

Surgical Sphincter Saving Approach and Topical Nifedipine for Chronic Anal Fissure with Hypertonic Internal Anal Sphincter

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Abbreviations:

CAPF - posterior chronic anal fissure;

IAS - internal anal sphincter;

CAF - chronic anal fissure;

LIS - lateral internal sphincterotomy;

MRP - maximum resting pressure;

MSP - maximum squeeze pressure;

USWA - ultraslow wave activity;

VAS - visual analogical scale

Rezumat

Abordare chirurgicală de conservare a sfincterului și nifedipină topică pentru fisura anală cronică cu sfincter anal intern hipertonic

Scop: Rolul tonului sfincterului anal intern mărit (IAS) în geneza posterioară fisura anală cronică (CAPF) este încă necunoscută. Sfincterotomia internă laterală este cea mai utilizată procedură chirurgicală, totuși este împovărată de incontinență anală postoperatorie cu risc ridicat. Scopul studiului nostru este de a evalua rezultatele procedurii de economisire a sfincterelor cu sfincterotomie farmacologică postoperatorie pentru pacienții afectați de CAPF cu hipertonie IAS.

Metode: Am înrolat 30 de pacienți, au fost supuși fisurectomiei și anoplastiei cu avansarea lamboului cutanat V-Y; toți pacienții au primit administrare topică de nifedipină 0,3% și lidocaină 1,5% terapie bazată pe unguent înainte și timp de 15 zile după operație. Scopul principal a fost cel al pacientului vindecarea completă și evaluarea incontinenței și a ratei de recurență; scopul secundar a inclus evaluarea parametrilor manometriei, ameliorarea simptomelor și complicațiile legate de administrarea nifedipinei și lidocainei.

Rezultate: Toate rănilor s-au vindecat în decurs de 40 de zile după operație. Nu am observat niciun „de novo” post-caz de incontinență anală operativă. Am raportat 2 cazuri de recidive, vindecate după conservatoare terapie. Nu am raportat nicio complicație locală

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legată de administrarea unguentului terapie; cu care toți pacienții au raportat o bună conformitate.
Concluzii: Fisurctomie și anoplastie cu clapă de avansare cutanată V-Y și topică administrarea de nifedipină și lidocaină, este un tratament eficient pentru CAPF cu hipertonie IAS.

Cuvinte cheie:

Abstract

Purpose: The role of augmented internal anal sphincter (IAS) tone in the genesis of posterior chronic anal fissure (CAPF) is still unknown. Lateral internal sphincterotomy is the most employed surgical procedure, nevertheless it is burdened by high risk post-operative anal incontinence. The aim of our study is to evaluate results of sphincter saving procedure with post-operative pharmacological sphincterotomy for patients affected by CAPF with IAS hypertonia.

Methods: We enrolled 30 patients, undergone fissurectomy and anoplasty with V-Y cutaneous flap advancement; all patients received topical administration of nifedipine 0.3% and lidocaine 1.5% ointment-based therapy before and for 15 days after surgery. The primary goal was patient's complete healing and the evaluation of incontinence and recurrence rate; the secondary goal included the evaluation of manometry parameters, symptom relief and complications related to nifedipine and lidocaine administration.

Results: All wounds healed within 40 days after surgery. We didn't observe any "de novo" post-operative anal incontinence case. We reported 2 cases of recurrences, healed after conservative therapy. We didn't report any local complications related to the administration of the ointment therapy; with whom all patients reported a good compliance.

Conclusions: Fissurectomy and anoplasty with V-Y cutaneous advancement flap and topical administration of nifedipine and lidocaine, is an effective treatment for CAPF with IAS hypertonia.

Key words:

Introduction

Chronic anal fissure (CAF) is a frequently occurring proctology lesion, which presents itself as a superficial tear in the cutaneous-mucosal transition zone of the anal canal. It is characterized by ellipsoid shape with an area of approximately 0.6-1 cm²; its edges are thickened and the internal anal sphincter (IAS) fibres can be seen on the bottom. At the top of the lesion we can often appreciate an hypertrophied papilla and a skin tag is present on the opposite side. CAF are more often located at the posterior anal commissure (CAPF), when it is so, a IAS hypertonia is frequently detected. To date, the role and genesis of this augmented IAS tone is still unknown, as a matter of fact, we still wonder

whether it is a cause or a consequence if CAF disease. During the last few decades, the treatment of this lesions aimed to reduce IAS hypertonia with medical or surgical approaches. Lateral internal sphincterotomy (LIS) represents nowadays the strategy of choice as for the treatment of CAF associated with IAS hypertonia, refractory to conservative therapies. This surgical procedure stands apart for a low rate of post-operative complications and a rate of healing of approximately 95%, it allows a fast resolution of clinical symptoms from the first post-operative defecation, leading to a complete healing within around 4-6 weeks. The greatest disadvantage of this latter procedure is represented by the high rate of anal incontinence occurrence, which accounts for up to 30-40%. A

meta-analysis from 2013 (1), which evaluated long-term incidence of anal incontinence after LIS, showed an overall continence alteration risk of 14%; however, on severity analysis, flatus incontinence and soilage/seepage were much more commoner than frank incontinence to liquid or solid stool. Anal incontinence has a strong impact on the quality of life of patients and it can be more disabling than CAF itself (2); actually, patients tend to better bear a recurrence than faecal incontinence (3), furthermore, LIS might distort plane for further anorectal surgeries that might become necessary. Finally, IAS tone has a tendency to shrink over the years, increasing the risk of late incontinence with aging. In order to preserve the anatomical and functional integrity of the sphincter system as well as to reduce the risk of post-operative anal incontinence, the mostly used surgical procedure for the treatment of CAPF is fissurectomy alone or in association with pharmacological sphincterotomy and/or cutaneous or mucosal flap advancement.

The aim of our study is to evaluate the results of fissurectomy and anoplasty with V-Y cutaneous flap advancement in association with topical administration of ointment based nifedipine 0.3% and lidocaine 1.5% as treatment for patients affected by CAPF with IAS hypertonia.

Materials and Methods

We enrolled 30 patients, all affected by idiopathic and non-recurrent CAPF with hypertonic IAS, who underwent fissurectomy and anoplasty with V-Y cutaneous flap advancement and topical administration of nifedipine 0.3% and lidocaine 1.5%, from March 2015 until March 2018. None of the patients was affected by inflammatory bowel disease or underwent to previous proctology surgical procedure. All patients were followed up for at least 2 years after the surgical procedure.

Informed written consent was obtained from all individuals participants included in this study.

The patients' outcome data were retrieved from a prospectively monitored database. All procedures have been approved by Ethical Committee Palermo 1 protocol number 340/20/ 20.

Preoperative manometric evaluation was performed after a reasonable period after suspension of all medical therapy influencing IAS tone. The manometric evaluation was carried out by a manometric sensor (2.1 mm external diameter) with four circle orifices and a latex microballoon at its extremity (Marquat C87; Boissy, St-Leger, France). The machine was connected to a polygraph (Narco; Byosystem MMS 200, Houston TX) using the station pull-through method with perfusion of normal saline and the patient lying in the right lateral position. At manometric evaluation, maximum resting pressure (MRP) and maximum squeeze pressure (MSP) were defined as the maximum pressure detected respectively, on resting and after voluntary contraction. Ultraslow wave activity (USWA) was defined as pressure's waves with frequency of less than 2/min and an amplitude greater than 25 cm H₂O (4).

Data collected on healthy subjects by our anorectal pathophysiological laboratory showed (5) that the normal values of MRP and MSP were respectively 68.1±12.3 mmHg mmHg and 112 ± 36.2 mmHg; USWA was detected in the 10% of patients. In accordance to Jones et al (6), normal range of MRP was 45-85 mmHg; so that CAF with hypertonic IAS were defined as those with MRP values > 85 mmHg. Manometric follow up was performed at 12 and 24 months after the surgery.

All patients, 30 minutes before surgery, received the topical administration inside the anal canal of 2 gr of ointment based 0.3% nifedipine and 1.5% lidocaine (Antrolin®).

All patients underwent fissurectomy and anoplasty with V-Y skin flap advancement lying in a gynecological position under spinal or general anesthesia. In order to expose the anal canal we used four Kocher pliers placed at 3,6,9 an 12 hours to avoid employing anal retractors; an Eisenhammer retractor or a speculum have been gently introduced just in case of necessity.

After injection of 5 ml of local anesthetic solution (100 mg cloridrate mepivacaine and 0.025 mg Ladrenaline), the fibrotic edges were excised with a scalpel until normal non-fibrotic anodermal tissue showed sufficient bleeding. The sentinel skin tag and hypertrophied papilla at the level of dentate line were excised when present according to Gupta and Kalaskar (7). The tissue at the base of the fissure was curetted until there were clean muscle fibers of the IAS. There hasn't been any use of diathermy and careful attention was payed at avoiding damages of the IAS (*Fig. 1*). Standard advancement anoplasty was performed using a flap of healthy skin tissue which was mobilized and then advanced with its blood supply to fill in the defect (*Fig. 2*). The flap was secured without tension to the anal canal and the skin was closed tension free in a V-Y manner with interrupted rapid absorbable suture behind the advancement flap. Before surgery, all patients received a small volume of phosphate-saline enema. Metronidazole was administered intravenously in a dose of 500mg 1h before surgery; subsequently, it was administered per os at the dosage of 250 mg for 7 days, three times daily. We prescribed for all patients topical administration inside the anal canal of 2 gr of ointment based 0.3% nifedipine and 1.5% lidocaine (Antrolin®) twice a day for 15 days.

During the first two weeks after the surgery, patients took variable doses of psyllium fibers. A laxative preparation (sennosides) was given orally to subjects who had not yet passed stools 3 days after surgery. Immediately after surgery, all patients received 100 mg of diclofenac intramuscularly for analgesia and were instructed to take only 100mg of nimesulide tablets as requires. The primary goal of the study was the patient's complete healing and the evaluation of incontinence and recurrence rate; the secondary goal included the evaluation of MRP, MSP, USWA, symptom relief (bleeding, itching and pain) and recording pro forma of the immediate an long time complications related to flap (anal stenosis, keyhole deformity, urinary retention, related side effects of nifedipine and lidocaine).



Figure 1. Intraoperative picture showing the excision of the anal fissure

A complete healing was defined as a complete epithelialization of the advancement skin flap. Both duration and intensity of pain post-defecation were evaluated. Pain intensity was scored with a visual analogical scale (VAS) from 0 to 10, where 0 corresponded to no pain



Figure 2. Intraoperative picture showing the preparation of the anoplasty V-Y advancement flap

and 10 to the worse pain conceivable. Anal incontinence was assessed preoperatively and after 1, 6, 12 and 24 months from surgery using the Pescatori grading system (8): A incontinence for flatus and mucus; B for liquid stool; C for solid stool; 1 for occasional; 2 for weekly and 3 for daily. Patients were discharged 24 hours after surgery, afterwards they were examined until they were completely healed and they were also followed up at 1, 6, 12 and 24 months following the surgical procedure.

Independently of the scheduled appointments, patients were seen on request.

Statistical Analysis

Continuous variables were expressed as a mean with standard deviation and qualitative data as absolute frequencies, MRP values were also given as median and range. Student's t-test with Welch correction was used to analyze the differences of pain score and pain duration at each registration point. Values of $P < 0.05$ were considered statistically significant.

Results

This study includes 10 women and 20 men. At the time of surgical procedure, the median age of the patient was 36 years (range 18-61). Demographic data of the patients object to study are reported in *Table 1*. Bowel function was normal in 5 patients, 20 patients suffered from constipation and 5 from diarrhea; bowel function was assessed according to the up-dated Rome IV diagnostic criteria.

Five women were nulliparous, 2 gave natural birth and all of them underwent an episiotomy and 3 patients gave birth throughout a caesarean section. Clinical features of AF are reported in *Table 2*.

Healing Fissure and Relief of Symptoms

All wounds healed completely within 40 days after surgery. Intensity and duration of post-defecation pain was significantly reduced with respect to the pre-operative values starting

Table 1. Demographic data of the patients object to study

	No	%
Gender		
Men	20	66,6
Women	10	33,3
Bowel function		
Normal	5	16,6
Constipation	20	66,6
Diarrhea	5	16,6
Delivery		
Nulliparous	5	50
Natural	2	20
Caesarean section	3	30

from the first defecation ($p < 0.01$) (*Fig. 3*). None of the patients complained about pain, bleeding or itching 40 days after surgery. Analgesics consumption decreased significantly after first defecation (data not shown).

Incontinence

We recorded 2 cases of pre-operative anal incontinence (6.6%), Both cases were type A1 according to Pescatori grading system (8). In none of these patients, anal incontinence resulted worsened. We didn't observe any "de novo" post-operative anal incontinence occurrence.

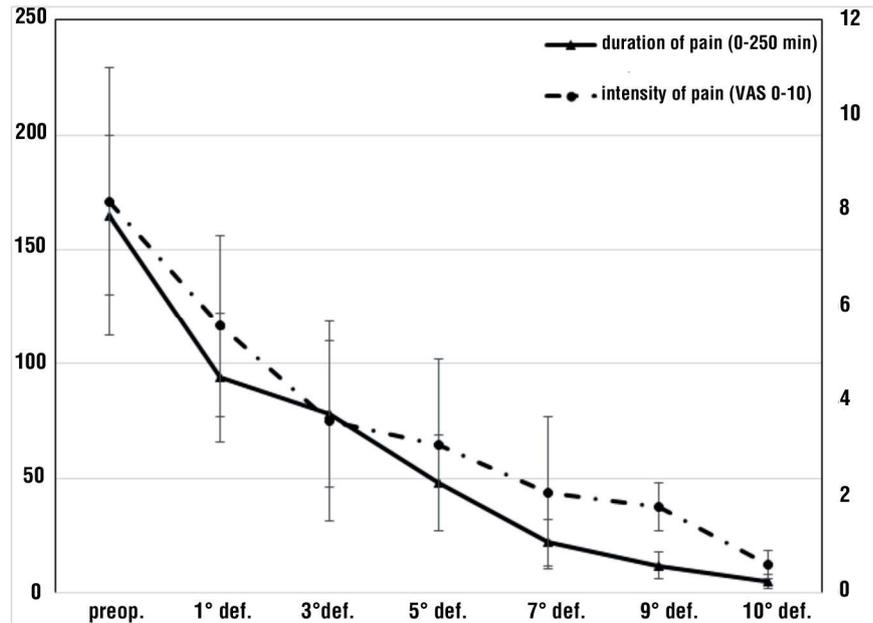
Recurrences

We reported only 2 cases of recurrences, all of them occurred within 2 years from surgery, they were located in a different place in comparison with the first one. Both patients

Table 2. Clinical features of chronic anal fissure

	No	Percent
Hypertrophied anal papilla	24	80
Skin tags	18	60
Symptoms		
Pain	30	100
Bleeding	21	70
Pruritus	15	50
Duration of Symptoms		
Months (mean \pm standard deviation)	18,7 \pm 12,3	

Figure 3. Intensity and duration of pain related to defecation after fissurectomy and anal advancement flap and ointment based nifedipine 0,3% and lidocaine 1,5% administration



underwent a medical treatment consisting in fibres implementation in the diet and employ anal dilators and responded to the conservative treatment with a complete healing. Immediate and long-term postoperative complications are reported in *Table 3*.

Manometry Findings

Preoperative values of MRP were significantly higher as compared with healthy subjects (108 ± 14 mmHg; $p=0.001$), whereas MSP values were only slightly increased (128 ± 15.9 mmHg; $p=n.s.$).

At 12 months and 24 months after surgery MSP values didn't significantly differ as compared both with pre-operative levels and healthy control subjects.

At 12 months follow up, MRP values were

significantly lower as compared with pre-operative values ($p<0.001$). As compared with healthy controls, MRP values were still increased ($p<0.01$).

At 24 months MRP values were similar compared with healthy control subjects ($p=n.s.$).

Pre-operative, the presence of USWA was detected in 18 out of 30 patients (60%). A comparison among healthy subjects and patients with CAPF showed a significant difference ($p<0.001$).

At 12 months follow-up, the detected rate of USWA was lower in comparison to pre-operative values ($p<0.05$) but they were not significantly higher as compared with healthy subjects. At 24 months follow up the USWA values of CAPF patient were not statistically significantly different from the ones of healthy subjects.

Table 3. Immediate and long-term post-operative complications

Complication	No	%
Infection	1	3.3
Partial break of the flap	1	3.3
Recurrence	2	6.6
Anal Incontinence	0	0

Complications and Follow up

There were no cases of urinary retention, anal stenosis or keyhole deformity. No necrosis of the transposed flap was observed. We didn't report any local complications related to the

administration of nifedipine and lidocaine; all patients reported a good compliance with the ointment-based therapy. The only complications recorded post-operatively were of slight entity and in no case required further surgery; in particular, 1 infection were detected in the donor site and a partial break down of the flap occurred in one case.

Discussion

The results of our study show that fissurectomy and anoplasty associated with post-operative topical administration of nifedipine and lidocaine, as a treatment for patients affected by CAPF with IAS hypertonia, allows an early resolution of clinical symptoms as well as a fast healing of the wounds. We recorded a low rate of recurrence (6.6%); we didn't observe any "de novo" case of post-operative anal incontinence; both patients who were already suffering didn't experienced any worsening. Moreover, MRP values start significantly reducing from 12 months after the procedure to reach, at 24 months after surgery, values which were similar to healthy subjects.

Anal fissure (AF) arise from continuous microtrauma in the perianal area often induced by long term constipation or diarrhea. Intense pain caused by this injury produces IAS contraction, which in turn leads to avoiding defecatory act; this cause a progressive hardening of stools and subsequently a worsening of the proctology disease. IAS hypertonia has a strong role in the pathogenesis of CAPF. Various studies in vivo (9) and post-mortem (10) revealed that posterior anal commissure is poorly perfused in comparison with other section of the anal canal, hence, IAS hypertonia might aggravate this hypoperfusion and slow down the healing process, enabling the disease to become chronic. Several researches showed that surgical procedure aiming to reduce the IAS tone allows a complete healing in most patients (11,12); other series proved instead, that the healing process of CAF is independent from the anal pressure. Pascual et al (13) confirmed that there are no statistically significant

differences in manometry or endoanal ultrasound findings between healed or not healed CAF, as concerning the anal pressure. Furthermore, surgical procedures, such as fissurectomy and anoplasty with flap advancement may lead to the resolution of CAF without interfering with IAS tone (14-17), furthermore, years after this procedure we can observe a normalisation of the IAS tone, which occurs concurrently with CAF healing (18).

Under the light of this latter considerations, we find reasonable to treat CAPF with IAS hypertonia employing a surgical procedure which allows to preserve the integrity of the IAS, throughout the association with pharmacological sphincterotomy aiming to improve anal canal blood perfusion.

Fissurectomy is the most common surgical procedure used in order to preserve structural and functional integrity of the IAS. Fissurectomy, as a wound debridement, removes the bradytrophic scar tissue and produces fresh wound edges, creating an acute fissure. This latter surgical procedure has been associated with pharmacological sphincterotomy in order to improve its results, as well as reduce its complications (19-24). After surgical fissurectomy, with or without association with chemical sphincterotomy (25-32), we observe a complete second intention wound healing, even after 10 weeks and the rate of failure can reach the 34% (30). The rate of recurrence reaches up to the 37% in some series (28). The high rate of recurrence and healing failure of fissurectomy might be related to the fact that this surgical procedure leaves a naked ischemic area, whose previously blood supply arrives from some branches of rectal inferior arteries, which cross the hypertonic IAS fibres (9,10,33); in this regard the employ of drugs enabling to reduce the IAS tone aims to improve the blood supply of the naked area. The use a flap to cover up for the naked area after fissurectomy is designed to relocate on this area healthy and fresh blood supplied tissue, perfused by other arterial districts. Another possible advantage of using a flap might be represented by the enlarging effect on the cutaneous circumference of the anal

canal, which reduces the risk of splitting. Several surgical techniques for the use of flaps have been described, we number among them the employ of skin or mucous flaps, skin ones are most frequently hired. Various type of skin flaps are known, such as sliding skin grafts, house advancement flap, V-Y advancement anoplasty, island advancement flap and rotation flaps (15,34-38).

Surgical procedures that involve the employment of flap guarantee shorter healing period and lower incidence of non-healed wound or recurrence and a minimal interference with the anal continence than the ones observed after surgical fissurectomy itself with or without association with pharmacological sphincterotomy (16,17,39,40). Fissurectomy associated with anoplasty is a surgical procedure employed for both patients with hypertonic IAS and normotonic IAS (38,41).

Under the light of the brilliant results of this surgical procedure, some authors suggest using fissurectomy with anal advancement flap as the first line therapy for CAF (15,17,42,43).

At the best of our knowledge, the association of fissurectomy with anoplasty and pharmacological sphincterotomy has been performed only by using botulinum toxin, as reported in few works (41,44-46).

The benefits of nifedipine might be due also to its anti-inflammatory action not only to its induced reduction of the IAS tone(47-52), carried through the inhibition of calcium flow into the sarcoplasm of IAS. Experimental studies indicate that nifedipine has a modulating effect on microcirculation (53), as well as a local anti-inflammatory effect (54). Moreover, nifedipine might contribute to the healing process of CAF due to its additional free radical scavenging properties (55). In our study we didn't observe any adverse effects related to the employ of nifedipine such as headache or perianal dermatitis, patients' compliance has been excellent.

The only surgical related complications we were able to record were of slight entity and they never required further surgery.

Furthermore, we recorded 2 cases of recurrence, which have not occurred at the same site as the original lesion and all healed with medical therapy; this might be because of the durability of the advancement flap (15).

Conclusion

Our preliminary work shows that fissurectomy and anoplasty with V-Y cutaneous advancement flap, associated with topical administration of nifedipine and lidocaine, was highly effective as a treatment for CAPF with IAS hypertonia; this approach stands apart for low recurrence rate and no incidence of "de novo" case of post-operative anal incontinence nor adverse effect.

Nevertheless, we must underline the necessity of further randomized trial comparing fissurectomy alone versus fissurectomy combined with graft, with or without pharmacological sphincterotomy, in order to better define the role of those latter approaches as a treatment for CAPF with IAS hypertonia.

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Conflict of Interest

The Authors report no conflict of interest in this work. The Authors declare that they have no competing interests.

Author's Contributions

All authors contributed to the study. D'Orazio B., Famà F. and Di Vita G. conceived, devised and designed the manuscript. Cali D., Terranova G. and Corbo G. collected the case and iconography. D'Orazio B. Bonventre S. and Geraci G. wrote the manuscript and participated in the sequence alignment. Di Vita G., Sciumé C. and Martorana G. revised and approved the final manuscript and its conclusions.

Consent Section

Informed written consent was obtained from all individuals participants included in this study.

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Our institution's ethical committee did not deem it necessary to explicit its approval for this study.

Availability of Data

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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