Anal Fissure: to Cut or not to Cut?

Julio Garcia-Aguilar, MD, PhD
Professor of Surgery
University of California, San Francisco
Anal Fissures

- Linear ulceration from the dentate line to the anal verge
- Most located in the posterior midline (25% anterior in females)
- Common cause of anal pain
- 5-15% office visits to a proctologist
- 10% of all interventions
- Most are idiopathic
- Few are secondary to other conditions
- Affects both genders
Definition of Chronicity

• **Chronology**
  - Pain for more than 6 weeks
    • 50% of patients had pain for a period of time between one and six months
    • 30% of patients had intermittent pain for almost a year

• **Morphology**
  - Visible fibers of internal sphincter
  - Indurated edges
  - Hypertrophied anal papillae
  - Sentinel pile
"the presence of visible transverse internal anal sphincter fibers at the base of an anal fissure of duration not less than 6 weeks"

Lindsey et al, BJS 2004;91:270-279
**Atypical Anal Fissure**

**Characteristics**
- lateral location
- multiple
- painless
- systemic symptoms

**Differential Diagnosis**
- Crohn's
- Anal cancer
- Leukemia
- Herpes
- Tuberculosis
- Trauma
Symptoms

• Pain with defecation
• Pain that lingers after BM
• May have started with hard BM or period of constipation
• Bleeding
Pathogenesis

- Anal Trauma
- Internal Anal Sphincter Hypertonia
- Relative Ischemia to Anoderm
Anal Sphincter Function

- **Intrinsic Myogenic Tone**
  - Depends on extracellular calcium levels entering via L-type calcium channels

- **Enteric Nervous System**
  - Responsible for peristalsis and rectoanal inhibitory reflex
  - Nitrous oxide is the neurotransmitter - relaxation
  - L-arginine is the precursor of nitrous oxide
Pressure Profiles and Anal Fissure

- Elevate resting pressure
- More ultraslow pressure waves
- "Overshoot" phenomenon
- 52% to 62% patients with anal fissure have normal or low resting pressure
- Poor correlation between clinical exam and manometry
An Ischemic Ulcer?

- 85% of ‘normal’ cadavers have “hypovascularity” in the posterior midline
- Terminal arterioles must cross internal anal sphincter to perfuse anoderm
- Blood supply from right and left side end in anterior and posterior midline
However,

- 85% of the population don’t develop fissures despite ‘hypovascularity’
- Fissures develop in young, not elderly, patients
- No association with peripheral vascular disease
Ischemia + Anal Hypertonia?

• Posterior midline anoderm has lowest blood flow of all four quadrants
• Posterior midline perfusion inversely proportional to resting pressure
• Anal fissure pts with highest pressure, lowest blood flow
• Pain increases sphincter spasm
• Sphincterotomy corrects both hypertonia and hypoperfusion and leads to healing

Schouten WR et al. DCR 1994, BJS 1996
Treatment

- Water
- Bulking agents
- Sit baths
- Topical analgesics
- Nitroglycerine ointment
- Calcium channel blockers
- Botulinum toxin
- Lateral internal sphincterotomy
Initial Treatment

For acute fissure and those who have not tried any treatment

1. Fiber supplementation and water:
   - bulk up stools
   - hasten transit
   - reduce consistency of stool

2. Warm tub soaks
   - relax pelvic muscles
   - increase blood flow to area
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Healing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bran/sitz baths</td>
<td>88</td>
</tr>
<tr>
<td>2% Lignocaine</td>
<td>82</td>
</tr>
<tr>
<td>2% Hydrocortisone</td>
<td>60</td>
</tr>
</tbody>
</table>

Jensen 1986
Lateral Internal Sphincterotomy
## Results of Lateral Internal Sphincterotomy 1980-1999 (20 series)

<table>
<thead>
<tr>
<th></th>
<th>Range (%)</th>
<th>Mean (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success</td>
<td>90-100</td>
<td>98</td>
</tr>
<tr>
<td>Recurrence</td>
<td>0-20</td>
<td>6</td>
</tr>
<tr>
<td>Incontinence</td>
<td>0-38</td>
<td>9</td>
</tr>
</tbody>
</table>

Madoff & Fleshman, Gastro 2003
DON’T ASK..................
DON’T TELL
Table 2. Results of Lateral Internal Sphincterotomy

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Success (%)</th>
<th>Recurrence (%)</th>
<th>Incontinence (%)</th>
<th>Follow-up (type)</th>
<th>Follow-up (%)</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abcarian</td>
<td>1980</td>
<td>150</td>
<td>100</td>
<td>1.3</td>
<td>0</td>
<td>C</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Keighley et al.</td>
<td>1981</td>
<td>71</td>
<td>100</td>
<td>25</td>
<td>2</td>
<td>I, E</td>
<td>89</td>
<td>12</td>
</tr>
<tr>
<td>Ravikumar et al.</td>
<td>1982</td>
<td>60</td>
<td>97</td>
<td>0</td>
<td>5</td>
<td>C</td>
<td>100</td>
<td>24 minimum</td>
</tr>
<tr>
<td>Hsu et al.</td>
<td>1984</td>
<td>89</td>
<td>100</td>
<td>5.6</td>
<td>0</td>
<td>C</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Jensen et al.</td>
<td>1984</td>
<td>30</td>
<td>100</td>
<td>3</td>
<td>0</td>
<td>Q, E</td>
<td>100</td>
<td>18 median</td>
</tr>
<tr>
<td>Walker et al.</td>
<td>1985</td>
<td>306</td>
<td>100</td>
<td>5</td>
<td>0</td>
<td>I</td>
<td>33</td>
<td>52 mean</td>
</tr>
<tr>
<td>Gingold</td>
<td>1987</td>
<td>86</td>
<td>100</td>
<td>3.5</td>
<td>0</td>
<td>C</td>
<td>NS</td>
<td>24 median</td>
</tr>
<tr>
<td>Weaver et al.</td>
<td>1987</td>
<td>39</td>
<td>93</td>
<td>5.1</td>
<td>2.5</td>
<td>I, E</td>
<td>86</td>
<td>17 mean</td>
</tr>
<tr>
<td>Lewis et al.</td>
<td>1988</td>
<td>350</td>
<td>94</td>
<td>6</td>
<td>6</td>
<td>I</td>
<td>100</td>
<td>37 median</td>
</tr>
<tr>
<td>Zinkin</td>
<td>1988</td>
<td>151</td>
<td>94.7</td>
<td>NS</td>
<td>NS</td>
<td>none</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Khubchandani et al.</td>
<td>1989</td>
<td>717</td>
<td>97.7</td>
<td>NS</td>
<td>NS</td>
<td>Q</td>
<td>52.9</td>
<td>NS</td>
</tr>
<tr>
<td>Kortbeek et al.</td>
<td>1992</td>
<td>112</td>
<td>95.5</td>
<td>NS</td>
<td>NS</td>
<td>I</td>
<td>NS</td>
<td>1.5</td>
</tr>
<tr>
<td>Pernikoff et al.</td>
<td>1994</td>
<td>500</td>
<td>99</td>
<td>2</td>
<td>16</td>
<td>Q</td>
<td>78</td>
<td>67</td>
</tr>
<tr>
<td>Romano et al.</td>
<td>1994</td>
<td>44</td>
<td>100</td>
<td>0</td>
<td>9</td>
<td>E</td>
<td>NS</td>
<td>8</td>
</tr>
<tr>
<td>Leong et al.</td>
<td>1995</td>
<td>20</td>
<td>100</td>
<td>NS</td>
<td>0</td>
<td>I, E</td>
<td>NS</td>
<td>6.5 median</td>
</tr>
<tr>
<td>Prohm et al.</td>
<td>1995</td>
<td>177</td>
<td>96</td>
<td>3.3</td>
<td>1.6</td>
<td>E</td>
<td>NS</td>
<td>1-1.5</td>
</tr>
<tr>
<td>Usatoff et al.</td>
<td>1995</td>
<td>98</td>
<td>90</td>
<td>20</td>
<td>18</td>
<td>Q</td>
<td>80</td>
<td>41 mean</td>
</tr>
<tr>
<td>Garcia-Aguilar et al.</td>
<td>1996</td>
<td>864</td>
<td>96</td>
<td>11</td>
<td>37.8</td>
<td>Q</td>
<td>63.5</td>
<td>36 mean</td>
</tr>
<tr>
<td>Haneliel et al.</td>
<td>1997</td>
<td>312</td>
<td>98.6</td>
<td>1.4</td>
<td>–</td>
<td>C</td>
<td>93.3</td>
<td>NS</td>
</tr>
<tr>
<td>Littlejohn et al.</td>
<td>1997</td>
<td>352</td>
<td>99.7</td>
<td>1.4</td>
<td>1.4</td>
<td>C</td>
<td>81.5</td>
<td>9 mean</td>
</tr>
<tr>
<td>Nyam et al.</td>
<td>1999</td>
<td>585</td>
<td>96</td>
<td>8</td>
<td>15</td>
<td>Q</td>
<td>83</td>
<td>72 mean</td>
</tr>
</tbody>
</table>

Used standardized incontinence questionnaires
Continence Defects after LIS

- Gas soiling
  - Open: 30%
  - Closed: 23%
- Stool soiling
  - Open: 27%
  - Closed: 16%
- Stool
  - Open: 12%
  - Closed: 4%

Garcia-Aguilar J et al, DCR 1996
Lateral Internal Sphincterotomy
Meta-Analysis of Surgical Techniques

- anal stretch vs. sphincterotomy
- open vs. closed lateral sphincterotomy
- posterior midline vs. lateral sphincterotomy
- outcome: persistence incontinence

Nelson R, DCR 1999
## Operative Technique?

<table>
<thead>
<tr>
<th>Technique</th>
<th>N</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Persistence</td>
</tr>
<tr>
<td>Anal Stretch vs. LIS</td>
<td>6</td>
<td>1.16</td>
</tr>
<tr>
<td>Open vs. Closed</td>
<td>4</td>
<td>1.61</td>
</tr>
<tr>
<td>Posterior vs. Lateral</td>
<td>4</td>
<td>2.12</td>
</tr>
</tbody>
</table>

* * p<0.05  
Pharmacologic IAS Relaxants

• **Topical nitrates**
  - Nitroglycerine
  - Isosorbide dinitrate
  - L-Arginine

• **Calcium channel blockers**
  - Nifedipine
  - Diltiazem

• **Neurotoxins**
  - Botulin toxin A
  - Gonyautoxin

• **Other agents**
  - $\alpha_1$-adrenergic antagonists: Indoramin
  - Muscarinic cholinergic agonists: Bethanecol
  - Phosphodiesterase inhibitors: Sildenafil
## Results of Treatment with Nitroglycerin

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Concentration</th>
<th>Duration</th>
<th>Healed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watson</td>
<td>1996</td>
<td>19</td>
<td>0.2%</td>
<td>6 weeks</td>
<td>47%</td>
</tr>
<tr>
<td>Lund</td>
<td>1996</td>
<td>21</td>
<td>0.2%</td>
<td>6 weeks</td>
<td>68%</td>
</tr>
<tr>
<td>Kennedy</td>
<td>1999</td>
<td>24</td>
<td>0.2%</td>
<td>4 weeks</td>
<td>59%</td>
</tr>
<tr>
<td>Brisinda</td>
<td>1999</td>
<td>25</td>
<td>0.2%</td>
<td>8 weeks</td>
<td>60%</td>
</tr>
<tr>
<td>Richard</td>
<td>2000</td>
<td>44</td>
<td>0.25%</td>
<td>6 weeks</td>
<td>29%</td>
</tr>
<tr>
<td>Palazzo</td>
<td>2000</td>
<td>45</td>
<td>0.5%</td>
<td>6 weeks</td>
<td>73%</td>
</tr>
<tr>
<td>Hasegawa</td>
<td>2000</td>
<td>40</td>
<td>0.2%</td>
<td>12 weeks</td>
<td>50%</td>
</tr>
<tr>
<td>Skinner</td>
<td>2001</td>
<td>51</td>
<td>0.2%</td>
<td>4 weeks</td>
<td>43%</td>
</tr>
<tr>
<td>Evans</td>
<td>2001</td>
<td>33</td>
<td>0.2%</td>
<td>8 weeks</td>
<td>61%</td>
</tr>
<tr>
<td>Bailey</td>
<td>2002</td>
<td>304</td>
<td>0.2-0.4%</td>
<td>8 weeks</td>
<td>39%</td>
</tr>
</tbody>
</table>
### Largest RCTs
#### Treatment with Nitroglycerin

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Healed(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lund 1997</td>
<td>80</td>
<td>68*</td>
</tr>
<tr>
<td>Carapeti 1999</td>
<td>70</td>
<td>66*</td>
</tr>
<tr>
<td>Richard 2000</td>
<td>82</td>
<td>27</td>
</tr>
<tr>
<td>Altomare 2000</td>
<td>119</td>
<td>38</td>
</tr>
<tr>
<td>Bailey 2002</td>
<td>304</td>
<td>39</td>
</tr>
<tr>
<td>Sonmez 2002</td>
<td>47</td>
<td>65</td>
</tr>
</tbody>
</table>

* 27% Relapse Rate in follow up studies of healed pts
Treatment with Nitroglycerin

Bailey, et al, DCR, 2002
Nitroglycerin
“Healing Or Headache?”

<table>
<thead>
<tr>
<th>Study</th>
<th>Headache (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lund 1997</td>
<td>58</td>
</tr>
<tr>
<td>Dorfman 1999</td>
<td>63</td>
</tr>
<tr>
<td>Carapeti 1999</td>
<td>27</td>
</tr>
<tr>
<td>Kennedy 1999</td>
<td>29</td>
</tr>
<tr>
<td>Altomare 2000</td>
<td>34</td>
</tr>
<tr>
<td>Sonmez 2002</td>
<td>9</td>
</tr>
<tr>
<td>Bailey 2002</td>
<td>3</td>
</tr>
</tbody>
</table>
Nitroglycerin vs. LIS

- Chronic anal fissure patients
- Multicenter randomized, controlled trial of Canadian Colorectal Surgical Trials Group
- LIS vs. 0.25% GTN TID
- Standardized conservative therapy
- Follow-up at 6 wks and 6 mos

Richard CS et al DCR 2000
Nitroglycerin vs. LIS

Healing

% healed

0 50 100

6 weeks 6 months

0.25% GTN
LIS

* p=5×10⁻⁸
** p=3×10⁻⁹

Richard CS et al DCR 2000
Nitroglycerin vs. LIS

Richard CS et al DCR 2000

* p < 0.001
** p = 9 x 10^{-6}
Nitroglycerin vs. LIS

• 9/44 GTN patients (21%) discontinued therapy due to headache (8) or syncope (1)

• No continence disturbance noted in LIS group
Nitroglycerin vs. LIS

Recurrence (79 months f/u)

Brown CJ et al, DCR 2007
Nitroglycerin vs. LIS

Recurrence (79 months f/u)

- Satisfied repeat treatment
  - 0.25% GTN
  - LIS

* $p = 5 \times 10^{-8}$
** $p = 3 \times 10^{-9}$

Brown CJ et al, DCR 2007
Calcium Channel Blockers

Side effects                         rare
Long term follow-up              unknown

% RAP

Oral
Nifedipine 33
Diltiazem 17

Topical
0.2% Nifedipine 30
2% Diltiazem 28
### Topical Calcium Channel Blockers

<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Agent</th>
<th>Healing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antropoli</td>
<td>1999</td>
<td>2% Nifedipine</td>
<td>95%</td>
</tr>
<tr>
<td>Carapeti</td>
<td>2000</td>
<td>2% Diltiazem</td>
<td>67%</td>
</tr>
<tr>
<td>Knight</td>
<td>2001</td>
<td>2% Diltiazem</td>
<td>75%</td>
</tr>
<tr>
<td>Jonas</td>
<td>2001</td>
<td>2% Diltiazem</td>
<td>65%</td>
</tr>
</tbody>
</table>
Diltiazem vs. Nitroglycerin

Healed/Improved

Headsche

From Sajid et al, Int J Colorectal Dis 2008
Botulinum Toxin

- Exotoxin produced by *Clostridium botulinum*
- Neurotoxin that causes botulism
- Local muscle relaxant
- Prevents acetylcholine release from presynaptic nerve terminals
- Clinical duration of action approximately 3 months
Botulinum Toxin - Initial Report

Series of 100 patients

78 pain free at 3 days

82 healed at 3 months
79 healed at 6 months

8 relapse
9 transient incontinence (7 flatus, 2 stool)

Jost DCR 1997
Botox vs. Nitroglycerin

- 3 RCT
- Both equally effective healing fissure
- Nitroglycerine associated with more side effects, in particular headache
- 33% recurrence rate in both arms at 3 years

From Sajid et al, Colorectal Dis 2007
# Botox vs Sphincterotomy

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Healing</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mentes 2003</td>
<td>111</td>
<td>75%</td>
<td>94%</td>
</tr>
<tr>
<td>Iswariah 2005</td>
<td>38</td>
<td>41%</td>
<td>91%</td>
</tr>
<tr>
<td>Arroyo 2005</td>
<td>80</td>
<td>45%</td>
<td>93%</td>
</tr>
</tbody>
</table>
Botox vs Sphincterotomy
Healed/Improved

From Sajid et al, Colorectal Dis 2007
Botox vs Sphincterotomy

Complications

From Sajid et al, Colorectal Dis 2007
Botox vs Sphincterotomy
Fecal Incontinence

From Sajid et al, Colorectal Dis 2007
Botox vs Sphincterotomy

Recurrence

From Sajid et al, Colorectal Dis 2007
Gonyautoxin

- Phytotoxin from microscopic planktonic algae
- Neurotoxin that causes PSP: paralytic shellfish poisoning
- Binds to receptor of voltage gated sodium channels on excitable cells blocking neuronal transmission
Gonyautoxin
(Garrido R et al. DCR 2005, Colorectal Dis 2007)

- 50 patients with acute or chronic fissure
- 100 units injected into IAS on both sides of fissure
- 56% reduction in maximum anal resting pressure 2 minutes after injection
- 98% healing by 28 days
- 2% relapse rate in 14 months follow up
- No side effects seen
- No fecal incontinence observed
Fisurectomy

from Pelta et al, DCR 2007
## Botox and Fisurectomy

<table>
<thead>
<tr>
<th>author</th>
<th>patients</th>
<th>healed</th>
<th>incont.</th>
<th>follow/up months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lindsey 2004</td>
<td>35</td>
<td>93%</td>
<td>7%</td>
<td>4</td>
</tr>
<tr>
<td>Scholtz 2007</td>
<td>40</td>
<td>79%</td>
<td>2%</td>
<td>12</td>
</tr>
<tr>
<td>Baraza 2008</td>
<td>46 (16 lost)</td>
<td>50%</td>
<td>3%</td>
<td>22</td>
</tr>
</tbody>
</table>
Summary

- Most anal fissures heal with fiber, water, and heat
- Use Calcium Channel Blockers for pharmacological relaxation of the anal sphincter
- Sphincterotomy is very effective, and relatively safe for patients who fail medical therapy
- Fisurectomy and Botox are an alternative when the risk of incontinence is high