.
2. Bhattacharya K, Bhattacharya N. Abu Al Qasim Al Zahrawi: the father of operative surgery. Indian J Surg 2023;85:946–9.
3. Garg P, Kaur B, Yagnik VD, Dawka S. A new anatomical pathway of spread of pus/sepsis in anal fistulas discovered on MRI and its clinical implications. Clin Exp Gastroenterol 2021;14:397–404.
4. Garg P, Kaur B. The new pathways of spread of anal fistula and the pivotal role of MRI in discovering them. Abdom Radiol (NY) 2021;46:3810–4.
5. Garg P, Dawka S, Yagnik VD, Kaur B, Menon GR. Anal fistula at roof of ischiorectal fossa inside levator-ani muscle (RIFIL): a new highly complex anal fistula diagnosed on MRI. Abdom Radiol (NY) 2021;46:5550–63.
6. Garg P, Yagnik VD, Dawka S, Kaur B, Menon GR. Guidelines to diagnose and treat peri-levator high-5 anal fistulas: supralevator, suprasphincteric, extrasphincteric, high outersphincteric, and high intrarectal fistulas. World J Gastroenterol 2022;28:1608–24.
7. Yagnik VD, Kumar S, Thakur A, Bhattacharya K, Dawka S, Garg P. Recent advances in the understanding and management of anal fistula from India. Indian J Surg 2024 Feb 13 [Epub]. https://doi.org/10.1007/s12262-024-04050-9
8. Garg P, Goyal A, Yagnik VD, Dawka S, Menon GR. Diagnosis of anorectal tuberculosis by polymerase chain reaction, GeneXpert and histopathology in 1336 samples in 776 anal fistula patients. World J Gastrointest Surg 2021;13:355–65.
9. Garg P, Garg M, Das BR, Khadapkar R, Menon GR. Perianal tuberculosis: lessons learned in 57 patients from 743 samples of histopathology and polymerase chain reaction and a systematic review of literature. Dis Colon Rectum 2019;62:1390–400.
10. Garg P, Singh P, Kaur B. Magnetic resonance imaging (MRI):

https://doi.org/10.3393/ac.2024.00325.0046

operative findings correlation in 229 fistula-in-ano patients. World J Surg 2017;41:1618–24.
11. Vo D, Phan C, Nguyen L, Le H, Nguyen T, Pham H. The role of magnetic resonance imaging in the preoperative evaluation of anal fistulas. Sci Rep 2019;9:17947.
12. Lefrançois P, Zummo-Soucy M, Olivié D, Billiard JS, Gilbert G, Garel J, et al. Diagnostic performance of intravoxel incoherent motion diffusion-weighted imaging and dynamic contrast-enhanced MRI for assessment of anal fistula activity. PLoS One 2018;13:e0191822.
13. Liu X, Wang Z, Ren H, Ren A, Wang W, Yang X, et al. Evaluating postoperative anal fistula prognosis by diffusion-weighted MRI. Eur J Radiol 2020;132:109294.
14. Sudoł-Szopińska I, Santoro GA, Kołodziejczak M, Wiaczek A, Grossi U. Magnetic resonance imaging template to standardize reporting of anal fistulas. Tech Coloproctol 2021;25:333–7.
15. Iqbal N, Sackitey C, Gupta A, Tolan D, Plumb A, Godfrey E, et al. The development of a minimum dataset for MRI reporting of anorectal fistula: a multi-disciplinary, expert consensus process. Eur Radiol 2022;32:8306–16.
16. Garg P, Kaur B, Yagnik VD, Dawka S. Including video and novel parameter-height of penetration of external anal sphincter-in magnetic resonance imaging reporting of anal fistula. World J Gastrointest Surg 2022;14:271–5.
17. Sudoł-Szopińska I, Garg P, Mellgren A, Spinelli A, Breukink S, Iacobellis F, et al. Structured MRI and endoanal ultrasound anal fistulas reporting template (SMART): an interdisciplinary Del phi consensus. World J Gastrointest Surg 2024;(Accepted; under print).
18. Guz W, Ożóg Ł, Aebisher D , Filip R. The use of magnetic resonance imaging technique and 3D printing in order to develop a three-dimensional fistula model for patients with Crohn's disease: personalised medicine. Prz Gastroenterol 2021;16:83–8.
19. Garg P, Yagnik VD, Kaur B, Menon GR, Dawka S. Role of MRI to confirm healing in complex high cryptoglandular anal fistulas: long-term follow-up of 151 cases. Colorectal Dis 2021;23:2447–55.
20. Garg P, Kaur B, Yagnik VD, Dawka S, Menon GR. Guidelines on postoperative magnetic resonance imaging in patients operated for cryptoglandular anal fistula: experience from 2404 scans. World J Gastroenterol 2021;27:5460–73.
21. Garg P. Comparison of preoperative and postoperative MRI after fistula-in-ano surgery: lessons learnt from an audit of 1323 MRI at a single centre. World J Surg 2019;43:1612–22.
22. Xu H, Xiao GZ, Zheng YH, Fu YJ, Zhong SL, Ren DL, et al. A magnetic resonance imaging-based decision-making tool for predicting complex anal fistulas healing in the early postoperative period. BMC Gastroenterol 2023;23:372.
23. Garg P, Yagnik VD, Dawka S, Kaur B, Menon GR. A novel MRI and clinical-based scoring system to assess post-surgery healing and to predict long-term healing in cryptoglandular anal fistulas. Clin Exp Gastroenterol 2022;15:27–40.
24. Dawka S, Yagnik VD, Kaur B, Menon GR, Garg P. Garg scoring system to predict long-term healing in cryptoglandular anal fistulas: a prospective validation study. Ann Coloproctol 2022 Oct 11 [Epub]. https://doi.org/10.3393/ac.2022.00346.0049
25. Tang H, Peng C, Zhao Y, Hu C, Dai Y, Lin C, et al. An applicability study of rapid artificial intelligence-assisted compressed sensing (ACS) in anal fistula magnetic resonance imaging. Heliyon 2023;10:e22817.
26. Ren J, Bai W, Gu L, Li X, Peng X, Li W. Three-dimensional pelvic ultrasound is a practical tool for the assessment of anal fistula. BMC Gastroenterol 2023;23:134.
27. Sayed A, El-azizi HM, El-barmelgi MY, Azzam H. Role of endoanal ultrasound in the assessment of perianal fistula in correlation with MRI fistulography. Egypt J Radiol Nucl Med 2022;53:195.
28. Akhoundi N, Bozchelouei JK, Abrishami A, Frootan M, Siami A, Alimadadi E, et al. Comparison of MRI and endoanal ultrasound in assessing intersphincteric, transsphincteric, and suprasphincteric perianal fistula. J Ultrasound Med 2023;42:2057–64.
29. Abdelzaher AA, Elbarmelgi MY, El Azizi HM, Mohamed AS, Abdelatty MA, Azzam HA. 3D endoanal ultrasound versus external phased array MRI in detection and evaluation of anal sphincteric lesions. Egypt J Radiol Nucl Med 2024;55:96.
30. Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. Br J Surg 1976;63:1–12.
31. Morris J, Spencer JA, Ambrose NS. MR imaging classification of perianal fistulas and its implications for patient management. Radiographics 2000;20:623–37.
32. Garg P. Garg classification for anal fistulas: is it better than existing classifications?: a review. Indian J Surg 2018;80:606–8.
33. Garg P. Comparing existing classifications of fistula-in-ano in 440 operated patients: is it time for a new classification? A retrospective cohort study. Int J Surg 2017;42:34–40.
34. Armstrong DN, Sudoł-Szopińska I, de Par ades V, Litta F, Limbert M, James KC. Pankaj Garg: a community doctor to a master innovator to a global icon. Glob J Med Pharm Biomed Update 2023;18:16.
35. Garg P. Assessing validity of existing fistula-in-ano classifications in a cohort of 848 operated and MRI-assessed anal fistula patients: cohort study. Ann Med Surg (Lond) 2020;59:122–6.
36. Garg P. Is fistulotomy still the gold standard in present era and

is it highly underutilized?: an audit of 675 operated cases. Int J Surg 2018;56:26–30.
37. Garg P. A new understanding of the principles in the management of complex anal fistula. Med Hypotheses 2019;132:109329.
38. Garg P, Mongia A. Transanal opening of the intersphincteric space (TROPIS): a novel procedure on the horizon to effectively manage high complex anal fistulas. Ann Coloproctol 2024;40:74–81.
39. Garg P, Kaur B. Transanal opening of intersphincteric space: a novel procedure to manage highly complex anal fistulas. Dis Colon Rectum 2023;66:e292–3.
40. Garg P. Transanal opening of intersphincteric space (TROPIS): a new procedure to treat high complex anal fistula. Int J Surg 2017;40:130–4.
41. Garg P, R Menon G, Kaur B. Comparison of different methods to manage supralevator rectal opening in anal fistulas: a retrospective cohort study. Cir Esp (Engl Ed) 2022;100:298–301.
42. Garg P, Kaur B, Singla K, Menon GR, Yagnik VD. A simple protocol to effectively manage anal fistulas with no obvious internal opening. Clin Exp Gastroenterol 2021;14:33–44.
43. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum 1993;36:77–97.
44. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. Gut 1999;44:77–80.
45. Garg P, Sudol-Szopinska I, Kolodziejczak M, Bhattacharya K, Kaur G. New objective scoring system to clinically assess fecal incontinence. World J Gastroenterol 2023;29:4593–603.
46. Clemente N, Yagnik VD, James KC. A new scoring system on the horizon to assess fecal incontinence: Garg Incontinence Scores (GIS). Updates Surg 2024;76:723–4.
47. Tsarkov P, Tulina I, Sheikh P, Shlyk DD, Garg P. Garg incontinence scores: new scoring system on the horizon to evaluate fecal incontinence: will it make a difference? World J Gastroenterol 2024;30:204–10.
48. Litta F, Parello A, De Simone V, Grossi U, Orefice R, Ratto C. Fistulotomy and primary sphincteroplasty for anal fistula: long-term data on continence and patient satisfaction. Tech Coloproctol 2019;23:993–1001.
49. Hiremath SC, Patil R. Fistulotomy versus fistulectomy for fistula-in-ano: a randomized prospective study. Surg J (N Y) 2022;8:e336–40.
50. Seyfried S, Bussen D, Joos A, Galata C, Weiss C, Herold A. Fistulectomy with primary sphincter reconstruction. Int J Colorectal Dis 2018;33:911–8.
51. Ratto C, Litta F, Donisi L, Parello A. Fistulotomy or fistulectomy and primary sphincteroplasty for anal fistula (FIPS): a systematic review. Tech Coloproctol 2015;19:391–400.
52. Wang C, Huang T, Wang X. Efficacy and safety of transanal opening of intersphincteric space in the treatment of high complex anal fistula: a meta-analysis. Exp Ther Med 2024;28:306.
53. Huang H, Ji L, Gu Y, Li Y, Xu S. Efficacy and safety of sphincter-preserving surgery in the treatment of complex anal fistula: a network meta-analysis. Front Surg 2022;9:825166.
54. Yagnik VD, Kaur B, Dawka S, Sohal A, Menon GR, Garg P. Non-locatable internal opening in anal fistula associated with acute abscess and its definitive management by Garg Protocol. Clin Exp Gastroenterol 2022;15:189–98.
55. Emile SH, Khan SM, Adejumo A, Koroye O. Ligation of intersphincteric fistula tract (LIFT) in treatment of anal fistula: an updated systematic review, meta-analysis, and meta-regression of the predictors of failure. Surgery 2020;167:484–92.
56. Jayne DG, Scholefield J, Tolan D, Gray R, Senapati A, Hulme CT, et al. A multicenter randomized controlled trial comparing safety, efficacy, and cost-effectiveness of the surgisis anal fistula plug versus surgeon's preference for transsphincteric fistula-in-ano: the FIAT trial. Ann Surg 2021;273:433–41.
57. Lau YC, Brown KG, Cheong J, Byrne C, Lee PJ. LIFT and BioLIFT: a 10-year single-centre experience of treating complex fistula-in-ano with ligation of intersphincteric fistula tract procedure with or without bio-prosthetic reinforcement (BioLIFT). J Gastrointest Surg 2020;24:671–6.
58. Rezk M, Emile SH, Fouda EY, Khaled N, Hamed M, Omar W, et al. Ligation of intersphincteric fistula tract (LIFT) with or without injection of bone marrow mononuclear cells in the treatment of trans-sphincteric anal fistula: a randomized controlled trial. J Gastrointest Surg 2022;26:1298–306.
59. Maralcan G, Başkonuş I, Aybasti N, Gökalp A. The use of fibrin glue in the tr eatment of fistula-in-ano: a prospective study. Surg Today 2006;36:166–70.
60. Garg P, Song J, Bhatia A, Kalia H, Menon GR. The efficacy of anal fistula plug in fistula-in-ano: a systematic review. Colorectal Dis 2010;12:965–70.
61. Grossberg SJ, Harran N, Bebington B, Lutrin DL. Use of the OVESCO OTSC® Proctology Clip for closure of fistula-in-ano at Wits Donald Gordon Medical Centre: a single centre experience. S Afr J Surg 2020;58:74–7.
62. La Torre M, Goglia M, Micarelli A, Fiori E, D'Andrea V, Grossi U, et al. Long term results of video-assisted anal fistula treatment for complex anal fistula: another shattered dream? Colorectal Dis 2023;25:2017–23.
63. Tümer H, Bulbuloglu GC. A comparison of laser and fistulotomy techniques in the treatment of fistula-in-ano. Cureus 2023;15:e37053.

https://doi.org/10.3393/ac.2024.00325.0046

64. Tang CY, Roslani AC. Laser ablation of anal fistulae: a 6-year experience in a tertiary teaching hospital in Malaysia. Lasers Med Sci 2022;37:3291–6.
65. Kasiri MM, Riss S, Stift A, Binder AD, Kogovšek U, Huth M, et al. Optimized fistulectomy using the novel FiXcision® device: a technical feasibility study and evaluation of short term healing rates. Tech Coloproctol 2019;23:579–82.
66. Khamar J, Sachdeva A, McKechnie T, Lee Y, Tessier L, Hong D, et al. Cutting seton for the treatment of cryptoglandular fistula-in-ano: a systematic review and meta-analysis. Tech Coloproctol 2023;28:12.
67. Garg P, Garg PK, Sodhi GS. Cutting seton is an inferior version of fistulotomy and is associated with increased morbidity in the management of anal fistulas. Tech Coloproctol 2024;28:57.
68. Garg P. Tube in tract technique: a simple alternative to a loose draining seton in the management of complex fistula-in-ano: a video vignette. Colorectal Dis 2016;18:107.
69. Aryanti C, Faruk M. Optimum management for complex anal fistula: a network meta-analysis of randomized controlled trials. Surg Open Sci 2024;18:117–22.
70. Wang Y, Rao Q, Ma Y, Li X. Platelet-rich plasma in the treatment of anal fistula: a systematic review and meta-analysis. Int J Colorectal Dis 2023;38:70.
71. Wang H, Jiang HY, Zhang YX, Jin HY, Fei BY, Jiang JL. Mesenchymal stem cells transplantation for perianal fistulas: a systematic review and meta-analysis of clinical trials. Stem Cell Res Ther 2023;14:103.
72. Garcia-Arranz M, Garcia-Olmo D, Herreros MD, Gracia-Solana J, Guadalajara H, de la Portilla F, et al. Autologous adipose-derived stem cells for the treatment of complex cryptoglandular perianal fistula: a randomized clinical trial with long-term follow-up. Stem Cells Transl Med 2020;9:295–301.