14 Echo-Assisted Intersphincteric Autologous Microfragmented Adipose Tissue Injection to Control Fecal Incontinence in Children

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14.1 Introduction

14.1.1 Fecal Incontinence

First of all it is important to highlight that it is possible to properly speak about continence only in children who completed toilet training: a report prepared for the Agency for Healthcare Research and Quality (AHRQ) of the U.S. Department of Health and Human Services (2006) suggested that most children between the ages of 18 and 30 months have the prerequisite skills to begin toilet training, and Brazelton et al. (1999) found that most children complete toilet training when 36 months old.

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Fecal incontinence is defined as accidentally having bowel movements in patients who completed toilet training; it is a common condition in the pediatric population and can cause social unacceptance and embarrassment in both the parents and children the more the patients grow up.

Possible causes of fecal incontinence could be medically acquired conditions (like chronic constipations) or congenital anomalies (anorectal malformations, Hirschsprung disease, or spinal anomalies).

It is possible to distinguish the following:

True fecal incontinence: It regards children affected by anorectal malformations (ARM), Hirschsprung disease (HD), and spinal problems since these conditions prevent the patients from developing normal anatomical structures required for an efficient bowel control. Children with true fecal incontinence, in order to better evaluate the proper therapeutic protocol, should be further divided into patients with slow (**hypomotility**) or fast (**hypermotility**) bowel movements.

Pseudoincontinence or **encopresis**: It occurs in children with the ability to toilet train but who have developed a severe chronic constipation or in patients in whom the underlying disease predisposes them to develop constipation. In these patients, feces accumulate along the colorectal tract and the wateriest stools percolate through the hardest ones determining a fecal overflow that cannot be controlled even by a well-toilet-trained child without anatomical anomalies.

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Defecation is a result of a series of complex processes that requires three undamaged elements working together: **voluntary muscle control**, **sensation**, and colon's involuntary peristalsis (**motility**).

Voluntary muscles: The muscle complex of the perineum is under the conscious control of the baby: once stools arrive to the anal canal, the child is free to decide whether to relax the muscle complex (and then to defecate) or to hold the stool contracting the muscles.

The sphincter muscles can be weak in children born with ARM or spinal defects.

Sensation: The ability of the baby to feel the feces in the ampulla. The anal canal and ampulla, with their fine and reach innervation, are able to give the baby's brain extremely precise sensory information of their filling state to let him/her know when it is time to empty the ampulla.

Surgery and spinal defects could alter this perception making the brain no longer able to understand when the rectum is full of feces.

Motility: Continence issue could also arise from an altered speed of stool progression from the colon to the anal canal. In cases of hypomotility feces tend to gather in the ampulla determining a chronic constipation and then soiling to overflow. Hypermotility is a characteristic of postoperative patients who have the colon parts removed: these children experience a fast progression of feces, especially if watery, that leak out of the anus even in well-toilet-trained babies.

Treatment of fecal incontinence in children should always start from dietary changes and an accurate bowel management eventually powered by transanal irrigation systems.

In case of ineffectiveness of the previous mentioned methods, surgery could be taken into account.

Here the authors describe a novel echo-guided technique to enhance the continence ability of patients based on the intersphincteric injection of adipose tissue derived from the patients themselves (autologous), also called anal lipofilling.

14.1.2 Adipose Tissue

Adipose tissue is a specialized connective tissue consisting of lipid-rich cells called adipocytes. As it comprises about 20–25% of total body weight in healthy individuals, the main function of adipose tissue is to store energy in the form of lipids (fat). Based on its location, fat tissue is divided into parietal (under the skin) and visceral (surrounding organs). Depending on the adipocyte morphology, there are two types of adipose tissue: white adipose tissue, mainly found in adults, and brown adipose tissue, mainly found in newborns.

Besides energy storing, fat tissue has several other important functions in the human body. These include thermal isolation, cushioning the organs, an endocrine role, and production of numerous bioactive factors.

Like every other tissue, adipose tissue consists of cells and extracellular matrix. The cells are the most abundant structural elements of this tissue, predominating over the small amount of extracellular matrix. The main cells that compose adipose tissue are the adipocytes. Besides adipocytes, several other cell types are present: fibroblasts, capillary endothelial cells, macrophages, and stem cells. These non-adipocyte cells collectively form the stromal vascular fraction, and their main function is to support and protect the adipose tissue. The extracellular matrix is produced by both adipocytes and stromal cells. It consists of a fine network of reticular fibers (type III collagen), whose function is to hold the cells in place. Adipose tissue is richly supplied with blood vessels and unmyelinated nerve fibers.

The abundance of the adipose tissue in the human body, its ease of obtaining, and its stem cell fraction make this tissue the best candidate for our technique (Fig. 14.1).

14.2 The Anal Lipofilling

Patients with fecal incontinence not responsive to medical treatments and bowel management, before more invasive surgical approach, may benefit from echo-assisted intersphincteric autologous microfragmented adipose tissue injection (anal lipofilling).

The ratio of this technique is that the injected fat tissue acts as a bulky agent increasing resting pressure as verified with anorectal manometry in various studies and thickens the anal sphincter as

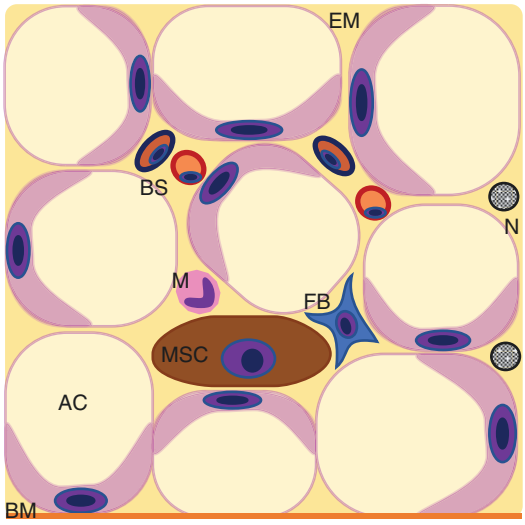

Fig. 14.1 Adipose tissue composition. *EM* Extracellular matrix, *BS* Blood supply, *N* Nerves, *M* Macrophages, *FB* Fibroblasts, *AC* Adipocyte, *MSC* Mesenchymal stem cells, *BM* Basal membrane

documented by anal endosonography by some authors.

Before its application in children, several studies reported its feasibility, safety, and encouraging results in adults.

The role of mesenchymal stem cells (MSCs) has still to be understood since in other disciplines (like orthopedics and cosmetics) a certain grade of tissue regeneration has been reported; therefore, MSCs may differentiate in order to implement the amount of sphincter muscle fibers but more studies are needed to clarify this point.

The main limits of autologous fat graft, also for anal lipofilling, remain to be the unpredictable viability and reabsorption of transferred fat. Therefore, the procedure needs to be repeated to maintain its efficacy.

14.2.1 Background of Fat Graft Application

Autologous adipose tissue transplantation is a well-established method with several clinical applications in plastic surgery.

It is based on the removal of fat graft from a donor site, its processing in order to make the tissue as suitable as possible for the recipient site, and the reimplantation of the processed tissue in a selected area.

The autologous adipose tissue has the main advantage of being completely biocompatible and easily available, also in pediatric patients, without morbidity for the donor site and without significant additional costs for the operating room. It is mainly used to correct a volumetric deficit, applicable in every part of the body. The transfer of autologous fat with filler purpose has been performed as whole grafts since the 1890s [1] and as injectable grafts since the 1920s [2] (breast reconstruction, facial and body contouring, post-traumatic treatments). Fat is the ideal filler: it is readily available and inexpensive to harvest, it is autologous and therefore lacks a host immune response, it is safe and noncarcinogenic, and it is acquired with a minimally invasive procedure. However, it is only within the last 15 years that the popularity of autologous fat graft for its regenerative purposes has increased within the plastic surgery and other surgical fields. Despite the well-known clinical advantages of the autologous fat graft, the main limit remains the unpredictable viability of transferred fat. During the years, several methods have been described to improve graft survival, better volume prediction, and regenerative capacity. Fat tissue is available in enough amount in most patients, also children, and can be harvested easily with a minimally invasive approach. Since the first description [3, 4], several studies have focused on the technical improvement and the optimization of the fat grafting technique described by Coleman. Simple lipoaspiration, gravity separation, Coleman fat centrifugation, washing, microfat, and nanofat techniques are the most cited and used approaches. Fat tissue offers a highly viable mesenchymal stem cell (MSC) population with optimal differentiation potential independent of the donor's age. The regenerative potential of adipose tissue-derived MSCs is similar to that reported in other tissues, but it is much more abundant compared with the widely used source of MSCs as bone marrow, and by their easy access [5]. A recent study compared the classical lipofilling technique with three commercial devices to obtain a fat

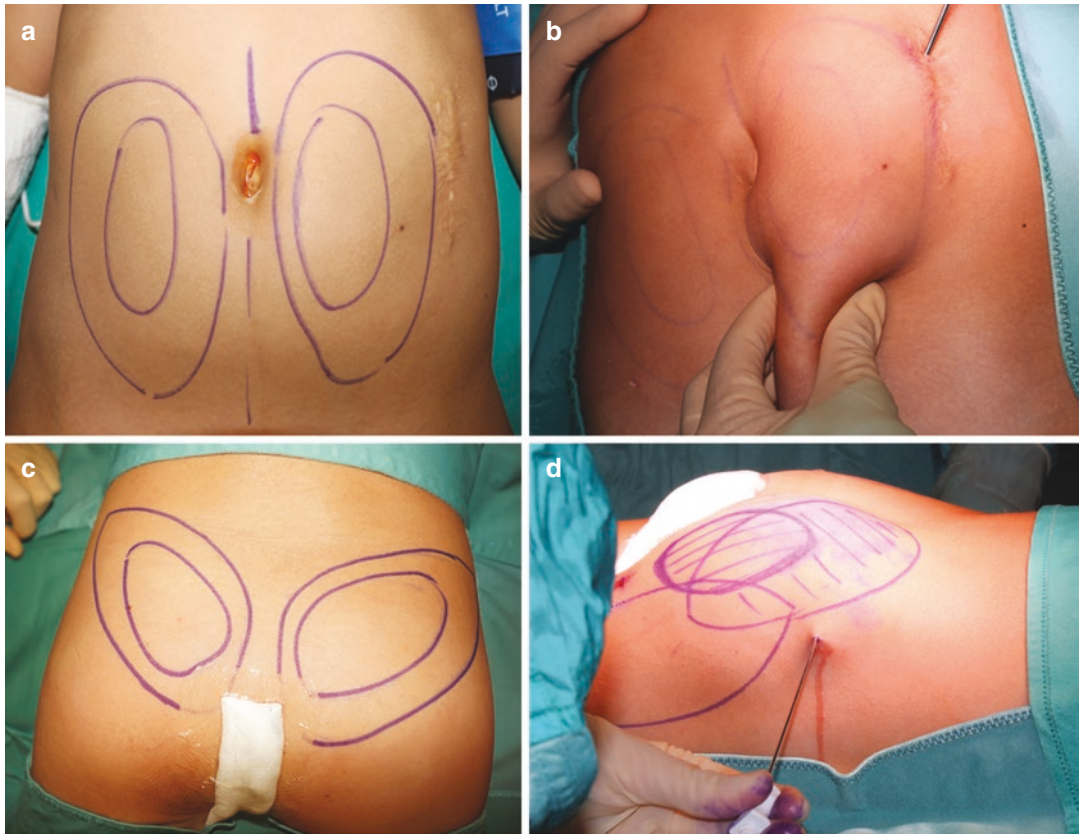

Fig. 14.2 Donor sites: (**a**) Abdominal region, (**b**) pinch test, (**c**) supragluteal area, (**d**) supragluteal fat graft harvesting

derivative enriched in MSCs, confirming that a greater amount of MSCs leads to better and more stable results [6]. Several studies showed greater tissue viability and a lower percentage of contaminants in fat tissue washed and filtrated within a closed system [7].

14.2.2 Surgical Procedure

The procedure of ano-lipofilling consists of three distinct phases performed in a single surgical time:

- Fat tissue harvesting
- Fat tissue processing
- Lipotreated tissue injection

14.2.3 Fat Tissue Harvesting

Each patient was examined preoperatively in orthostatic position with the pinch test, to precisely evaluate and draw the area to be lipoaspirated (Fig. 14.2).

The ideal donor site is represented by the abdomen, for different reasons.

Usually, abdominal area is chosen as the donor site because of its ease of access and availability; it is unique and median (for which we do not need to take bilateral sample as from the hips, thighs, and buttocks to avoid morpho-volumetric asymmetries). Further, the abdominal area as donor site allows to place the patient in supine position and easily converts it into a lithotomic position, needed for the injection time.

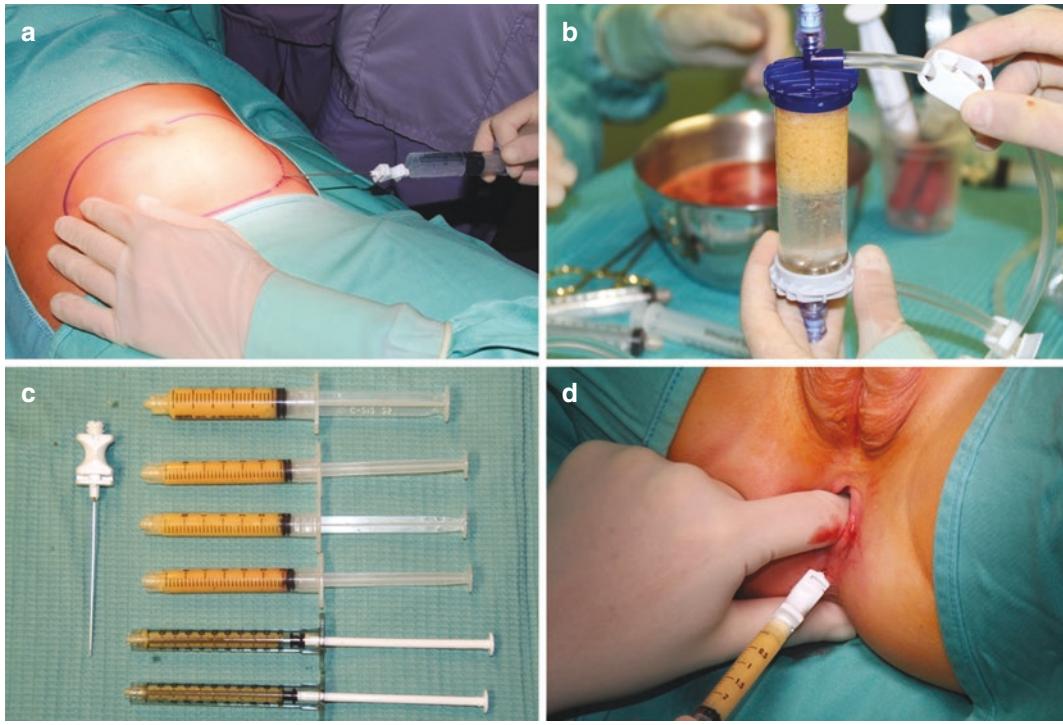

Fig. 14.3 Lipofilling procedure: (**a**) Local infiltration, (**b**) adipose tissue processing technique, (**c**) adipose tissue ready for injection, (**d**) intersphincteric adipose tissue injection

In very thin patients, the supragluteal region and inner knees are the best donors of adipose tissue but require bilateral sampling to preserve the contouring of the buttock; further they require to move the position with the patient's pronation-supination.

The first step is the infiltration in the donor site of a solution composed of epinephrine 2 mcg/mL in saline solution (1:500), using a 17-gauge cannula connected to the Luer Lock® syringe included in the kit (Fig. 14.3a).

After 10 min, lipoaspiration of a small amount of fat tissue is performed in a standardized fashion of the liposuction through a millimetric skin incision. Fat is harvested from the selected area using manual suction with a 20 mL VacLok® syringe and a 3 mm 13-gauge blunt cannula included in the Lipogems® kit (about 50/60 mL depending on the patient's body habitus). Sequential steps for fat tissue harvesting are reported in Table 14.1.

Table 14.1 Standard surgical liposuction: sequential steps

Standard surgical liposuction	
1	Skin incision with a 11 blade (peripheral area of the donor site) – *Hidden skin incision* – *Skin folds/umbilicus* – *Previous scars*
2	Infiltration of saline solution/epinephrine 2 mcg/mL in saline solution 1:500.000 in the selected area using disposable infiltration 17 G cannula (included in the Lipogems® kit)
3	Waiting for 10 min
4	Harvesting fat tissue in the selected area by using a blunt 13 G cannula with multiple elliptical holes (included in the Lipogems® kit) connected with a 20 cc self-locking Luer Lock syringe (VacLok®)
5	Transfer of the harvested fat tissue in the Lipogems® system

14.2.4 Fat Tissue Processing

Processing of the harvested fat is carried out with the Lipogems® device [5] (Fig. 14.3b), a closed,

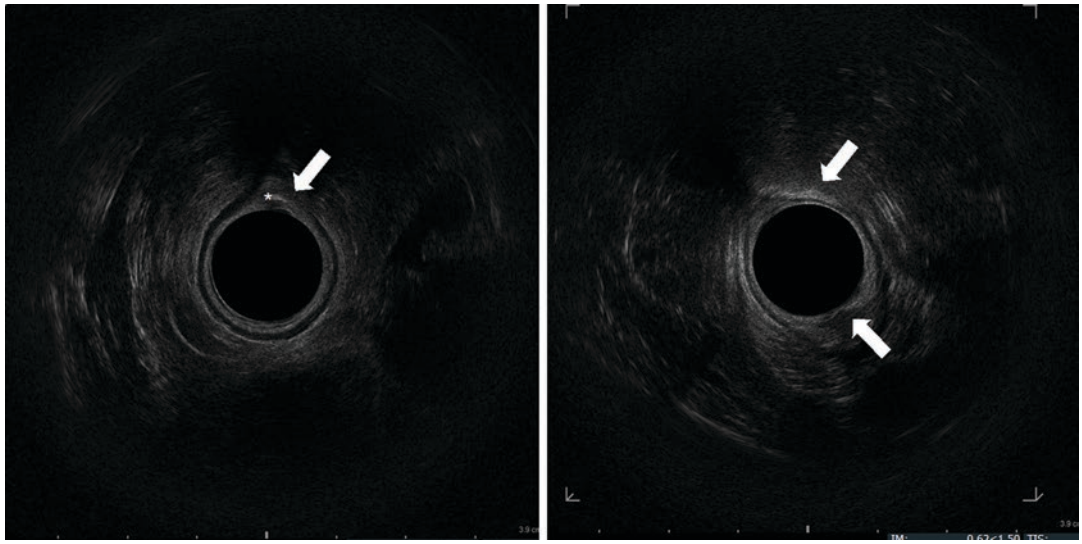

Fig. 14.4 Endosonographic axial sections of the middle anal canal. Asterisk: needle in the internal anal sphincter; arrow: injected fat tissue h 6 and 12

full-immersion, low-pressure cylindrical system, to obtain a gradual reduction in the adipose tissue clusters and remove impurities (blood, oil, and cell debris), producing an injectable fluid containing many pericytes/MSCs.

Lipogems® is a simple system patented in 2010 and clinically available since 2013, designed to harvest, process, and transfer refined adipose tissue, and is associated with great regenerative potential and optimal handling ability [5]. Thanks to this Italian system technology, fat tissue is microfragmented gently and washed from proinflammatory oil and blood residues, without enzymes or other additives. The processed fat is subjected to only slight mechanical forces, with no detrimental effects on the integrity of the stromal vascular components and on the tissue itself.

The processing procedure consists of five consecutive steps well described by the manufacturer; directions for use are supplied with the device. The system core is represented by a plastic cylinder containing five stainless steel marbles and connected to two hoses. The fat cluster reduction and purification are allowed by a mechanical system of metallic filters. The manual vertical shaking permits the steel spheres to emulsify and microfracture the adipose tissue. The fat is washed and emulsified, and adipose cluster size is gradually reduced to about 0.3–0.8 mm. This procedure will be repeated till washing saline solution will be clear and transparent. At this time, processed and purified fat graft, containing MSCs, is ready to be isolated and injected in the anal area.

In the resulting microfragmented fat, pericytes are retained within an intact stromal vascular niche and are ready to interact with the recipient tissue after injection, thereby becoming MSCs and starting the regenerative process (Fig. 14.3c).

14.2.5 Echo-Assisted Injection

Having completed the liposuction procedure and processed the adipose tissue, the patient is set in gynecological position and three injections of about 10 mL of adipose tissue are performed at three out of four quadrants of middle anal canal (Fig. 14.3d) under endoanal US guidance, precisely in the intersphincteric plane (Fig. 14.4).

As regards the echo-assistance, we use an anorectal 3D 2052 transducer (17 mm diameter, 13 MHz); endoanal ultrasound guarantees a more precise transplantation site.

Table 14.2 Donor-site treatment

Donor-site treatment
5.0 Prolene skin suture (single stitch): 1 week
Application of gauzes soaked with iced saline solution to reduce ecchymosis: up to postoperative dressing
Antibiotic therapy (amoxicillin): 5 days
Elastic and compressive dressing: 1 week
Heparan sulfate 1% cream to reduce ecchymosis

14.2.6 Postoperative Time

Immediate bulging and mechanical effect of the fat graft can be showed, while improvement of mucosal quality of the treated region is generally observed a few months after fat grafting. Compression dressing is applied on the donor site for 1 week. Antibiotic therapy (amoxicillin) is administered for 5 days. Heparan sulfate ointment is indicated to reduce ecchymosis (Table 14.2).

14.2.7 Complications

No hematomas, infections, and vascular or nervous injuries were reported in the treated children. No significant further surgical complications, from either the donor site or the injected site, were reported. Mild edema and bruising were frequent during the first postoperative week. Further possible described complications of this procedure could be visible irregularities of the liposuction site that are extremely rare considering the small amount of lipoaspiration and accurate preoperative evaluation. Major complications such as fat embolism syndrome present a low risk considering the small caliber of the blunt cannula used for lipoaspiration.

14.3 Authors' Experience

In our center we decided to apply this technique to patients with fecal incontinence due to ARM [8].

Table 14.3 International classification (Krickenbeck) for postoperative results in ARM

1. Voluntary bowel movements
Feeling of urge, capacity to verbalize and hold the bowel movements
1.0 No
1.1 Yes
2. Soiling/fecal incontinence
2.0 No
2.1 Occasionally (once/twice a week)
2.2 Every day, no social problem
2.3 Constant, social problem
3. Constipation
3.0 No
3.1 Manageable with diet
3.2 Requires laxatives
3.3 Resistant to diet and laxatives

We monitored the efficacy at follow-up using the international classification (Krickenbeck) for postoperative results in ARM (Table 14.3) [9].

We therefore treated four patients: they were all male, three rectourethral fistulas (75%), and one recto-perineal fistula (25%), and underwent the first anal lipofilling at a mean age of 13 ± 4.2 years (range: 8–17 years). All four patients suffered from total fecal incontinence; presented the same score at Krickenbeck scale, 1.0, 2.3, and 3.0; and needed an enema every day to help in bowel control.

The total number of procedures performed was 9 and the mean number of procedures per patient was 2.0 ± 1.3 (range: 1–4).

Three patients treated (75%) showed a significant improvement in continence with a KS score of 1.0, 2.1, and 3.0 after every single procedure and a reduction of the number of enemas from once daily to 1 or 2 weekly (Fig. 14.5).

One patient (25%) did not benefit from the anal lipofilling, and no changes on the KS were recorded before and after the procedure (Fig. 14.5).

The mean interval between the procedures in the ones who underwent more than one anal lipofilling was 343.8 days ±220.1 days (range 203–733 days).

No complications were recorded during and after the procedure.

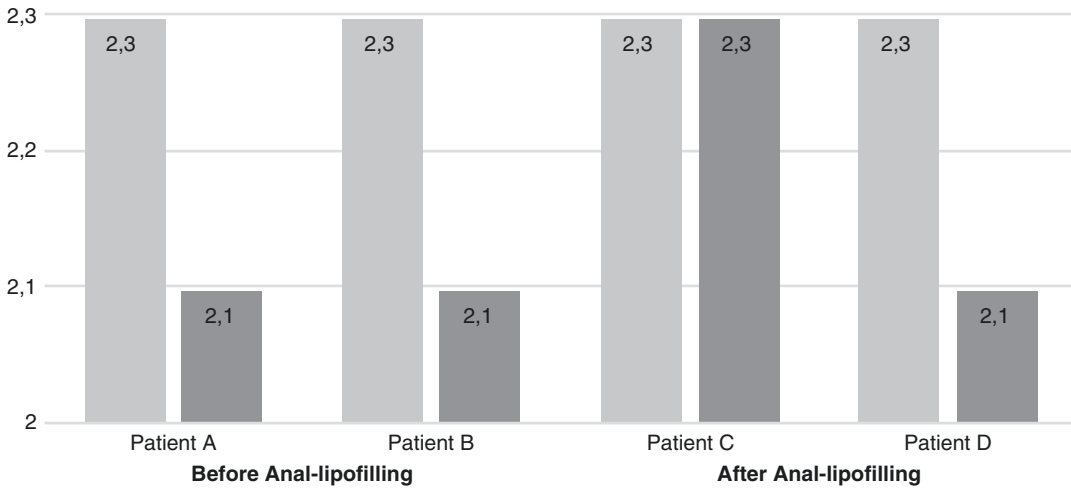

Fig. 14.5 Results of anal lipofilling on soiling reported as Krickenbeck scale (KS) score

14.4 Conclusions

The treatment of ARMs consists of a wide range of surgical and nonsurgical procedures [10].

Thanks to the optimal size of the clusters, allowing easy injection of the product and its regenerative capacity, fat graft and microfragmented fat have been tested and used safely in various clinical applications [11–16]. Fat grafting is a simple, effective, and reproducible technique, with a high satisfaction rate and few disadvantages or complications. According to our preliminary experience, fat tissue fits with authority into the portfolio of therapeutic options for patients with anorectal malformations. The microfragmentation technology (Lipogems®) improves and optimizes the natural properties of adipose tissue, without the use of enzymes, additives, or separation centrifugation. The opportunity to promote local tissue regeneration, thanks to mechanical MSC selection, makes local tissue more viscoelastic and represents a very promising approach for ARMs. The entire procedure is performed in a single surgical time and can be repeated without compromising the execution of further more invasive and traditional surgical procedures in the future.

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