

# World Journal of *Clinical Cases*

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## Case Control Study

**Botulinum toxin associated with fissurectomy and anoplasty for hypertonic chronic anal fissure: A case-control study**

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**Institutional review board statement:** 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. The protocol for this study was submitted to the Ethical Committee of our institution "Ethical Committee Palermo 1-AUOP P. Giaccone" on March 1, 2018, which did not consider it necessary to approve it and waved, in that occasion, the requirement for ethical approval.

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**Abstract****BACKGROUND**

Lateral internal sphincterotomy is still the approach of choice for the treatment of chronic anal fissure (CAF) with internal anal sphincter (IAS) hypertonia, but it is burdened by high-risk postoperative faecal incontinence (FI). Sphincter saving procedures have recently been reconsidered as treatments to overcome this risk. The most employed procedure is fissurectomy with anoplasty, eventually associated with pharmacological sphincterotomy.

**AIM**

To evaluate whether fissurectomy and anoplasty with botulinum toxin injection improves the results of fissurectomy and anoplasty alone.

**METHODS**

We conducted a case-control study involving 30 male patients affected by CAF with hypertonic IAS who underwent fissurectomy and anoplasty with V-Y cutaneous flap advancement. The patients were divided into two groups: Those in group I underwent surgery alone, and those in group II underwent surgery and a botulinum toxin injection directly into the IAS. They were followed up for at least 2 years. The goals were to achieve complete healing of the patient and to assess the FI and recurrence rate along with manometry parameters.

**RESULTS**

**Informed consent statement:**

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

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The intensity and duration of post-defecatory pain decreased significantly in both groups of patients starting with the first defecation, and this reduction was higher in group II. Forty days after surgery, we achieved complete wound healing in all the patients in group II but only in 80% of the patients in group I ( $P < 0.032$ ). We recorded 2 cases of recurrence, one in each group, and both healed with conservative therapy. We recorded one temporary and low-grade postoperative case of “*de novo*” FI. Manometry parameters reverted to the normal range earlier for group II patients.

**CONCLUSION**

The injection of botulinum toxin A in association with fissurectomy and anoplasty with a V-Y advancement flap improves the results of surgery alone in patients affected by CAF with IAS hypertonia.

**Key Words:** Proctology; Fissurectomy; Anoplasty; Anal fissure; Botulinum toxin

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**Core Tip:** Surgical sphincterotomy is still the approach of choice for the treatment of chronic anal fissure with internal anal sphincter hypertonia, even if it is burdened by a high risk of postoperative faecal incontinence. For this reason, sphincter-saving surgical procedures have recently been reconsidered to overcome this risk. In our work, we consider fissurectomy with anoplasty, and we wonder if the association with pharmacological sphincterotomy with botulinum toxin A injection may improve the outcomes in patients affected by chronic anal fissure with hypertonic internal anal sphincter. Therefore, this study aims to evaluate the results of the associated procedures in terms of reduction of faecal incontinence risk and recurrence rate and improvement of overall results in comparison with conventional sphincterotomy.

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**INTRODUCTION**

Chronic anal fissures (CAFs), which are refractory to dietary, hygienic, and pharmacological therapy, require a surgical approach. A hypertonic internal anal sphincter (IAS) is associated with 40%-60% of CAFs[1-4]. To date, the role and genesis of the augmented IAS tone remains unknown; in fact, we wondered whether it is a cause or a consequence of CAF. During the last few decades, the treatment of this disease aimed to reduce IAS tone with medical and surgical approaches, and lateral internal sphincterotomy (LIS) currently represents the preferred approach.

This latter stands apart for its low rate of postoperative complications as well as its high rate of success, which reaches approximately 95%; furthermore, it allows a fast resolution of clinical symptoms since the first postoperative defecation, leading to complete healing within approximately 4-6 wk. Nevertheless, the greatest disadvantage of the abovementioned procedure is the high rate of faecal incontinence (FI) occurrence, which accounts for 30%-40% of cases. A meta-analysis from 2013 evaluated the long-term incidence of FI after LIS and showed an overall continence alteration risk of 14%[5].

Sphincter-saving procedures have been recently reconsidered as a valuable alternative to reduce the risk of FI in both children and adults[6]. Among the latter, fissurectomy and anoplasty with a V-Y advancement flap have been employed by our team for a few years, with outstanding results[1,7].

The aim of our study was to examine whether fissurectomy and anoplasty with botulinum toxin A (BT) injection improves the results of surgery alone in patients affected by CAF with IAS hypertonia. Therefore, we conducted a case-control study

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between two groups of patients who underwent fissurectomy and anoplasty with or without BT injection.

## MATERIALS AND METHODS

This case-control study involved 30 male patients, all affected by idiopathic and nonrecurrent CAFs with hypertonic IAS. Fifteen underwent fissurectomy and anoplasty from April 2018 until January 2019 (group I), and 15 underwent fissurectomy and anoplasty with BT injection from 2011 until 2015 (group II). The two groups were matched for demographic and clinical data (Table 1).

The exclusion criteria for the study were the presence of multiple fissures, fistulas in ano, syphilis, inflammatory bowel disease, anal abscess, malignant disease, and previous proctology surgery. All patients were followed up for at least 2 years after the surgical procedure. The patients' outcome data were retrieved from a prospectively monitored database.

We conducted this study in compliance with the principles of the Declaration of Helsinki. The protocol for this study was submitted to the Ethical Committee of our institution, which did not consider it necessary to approve. Written informed consent was obtained from all study participants.

Preoperative manometric evaluation was performed after a reasonable period of suspension of all medical therapies influencing IAS tone, and it was carried out by a manometric sensor using station pull-through as described in our previous work[7]. Then, we performed postoperative manometric evaluations at 12 and 24 mo.

Data collected on healthy subjects by our anorectal pathophysiological laboratory showed that normal values of maximum resting pressure (MRP) and maximum squeeze pressure (MSP) were  $68.1 \pm 12.3$  mmHg and  $112 \pm 36.2$  mmHg, respectively [7]. Ultraslow wave activity (USWA) was detected in only 10% of healthy patients. The normal range of MRP, according to Jones *et al*[8], was 45-85 mmHg; therefore, CAF without hypertonic IAS was defined as those with MRP values < 85 mmHg.

All patients underwent fissurectomy and anoplasty with V-Y skin flap advancement lying in a gynaecological position under spinal or general anaesthesia.

The sentinel skin tags, and hypertrophied anal papilla located at the dentate line were excised, if present; the tissue at the base of the fissure was curetted until clean IAS muscle fibres were reached. Technical details concerning the surgical procedure have already been widely explained in a previous work from our group[9,10].

Once fissurectomy was performed, patients in group II underwent a local injection of 30 UI of BT (Botox, Allergan Westport, Ireland)[11] directly into the IAS. Each patient received a total of 30 UI of BT: 15 UI injected at 3 h in gynaecological position and 15 UI injected at 9 h. None of the patients were taking concomitant oral medication that could interfere with the action of BT (*e.g.*, aminoglycoside, baclofen, dantrolene, diazepam), and we did not register any case of hypersensitivity to any component of BT. Metronidazole was administered intravenously at a dose of 500 mg 1 h before surgery; subsequently, it was administered *per os* at a dosage of 250 mg three times a day for 7 d. During the first 2 weeks after the surgery, the patients took variable doses of psyllium fibres. A laxative preparation (sennosides) was administered orally to patients who had not yet passed stools for 3 d after surgery. All patients received 100 mg of diclofenac intramuscularly immediately after surgery, and they were instructed to take only 100 mg of nimesulide tablets at home if needed.

Complete healing was defined as complete epithelialization of the advancement skin flap. Recurrent CAFs were defined as those that occurred after the complete healing of the previous wound. Both the duration and intensity of post-defecatory pain were evaluated; the intensity was evaluated with a visual analogue scale.

FI was assessed preoperatively and 6, 12 and 24 months after surgery according to Pescatori's grading system[12]: 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 within 24 h after surgery; afterwards, they were examined until they healed completely, and they were also followed up until 24 months after the surgical procedure. Regardless of the scheduled appointments, patients were seen on request.

### Statistical analysis

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

Table 1 Demographic data and clinical features of chronic anal fissure

	Group I		Group II		P value
	n	%	n	%	
Age in yr <sup>1</sup>	35.2 ± 10.8		29.9 ± 13.9		NS
Hypertrophied anal papilla	11	73.3	12	80	NS
Skin tags	9	60	8	53.3	NS
<b>Symptoms</b>					
Pain	15	100	15	100	NS
Bleeding	10	66.6	9	60	NS
Pruritus	8	53.3	8	53.3	NS
Duration of symptoms in mo <sup>1</sup>	19 ± 133.5		20.8 ± 12.9		NS

<sup>1</sup>Values expressed as mean ± SD. NS: No statistically significant differences.

significant.

## RESULTS

This study included 30 men. At the time of the surgical procedure, the median age of the patients was 35 years in group I and 29 years in group II (range 18-61). We did not report any significant differences between the two groups of patients regarding bowel function, preoperative FI, intensity and duration of post-defecation pain, IAS tone or USWA detection. Demographic data of the patients in the study and clinical features of CAFs are reported in Table 1.

### Healing fissure and relief of symptoms

We achieved complete wound healing within 40 d for all patients in group II and for 80% of those in group I ( $P < 0.032$ ). All patients in group I reached complete healing within 50 d.

The intensity and duration of post-defecatory pain were significantly reduced in comparison to the preoperative values starting with the first postoperative defecation in both groups; they were greatly reduced in group II patients ( $P < 0.0001$ ) (Figure 1), while we observed less reduction in both the intensity ( $P < 0.0095$ ) and duration ( $P < 0.014$  in group I) of pain in group I patients (Figure 2).

None of the patients complained about itching, bleeding, or pain 40 d after surgery. Analgesic consumption decreased significantly after the first defecation.

### FI

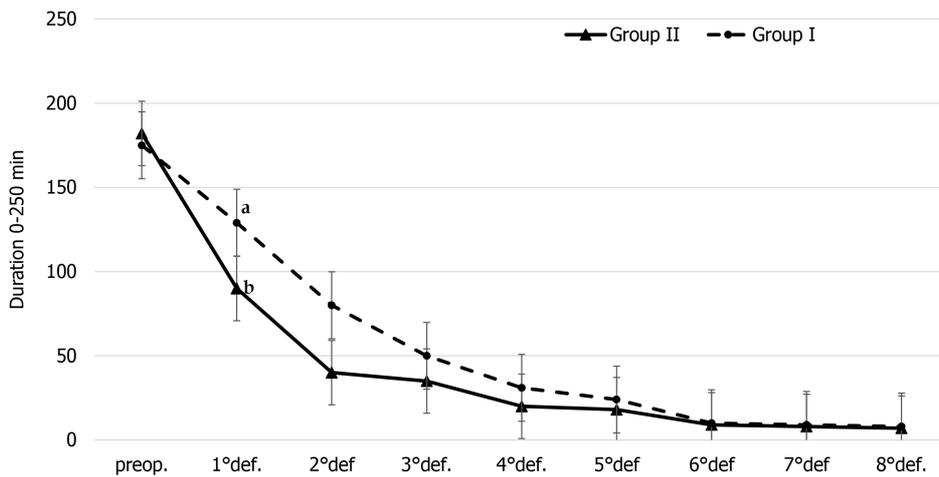
We recorded 2 cases of preoperative FI, one in each group of patients and both of grade A1 according to Pescatori's grading system[12]. In group II, FI worsened 1 month after surgery, while at 3 months after the procedure, its grading was similar to that of the preoperative FI. We observed only 1 case of postoperative "de novo" FI in group II, which was temporary and of grade A1.

### Recurrence

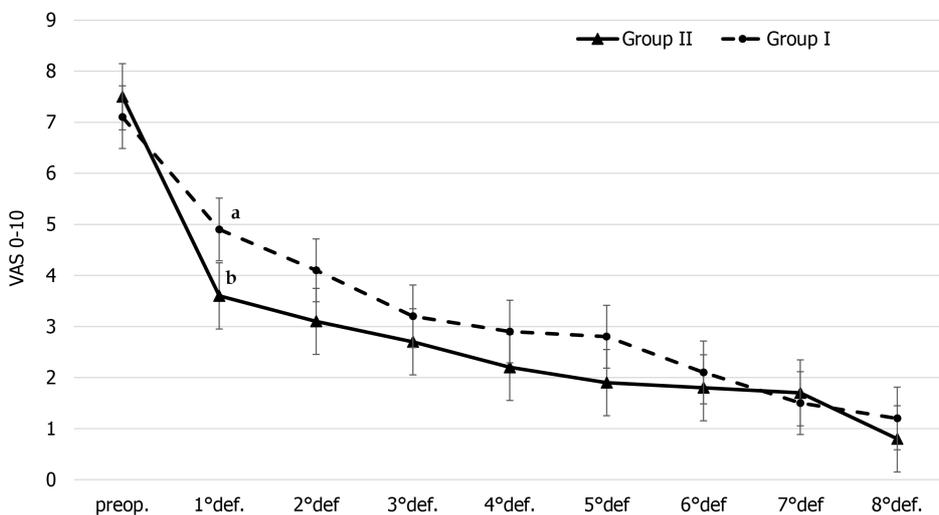
We observed only 2 cases of recurrence, one in each group of patients. The site of recurrence was different from the primary location; both occurred within 2 years of surgery and were characterized by the persistence of IAS hypertonia. Both patients underwent medical treatment consisting of implementation of fibre in the diet, employment of local products containing nifedipine or lidocaine and anal dilators. The patients responded to conservative therapy with complete healing.

### Manometry findings

Preoperative values of MRP were significantly higher than those of healthy subjects in both groups of patients ( $P < 0.001$ ), while MSP values were only slightly increased ( $P = NS$ ).



**Figure 1** Duration of post-defecatory pain preoperatively and after fissurectomy and anoplasty with V-Y advancement flap alone (group I) and associated with botulinum toxin A injection in the internal anal sphincter (group II). Significant difference vs preoperative values: <sup>a</sup> $P < 0.014$ ; <sup>b</sup> $P < 0.0001$ .



**Figure 2** Intensity of post-defecatory pain preoperatively and after fissurectomy and anoplasty with V-Y advancement flap alone (group I) and associated with botulinum toxin A injection in the internal anal sphincter (group II). Significant difference vs preoperative values: <sup>a</sup> $P < 0.0095$ ; <sup>b</sup> $P < 0.0001$ .

In both groups of patients, MSP values at 12 and 24 mo after surgery did not significantly differ from the preoperative values or those of healthy subjects. In group I patients, MRP values at 12 mo after surgery were significantly lower than the preoperative values ( $P < 0.02$ ), while they were still increased compared with healthy subjects ( $P < 0.005$ ). At 24 months after surgery, MRP values were similar to those of healthy subjects ( $P = NS$ ).

In group II patients, MRP values at 12 months after surgery were significantly lower than the preoperative values ( $P < 0.001$ ), while they were still increased compared to healthy subjects ( $P < 0.01$ ). At 24 months after surgery, MRP values were similar to those of healthy subjects ( $P = NS$ ). Preoperative detection of USWA in both groups was significantly higher than that in healthy subjects ( $P < 0.001$ ). This value decreased significantly after 12 months and was within the normal range after 24 months.

**Complications and follow-up**

There were no cases of urinary retention, anal stenosis or keyhole deformity. No necrosis of the transposed flap was reported. We did not observe any local complications related to the injection of the BT. The few postoperative complications recorded were of slight severity and in no case required further surgery; in particular, two infections were detected in the donor site, and a partial breakdown of the flap

occurred in 1 case.

## DISCUSSION

This study shows that the association of BT injection with fissurectomy and anoplasty improves the results compared with the surgery procedure alone. In fact, we observed a faster and greater reduction in both the intensity and duration of post-defecatory pain as well as a quicker healing of wounds and normalization of IAS tone in patients treated with BT injection. Regarding FI occurrence, we recorded a worsening of preoperative cases and 1 “*de novo*” postoperative case in group II.

The role of hypertonic IAS in the pathogenesis of this disease is still unclear. Various studies, both *in vivo* and with corpses[13,14], demonstrate that small arterial branches arising from the rectal artery pass through the IAS to ensure blood supply to the transition zone so that a hypertonic IAS might worsen the blood perfusion and prevent the healing process, leading to the genesis of CAF. However, hypertonic IAS is present only in 40%-60% [1-4] of CAFs, and as some research has indicated, the healing process takes place regardless of the IAS pressure. Pascual *et al*[3] showed that there were no significant differences concerning anal pressure, assessed with manometry or endoanal ultrasound, between healed and non-healed CAFs. Furthermore, surgical procedures, such as fissurectomy and anoplasty with flap advancement, lead to the resolution of CAF without interfering with the IAS tone, and even years after the procedure, we might record a normalization of IAS tone concurrently with CAF healing[15].

Considering the above findings, LIS should be reconsidered given the high incidence of FI resulting from the entity of the IAS section and, above all, considering that FI worsens naturally with ageing.

Fissurectomy is the most employed procedure to preserve the structural and functional integrity of the IAS. The fissurectomy itself produces wound debridement and removes the brady-trophic scar tissue, from which fresh wound edges and an acute fissure arise. This surgical procedure has been performed alone[16-18] or in association with pharmacological sphincterotomy to improve its outcome[19-25] and reduce its complications. After surgical fissurectomy, which may or may not be followed by chemical sphincterotomy, we observed complete second intention healing even after 10 weeks, with a rate of failure up to 34%. The rate of recurrence and healing failure of fissurectomy might be a consequence of the naked ischaemic area left at the wound site; therefore, the use of a flap to cover up this area is designed to relocate healthy and blood-supplied tissue coming from different arterial districts[26-36]. Another advantage of using a flap may be represented by the boosting effect on cutaneous circumference of the anal canal, which reduces the risk of splitting. Lastly, the employment of drugs enables the reduction of IAS tone and leads to an improvement in the blood supply of the naked area[37-39].

## CONCLUSION

This study shows that the association of BT injection with a sphincter-saving procedure enables a temporary reduction of the IAS tone, improving the outcomes.

## ARTICLE HIGHLIGHTS

### Research background

Lateral internal sphincterotomy is still the approach of choice for the treatment of chronic anal fissure (CAF) with internal anal sphincter (IAS) hypertonia, but it is burdened by high-risk postoperative faecal incontinence.

### Research motivation

Sphincter-saving procedures have been recently reconsidered as treatments to overcome this risk.

### Research objectives

The aim of our study was to evaluate whether fissurectomy and anoplasty with

botulinum toxin injection improves the results of fissurectomy and anoplasty alone.

### Research methods

We conducted a case-control study involving 30 male patients affected by CAF with hypertonic IAS who underwent fissurectomy and anoplasty with V-Y cutaneous flap advancement. The patients were divided into two groups: Those in group I underwent surgery alone, and those in group II underwent surgery and a botulinum toxin injection directly into the IAS. They were followed up for at least 2 years.

### Research results

The intensity and duration of post-defecatory pain decreased significantly in both groups of patients starting with the first defecation, and this reduction was higher in group II. Forty days after surgery, we achieved complete wound healing in all the patients in group II but only in 80% of the patients in group I ( $P < 0.032$ ). We recorded 2 cases of recurrence, one in each group, and both healed with conservative therapy. We recorded one temporary and low-grade postoperative case of “*de novo*” faecal incontinence. Manometry parameters reverted earlier to the normal range in group II patients.

### Research conclusions

The injection of botulinum toxin A in association with fissurectomy and anoplasty with a V-Y advancement flap improves the results of surgery alone in patients affected by CAF with IAS hypertonia.

### Research perspectives

Further studies with larger samples of patients are necessary to ensure a greater foundation for our findings. The outcomes of this study might be considered a starting point to consider the sphincter-saving procedure, eventually associated with pharmacological sphincterotomy, as the treatment of choice for all patients affected by chronic anal fissure regardless of the internal anal sphincter tone.

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