



Rectal advancement flap plus adipose lipofilling (RAFAL) for the treatment of rectourethral fistulas after radical prostatectomy

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Received: 12 March 2019 / Accepted: 5 September 2019 / Published online: 18 September 2019
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Abstract

Background Rectourethral fistula (RUF) is a rare but significant complication after radical prostatectomy. Many different approaches have been used, but none of them has become the standard of care.

Methods We present our series of seven patients treated with a transanal rectal advancement flap plus the injection of mesenchymal stem cells, to facilitate the healing of the fistula. Mesenchymal cells were obtained by a new mechanical device known as LIPOGEMS[®]. We called this technique RAFAL (rectal advancement flap plus adipose lipofilling). In all patients the RUF was a complication of laparoscopic radical prostatectomy. Fistula size ranged from 0.3 to 0.5 cm (median 0.4 cm).

Results After a median follow-up of 53 months (range 6–163 months), 2 out of 7 patients experienced RUF recurrence. In both cases recurrence was successfully treated by the York-Mason technique in one case and by redo RAFAL in the other. Success rate of RAFAL was 71% (5 of 7). The total success rate of primary RAFAL and redo-RAFAL was 85.7% (6 of 7). No short- or long-term complications were seen.

Conclusions In our patient population this new procedure was safe and effective.

Keywords Rectourethral fistula · Transanal advancement flap · Mesenchymal stem cells (MSCs) · LIPOGEMS[®]

Introduction

Rectourethral fistula (RUF) is an abnormal communication between the rectum and urethra which can be congenital or acquired, resulting from radiation, trauma, inflammation and especially after surgery. RUF is a rare but significant complication after radical prostatectomy. It is usually located at or near the anastomosis between the urethra and the bladder

and it can occur during apical dissection, while attempting to develop the plane between the rectum and Denonvilliers' fascia. Intraoperative accidental rectal injury and radiation therapy prior to surgery are major risk factors for its formation. A RUF is usually diagnosed because of faecaluria and/or pneumaturia and/or watery stool.

Many different techniques for RUF repair have been described in the literature, with the Lydston and the York-Mason procedures as the most frequently used. However, because of the rarity of cases and the absence of randomized control trials, there is no consensus about the optimal method of repair.

We describe a new minimally invasive technique which allows RUF repair from both the urethral and the rectal side; the rectal side is repaired by a fistulectomy and the creation of an endorectal advancement flap; the urethral side is repaired by the infiltration of adipose lipofilling containing mesenchymal stem cells (MSCs), which has already been used to repair muscle damage in patients with urinary and anal incontinence [1].

We call this technique rectal advancement flap plus adipose lipofilling (RAFAL).

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Materials and methods

From 2004 to 2017 all patients presenting with RUF had RAFAL. There were seven patients [median age 61 years (range 52–66 years)]. All the patients had had laparoscopic radical prostatectomy for prostate cancer. None of them had a history of radiation therapy. All patients experienced faecaluria, with a median onset of 15 days (range 12–27 days) after prostatectomy. Median RUF size was 0.4 cm (range 0.2–0.5 cm). Patients' characteristics are listed in Table 1. Diagnosis of RUF was made based on symptoms, sigmoidoscopy and cysto-urethrography. At the onset of faecaluria each patient had bladder catheterization, oral antibiotic therapy and a laparoscopic colostomy. After a median period of 6 months for spontaneous RUF closure (that did not occur in any case) our patients underwent the RAFAL procedure. Informed consent was obtained from all individual participants included in the study.

Surgical technique:

1. Patient in lithotomy, under spinal anaesthesia and sedation;
2. At proctoscopy, 1:10.000 adrenaline solution is injected into the fistula margins;
3. Fistulectomy with a scalpel blade (to avoid tissue necrosis) is performed, until reaching the bladder wall; fistulous tract is sent to pathologist to be analysed;
4. Preparation of a rectal advancement flap with rectal mucosa and submucosa;
5. Suture of the muscular plane at the fistula site with interrupted polydioxanone 2.0 stitches;
6. Suture of the advancement flap with Monosyn 3.0 stitches to cover the fistulous orifice;
7. At cystoscopy (it is important to maintain a low flow pressure to avoid flap rupture due to internal bladder pressure):

- 7.1. Identification of the ureteral ostia, which are cannulated to ensure their patency with bilateral mono J stent;
- 7.2. Identification of the internal orifice of the fistulous tract;
- 7.3. With a 21G needle (Coloplast needle for bladder injections, CH/Fr 0.5 × 35 cm) injection of 40 ml of MSCs solution into bladder submucosa within fistula margins;
- 7.4. Diathermocoagulation of the fistula margin with monopolar electrocautery to create subsequent fibrosis;
8. Checking the sealing of sutures on the rectal side;
9. The MSC solution was obtained as follows:
 - 9.1. From 2007 to 2012 (3 patients), we used Contigen, a MSC solution formed by cross-linking bovine dermal collagen with glutaraldehyde; Contigen is used for the treatment of urinary incontinence with favourable results [2]. From 2012 we decided to stop the use of this product because of the risk related to prion diseases. We did not experience any adverse reaction with its use and those patients are still alive with no health problems;
 - 9.2. From 2012 (4 patients) we used an adipose lipofilling of autologous origin. We collected 150 ml of fatty tissue from patient's abdominal wall and used LIPOGEMS® to obtain a MSCs solution. In 2014, LIPOGEMS® received the Food and Drug Administration clearance as a class II medical device for processing autologous adipose tissue. It is a mechanical device containing stainless steel ball bearings that separate the oily from the vascular part of adipose tissue, thus obtaining autologous MSCs, which are located near the blood

Table 1 Patient characteristics

Case no.	Age, years	Comorbidity	pT ^a	Gleason score	RUF onset ^b	Symptoms	Fistula size (cm)	Ostomy
1	65	Cardiovascular disease	pT2c	3+3	12	Faecaluria	0.5	Lps colostomy
2	66	Hypertension + diabetes mellitus	pT2a	4+4	13	Faecaluria	0.4	Lps colostomy
3	66	Hypertension	pT3	4+5	13	Faecaluria	0.5	Lps colostomy
4	52	None	pT2a	3+4	14	Faecaluria	0.5	Lps colostomy
5	60	None	pT2c	4+4	27	Faecaluria	0.2	Lps colostomy
6	57	None	pT2c	3+3	12	Faecaluria	0.3	Lps colostomy
7	65	Neurological disease	pT2a	4+5	14	Faecaluria	0.5	Lps colostomy

RUF rectourethral fistula, Lps laparoscopic

^apT of prostate cancer

^bPostoperative day

vessels of the adipose tissue. The system consists of a transparent plastic cylinder containing stainless steel microspheres in which patient's adipose tissue and a washing solution are inserted; after 20 min of gentle mechanical agitation, at the other end of the cylinder of adipose lipofilling containing MSCs fills a syringe, while waste products are collected in a bag (Fig. 1). From a 50-ml sample of lipoaspirate 20 ml of final product are obtained. LIPOGEMS® is time-saving: a ready-to-use product is obtained in approximately 20 min, compared to the several hours or days required for enzymatic digestion [3]. All patients were discharged with a urinary catheter, oral antibiotics and a residue-free diet the first day after surgery. Follow-up was performed with anosco-

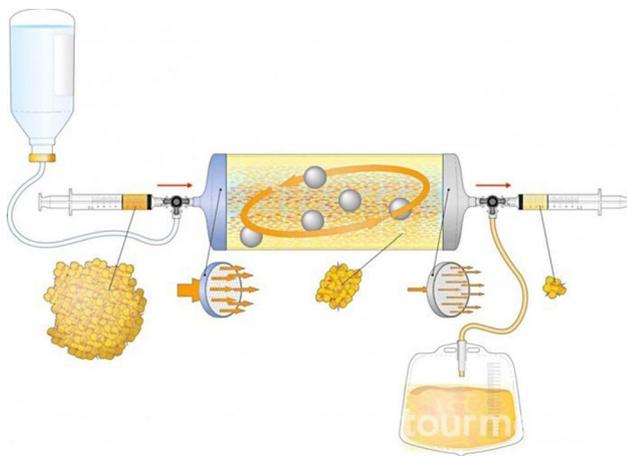


Fig. 1 LIPOGEMS system: a transparent plastic cylinder containing stainless steel microspheres in which the patient's adipose tissue and a washing solution are introduced; after 20 min of mechanical agitation, at the other end of the cylinder we obtain a syringe of adipose lipofilling containing MSC, a ready-to-use product

py and cysto-urethrography 30 and 60 days after surgery. After confirmation of successful fistula closure, bladder catheter was removed (2 months after surgery) and colostomy reversed 5 months after surgery. Intraoperative data are provided in Table 2.

Results

All patients were treated with the same standardized protocol. Median operative time was 162 min (120–205) and blood loss was inferior to 50 ml in all cases. All patients were discharged on the first day after surgery. Pain was well controlled with oral analgesic therapy. There were no intraoperative or postoperative complications. There were no early or late adverse reactions to the mesenchymal cells injected. Cancer was not found in any of the specimens. Median time between prostatectomy and RAFAL was 6 months (range 2–18 months).

There were 2 RUF recurrences: one patient experienced urinary loss from the rectum 4 days after the removal of bladder catheter and after 24 days the fistula was successfully repaired with the York-Mason technique. The second experienced symptoms of RUF 4 months after surgery; the colostomy was maintained and a redo-RAFAL procedure was successfully performed.

In the other five patients complete healing of the fistula was observed after the 30-day, 60-day cysto-urethrography. They had colostomy reversal after 5 months with no faecal incontinence. After a median follow-up of 53 months (range 6–163 months) they had no symptoms of recurrence (Table 3).

The success rate of primary RAFAL was 71%. The total success rate of primary RAFAL and redo-RAFAL was 85.7%.

Table 2 Operative data

Case no.	Operative time ^b	Mesenchymal cells origin	Blood loss ^c	Time prostatectomy—RAFAL ^a
1	120	Contigen-B	< 50	3
2	120	Contigen-B	< 50	7
3	135	Contigen-B	< 50	2
4	180	LIPOGEMS®	< 50	4
5	180	LIPOGEMS®	< 50	5
6	195	LIPOGEMS®	< 50	6
7	205	LIPOGEMS®	< 50	18

RAFAL rectal advancement flap plus adipose lipofilling

^aTime expressed in months

^bTime expressed in minutes

^cMillilitres

Table 3 Postoperative results

Case no.	30-day FU	60-day FU	Reversed colostomy ^a	FU ^a
1	No recurrence	Recurrence 4 days after bladder catheter removal	5	163
2	No recurrence	No recurrence	5	103
3	No recurrence	No recurrence	8	66
4	No recurrence	No recurrence	5	48
5	No recurrence	No recurrence	5	26
6	No recurrence	No recurrence	5	22
7	No recurrence	Recurrence 4 months after RAFAL	5	6

FU follow-up

^aTime expressed in months

Discussion

The treatment of RUF is complex because of the heterogeneity of causes, the dimensions of the parietal defect and previous radiotherapy. Moreover, because of the lack of randomized controlled trials and guidelines, there is no consensus about the treatment of RUF and every surgeon uses the technique with which he/she is most comfortable.

The first step for RUF treatment is a conservative approach, consisting of bladder catheterization and faecal diversion with an ostomy. This approach seems to be effective in a small number of cases (from 14 to 33%) [4], especially for severely symptomatic ones. The generally accepted time for healing of the RUF after conservative treatment is 3 months. After 3 months surgical therapy is needed.

In the literature, the commonly used surgical method for simple RUF (less than 2 cm) repair is the York-Mason procedure. First described in 1969 it consists of a full-thickness opening of the anal canal and of the levators muscles, fistulectomy and closure by layers. The main advantage of this technique is the preservation of sexual potency, urinary continence and rectal innervation. However, it is associated with the risk of faecal incontinence (due to the division of the anal sphincter), even though the complication rate is less than 1%. The overall success rate of this procedure is 94.7% and 75%, in non-irradiated and irradiated patients, respectively [5]. In 1904, Lydston first described the transperineal approach, the most commonly used method for complex RUF (more than 2 cm) repair in the literature. This approach allows a wide exposure of the urethra and rectum, which facilitates reconstruction of anatomical structures. The interposition of a flap, in particular the gracilis muscle, seems to increase success rate, which is nearly 100% in most published literature. Its main disadvantage is the risk of stress urinary incontinence, a complication that occurs in 70% of cases in some reports [5]. The use of a transanal rectal advancement flap

to repair RUF was first described by Jones et al. in 1987. This is not a widely used approach, but it is associated with minimal postoperative morbidity, a shortened hospital stay and a success rate of fistula closure of nearly 80% [6].

Our approach to RUF repair has four main advantages in respect to other published techniques:

1. RAFAL is a minimally invasive technique. Patients can be discharged the first day after surgery, with little postoperative pain, minimal morbidity and a faster resumption of daily activities.
2. RAFAL allows RUF repair from both the rectal side (fistulectomy and rectal advancement flap) and the urethral side (diathermocoagulation of fistula margin), leading to a lower risk of RUF recurrence;
3. The use of lipofilling allows the consolidation of surgical sutures, thus reducing the risk for RUF recurrence. Adipose tissue has a high concentration of MSCs, between 50 and 500 times higher than in bone marrow. MSCs have a physiologically immunomodulatory and trophic function (suppression of immune surveillance of injured tissues, tissue regeneration and angiogenesis) and they can also differentiate in several cell lineages, such as adipocytes, chondrocytes, osteoblasts and myoblasts [7]; a MSC solution has been reported to be effective in the treatment of urinary incontinence [2], perianal fistulas and faecal incontinence [8].
4. LIPOGEMS[®] MSC solutions can be obtained by enzymatic digestion processes, requiring several days or hours with the subsequent delay in clinical application. LIPOGEMS[®] is easy to use in every operating-room; a ready-to-use product can be obtained in approximately 20 min. After the patient's own adipose tissue has been collected, the LIPOGEMS[®]'s device makes it possible to obtain an autologous adipose lipofilling.

Conclusions

As shown by our data, the rectal advancement flap plus mesenchymal cells is a safe and effective method for RUF repair after radical prostatectomy. Injection of mesenchymal cells into the urethral side is safe and effective since it may increase the chance of healing. Further studies with larger series are needed to define the real effectiveness of the technique.

Author contributions Conception and design: SC, RM, ZM, AA. Acquisition, analysis, or interpretation of data: ZM, SC, AA, BM, RM. Draft of the manuscript: ZM. Critical revision of the manuscript: SC, ZM. Final approval of the version to be published: ZM, RM, AA, DZ, BM, PM, RB, SC. All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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