# Anal Fissure

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## ABSTRACT

Anal fissure is one of the most common anorectal problems. Anal fissure is largely associated with high anal sphincter pressures and most treatment options are based on reducing anal pressures. Conservative management, using increased fiber and warm baths, results in healing of approximately half of all anal fissures. In fissures that fail conservative care, various pharmacologic and surgical options offer satisfactory cure rates. Lateral internal sphincterotomy remains the gold standard for definitive management of anal fissure. This review outlines the key points in the presentation, pathophysiology, and management of anal fissure.

**KEYWORDS:** Anal fissure, fissure in ano, sphincterotomy, anal sphincter hypertonia

**Objectives:** On completion of this article, the reader should be able to summarize the etiology and management of anal fissure.

Anal fissure is a tear in the anoderm distal to the dentate line. It can be categorized as acute or chronic. Acute fissures present with anal pain, spasm, and/or bleeding with defecation. The diagnosis can typically be confirmed by physical examination and anoscopy in the office if tolerated by the patient. By gentle separation of the buttocks and examination of the anus, a linear separation of the anoderm can be identified at the lower half of the anal canal. Approximately 90% of anal fissures in both men and women are located posteriorly in the midline. Anterior fissures occur in 10% of patients, more commonly women. Fewer than 1% of fissures are located off a midline position or are multiple in number. These atypical fissures may be associated with Crohn's disease, sexually transmitted diseases (human immunodeficiency disease [HIV], syphilis, or herpes), anal cancer, or tuberculosis. Whereas acute fissures typically heal with medical management after 4 to 6 weeks, chronic fissures persist beyond 6 weeks. Chronic fissures are also associated with raised edges, exposed internal sphincter muscle, distal sentinel tag, and hypertrophied anal papilla at the internal apex.

## PATHOGENESIS

Despite extensive investigation of this disease, the exact etiology of anal fissure remains unclear. It appears that constipation with passage of hard stools or anal trauma may instigate the fissure. However, in many instances patients do not report constipation or may have a history of watery diarrhea. In addition, many fissures heal within weeks whereas others go on to become chronic in nature. Various studies have suggested that both anorectal mechanics and blood flow to the anal canal may play a role in anal fissure development. Initial reports from the 1970s and 1980s have implicated internal sphincter hypertonia in anal fissure pathogenesis.[1–3] More recent studies have used anorectal manometry to demonstrate hypertonia of the internal sphincter and have shown fewer internal anal sphincter relaxations in patients with

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chronic anal fissures.[4,5] In addition, relative ischemia of the posterior anal canal has been implicated in chronic, nonhealing anal fissures. Postmortem angiography of the inferior rectal artery has demonstrated that the posterior commissure of the anal canal is poorly perfused in 85% of patients compared with other sections.[6] Anal hypertonicity may aggravate perfusion to the anal canal. Pressure on the vessels passing perpendicularly through the internal anal sphincter muscle during increased sphincter tone may compromise perfusion to the posterior commissure where blood flow is already sparse.[6] Doppler laser flow studies have clearly shown lower anodermal blood flow at the fissure site compared with the posterior commissure of controls.[5,7] Internal sphincterotomy, the gold standard for the treatment of anal fissure, has been shown to decrease internal sphincter pressures and increase anodermal blood flow.[7] In addition, it has been demonstrated that administration of anesthesia both decreases anal pressure and increases anodermal blood flow.[5]

The pathophysiology of anterior fissures may be different than chronic posterior fissures. Jenkins and colleagues showed that anterior fissure patients were significantly more likely to have occult external sphincter injury and impaired external sphincter function compared with posterior fissure patients. In addition, anterior fissures were identified in a younger and predominantly female group of patients. In these patients, maximum squeeze pressure was significantly lower compared with the posterior fissure group. Also, maximum resting pressure was not significantly elevated compared with controls, but was significantly elevated in posterior fissures. These findings may have important implications for the management and treatment of this common subgroup of anal fissure patients.[8]

## NONOPERATIVE MANAGEMENT

The majority of initial anal fissures can be managed medically. In fact, almost half will heal with conservative therapy alone using warm baths and increased fiber intake.[9–11] Warm sitz baths may lead to healing of anal fissures via a somatoanal reflex that results in relaxation of the internal anal sphincter.[12] In a randomized study conducted by Jensen, treatment with 10 g of unprocessed bran twice daily and warm sitz baths for 15 minutes twice daily and after each bowel movement resulted in quicker symptomatic relief and better healing at 3 weeks (88%) compared with 2% lignocaine ointment or 2% hydrocortisone cream.[13] In a separate randomized prospective study, treatment with 15 g of unprocessed bran in three divided doses daily was shown to have significantly fewer recurrences (16%) compared with patients receiving 7.5 g of bran daily (60%) ($p < 0.01$).[14] According to the practice parameters set by the American Society of Colon and Rectal Surgeons, increased fluid and fiber ingestion, the use of sitz baths, and if necessary, the use of stool softeners are safe, have few side effects, and should be the initial therapy for all patients with anal fissure.[15]

When conservative measures fail, the next step in the management of anal fissure has traditionally been surgery. However, given the potential risk of incontinence with surgery, the last decade has brought significant interest and investigation in the use of pharmacologic agents to reduce anal pressures and avoid surgical intervention.

### Topical Nitrates

Organic nitrates such as glyceryl trinitrate (GTN) undergo cellular metabolism to release nitric oxide (NO).[16] Nitric oxide works as an inhibitory neurotransmitter in the internal anal sphincter resulting in sphincter relaxation.[17] The topical application of GTN in dilute form (0.2%) has been shown to cause decreased anal resting pressures.[18] Various studies have since emerged to investigate the use of GTN to treat anal fissures. In a Cochrane Review of 53 randomized controlled trials (RCTs) of nonsurgical therapies for anal fissures and 15 RCTs that specifically looked at GTN versus placebo, GTN was found to be marginally but significantly better than placebo in healing anal fissures (49% vs 37%, $p < 0.004$). However, late recurrence was shown to be common ($> 50\%$) in those initially cured.[19] In addition, dose made no difference in healing of anal fissures in three studies that compared doses of GTN ranging from 0.05% to 0.4% GTN.[20–22] Cure rates were similar with the use of a topical application of GTN around the anus versus a dermal patch at a distant location.[23,24] The key drawback, however, to GTN therapy is the high incidence of side effects, primarily headaches and light-headedness. In fact, up to 20% of patients cease GTN therapy due to the severity of their headaches.[25–27]

### Calcium Channel Blockers

Calcium channel blockers (CCBs) relax the internal anal sphincter by blocking the influx of calcium into the cytoplasm of smooth muscle cells.[28] It has been shown that both nifedipine (0.2–0.5% gel) and diltiazem (2% cream) promote fissure healing by decreasing mean anal resting pressure.[29–31] Topical CCBs have been shown to be better than both lignocaine ointment and hydrocortisone cream, with up to 95% remission in two studies.[31,32] Compared with GTN, topical application of CCBs has been shown to be equally effective with fewer side effects in various prospective, randomized studies.[33–35] The principal side effect is mild headache, seen in up to 25% of patients.[33] Topical nifedipine has also been compared with lateral internal sphincterotomy

with healing rates of 97% and 100% at 8 weeks. Long-term follow up at 19 months showed healing rates of 93% and 100% for the nifedipine and lateral internal sphincterotomy (LIS) groups, respectively.[36] On the other hand, oral calcium channel blockers have been shown to have poor healing rates (< 20% at 4 weeks in one study), high side-effect profile, and high therapeutic dropout.[30,37] Thus, with reasonable healing potential and minimal risk to the patient, topical CCBs are an acceptable choice for the medical management of chronic anal fissure.

## Botulinum Toxin

Botulinum toxin is produced by *Clostridium botulinum* and acts as an inhibitory neurotransmitter preventing release of acetylcholine from the presynaptic terminals. It has been shown to cause relaxation of both the external and internal anal sphincters lasting for up to 3 months.[28,38] Jost and Schimrigk reported the first case of anal fissure treated with botulinum toxin in 1993.[39] Since then, there has been increased interest in the use of botulinum toxin injections for the treatment of anal fissures.

There have been various studies on dosing and location of injection of the botulinum toxin, but the most common location is directly into the internal anal sphincter on either side of midline.[27,40–43] Retrograde endoscopic delivery of BOTOX® (Allergan, Inc., Irvine, CA) into the internal anal sphincter has also been described as being more accurate and better tolerated by patients in one group.[44] The value of this dosing regime awaits validation. Doses have varied between 5 to 100 units of BOTOX®,[45,46] with various studies suggesting a dose-dependent efficacy of BOTOX® treatment.[47–49] It appears that the type of botulinum toxin A preparation (Dysport®; Speywood Biopharm Ltd, Wrexham, UK vs the American preparation BOTOX®; Allegran, Irvine, CA) does not influence efficacy.[49]

Compared with placebo, injection of botulinum toxin into the internal anal sphincter has been shown to be significantly better at healing anal fissures (73%) and in symptomatic relief (87%) at 2-month follow up.[40] Botulinum toxin has also been compared with other means of "chemical sphincterotomy." Various randomized prospective studies have compared botulinum toxin injection with glyceryl trinitrate for the treatment of chronic anal fissures.[27,50,51] According to a meta-analysis of 180 patients included in these studies, botulinum toxin and glyceryl trinitrate had equal healing rates, but glyceryl trinitrate had higher side effects and headaches.[52] In another prospective study, overall cure rates between nitroglycerine ointment, diltiazem ointment, and botulinum toxin injection were similar at 54%, 53%, and 51%, respectively.[53] Overall recurrence of anal fissure with botulinum toxin therapy is common (up to 55%),[46] but retreatment with a higher dose may be effective.[45,48] The main side effect with botulinum toxin injection is mild incontinence to flatus and stool, lasting up to 3 weeks.[45,50] Although the risk is significantly lower compared with lateral internal sphincterotomy, there have been two case reports of long-term fecal incontinence with botulinum toxin injection of the anal canal.[54,55] Nonetheless, comparison with lateral internal sphincterotomy reveals that botulinum toxin injection of the internal anal sphincter has lower healing rates and higher recurrence, but comes with a lower chance of long-term incontinence. In a randomized controlled trial by Arroyo and colleagues, one-year healing with botulinum toxin injection was 45% versus 93% with lateral internal sphincterotomy. Fissure recurrence was 55% within one year compared with 8% with lateral internal sphincterotomy.[46] One single-center, retrospective study found that the use of botulinum toxin injection helped prevent surgery in 73% of patients who presented with anal fissure in 2004 compared with patients in 1993 when sphincterotomy was first-line therapy.[56] Thus, botulinum toxin injection offers reasonable success with minimal side effects and is a reasonable option for "chemical sphincterotomy" in the management of chronic anal fissure.

Yet, the question remains as to whether botulinum toxin injection can be used when other medical therapy has failed. Two prospective randomized trials evaluating patients with chronic anal fissures that have failed previous pharmacologic management showed poor healing rates (as low as 27%) with subsequent botulinum toxin injection.[57,58] In the study by Jones et al, 37% of all patients treated with botulinum toxin resorted to surgery. Interestingly, 12 of 30 patients in this study had low baseline mean resting anal pressures (mean of 56 mm Hg) and had a paradoxical response to treatment with botulinum toxin, with a rise in their mean resting pressures.[58] This patient population may have a different anal fissure pathophysiology not based on sphincter hypertonia. Thus, attempts at botulinum toxin injection in patients that have already failed other chemical sphincterotomy may be futile. The use of botulinum toxin injection for treatment of recurrent anal fissure after lateral internal sphincterotomy has been investigated, but the study was flawed with an extremely high incidence of recurrent anal fissures after sphincterotomy.[59]

## Unproven Therapies

The internal anal sphincter is stimulated by $\alpha_1$-adrenergic innervation and is inhibited by cholinergic innervation by the sacral parasympathetic fibers[60]. Topical bethanechol, a muscarinic agonist, has been shown to cause a dose-dependent reduction of anal pressure, with

a maximal 24% reduction seen with 0.1% bethanechol.[61] In a subsequent study, 0.1% bethanechol yielded a 60% healing rate at 8 weeks with no reported side effects in a small series of 15 patients.[62] Although this data appears promising, large, prospective studies are needed before any treatment recommendations can be made. Indoramine, an $\alpha_1$-adrenoreceptor antagonist and minoxidil, a smooth muscle relaxer, have been ineffective at healing anal fissure in small RCTs.[63,64]

## OPERATIVE MANAGEMENT

When conservative measures fail, a surgical approach becomes necessary for the definitive management of the chronic anal fissure. Dilation of the anal canal for the treatment of anal fissure was first described in the 1860s, but was popularized in the 1960s. In 1964, Watts and colleagues reported on 99 patients with anal fissures treated with anal stretch. They describe the procedure as a manual stretching of the anal canal with two, then four fingers applying considerable outward force on the lateral walls of the anal canal. Dilation is performed for no less than 4 minutes. They reported satisfactory early relief of symptoms in 95% of patients, with fissure recurrence noted in 16% of patients.[65] Since that time, various studies have emerged comparing anal stretch procedure with other surgical procedures, primary lateral internal sphincterotomy. Despite extensive study, there has been significant variability in the reported outcomes due to lack of standardization and reproducibility of the techniques employed. In addition, anal stretch has been scrutinized for causing extensive damage to internal and external sphincters leading to incontinence. A recent randomized controlled trial enrolled 108 patients assigned to anal dilation (AD) versus left lateral sphincterotomy (LLS). Average follow-up was 11.2 months. Significantly more patients reported minor incontinence in the AD than in the LLS group. Recurrence occurred in 11% of AD patients versus 2% of LLS patients.[66] In addition, a Cochrane Review of seven randomized controlled trials, comparing anal stretch with internal sphincterotomy significantly favored sphincterotomy over anal stretch for efficacy (OR = 3.35; 95% CI = 1.55–7.26) and incontinence to flatus or feces (OR = 4.03; 95% CI = 2.04–7.46).[67]

In an effort to standardize the method of anal dilation, pneumatic balloon dilation (PBD) has been developed. Sohn and colleagues first described PBD using a 40-mm rectosigmoid balloon.[68] A recent randomized controlled trial looked at PBD rather than manual dilation in comparison to lateral internal sphincterotomy (LIS) for the treatment of chronic anal fissure. Pneumatic dilation was performed with a 40-mm diameter by 60-mm-long anal balloon (Microvasive, Genova, Italy) with the balloon inflated to 20 psi for 6 minutes. Overall healing rates at 6 weeks were 83 and 92% for PBD and LIS, respectively. Based on preoperative and postoperative manometry, both techniques reduced anal pressures by ~30%. The PBD group did demonstrate mild transient fecal incontinence; however, at 24-month follow-up, the incidence of incontinence in the PBD group was 0%, but 16% in the LIS group ($p < 0.0001$).[69] Thus, with a better ability to standardize the technique and produce reproducible results, pneumatic balloon dilation may become a preferable alternative to anal dilation.

Nonetheless, lateral internal sphincterotomy still stands as the surgical treatment of choice for refractory anal fissures and may be offered without pharmacologic treatment failure according to the practice parameters by the American Society of Colon and Rectal Surgeons.[15] Reports of sphincterotomy for various anal pathologies probably date back to the 1700s.[70] However, internal sphincterotomy for the management of anal fissure was first described and popularized in the 1950s by Eisenhammer.[71,72] Lateral internal sphincterotomy quickly gained recognition as the posterior approach was found to result in large wounds and incontinence due to a "keyhole deformity." Lateral internal sphincterotomy is performed with a radial incision in the anoderm laterally exposing the internal sphincter muscle fibers. Then, under direct vision, the distal 4/5th of the internal sphincter muscle is divided with a scalpel or scissors. The wound can be left open or closed primarily. In 1969, Notaras described a technique that he called lateral subcutaneous sphincterotomy, now also known as a closed lateral internal sphincterotomy. This resulted in even smaller wounds and fecal soiling rates dropped to 6% compared with 30–41% with a posterior internal sphincterotomy.[73] This technique involves a narrow-bladed scalpel such as a cataract knife introduced through the perianal skin on the lateral side and pushed subcutaneously upwards between the internal sphincter and the skin lining the anal canal. When the point of the blade is at the dentate line the internal sphincter is divided by cutting medial to lateral. A defect can be felt under the skin between the retracted edged of the internal sphincter. A second approach for closed lateral internal sphincterotomy is the lateral to medial approach. In this operation, the scalpel is inserted into the intersphincteric groove and directed up to the dentate line. At this point, the internal sphincter is divided, cutting laterally to medially toward the surgeon's finger in the anal canal.[74–77]

Since the 1950s and 1960s, numerous studies have evaluated different methods of sphincterotomy. Various randomized controlled trials have compared open versus closed techniques. Healing rates appear to be similar, with open techniques ranging from 93% to 95% and closed approaches ranging from 90% to 97%. There appears to be no difference in major incontinence rates, which range from 2% to 5%.[75,76,78]

A meta-analysis of operative techniques for anal fissure also demonstrated no difference for persistence or incontinence between the open or closed technique.[79] When comparing lateral internal sphincterotomy with midline posterior sphincterotomy, again there appears to be no significant difference in persistence of symptoms or incontinence in two meta-analyses of retrospective studies.[67,74,79] Several studies have evaluated adjuncts to various surgical approaches. For example, one study reported higher patient satisfaction rates when hypertrophied anal papillae and fibrous anal polyps were removed at the time of LIS.[80] The value of this maneuver, however, remains unclear as the results have not been validated.

Since the description of the technique of lateral internal sphincterotomy by Eisenhammer in the 1950s,[71,72] current practice remains that the division of the internal sphincter be taken to the dentate line. However, with high reports of incontinence with LIS, there has been a more prudent approach to division of the sphincter that may yield lower incontinence rates. Littlejohn and colleagues described a technique of tailored left lateral sphincterotomy, wherein the sphincter is divided up to the height of the fissure.[81] They showed a 99% initial healing rate, 0.7% incidence of urgency, 1% gas incontinence, and 35% minor staining. Since then, various randomized, prospective studies have compared this technique with a larger sphincterotomy. Sphincterotomy to the fissure apex has been shown to have lower rates of mild incontinence (2%) compared with sphincterotomy to the dentate line (11%).[82] However, this comes with a higher overall treatment failure rate on long-term follow-up (13%) compared with a larger sphincterotomy either to the dentate line (0%) or to an anal diameter of 30 mm (3%).[82–84] Thus, a traditional, longer sphincterotomy, with fewer treatment failures and an acceptable rate of mild incontinence, appears to be the preferred technique.

Other complications associated with lateral internal sphincterotomy are ecchymosis, hematoma, and wound infection. In the past, there has been fear that closure of these wounds would result in a higher complication rate, such as wound infection. Two prospective, randomized studies compared primary closure of the wound after LIS with leaving the wound open to heal secondarily.[85,86] In the study by Aysan and colleagues, there was a significantly faster healing rate of $15.05 \pm 5.60$ days with wound closure versus $33.94 \pm 6.67$ days when wounds were left open ($p < 0.001$).[85] In a combined analysis, the advantage of closure was not statistically significance ($p = 0.35$, 95% CI: 0.13–1.00).[67] Also, there was no significant difference in the complication rate between primary wound closure versus leaving the wound open to heal secondarily.[85,86]

The management of anal fissure largely relies on relieving anal hypertonicity. Patients with anterior anal fissures have been shown to have significantly lower anal pressures, suggesting a different pathophysiology in the development of these fissures.[8,87] In support of this idea, there have also been reports of a paradoxical contraction response of low-pressure fissures to treatment with botulinum toxin.[58,88] These patients are at particularly high risk for incontinence with measures directed at reducing anal hypertonia. Various small studies have shown success with advancement anoplasty, or fissurectomy with advancement anoplasty, in patients with low-pressure anal fissures with success rates ranging from 87% to 100%.[89–91] Thus, it is especially important to approach anterior and low-pressure fissures more cautiously. Advancement flap surgery may be an acceptable first approach to low-pressure fissures. When encountered with a patient with an anterior fissure, it may be beneficial to perform anorectal manometry before proceeding with a treatment algorithm.

Various studies have also evaluated advancement flap surgery for all chronic anal fissure types. The procedure typically involves a subcutaneous flap with an incision made from the anal verge extending caudally. The skin flap is then advanced into the anal canal and positioned to cover the anal fissure and sutured in place. Two independent studies showed 98% success rate with advancement anoplasty for the treatment of chronic anal fissure, irrespective of anal tone.[92,93] Another study showed 100% success rate and no recurrence at 12 months in 10 patients who underwent fissurectomy and V-Y anoplasty with injection of botulinum toxin in the treatment of anterior chronic fissure with hypertonia of the internal anal sphincter.[94] In a recent pilot study of 8 patients, autologous adipose tissue transplant has also shown 75% healing of anal fissure and 80% resolution of anal stenosis in patients with chronic anal fissure who failed previous medical and surgical therapy.[95] Although these studies have shown promising results, larger prospective studies and longer follow-up is needed before further recommendations can be made in comparison to lateral internal sphincterotomy.

## SPECIAL CONSIDERATIONS

Anal fissure is a common finding in patients with perianal Crohn's disease.[96–98] In the past, fissures associated with Crohn's disease were thought to be asymptomatic and more commonly located off-midline.[96,98] However, more recent data suggests that the majority are actually symptomatic (up to 85%) and posterior (up to 66%), although off midline, multiple, and asymptomatic fissures occur more commonly in Crohn's disease patients compared with the general population.[97,99] Various reports have suggested that perianal Crohn's disease can be successfully treated with topical ointments, metronidazole, prednisone, or sulfasalazine.[97,98,100] In addition, surgical management of these

Crohn's disease patients with anal fissure has been feared due to presumed risks of incontinence in a population prone to diarrhea as well as poor wound healing, infections, and fistula formation. However, more recent reports have shown successful healing of Crohn's disease fissures after anorectal surgery.[97,99,101] Fleshner and associates showed 88% healing of anal fissures after fissurectomy, closed lateral internal sphincterotomy, or a combination of both. In comparison, medical management alone healed 50% of fissures. Abdominal surgery for Crohn's disease offered no significant healing of anal fissures compared with medical management alone. Factors found to be predictive of healing with medical therapy include male gender, painless fissure, and acute fissure. On long-term follow-up, 26% of patients developed a fistula or abscess from the base of the fissure, but there was no significant difference in medically or surgically treated patients.[99] Thus, most fissures associated with Crohn's disease can be treated medically, but those who fail to resolve and remain symptomatic can be managed surgically with acceptable risk.

Anal lesions in HIV-positive patients are a difficult problem with early reports of poor healing and high rates of incontinence after surgery.[102,103] Appropriate classification of these lesions is necessary for proper management. Benign anal fissures are narrow, usually located low in the anal canal and associated with a hypertonic anal sphincter. These must be differentiated from HIV-associated anal ulcers, which are typically broad-based, deep, or cavitating lesions associated with low anal sphincter tone.[104] For the management of benign anal fissures, Viamonte and colleagues advocate conservative therapy followed by lateral internal sphincterotomy after failure of medical therapy. On the other hand, anal ulcers are much more difficult to treat, and these patients should undergo examination under anesthesia, cultures, biopsy, and wide debridement.[104] Various other studies have reported sphincterotomy results for anal fissure in the HIV-positive population. However, these are mostly small series, without long-term follow-up, thus making if difficult to make any strong treatment recommendations.[103,105] In addition, the incidence of anal lesions has not changed significantly since introduction of highly active retroviral therapy (HAART).[106] Thus, anal fissure remains a difficult problem in the management of HIV-patients and should be approached cautiously, especially in a setting of advanced disease or baseline incontinence.

## CONCLUSION

Anal fissure is a common problem. The pathophysiology is based on high sphincter pressures and management is generally aimed toward reducing anal pressures. Anal fissures can generally be treated with conservative management, but pharmacologic management with topical calcium channel blockers, topical nitrates, and botulinum toxin injection are reasonable options with minimal side effects and good cure rates. Lateral internal sphincterotomy remains the gold standard for definitive management of anal fissures, but comes with a risk of incontinence. Open or closed techniques can be used with similar healing and complication rates. Anal stretch should be abandoned in the management of anal fissure. Larger studies with longer follow-up are needed before recommendations can be made about various other treatment modalities for anal fissure. Particular attention must be paid to anterior anal fissures as they are typically associated with low anal pressures. These patients should undergo anorectal manometery testing preoperatively. Those patients with sphincter hypotonia who fail conservative management should undergo advancement anoplasty. Atypical anal fissures associated with Crohn's disease or HIV should be approached cautiously. However, recent data suggests that lateral internal sphincterotomy may be tolerated well in these patients when conservative management fails.

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