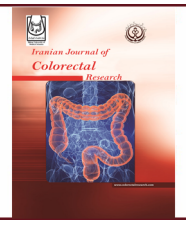
Review Article

Iran J Colorectal Res 2026;14(2):6-18.

Iranian Journal of Colorectal Research



Injectable Non-Animal Stabilized Hyaluronic Acid/Dextranomer (NASHA/Dx) for Adult Fecal Incontinence: Mechanisms, Clinical Outcomes, and Its Role in Contemporary Management

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Received: 2026-04-12
Revised: 2026-06-30
Accept: 2026-06-30

Abstract

Background: Adult fecal incontinence (FI) is a common and debilitating condition that significantly impairs physical, psychological, and social quality of life (QoL). Injectable non-animal stabilized hyaluronic acid/dextranomer (NASHA/Dx) has emerged as a minimally invasive treatment option for patients who remain symptomatic despite optimized conservative therapy. This narrative review evaluates the mechanism of action, clinical outcomes, patient selection criteria, and the contemporary role of NASHA/Dx in the management of adult FI.

Methods: A comprehensive literature search was performed in PubMed/MEDLINE, Embase, and Scopus, emphasizing high-quality evidence published from 2010 through June 2026. Landmark randomized controlled trials, long-term prospective studies, systematic reviews, and contemporary international clinical practice guidelines were critically evaluated and narratively synthesized.

Results: NASHA/Dx acts through immediate tissue augmentation, followed by progressive collagen deposition and tissue remodeling around dextranomer microspheres. Clinical studies demonstrate significant reductions in FI episodes, sustained improvements in QoL, and a favorable safety profile in appropriately selected patients, particularly those with passive FI associated with internal anal sphincter dysfunction. Repeat ("top-up") injections may enhance or maintain therapeutic benefits in selected individuals. Current evidence supports NASHA/Dx as an effective intermediate treatment between conservative management and more invasive interventions.

Conclusion: Injectable NASHA/Dx is a safe, minimally invasive, and evidence-based treatment for selected adults with FI who do not respond to conservative management. Careful patient selection and integration within a multidisciplinary treatment pathway are essential to achieving optimal outcomes. Further research should focus on long-term durability, standardized outcome measures, and refinement of patient selection criteria.

Keywords: Fecal Incontinence; Hyaluronic Acid; Dextranomer; Injections; Treatment Outcome; Patient Selection

Please cite this paper as:
Salati SA, Salati AA. Injectable Non-Animal Stabilized Hyaluronic Acid/Dextranomer (NASHA/Dx) for Adult Fecal Incontinence: Mechanisms, Clinical Outcomes, and Its Role in Contemporary Management. *Iran J Colorectal Res*. 2026;14(2):6-18. doi:

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Introduction

Adult fecal incontinence (FI), defined as the involuntary loss of solid or liquid stool, is a common and often debilitating condition that substantially impairs physical, psychological, and social well-being (1). Despite its considerable impact on quality of life (QoL), FI remains underrecognized and undertreated because many affected individuals are reluctant to seek medical attention due to embarrassment, social stigma, and misconceptions that incontinence is an inevitable consequence of aging (1, 2). Consequently, the true prevalence of FI is likely underestimated. Current epidemiological studies suggest that FI affects approximately 1% to 21% of adults worldwide, with substantially higher rates reported among institutionalized older adults and individuals with multiple comorbidities (1, 2). Beyond the physical burden of uncontrolled bowel leakage, FI is associated with social isolation, anxiety, depression, loss of independence, reduced work productivity, and significant healthcare utilization, making it an important public health issue (1).

The pathophysiology of FI is complex and multifactorial, involving disruption of the intricate mechanisms responsible for maintaining continence. Normal continence depends on the coordinated function of the internal and external anal sphincters, pelvic floor musculature, anorectal sensation, rectal compliance, stool consistency, and intact neurological pathways (2). Dysfunction of any of these components—including internal anal sphincter degeneration, external anal sphincter injury, pudendal neuropathy, impaired rectal sensation, altered rectal compliance, or chronic diarrhea—may contribute to incontinence, often occurring in combination rather than in isolation (1, 2). Consequently, effective management requires individualized treatment strategies tailored to the predominant underlying pathophysiological mechanisms rather than a uniform therapeutic approach.

Contemporary management of FI follows a stepwise escalation from conservative to increasingly invasive interventions (2, 3). First-line treatment focuses on optimization of stool consistency through dietary modifications, fiber supplementation, regulation of bowel habits, and antidiarrheal medications when appropriate, often combined with pelvic floor muscle training and biofeedback therapy (2, 3). Although these measures improve symptoms in many patients, a substantial proportion continue to experience persistent or bothersome incontinence despite optimized conservative management (3, 4). At the other end of the therapeutic spectrum, surgical interventions such as sphincteroplasty and neuromodulatory therapies, particularly sacral neuromodulation (SNM), offer effective treatment for carefully selected patients but require invasive procedures, specialized expertise, and considerable healthcare resources (2, 5, 6). Furthermore, not all patients are suitable candidates for these interventions because of advanced age, medical comorbidities, unfavorable sphincter anatomy, patient preference, or limited access to specialized centers.

This therapeutic gap has driven the development of minimally invasive interventions that bridge the transition between conservative therapy and definitive surgical management. Injectable bulking agents were introduced to improve passive anal canal closure by augmenting submucosal tissue volume and enhancing tissue coaptation. Earlier bulking materials—including autologous fat, silicone, collagen, and polytetrafluoroethylene—demonstrated inconsistent efficacy and were frequently limited by poor durability, inflammatory reactions, migration, or other safety concerns (4). The introduction of non-animal stabilized hyaluronic acid with dextranomer microspheres (NASHA/Dx) provided an injectable approach combining tissue augmentation with subsequent host-tissue remodeling (4, 7). The landmark randomized, sham-controlled trial by Graf and colleagues provided pivotal evidence supporting the clinical efficacy of NASHA/Dx, demonstrating a significantly greater proportion of responders among treated patients compared to those receiving sham injections (7).

Although NASHA/Dx has become an established minimally invasive treatment option for selected patients with FI, its precise role within modern treatment algorithms continues to evolve. The increasing adoption of SNM, growing interest in regenerative therapies, variable long-term durability, and uncertainty regarding optimal patient selection have generated ongoing debate about the appropriate place of injectable bulking therapy in contemporary practice (2, 5, 6, 8). Additionally, issues such as the use of top-up injections, predictors of sustained treatment response, cost-effectiveness, and the recognition of persistent NASHA/Dx deposits on cross-sectional imaging remain clinically relevant and continue to influence therapeutic decision-making (8-10). Existing reviews have generally focused on efficacy and safety, while relatively less emphasis has been placed on integrating current evidence regarding biological mechanisms, long-term outcomes, patient selection, radiological considerations, and the role of NASHA/Dx within modern multidisciplinary management pathways.

In this narrative review, we critically examine the contemporary evidence supporting injectable NASHA/Dx for adult FI. We review its biological mechanisms of action, procedural principles, clinical efficacy, long-term durability, safety profile, imaging characteristics, and predictors of treatment success. Additionally, we discuss its evolving role within current multidisciplinary treatment algorithms, highlighting unresolved questions and future directions for clinical practice and research.

Methods

i. Literature Search Strategy

A comprehensive literature search was performed in PubMed/MEDLINE, Embase, and Scopus, emphasizing high-quality evidence published from 2010 through June 2026. Landmark randomized controlled trials, long-term prospective studies, systematic reviews, and contemporary international clinical practice guidelines were identified and critically evaluated to provide an up-to-date overview of the mechanism, clinical outcomes, and current role of injectable NASHA/Dx in adult FI.

The search strategy combined controlled vocabulary terms (Medical Subject Headings [MeSH] and Emtree) with free-text keywords, including *fecal incontinence*, *faecal incontinence*, *anal incontinence*, *injectable bulking agents*, *dextranomer*, *non-animal stabilized hyaluronic acid*, *NASHA/Dx*, *Solesta*, *hyaluronic acid*, *anal bulking agents*, and related terms. Additionally, reference lists of relevant review articles, clinical guidelines, randomized controlled trials, and observational studies were manually screened to identify additional eligible publications not retrieved through the electronic database search.

ii. Literature Selection

This article was designed as a narrative review rather than a systematic review or meta-analysis. Studies were selected based on their scientific quality, clinical relevance, and contribution to understanding the evolving role of NASHA/Dx in adult FI. Particular emphasis was placed on high-quality evidence, including randomized controlled trials, prospective cohort studies, long-term follow-up investigations, multicenter clinical studies, systematic reviews, landmark publications, and contemporary international clinical practice guidelines.

Studies evaluating patient selection, injection techniques, repeat ("top-up") injections, long-term durability, safety outcomes, radiological findings, and comparative effectiveness with other therapeutic modalities were preferentially included. Earlier studies evaluating historical injectable bulking agents were considered only when they provided important context for the evolution of contemporary injectable therapies. Only articles published in English were included.

iii. Data Synthesis

The selected literature was critically reviewed and synthesized narratively. The evidence was organized into thematic sections addressing biological mechanisms of action, procedural considerations, clinical efficacy, long-term durability, patient selection, safety profile, radiological characteristics, comparative effectiveness, current position within contemporary treatment algorithms, and future perspectives.

Because this was a narrative review, no formal risk-of-bias assessment or quantitative meta-analysis was undertaken. Instead, the available evidence was interpreted within the context of current international guideline recommendations and expert opinion to provide a clinically relevant overview for surgeons and physicians involved in the multidisciplinary management of adult FI.

Biological Mechanisms and Clinical Considerations

i. Composition and Biomaterial Properties

Injectable NASHA/Dx is a biocompatible bulking agent composed of two complementary components: NASHA, which functions as the carrier gel, and dextranomer microspheres suspended within the gel matrix (4, 7). Hyaluronic acid is a naturally occurring glycosaminoglycan with excellent biocompatibility and viscoelastic properties, providing immediate volumetric augmentation following injection. The dextranomer microspheres serve as a durable scaffold that remains within the submucosal tissue after the gradual degradation of the hyaluronic acid carrier, thereby promoting long-term tissue remodeling and sustained therapeutic benefit (4, 7).

Unlike earlier injectable bulking materials, including autologous fat, silicone, collagen, and polytetrafluoroethylene,which primarily acted as inert space-occupying fillers and were limited by variable durability, inflammatory reactions, particle migration, or foreign-body responses, NASHA/Dx combines immediate mechanical augmentation with biologically mediated tissue integration (4). This dual mechanism represents a significant advancement in injectable biomaterials for the treatment of FI.

ii. Biological Mechanism of Action

The therapeutic effect of NASHA/Dx is achieved through two sequential yet complementary biological phases. Immediately after injection, the hyaluronic acid carrier gel produces submucosal volume expansion, increasing tissue bulk within the anal canal and improving the apposition of the anal cushions. This immediate augmentation enhances passive anal canal closure and reduces involuntary leakage, particularly during periods of low resting sphincter pressure (4, 7).

The second phase involves the degradation of the hyaluronic acid carrier and the persistence of dextranomer microspheres within the injected tissue, followed by host tissue remodeling around the microspheres. Fibroblast infiltration and collagen deposition contribute to the formation of a tissue response surrounding the injected material (4, 7). Rather than functioning solely as a temporary filler, NASHA/Dx promotes structural tissue integration, which contributes to the prolonged augmentation of the anal canal and the maintenance of tissue coaptation.

Clinical follow-up studies have demonstrated sustained improvements in continence and QoL for

up to 36 months in a proportion of treated patients, although the magnitude and durability of these benefits vary among individuals (8). Patients with recurrent symptoms or an incomplete initial response may experience additional benefits from top-up injections, which can enhance tissue augmentation while maintaining the favorable safety profile of the procedure (4, 9).

iii. Injection Technique and Procedural Considerations

NASHA/Dx is administered as a minimally invasive transanal injection into the deep submucosal layer immediately above the dentate line, an anatomically favorable location that minimizes procedural discomfort while effectively augmenting the anal canal (4, 5). The procedure is typically performed in an outpatient or office-based setting under local anesthesia or minimal sedation and generally does not require hospitalization, making it an attractive therapeutic option for patients who have failed conservative treatments but wish to avoid more invasive surgical interventions.

The pivotal clinical studies used injections at multiple sites within the anal canal, and a four-quadrant submucosal approach has since been widely adopted in clinical practice (7, 9). Uniform distribution of the injectable material creates submucosal cushions that improve resting anal canal closure by enhancing tissue coaptation. This four-quadrant technique has been consistently employed in the pivotal clinical studies evaluating NASHA/Dx and remains the recommended approach in contemporary clinical practice (9).

The procedure is generally well tolerated, with most patients resuming normal daily activities shortly after treatment. Although a single treatment session provides satisfactory symptom improvement for many patients, top-up injections may be considered for those with persistent or recurrent symptoms. Repeat injections may provide additional symptom relief in selected patients; however, evidence supporting standardized retreatment protocols remains limited (7, 10).

iv. Biological Basis of Clinical Efficacy

The clinical effectiveness of NASHA/Dx is closely linked to its mechanism of action. By increasing submucosal tissue volume and enhancing anal canal coaptation, the injected material strengthens the passive anal seal and improves resting continence. Subsequent collagen deposition and tissue remodeling help maintain this augmentation beyond the initial volumizing effect of the hyaluronic acid carrier, providing a biological explanation for the durability observed in long-term clinical studies (4, 7).

Because NASHA/Dx primarily improves passive anal canal closure rather than restoring voluntary sphincter contractility, treatment outcomes largely depend on the preservation of the underlying sphincter anatomy. Consequently, patients with predominantly passive FI and relatively preserved sphincter anatomy may be more suitable candidates for injectable bulking therapy. However, reliable anatomical or physiological predictors of treatment response have yet to be fully established (2, 11).

This mechanistic relationship provides the biological basis for contemporary patient-selection guidelines and underscores the importance of a thorough anatomical and physiological evaluation before considering injectable bulking therapy (Figure 1).

Clinical Outcomes, Safety Profile, and Long-Term Durability

i. Clinical Effectiveness

The principal objective of injectable NASHA/Dx therapy is to achieve a clinically meaningful improvement in FI rather than complete restoration of continence. In published clinical studies, treatment success is most commonly defined as a reduction of at least 50% in weekly FI episodes, accompanied by improvements in disease-specific quality-of-life measures (7, 9). Subsequent analyses have validated this ≥50% response threshold as a clinically meaningful endpoint, demonstrating that responders experience significant improvements in symptom severity, health-related QoL, and patient-reported treatment satisfaction (9).

The landmark randomized, sham-controlled trial by Graf et al. provided pivotal evidence supporting the clinical efficacy of NASHA/Dx. At six months, 52% of patients receiving NASHA/Dx achieved a ≥50% reduction in FI episodes compared with 31% of those receiving sham treatment, with significant improvements in FI-related outcomes (7). In addition to reducing symptom frequency, the treatment resulted in significant improvements in Fecal Incontinence Quality of Life (FIQL) scores, demonstrating that symptom reduction translated into meaningful functional and psychosocial benefits.

Subsequent prospective cohort studies and multicenter investigations have consistently confirmed these findings in routine clinical practice. Improvements have been observed not only in the frequency of incontinent episodes but also in passive leakage, urgency-related symptoms, patient satisfaction, and health-related QoL (8, 10, 12).

Although reported response rates vary across studies because of differences in patient selection, outcome measures, and follow-up duration, the overall body of evidence supports NASHA/Dx as an effective, minimally invasive treatment for appropriately selected patients with mild-to-moderate FI who remain symptomatic despite optimized conservative therapy.

ii. Long-Term Durability

The durability of therapeutic benefit remains one of the most important considerations when evaluating

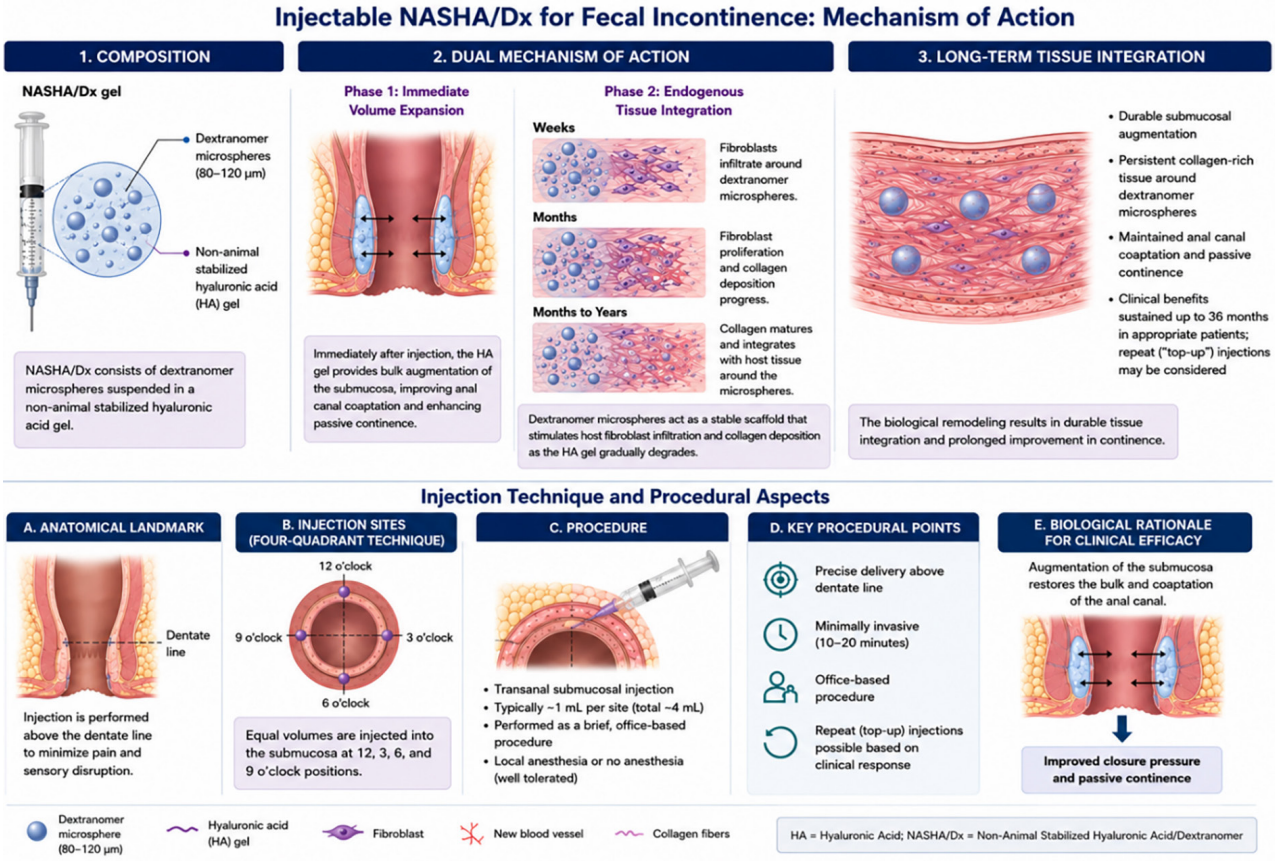


Figure 1: *Biological Mechanism of Action and Standard Injection Technique of Injectable NASHA/Dx for Adult Fecal Incontinence.* This figure illustrates the composition of NASHA/Dx, the sequential phases of tissue augmentation and remodeling, the standard four-quadrant injection technique administered above the dentate line, and the resulting improvement in anal canal coaptation that underlies its therapeutic efficacy.

injectable bulking therapies. Unlike temporary space-occupying fillers, NASHA/Dx promotes progressive tissue remodeling through fibroblast infiltration and collagen deposition, providing a biological basis for sustained clinical improvement beyond the initial injection (4, 10).

Long-term follow-up studies have demonstrated that therapeutic benefits can be maintained for up to 36 months in a substantial proportion of patients. In multicenter prospective studies, approximately two-thirds of treated patients continued to meet predefined responder criteria at 24 months, maintaining improvements in continence episodes and quality-of-life measures (10, 12). More recent prospective studies have confirmed that many patients experience durable symptom control through 36 months, although the magnitude of benefit varies considerably among individuals (8).

Nevertheless, long-term efficacy remains inconsistent. Some patients experience a gradual recurrence of symptoms over time, reflecting the multifactorial nature of FI rather than failure of the injected material alone. Longer-term observational data, including the study by Ezra et al. on intersphincteric NASHA/Dx implantation, suggest that clinical benefits may diminish over extended follow-up in some patients, although the small sample size limits the generalizability of these findings (13). Current evidence suggests that durable treatment response depends not only on the persistence of the implant but also on factors such as sphincter integrity, anorectal physiology, stool consistency, and progression of the underlying disease process. Consequently, careful patient selection remains one of the strongest determinants of long-term clinical success.

iii. Repeat ("Top-Up") Injections

An incomplete response following the initial procedure should not necessarily be regarded as treatment failure. Repeat injections have been administered to selected patients with incomplete or recurrent responses; however, evidence regarding the optimal timing, frequency, and long-term benefits of retreatment remains limited (10, 13, 14).

Rather than representing a limitation of therapy, retreatment should be considered an integral component of the therapeutic strategy for appropriately selected patients. Similar to other minimally invasive interventions, repeat treatments enable individualized optimization of clinical response according to symptom severity and patient-reported outcomes. However, further prospective studies are needed to establish standardized criteria regarding the optimal timing, frequency, and long-term effectiveness of repeat injections.

iv. Safety Profile

One of the principal advantages of NASHA/Dx is its favorable safety profile. Because the procedure is minimally invasive and performed via transanal submucosal injection, treatment avoids many of the risks associated with reconstructive surgery and implantable neuromodulation devices (2, 5).

Reported adverse events are generally mild to moderate and self-limiting. Proctalgia and fever are among the commonly reported treatment-related adverse events, although serious complications such as abscess formation have been reported rarely (7, 10, 12). These events usually resolve with conservative management and seldom require additional intervention.

Serious complications appear to be uncommon, although abscess formation has been reported in clinical trials (7). Appropriate injection technique and awareness of potential complications remain important. The favorable safety profile, combined with the absence of implanted hardware and the ability to perform the procedure in an outpatient setting, significantly enhances the appeal of NASHA/Dx as an intermediate treatment option between conservative therapy and more invasive surgical interventions.

v. Radiological Appearance and Diagnostic Challenges

As the dextranomer microspheres become incorporated into the submucosal tissues following NASHA/Dx injection, persistent submucosal deposits may be visible on cross-sectional imaging. Reported CT appearances include mural thickening with multiple rounded hypodense foci that can mimic abscesses or neoplastic disease (15). Their characteristic appearance may also resemble perianal abscesses, duplication cysts, postoperative collections, or other pelvic masses. Therefore, awareness of previous NASHA/Dx injection is important when interpreting these findings.

Recognition of these characteristic imaging findings is essential for both colorectal surgeons and radiologists. Correlating these findings with the patient's procedural history and understanding the expected imaging appearance of NASHA/Dx implants can prevent unnecessary diagnostic investigations, inappropriate surgical drainage, or biopsy of benign post-treatment changes.

Table 1: Landmark Clinical Studies Evaluating Injectable NASHA/Dx for Adult Fecal Incontinence

Study	Study Design	Study Population	Key Findings	Clinical Relevance
Graf et al.(7)	Multicenter, Randomized, Double-Blind, Sham-Controlled Trial	Adults with FI refractory to conservative treatment	Fifty-two percent of treated patients achieved a ≥50% reduction in FI episodes at six months, compared with 31% after sham treatment.	Established the efficacy and safety of NASHA/Dx, providing pivotal evidence to support regulatory approval.
Sanchez et al.(9)	Post Hoc Analysis of a Randomized Clinical Trial	Responders and non-responders from the pivotal NASHA/Dx trial	Demonstrated that a ≥50% reduction in FI episodes represents a clinically meaningful endpoint associated with improved symptom severity, enhanced quality of life, and increased patient satisfaction.	Validated the ≥50% responder threshold as an appropriate outcome measure in clinical trials and routine practice.
Mellgren et al.(10)	Prospective Long-Term Follow-Up Study	Patients treated with NASHA/Dx	Demonstrated sustained clinical benefits and acceptable safety over 36 months in a prospective multicenter cohort.	Demonstrated medium-term durability of the treatment benefit.
La Torre et al.(12)	Prospective Observational Study	Adults undergoing NASHA/Dx injections	Sustained improvements in continence and quality-of-life outcomes are observed with repeat ("top-up") injections where indicated.	Supported the role of repeated injections in optimizing long-term outcomes.
Franklin et al.(11)	Post Hoc Responder Analysis	Patients enrolled in the pivotal randomized trial	Better outcomes were associated with milder baseline symptoms, shorter symptom duration, obstetric etiology, and fewer previous FI treatments.	Highlighted the importance of careful patient selection to maximize therapeutic success.
Ezra et al.(13)	Retrospective Long-Term Follow-Up Study	Patients undergoing intersphincteric NASHA/Dx implantation	Demonstrated meaningful short-term improvement, although efficacy declined over extended follow-up, emphasizing variability in long-term durability.	Reinforced realistic expectations regarding durability and emphasized the need for individualized patient selection.
Assmann et al. (UEG/ESCP/ ESNM/ESPCG Guideline)(2)	International Evidence-Based Clinical Practice Guideline	Adults with FI	Recommends individualized, stepwise management of FI. Injectable bulking agents, such as NASHA/Dx, may be considered for carefully selected patients with persistent symptoms despite optimized conservative therapy.	Defines the contemporary, evidence-based role of NASHA/Dx within multidisciplinary treatment algorithms and reinforces the importance of careful patient selection.

This important radiological consideration should form part of routine clinical assessment when evaluating patients who have undergone injectable bulking therapy.

The landmark clinical studies and evidence supporting the contemporary use of injectable NASHA/Dx for adult FI are summarized in Table 1.

Patient Selection and Predictors of Treatment Success

Appropriate patient selection is a crucial factor in the success of treatment with injectable NASHA/Dx. However, predictors of response have not yet been sufficiently established to allow reliable individual outcome prediction (2, 11). Treatment is most appropriate when the underlying mechanism of FI can be addressed through tissue augmentation. Therefore, a comprehensive assessment of symptoms, anorectal anatomy, and physiology, along with realistic counseling regarding the expected degree of improvement and the possibility of retreatment, is essential before considering NASHA/Dx therapy (2, 5, 11).

i. Ideal Candidates for NASHA/Dx Therapy

Current evidence and international clinical practice guidelines consistently support the use of NASHA/Dx in adults with mild-to-moderate FI who remain symptomatic despite optimized conservative management, including dietary modification, pharmacological therapy, and pelvic floor rehabilitation (2, 5). The greatest therapeutic benefit is observed in patients with passive FI resulting predominantly from internal anal sphincter (IAS) dysfunction, age-related IAS degeneration, or small structural sphincter defects that impair resting anal canal closure while preserving overall sphincter anatomy (2, 16).

Post hoc analyses of clinical trial data further suggest that certain baseline characteristics are associated with a greater likelihood of response in patients who have milder baseline symptoms, a shorter duration of FI, obstetric etiology, and limited prior treatment exposure. These findings emphasize the importance of careful patient selection to optimize treatment success (11).

Patients seeking a minimally invasive alternative to surgery, those with significant medical comorbidities that increase operative risk, and individuals who are either unsuitable for or unwilling to undergo SNM or reconstructive surgery may also be appropriate candidates for NASHA/Dx therapy. Because the procedure is performed in an outpatient setting with minimal recovery time, it represents an attractive option for older adults and other carefully selected patients in whom more invasive interventions may be undesirable (2, 5).

ii. Patients Less Likely to Benefit

The effectiveness of NASHA/Dx is considerably reduced in patients whose incontinence primarily results from major structural disruption of the continence mechanism. Patients with major structural sphincter disruption, severe neuromuscular dysfunction, or complex anorectal pathology may be less suitable candidates for injectable bulking therapy because NASHA/Dx does not restore sphincter contractility or correct major structural defects (2, 5). Active anorectal sepsis and significant inflammatory or structural anorectal pathology should be thoroughly evaluated and managed before considering injectable bulking therapy, with treatment selection individualized according to the underlying disorder (2, 5).

iii. Role of Endoanal Ultrasound and Anorectal Physiology

Objective assessment of anorectal structure and function provides valuable information for selecting patients for NASHA/Dx therapy. Endoanal ultrasound (EAUS) is a useful modality for assessing anal sphincter integrity and identifying structural defects when anatomical evaluation is clinically indicated (2, 5).

Anorectal manometry (ARM) complements anatomical assessment by evaluating resting and squeeze pressures, rectal sensation, and rectal compliance. It provides valuable information regarding resting and squeeze pressures, rectal sensation, and compliance. These findings may help characterize the predominant mechanism of FI. However, its ability to predict the response to NASHA/Dx treatment remains uncertain (2, 8).

Diagnostic findings alone are insufficient to predict therapeutic success; results from both investigations should be integrated with the broader clinical context, including the patient's history, bowel habits, symptom severity, and functional capacity.

iv. Clinical Factors Influencing Treatment Response

Several additional clinical factors can influence treatment outcomes.

Optimizing stool consistency is essential before considering injectable therapy. Persistent diarrhea or poorly controlled loose stools can compromise the improved anal seal achieved through tissue augmentation, thereby reducing therapeutic efficacy. Therefore, dietary modifications, fiber supplementation, and appropriate pharmacological treatments should be maintained alongside any procedural intervention (2, 17).

Patients with less severe baseline symptoms and relatively preserved sphincter anatomy generally demonstrate more favorable clinical outcomes than those with advanced disease, although no universally accepted predictors of long-term response have been established (8, 14). Previous sphincter repair does not necessarily preclude consideration of other treatments; however, selection should be individualized according to residual anatomy and symptoms (2, 5).

v. Shared Decision-Making

Shared decision-making is a crucial element in patient selection. Patients should be informed that the primary objective of NASHA/Dx therapy is to achieve a meaningful improvement in symptom severity and QoL rather than complete restoration of continence. Counseling should include a discussion of realistic expectations, the possibility of requiring top-up injections, and the potential need for alternative interventions if symptoms persist or recur. Incorporating patient preferences, functional goals, comorbidities, and quality-of-life considerations into therapeutic decision-making facilitates individualized treatment and promotes long-term patient satisfaction (2, 7).

vi. Practical Clinical Pearls

Based on the available evidence, several practical principles can assist clinicians in selecting appropriate candidates for NASHA/Dx therapy:

- Best outcomes are achieved in patients with passive FI associated with preserved sphincter anatomy and internal anal sphincter dysfunction.
- Injectable therapy should generally be considered after the failure of optimized conservative treatment but before proceeding to more invasive surgical interventions.
- Careful assessment using endoanal ultrasound and anorectal physiology enhances patient selection; however, these results should always be interpreted in conjunction with clinical findings.
- NASHA/Dx enhances passive anal canal closure but does not restore voluntary sphincter function; therefore, patients with major external sphincter defects or severe neuromuscular dysfunction should usually be considered for alternative therapies.
- Careful patient counseling about realistic expectations and the possible need for repeat injections is fundamental to achieving satisfactory long-term outcomes.

Position of NASHA/Dx within Contemporary Management Algorithms

The management of adult FI has evolved substantially over the past two decades with the introduction of neuromodulation techniques, refinements in sphincter-preserving surgery, and growing interest in regenerative therapies. Despite these advances, injectable NASHA/Dx continues to occupy a distinct therapeutic niche within the treatment algorithm because it offers a minimally invasive option for patients who remain symptomatic after conservative therapy but do not require, are unsuitable for, or prefer to avoid more invasive interventions (2, 5, 6).

Current international guidelines recommend a stepwise, individualized approach to FI management, beginning with optimization of stool consistency, dietary modifications, pharmacological therapy, pelvic floor muscle training, and biofeedback. Patients with persistent symptoms should then undergo detailed anatomical and physiological assessments to guide the selection of second-line interventions (2, 6). Within this framework, NASHA/Dx is best regarded as an intermediate treatment option rather than a replacement for neuromodulation or reconstructive surgery. Its principal strengths include technical simplicity, outpatient administration, preservation of anorectal anatomy, rapid recovery, and the possibility of repeat treatments without compromising future therapeutic options.

The emergence of SNM has significantly influenced the contemporary management of FI and has reduced the routine use of injectable bulking agents in many specialized centers. SNM is an established treatment option for selected patients with refractory FI and has expanded the range of effective interventions available after the failure of conservative therapy (2, 5, 6). Nevertheless, SNM requires staged implantation, specialized expertise, device maintenance, and incurs higher healthcare costs, factors that may limit its availability or acceptability in some clinical settings. Furthermore, certain patients are either medically unsuitable for neuromodulation or prefer to avoid permanent implanted devices. In these cases, NASHA/Dx remains an attractive alternative because of its favorable safety profile, minimal invasiveness, and low procedural burden.

Injectable bulking therapy should not be considered a direct alternative to sphincteroplasty or other reconstructive procedures. Patients with significant structural sphincter defects or complex anorectal pathology may require reconstructive or other mechanism- targeted interventions rather than tissue augmentation alone (2, 5). Conversely, patients with passive FI associated with internal anal sphincter dysfunction or minor structural abnormalities are more likely to benefit from NASHA/Dx, as its mechanism of action directly addresses impaired passive anal canal closure.

The role of NASHA/Dx should therefore be individualized rather than protocol-driven. Selection should consider symptom severity, anorectal anatomy, physiological findings, patient age, medical comorbidities, treatment preferences, local expertise, and resource availability (Figure 2). Importantly, injectable therapy does not preclude subsequent neuromodulation or reconstructive surgery if symptoms persist or recur, allowing it to serve as a reversible and anatomy-preserving step within a staged treatment strategy.

Since NASHA/Dx can be administered as a minimally invasive outpatient procedure without the need for implanted hardware, its relatively low procedural burden makes it an attractive option in settings where access to more complex interventions is limited. The procedure requires modest infrastructure, can usually be performed on an outpatient basis, and is associated with rapid recovery and low peri-procedural morbidity.

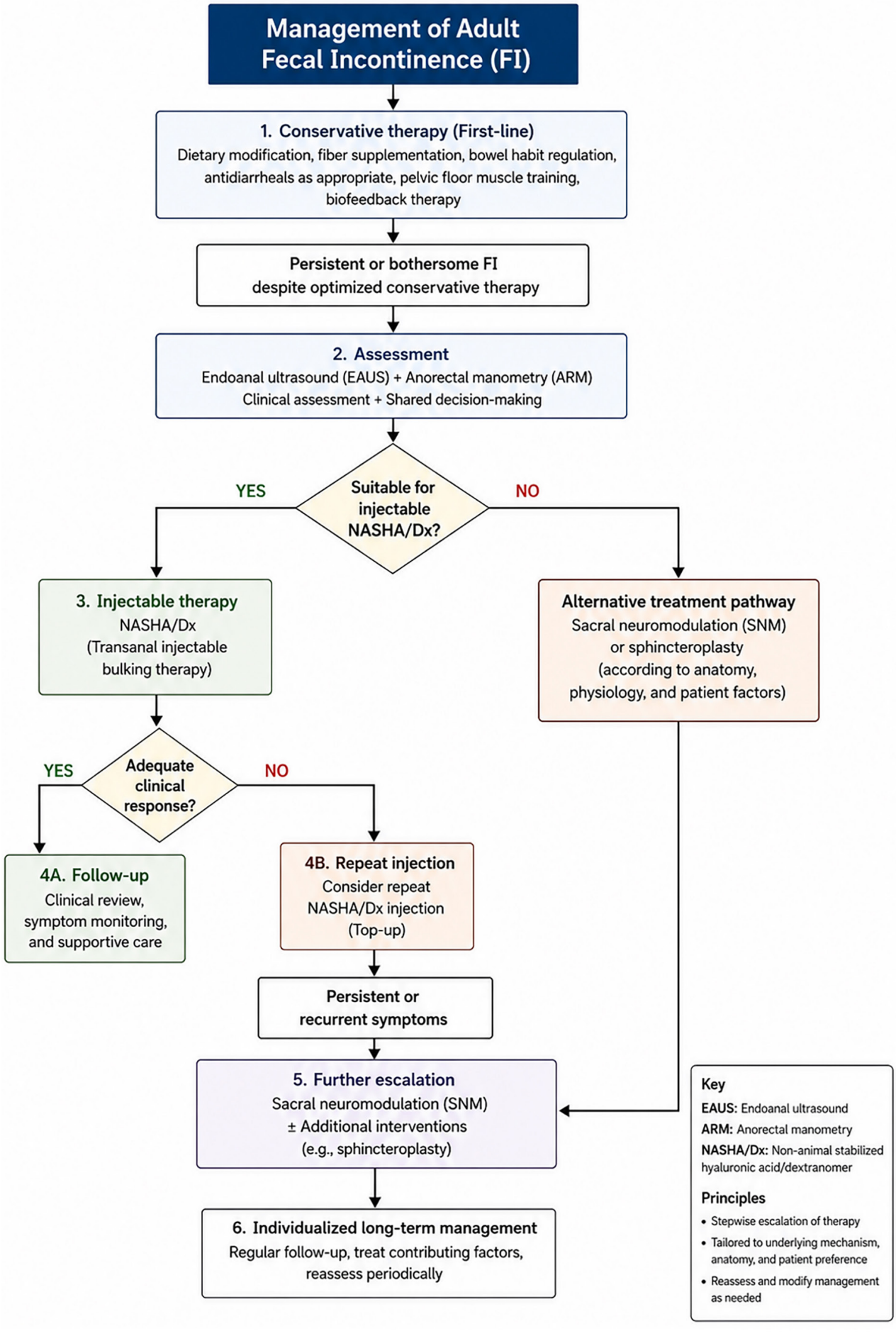


Figure 2: Position of Injectable NASHA/Dx within the Contemporary Management Algorithm for Adult Fecal Incontinence.

Although formal cost-effectiveness analyses remain limited and vary across healthcare systems, these practical advantages support the continued inclusion of NASHA/Dx within multidisciplinary treatment pathways, particularly in contexts where more resource-intensive interventions are not readily available.

Overall, contemporary evidence suggests that NASHA/Dx should no longer be viewed simply as a historical bulking agent, nor as a direct competitor to SNM. Instead, it should be considered a complementary therapeutic option occupying a well-defined position between optimized conservative management and more invasive interventions. Careful patient selection and shared decision-making remain essential to maximizing its clinical benefits and ensuring its appropriate integration into modern, individualized treatment algorithms.

Limitations of Current Evidence and Directions for Future Research

Although the available evidence supports injectable NASHA/Dx as a safe and effective minimally invasive treatment for carefully selected patients with adult FI, several important limitations continue to influence interpretation of the published literature and should be considered when applying these findings in routine clinical practice.

First, relatively few high-quality randomized controlled trials have evaluated NASHA/Dx, with much of the current evidence derived from prospective cohort studies, observational investigations, and long-term follow-up of the original pivotal clinical trials (7, 8, 10, 12). Although these studies consistently demonstrate clinically meaningful improvements in continence and QoL, variations in study design, inclusion criteria, outcome measures, and duration of follow-up make direct comparisons between studies challenging.

Second, considerable heterogeneity exists within patient populations. FI is a multifactorial disorder with diverse etiologies, including internal anal sphincter dysfunction, external sphincter injury, neurological diseases, altered rectal compliance, and bowel disturbances. Consequently, treatment outcomes reported in one patient population cannot necessarily be generalized to others. Greater standardization of patient selection criteria would facilitate more meaningful comparisons across future studies and improve the identification of individuals most likely to benefit from injectable therapy.

Third, although several studies have reported sustained clinical benefits for up to 36 months, evidence regarding durability beyond approximately three years remains limited and is largely based on observational follow-up and small cohorts. The natural history of implanted dextranomer microspheres, the optimal timing of top-up injections, and factors influencing long-term treatment persistence require further investigation through prospective longitudinal studies with extended follow-up periods.

Another important limitation is the lack of direct comparative studies between NASHA/Dx and other contemporary minimally invasive therapies. Although SNM is an established treatment option for selected patients with refractory FI, direct comparative evidence between SNM and NASHA/Dx remains limited, particularly regarding long-term patient-reported outcomes, retreatment rates, and cost-effectiveness. Conducting such studies would help better define the optimal role of injectable bulking therapy within modern multidisciplinary treatment pathways.

Future research should focus on identifying reliable predictors of treatment success. Integration of clinical characteristics, endoanal ultrasound findings, anorectal physiological assessments, and emerging imaging or biomarker-based approaches may facilitate more individualized patient selection and improve therapeutic outcomes. The development of validated prediction models could further assist clinicians in selecting patients most likely to derive durable benefits from injectable therapy.

Future regenerative therapies may eventually expand the therapeutic landscape beyond passive tissue augmentation. Experimental approaches using myogenic stem cells, biomaterial scaffolds, and controlled delivery of growth factors have demonstrated potential for improving external anal sphincter repair, tissue regeneration, and sphincter function in preclinical models (18-21). These strategies aim to promote the biological restoration of damaged sphincter tissue rather than simply augmenting the anal canal. However, most available evidence remains experimental, and substantial challenges regarding delivery methods, durability, safety, and clinical translation persist. Therefore, regenerative therapies should currently be regarded as investigational approaches that may complement or eventually redefine the role of injectable biomaterials in the management of FI (18-21).

Finally, future clinical trials should adopt standardized outcome measures that extend beyond reduction in incontinence episodes to include validated quality-of-life instruments, patient-reported outcome measures, functional status, retreatment rates, cost-effectiveness, and long-term durability. Such standardization would enhance comparability between studies, facilitate evidence synthesis, and provide clinicians with more meaningful information to guide patient-centered decision-making.

Overall, current evidence supports NASHA/Dx as a valuable component of contemporary FI management. However, further high-quality, multicenter studies with standardized methodologies, longer follow-up periods, and direct comparisons with alternative treatment modalities are required to

better define its long-term effectiveness and optimal role within individualized treatment algorithms.

Expert Perspectives and Practical Recommendations

The management of adult FI has evolved from a predominantly surgical discipline to a multidisciplinary, patient-centered approach that emphasizes individualized treatment selection. Within this evolving landscape, injectable NASHA/Dx should be regarded neither as an obsolete therapy nor as a universal solution, but rather as a valuable, minimally invasive intervention for carefully selected patients. Based on the available evidence and current international guideline recommendations, several practical considerations can assist clinicians in integrating NASHA/Dx into contemporary clinical practice.

i. Patient Selection Should Drive Treatment Success

The success of NASHA/Dx depends more on appropriate patient selection than on the injection procedure itself. Available evidence suggests that patients with less severe symptoms and relatively preserved anorectal anatomy are more likely to respond, although validated predictors of individual treatment success remain lacking (11).

ii. Injectable Therapy Should Occupy an Intermediate Position in the Treatment Algorithm

NASHA/Dx may be considered after optimized conservative management in appropriately selected patients, particularly when a minimally invasive, anatomy-preserving intervention is preferred or when other advanced therapies are unsuitable or unavailable (2, 5, 6).

iii. Objective Evaluation Improves Clinical Decision-Making

Comprehensive assessment should precede injectable therapy whenever feasible. Endoanal ultrasound, anorectal manometry, and careful evaluation of bowel habits help identify the predominant mechanism of incontinence and improve patient selection. These investigations should complement, rather than replace, careful clinical assessment and individualized decision-making (2).

iv. Patient Expectations Should Be Realistic

Patients should be counseled that the principal objective of NASHA/Dx treatment is a meaningful reduction in symptom severity and an improvement in QoL rather than complete restoration of continence. The discussion should include the possibility of requiring top-up injections and the potential need for subsequent alternative interventions if symptoms persist or recur. Establishing realistic expectations before treatment is likely to improve patient satisfaction and facilitate shared decision-making (7, 10).

v. Repeat Injections Represent Continuing Care Rather Than Treatment Failure

Recurrence of symptoms following an initially successful response should not be automatically interpreted as failure of therapy. Current evidence indicates that repeat injections can restore or maintain clinical benefits in selected patients while preserving the procedure's favorable safety profile. Decisions regarding retreatment should be individualized according to symptom recurrence, patient preferences, and functional outcomes rather than predetermined treatment intervals (10, 14).

vi. NASHA/Dx Remains Relevant in Contemporary Practice

The widespread adoption of SNM has appropriately expanded treatment options for patients with FI; however, it has not eliminated the role of injectable bulking agents. NASHA/Dx continues to offer several practical advantages, including outpatient administration, avoidance of implanted hardware, preservation of future treatment options, and low procedural morbidity. These characteristics make it particularly attractive for older adults, patients with significant comorbidities, individuals who decline implanted devices, and healthcare settings where access to advanced neuromodulation may be limited (2, 5, 6).

vii. Future Management Will Become Increasingly Individualized

Emerging advances in anorectal imaging, physiological assessment, biomaterial engineering, and regenerative medicine are expected to further refine the role of injectable therapies in adult FI. Rather than replacing existing treatment modalities, future innovations are likely to facilitate increasingly personalized, mechanism-based therapeutic approaches, integrating injectable biomaterials with pelvic floor rehabilitation, SNM, and regenerative strategies according to each patient's underlying pathophysiology.

Future prospective studies should focus on refining patient selection criteria, optimizing injection techniques, identifying predictors of long-term treatment success, and directly comparing NASHA/Dx with emerging minimally invasive therapies to better define its role in the multidisciplinary management of adult FI over the long term.

Practical Take-Home Messages

Based on the available evidence, the following principles can assist clinicians in everyday practice:

- Optimize conservative management before considering injectable therapy.
- Select patients based on the underlying mechanism of incontinence rather than solely on symptom severity.
- Use endoanal ultrasound and anorectal physiology studies to complement the clinical evaluation whenever available.

• Consider NASHA/Dx particularly for patients with predominantly passive FI and relatively preserved sphincter anatomy, while recognizing that reliable predictors of treatment response are not yet fully defined.
• Counsel patients that symptom improvement, rather than complete continence, is the realistic therapeutic goal.
• Consider repeat (top-up) injections for carefully selected patients who experience recurrent symptoms after an initial favorable response.
• Recognize the characteristic post-treatment appearance of NASHA/Dx deposits on cross-sectional imaging, particularly CT, to reduce the risk of misinterpreting them as abscesses or neoplastic disease (15).
• Incorporate NASHA/Dx into individualized, multidisciplinary treatment pathways rather than viewing it as a competitor to SNM or reconstructive surgery.

Overall, contemporary evidence supports NASHA/Dx as a safe, minimally invasive, and clinically valuable treatment for selected patients with adult FI. Its greatest strength lies not in replacing established therapies but in filling an important therapeutic niche between conservative management and more invasive interventions. Continued refinement of patient selection, procedural techniques, and biomaterial technology is likely to further define its role within personalized colorectal practice.

Conclusion

Injectable NASHA/Dx is a safe, minimally invasive, and evidence-based treatment for selected adults with FI who remain symptomatic despite optimized conservative management. By providing immediate tissue augmentation followed by sustained tissue remodeling, it offers meaningful improvements in continence and QoL, particularly in appropriately selected patients with persistent FI and relatively preserved sphincter anatomy.

Although SNM has expanded the therapeutic landscape, NASHA/Dx continues to occupy an important niche between conservative therapies and more invasive interventions. Careful patient selection, realistic patient counseling, and integration within a multidisciplinary treatment pathway remain key determinants of successful outcomes. Continued research focusing on long-term durability, optimized patient selection, and next-generation biomaterials will further define the role of injectable bulking therapy in the personalized management of adult FI.

AI Acknowledgments

The authors acknowledge the use of OpenAI's ChatGPT to assist with English language refinement and the conceptual design of Figures 1 and 2. Both authors independently reviewed and verified all scientific content, interpreted the literature, prepared and validated the final figures, and approved the final manuscript. The authors accept full responsibility for the accuracy, integrity, and originality of the work.

Author Contributions

Both authors contributed to the conception and design of the review, literature search, interpretation of the evidence, manuscript drafting, critical revision of the manuscript, and approval of the final version. SAS (first author) led the overall conceptualization, synthesis of evidence, and preparation of the final manuscript. Both authors agree to be accountable for all aspects of the work.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Data Availability Statement

No new datasets were generated or analyzed during the current study. All information supporting the findings of this review is available in the published literature cited in the reference list.

Ethics Approval and Consent to Participate

Not applicable. This study is a narrative review based exclusively on previously published literature and did not involve human participants, animals, or identifiable patient data.

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