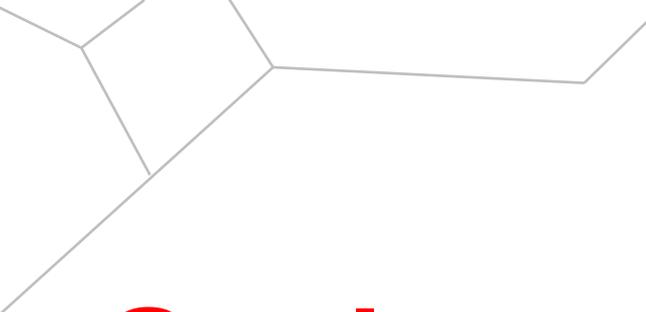


Post-op Gastrointestinal Leaks: A significant medical problem

Collaboration with Harvard Catalyst to investigate novel solutions to identify, detect, and prevent post-surgery GI leaks



Goal

To launch a multi-disciplinary effort to enhance understanding of the multi-factorial nature of post-surgery anastomotic leakage and develop innovative solutions.

* Open Access Surgery 2016:9

Johnson & Johnson INNOVATION

PROBLEM

Post-surgery GI leaks are a major medical problem with high morbidity and mortality.
Novel solutions are needed.

Background

- Anastomotic leakage has been the bane of intestinal surgery for over a century.
- High leak rates complicate the ~8 million colorectal surgeries/year world-wide.
- Patients with anastomotic leaks have increased lengths of hospital stay, higher readmission rates, and higher mortality rates.
- Where required, reoperation also results in negative impact on quality of life.
- Various surgical techniques and interventions have been developed to mitigate leaks; no effective solution is available.

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GI Anastomosis – Clinical Definition

Anastomotic Leak: a defect of the intestinal wall at or near the anastomotic site (including suture and staple lines of neorectal reservoirs), leading to a communication between the intra- and extraluminal compartments.

A pelvic abscess close to anastomosis is also considered an anastomotic leak.

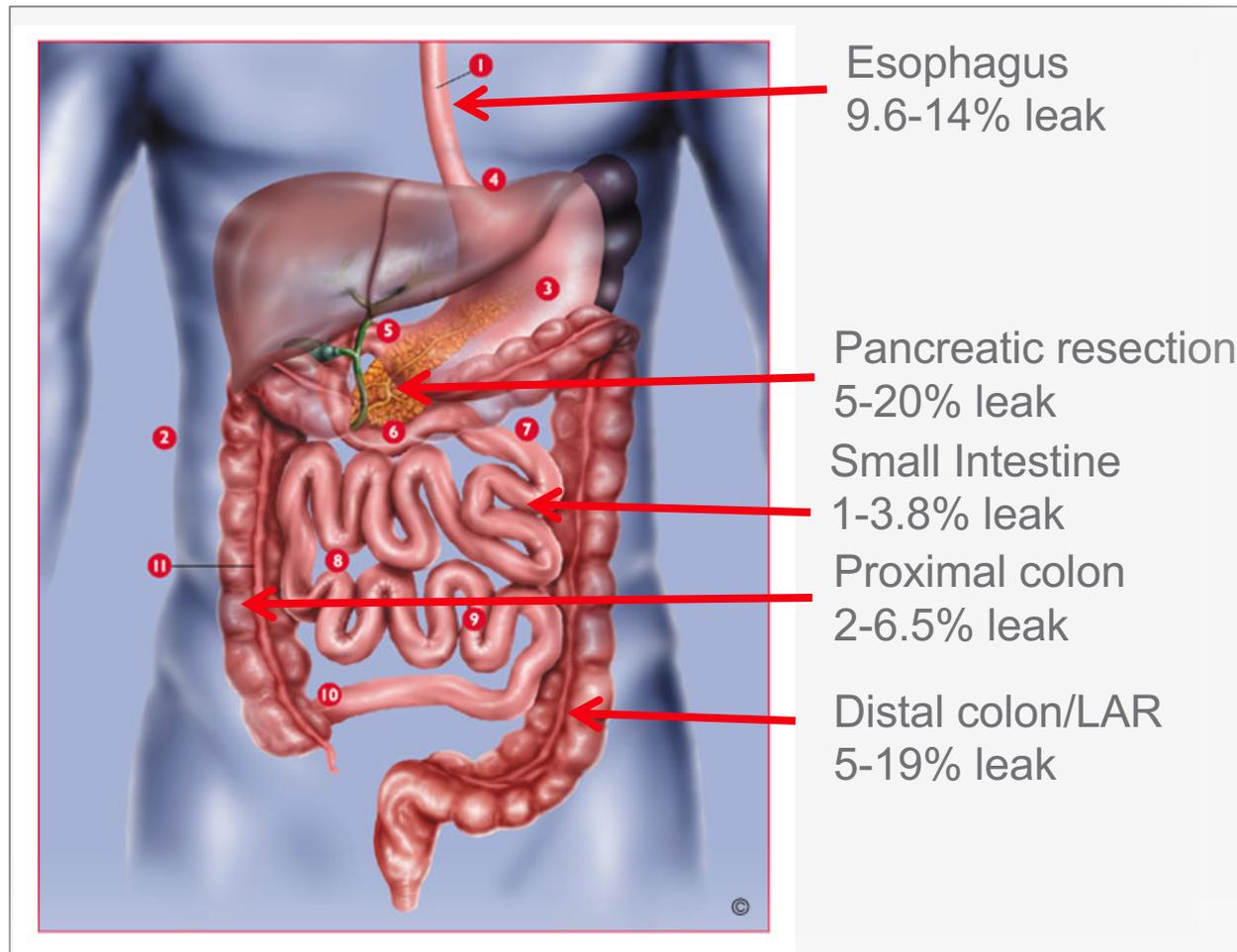
An anastomotic leak is one of the most severe complications of GI surgery, including common procedures:

- GI Resections - Lower Anterior Resection, Colectomy, Esophagectomy
- Bariatric Surgery
- Pancreatectomy

The clinical presentation of an anastomotic leak can vary:

- Peritonitis
- Pelvic abscess
- Pain
- Fever
- Tachycardia
- Drainages (Feculent or Purulent)

GI Leak Rates By Site and/or Procedure and Implications



Impact of GI Anastomotic Leaks

- 18% mortality
- Increased hospital Length of Stay (LOS)/
overall cost: for example: colorectal surgical
leaks
 - incurred additional LOS of +32.1 days,
 - increased hospital costs of +\$175,835
- Digestive stomas (ileostomy and colostomy)
- Patient discomfort / decreased QOL

Mechanisms of Action (MOA) of leak(s) are site specific due to local presentation of risk factors such as tissue/cellular morphology, locally present digestive enzymes, microbiota, underlying disease, etc.

Proposed Solutions therefore could also be different vary in order to account for this site specific MOA

Factors Increasing The Risk For Post Operative Leaks

Factors that may contribute to leaks include the following:

- Ischemia
- Steroid use
- Radiotherapy
- BMI > 30
- Diabetes
- Malnutrition
- Inflammatory bowel disease
- Poor wound healing
- Microbial dysbiosis
- Intra-operative hypoxia
- Tension on tissues
- Technical acumen
- Unknown factors – .i.e. leaks occur after uncomplicated surgery without identified risk factors

No standardized approaches other than good technique

* International Journal of Surgery 36 (2016) 183e200

Prevention Strategies to Date

Platform	Categories	Description	Products
Sealants	Biologic	<ul style="list-style-type: none"> Fibrin Glue BioGlue Gelatin 	<ul style="list-style-type: none"> Tisseel*, Tissucol (Baxter) BioGlue (CryoLife) LifeSeal (LifeBond)
		<ul style="list-style-type: none"> Autologous Platelet-Rich Fibrin Sealant 	<ul style="list-style-type: none"> (Vivostat A/S, Allerod, Denmark)
	Synthetic	<ul style="list-style-type: none"> Polyethylene Glycol (PEG) Polyurethane Cyanoacrylate Glue 	<ul style="list-style-type: none"> CoSeal (Baxter) Syls Surgical Sealant (Cohera Medical) GluBran 2 (GEM Italy)
Pads & Patches/ Buttress	Biologic	<ul style="list-style-type: none"> Collagen 	<ul style="list-style-type: none"> TachoSil (Takeda), Veritas (Baxter)
	Synthetic	<ul style="list-style-type: none"> Polyglycolic Acid: Trimethylene Carbonate (PGA:TMC) Intraluminal device (C-Seal) 	<ul style="list-style-type: none"> Seamguard (Gore) buttressing Polyganics B.V
Mechanical Methods		<ul style="list-style-type: none"> Intraluminal tubes Suture Clipping Drainage Compression Anastomosis 	<ul style="list-style-type: none"> Coloshield® (permanent), SBS tube® (absorbable) ColonRing (Novo GI, Israel)
Improved surgical technique		<ul style="list-style-type: none"> Real-time measurement of tissue oxygen saturation Omental wrap 	<ul style="list-style-type: none"> T.Ox™ (ViOptix)



Pros and Cons For GI Leaks Reduction Approaches

Fibrin Sealants / Other Biologics

- Physiological sealing
- Low inflammatory reaction
- No adhesion (pro or con)
- Rapid metabolism (pro or con)

Murphy button Endoluminal Stents (Mechanical barrier)

- Rigidity
- Inflammation
- Foreign body reaction
- Luminal stenosis

Synthetic Sealants

- Strong adhesion
- Inflammation
- Foreign body reaction

Synthetic gaskets Biodegradable rings (Mechanical barrier)

- Inflammation
- Foreign body reaction
- Adhesion
- Luminal stenosis
- Migration

Biomembranes and Patches

- Immunogenicity
- Foreign body reaction

Omental Wrap

- Adhesion
- Stricture

Challenges in Finding Solutions

- Anastomotic leaks are poorly understood and may be multi-factorial
- Well-established associations include:
 - Ischemia
 - Tension on tissue
 - Poor wound healing
 - Intra-op hypoxia
 - Patient health status / pre-conditions
- So far, leaks have been addressed mainly through mechanical means or surgical technique.
- We propose to launch a multi-disciplinary effort to enhance understanding of the multi-factorial nature of anastomotic leakage and invite innovators to propose research efforts to address them.

Summary

- A GI leak is a critical post-operative complication of procedures related to surgical anastomosis of the GI tract.
- The reasons for anastomotic leaks are poorly understood.
- The leak rate for GI anastomosis varies from 1-20% depending on the location, procedure and other risk factors and has not changed significantly for 40 years.
- Leaks are often diagnosed late because of nonspecific symptoms and suboptimal diagnostic approaches. Typically they occur from 3-7 days post-op and can result in infection, sepsis, and death.
- There is no clinically representative preclinical model of anastomotic leaks.
- Multiple solutions have been tried, addressing the problem mainly as a mechanical one.

Post-surgery GI leaks are a major medical problem with high morbidity and mortality.
Novel solutions are needed.