The Evolving Role of Surgery in IBD

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Advances in IBD, December, 2012

The Evolving Role of Surgery

- Safety and effectiveness of strictureplasty
- Approach to patients with complex perineal CD
- When is enough medical management of patients with CUC enough?
- Just how well is IPAA performing?
- Controversies concerning IPAA
- How do biologics impact surgery for IBD?

The Evolving Role of Surgery

- How safe is IPAA in IC patients? In CD patients?
- When is colectomy indicated for patients with dysplasia?
- Can you do IPAA in IBD patients with CRC?
- What is the risk of CRC after IPAA?
- Are enhanced recovery programs helpful?

The Evolving Role of Surgery

Is there a potential downside to attempts to control CD or CUC medically over longer and longer periods of time?

Crohn Disease

Rationale for Strictureplasty

- Disease involves whole intestine
- Impossible to cure by excision
- All diseased bowel does not need excision
- If only stenotic complications are present, these can be relieved without excision
Evolution

toward more complex strictureplasties

The Evolving Role of Surgery
Strictureplasty

<table>
<thead>
<tr>
<th>Strictureplasty types</th>
<th>N (%)</th>
<th>Morbidity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional strictureplasties</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H-M</td>
<td>356/6 (8)</td>
<td>400 (11)</td>
</tr>
<tr>
<td>Finney</td>
<td>43/1 (1)</td>
<td></td>
</tr>
<tr>
<td>Nonconventional strictureplasties</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Michelassi and various modifications</td>
<td>426/7 (1)</td>
<td>537 (12)</td>
</tr>
<tr>
<td>Jaboulay</td>
<td>68/13</td>
<td></td>
</tr>
<tr>
<td>Combined Finney and H-M</td>
<td>12/2</td>
<td></td>
</tr>
<tr>
<td>Double Wali</td>
<td>3/8 (3)</td>
<td></td>
</tr>
<tr>
<td>Judd</td>
<td>5/1</td>
<td></td>
</tr>
<tr>
<td>Moschel-Walsh-Neumeier</td>
<td>3/3 (1)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>20/4</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4336</td>
<td></td>
</tr>
</tbody>
</table>

N = number of strictureplasties; H-M = Hugos-Mikulicz strictureplasty

Bellolio, F; Cohen, Z; MacRae, H; et al. DCR 2012 55(6):714-726

Strictureplasty Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STF site leak</td>
<td>6/2 (3)</td>
</tr>
<tr>
<td>Anatomic leak</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Intra-abdominal abscess</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Fenestraneous fistula</td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>GI bleed</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Wound infection</td>
<td>4/2 (5)</td>
</tr>
<tr>
<td>Small bowel obstruction/fistula</td>
<td>3 (2.5)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (0.6)</td>
</tr>
</tbody>
</table>

STF = strictureplasty

One of the fistulas was from a STF site, the other was from an anastomotic site.

Bellolio, F; Cohen, Z; MacRae, H; et al. DCR 55(8):864-869, August 2012

AN APPROACH TO PATIENTS WITH PERINEAL FISTULAS AND CD

Surgery-free survival

Strictureplasty in Selected Crohn's Disease Patients

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Evolution toward upfront aggressive COMBINED medical AND surgical therapy for perineal Crohn’s Disease

Surgery for Crohn Disease Combination Therapy

<table>
<thead>
<tr>
<th></th>
<th>Initial Response (%)</th>
<th>Recurrence (%)</th>
<th>Time to Recurrence (Months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>82</td>
<td>79</td>
<td>3.6</td>
</tr>
<tr>
<td>EUA + Seton + Infliximab</td>
<td>100</td>
<td>44</td>
<td>13</td>
</tr>
</tbody>
</table>

*Regueiro M & Mardine H. Inflammatory Bowel Diseases, March 2003, 9(2):98-103

Response Based on Type of Fistula

<table>
<thead>
<tr>
<th>Simple fistula</th>
<th>Complex fistula</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EUA and infliximab</td>
</tr>
<tr>
<td></td>
<td>n=3</td>
</tr>
<tr>
<td></td>
<td>Infliximab alone n=0</td>
</tr>
<tr>
<td>Initial response</td>
<td>3 100%</td>
</tr>
<tr>
<td></td>
<td>9 100%</td>
</tr>
<tr>
<td>Recurrence rate</td>
<td>1 33.3%</td>
</tr>
<tr>
<td></td>
<td>5 56%</td>
</tr>
<tr>
<td>Mean time to recurrence (mo)</td>
<td>15 6.2 0.004</td>
</tr>
</tbody>
</table>


Surgery for Crohn Disease

“For perianal fistulizing CD, repeat doses of Infliximab improves clinical and radiological outcomes, although complete radiologic healing occurs in a minority of patients”


Surgery for Perineal Crohn Disease Summary

- Perianal fistulous disease is rarely cured
- Rather, fistulas are controlled by a combined approach including surgery (seton), immunosuppressives antibiotics and infliximab
- Setons are used to keep the tracts open, eliminating accumulation of pus and fostering tract quiescence

Surgery for Perineal Crohn Disease Summary

- When the tracts are dry, the setons are removed
- The perineum is reexamined regularly
- Only if fecal incontinence intervenes is proctectomy discussed
Risk factors for Proctectomy

- Extensive fistula/abscess vs simple
  26% vs. 6%
- Severe Proctitis vs none or mild
  37% vs. 10%
- Severe proctitis and extensive fistula/abscess
  46% proctectomy rate

Fecal Diversion

Patients undergoing diversion for perineal CD have <20% chance of successful restoration of intestinal continuity which is NOT improved with biologic therapy

Hong MK et al Colorectal Dis 2011 13 (2): 171-6

However.....

Fecal diversion is useful to quiet the perineum prior to repairing an R-V fistula and to promote healing postoperatively

Chronic Ulcerative Colitis

Evolution

Toward reasonable time frames for managing aggressive disease

Surgery for CUC....
when is enough, enough?

- For outpatients, it seems reasonable to treat with 5 ASA preparations, topical steroids, oral steroids, AZA and biologics until unable to steroid spare effectively
- For inpatients, reasonably aggressive treatment includes; IV steroids & IFX for 5 days [bleeding, >10 stools indicates fulminant disease]
- For deteriorating inpatients, GI & Surgeon need to decide together when enough is enough
- High grade dysplasia signifies enough is enough
- Low grade dysplasia probably signifies the same
Ileal Pouch-Anal Anastomosis

Evolution
Straight IPAA
- S pouch
- J pouch
- Long cuff
- Short cuff
- Double-stapled
- Laparoscopic IPAA (LAP, HALS, SILS)

Evolution of the IPAA data set

IPAA
Mayo Experience

Total: 3405
- CUC: 3048
- FAP: 304
- "other": 53

- 1981-2001 1,885 IPAA for CUC
- complete annual follow-up for 15 years
- n=409
- annual questionnaire (prospective database)
  - function and continence
  - QoL
  - complications (excluding pouch failure)

- Function (n=409)
- years follow-up: 1, 5, 10, 15
- Age (years): 33, 38, 43, 49
- Stool frequency:
  - Mean Stools/day: 5.5, 5.6, 5.6, 6.2, p<.001
  - Mean Stools/night: 1.1, 1.3, 1.5, 2.0, p<.001

Complications

Pouchitis

Quality of Life

Social Activities

Years after IPAA

Quality of Life

Social Activities

Work at Home

Years after IPAA

Quality of Life

Social Activities

Work at Home

Family Relationship

Years after IPAA

Quality of Life

Social Activities

Work at Home

Family Relationship

Travel

Sports

Recreation

Sexual Life

Summary

with ageing…

• good functional outcome

• good and stable QoL
**Conclusion**

IPAA is a durable operation with a good QoL and stable predictable outcomes over time.

**Minimally Invasive Surgery and IPAA**

**Evolution**

toward *Minimally Invasive Surgery (MIS)* for IBD

(Laparoscopy/Hand Assisted Laparoscopy (HALS))

**HALS IPAA**

Wt. = 227, BMI = 35.2

**IPAA (2007)**

- Total performed: 114
- Open: 29
- Minimally Invasive: 85 (75%)
- LAP/HALS: 37/48 (67%)
Surgical Evolution

**Age**
- 32pts >65 y/o matched to 32pts <65 y/o

**Outcomes:** older pts. had more readmission for volume depletion but functional results were the same over time

(Pinto RA et al Colorectal Dis 2011;13:177-83)

Fertility
- Weighted average infertility rate during medical treatment = 15% after IPAA = 48%


- Fecundity (probability of conception) is decreased after IPAA


- Ability to carry a pregnancy to term is not affected.


- Subtotal colectomy and BI or IRA is offered to young women who wish to become pregnant

Surgical Evolution

- Fewer pelvic/adnexal adhesions form after laparoscopic pelvic dissection* and

- Patients undergoing lap IPAA have a higher fertility rate than open patients**

**Laparoscopic IPAA may be the POC**


Biologics and Surgery for IBD

The widespread use of biologics has prompted a change in the surgical management of patients with CUC

<table>
<thead>
<tr>
<th>Author</th>
<th>Complication</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marchal*</td>
<td>Early Major</td>
<td>1.7 (3.0-7.7)</td>
</tr>
<tr>
<td>Belgium</td>
<td>Late Major</td>
<td>1.4 (4.5.0)</td>
</tr>
<tr>
<td>Colombel**</td>
<td>Septic</td>
<td>.9 (1.4-1.9)</td>
</tr>
<tr>
<td>Mayo</td>
<td>Non septic</td>
<td>1.0 (.5-2.0)</td>
</tr>
<tr>
<td>Nasir***</td>
<td>All Complic</td>
<td>30.3 (TNF) v 27.9%</td>
</tr>
<tr>
<td>Mayo</td>
<td>Abscess/leak</td>
<td>1.99 (TNF) v 3.4%</td>
</tr>
<tr>
<td>Appau****</td>
<td>30 d readmit</td>
<td>2.3 (1.5-3.1)</td>
</tr>
<tr>
<td>CCF</td>
<td>30 d sepasis</td>
<td>2.8 (1.1-6.1)</td>
</tr>
<tr>
<td></td>
<td>30 d abscess</td>
<td>5.8 (1.7-19.7)</td>
</tr>
</tbody>
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* Aliment Pharmacol Ther 2004;19:749-54
** AM J Gastroenterol 2004;99:878-83
*** J Gastrontrale Surg 2010;14:1859-1866
**** J Gastrontrale Surg 2008;12:1738-44

Surgical Challenges in IBD

IFX and Surgical Complications

<table>
<thead>
<tr>
<th>CD only</th>
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<tbody>
<tr>
<td>Author</td>
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<tr>
<td>Mayo</td>
</tr>
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<tr>
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<th>Complication</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selvasekar</td>
<td>Pouch specific</td>
<td>2.6 (0.9-7.5)</td>
</tr>
<tr>
<td>Mayo</td>
<td>Infectious</td>
<td>2.7 (1.1-6.7)</td>
</tr>
<tr>
<td>Schluender</td>
<td>Surgery</td>
<td>1.9 (0.6-5.9)</td>
</tr>
<tr>
<td>Cedars</td>
<td>Infectious</td>
<td>2.4 (0.6-9.6)</td>
</tr>
<tr>
<td>Mor</td>
<td>Sepsis</td>
<td>13.8 (1.8-105)</td>
</tr>
<tr>
<td>CCF Ferrante</td>
<td>Pouch specific</td>
<td>0.9 (0.8-9)</td>
</tr>
<tr>
<td>Belgium</td>
<td>Infectious</td>
<td>0.3 (0.07-1.4)</td>
</tr>
</tbody>
</table>

Pharmacokinetics of the Biologics

- Half lives
  - Infliximab (IFX) = 10-12 days
  - Adalimumab = 14 days
  - Certolizumab = 14 days
  - Natalizumab = 11 days

  - For all, drug is still detectable at 8 weeks with complete clearance by 12 weeks

Surgery and Biologics
Evolution

Because CUC patients are at higher risk for post-operative infectious complications when treated with a biologic, in order to maximize the chances of success of the operation

Consider more liberal use of subtotal colectomy prior to IPAA (3 staged IPAA)

IPAA for Crohn’s Disease
Evolving

- Among 20 CD patients in whom IPAA was intentionally performed:
  - Pouch in place - 85%
  - Fistula - 19%
  - Pouch/vag. Fistula - 13%
  - Stricture - 17%
  - Sepsis – 12%
  - Urgency - 30%
  - Incontin. - 28%
  - No. stools – 7

  Mean F/U = 5yr

IPAA for CD
Comment

- Patients with an IPAA constructed for CD may have better long-term outcomes than patients with supervening CD of the pouch

- The number of CD patients who are candidates for primary IPAA is tiny
In patients in whom CD develops *AFTER* IPAA

Aggressive combined medical/surgical management

Management of Crohn’s of the Pouch with Infliximab

- Patients treated with Infliximab for CD-related complications after IPAA – ileitis, fistulas

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>No.</th>
<th>Partial</th>
<th>Complete</th>
<th>No Resp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-term</td>
<td>26</td>
<td>23%</td>
<td>62%</td>
<td>15%</td>
</tr>
<tr>
<td>Long-term*</td>
<td>24</td>
<td>29</td>
<td>29%</td>
<td>42%</td>
</tr>
</tbody>
</table>

*21 months


Management of dysplasia in patients with CUC

Surgery

Management Scheme for Patients With CUC Undergoing Surveillance

- No dysplasia ——— Continue surveillance
- Indefinite dysplasia ——— Continue surveillance
- LGD (flat or sessile polyp) ——— Colectomy
- HGD ——— Colectomy
- CRC ——— Colectomy

CRC in IBD

- Between 1-9% of patients presenting for IPAA will have CRC
- Surgery is based on established oncologic principles
- Colon cancer → IPAA
- Rectal Cancer (mid-high Stage I and II) → IPAA
- Otherwise, TPC +BI

Dysplasia and Cancer *after IPAA*
**Dysplasia and Cancer after IPAA**

- **Dysplasia in the ATZ:** 7/210 (3%)*
  Associated with dysplasia or ACA in the colon or rectum at IPAA
- **Dysplasia in the pouch:** 0/37**
  (bx'd yearly x 7)
- **Total number of patients with cancer in the pouch or anal canal reported as of May 2011= 36**
  Incidence = 0.0015%***
  
*O'Riordan MG, et al: DCR, 2000;43:1660-1665
**Ettorre GM. DCR, 2000; 43:1743-1748 (Rome)
***O'Riordan JM. Int J Colorectal Dis 2011 (Toronto) on-line publication ahead of print

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**ATZ and Pouch Surveillance**

**Patients considered for post op surveillance:**

- Pre op ACA or Dysplasia
- Ongoing severe pouchitis
- Pouches in place 15 yrs and longer

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**Enhanced Recovery Protocol (ERP)**

**LOS = 2-5 days after IPAA**

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**Surgical Evolution in IBD**

- Strictureplasty safe and efficacious
- Surgical drainage and IFX is TOC for perineal CD
- Role for fecal diversion=?
- If steroid sparing not achieved-colectomy
- IPAA is maturing
- Fertility issues prompt consideration of family first/BI/IRA

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**Surgical Challenges in IBD**

- Biologics affect recovery from IPAA adversely prompting consideration of 3 rather 2 staged IPAA
- Biologics not cleared for ~12 weeks
- IPAA not OK for CD
- HGD AND LGD prompt colectomy
- IPAA not contraindicated for all IBD pts. with CRC
- Incidence of CRC after IPAA= 0.0015%
- Enhanced recovery protocols are effective

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**Ongoing Surgical Challenges in IBD**

- Quantifying patient centered/reported outcomes between medical and surgical treatment for IBD.
- Identify the optimal time for surgical intervention in CUC
- Identify high risk patients requiring alternate surgical planing to avoid complications
- Determine best follow-up regimen after IPAA
- Determine those most at risk for pouchitis preop and develop better management regimens.
- Identify the pertinent issues concerning fecundity in patients requiring IPAA
- Increasing utility of MIS in IBD (NOTES, SILS)