ACUTE COLONIC PSEUDO-OBSTRUCTION

= OGILVIE SYNDROME

19.01.14

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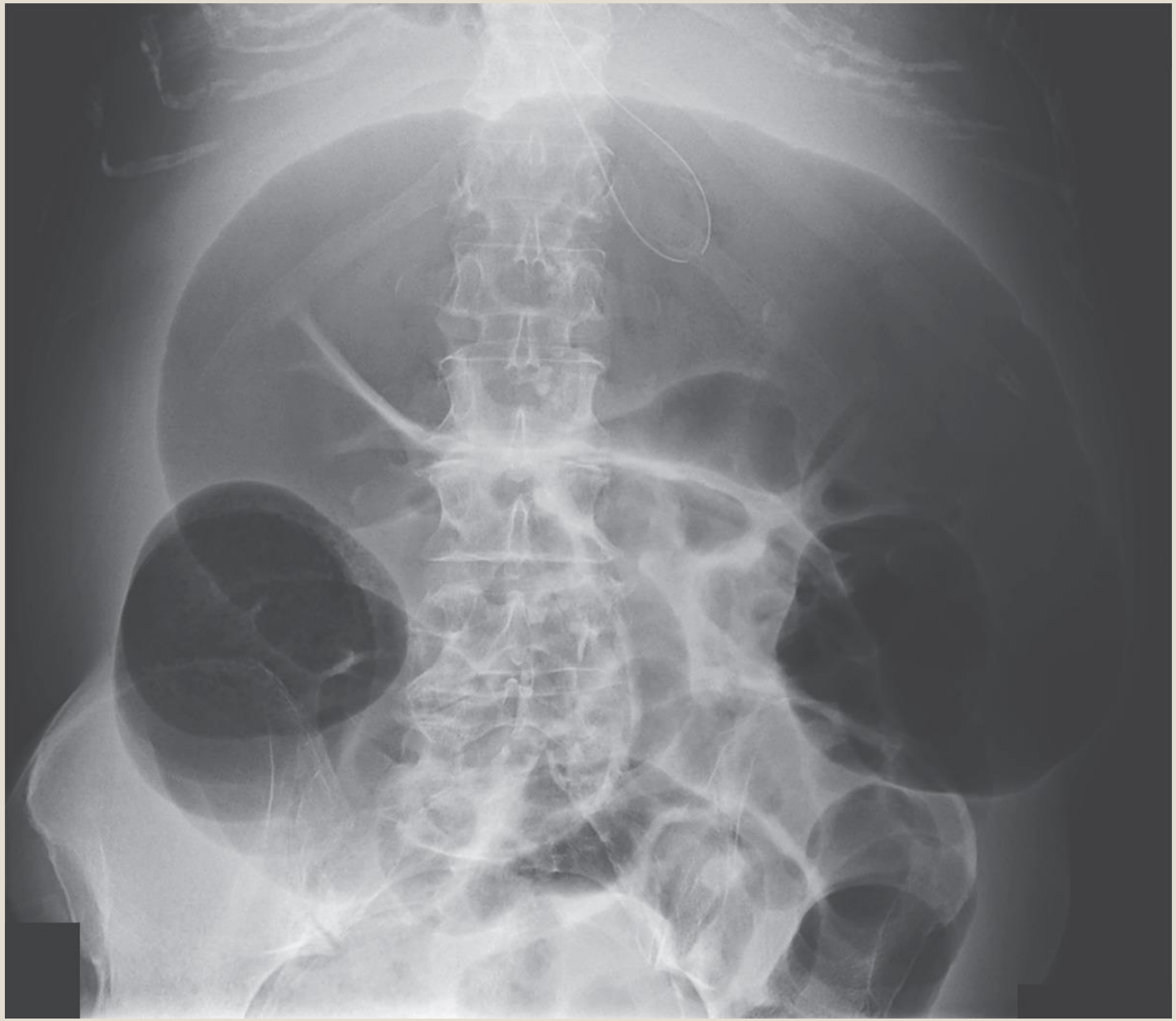
Acute colonic pseudo-obstruction

- **= Ogilvie syndrome**
  - First described by Sir William Ogilvie in 1948
    → use of this term discouraged d/t ambiguity
  - Many overlapping terms
    - adynamic ileus, pseudo-megaolon, non-mechanical large bowel ileus, intestinal pseudo-obstruction…

- **Rare condition** characterized **by acute colonic dilatation in the absence of mechanical obstruction or extrinsic inflammatory process**

- DDx
  - toxic megacolon (inflammatory, infective cause) or chronic intestinal pseudo-obstruction



Epidemiology

- Incidence : rare, 100/10000 inpatients admissions
- Mortality : 9.4%(1998) ~ 6.4%(2011) (d/t over-diagnosis?)
- Colonic perforation in 10-20% ➔ mortality up to 45%
  - ✓ risk factor : cecal diameter, duration of dilatation

- **Elderly, comorbid patients**
  - 50% : Acute illness on a background of chronic disease (cardiac, respiratory, neurological disease)
  - 50% : Post-op (cardiothoracic, orthopedic, abdominal, neurosurgical)

Etiology, pathophysiology

The pathophysiological mechanisms remains unclear

- **Autonomic imbalance**
- Colonic reflex arcs
- Intrinsic colonic dysfunction
- Chronic disease and pharmacological factors
- Obstetric causes
- Metabolic factors
- Viral enteroneropathy
- Other hypothesis

Autonomic imbalance

Most commonly suggested mechanism, Key role

- **Sympathetic vs. Parasympathetic tone**
  - Relative excess of sympathetic over parasympathetic tone
  - Increased Sympathetic And/Or Reduced Parasympathetic signal

- Sympathetic from paravertebral ganglia
  - Proximal colon appears to have a richer sympathetic innervation
- Parasympathetic supply via vagus nerve(mid gut) or Sacral outflow(hind-gut)

- In ACPO, transition point occurs usually near the **splenic flexure**

  → transition in innervation for both sympathetic & parasympathetic supply

  ➔ Supporting autonomic imbalance as a key step

Autonomic imbalance

- Most patients have **acute** illness → increased **sympathetic** drive ➔ potentially contributing **autonomic imbalance** at the level of colon

- ACPO cannot be reproduced in human or animals by splanchnic or pelvic nerve transection → more complex pathogenesis than excess or deficiency of autonomic activity alone

- Neostigmine (AchE inhibitor)

Colonic reflex arcs

- Several spinal and ganglionic reflex arcs
  - involved in regulating intestinal motor function
- Colonic inhibitory reflex
  - inhibition of proximal colon activity in response to distal colonic distention, Proximal distension also causes a reduction in basal intraluminal pressure in distal colon
- Via afferent mechanoreceptors synapsing with adrenergic efferent neurons in the prevertebral ganglia and spinal cord
- **Success of epidural anesthesia, splanchnic nerve block** as evidence for this mechanism

Intrinsic colonic dysfunction

- **Interstitial cell of cajal (ICC)** : Modulated by the ENS, resulting in the rhythmic contractile activity of intestine

- Despite their importance, **Few studies** were identified specially investigated the role of ICC in ACPO
  - Jain et al, in ACPO, normal number and distribution of ICC, however, affected ICC function remained unknown
  - Choi et al, reported reduction and degeneration of enteric ganglionic cell in resected specimen of patient with pseudo-obstruction, but it is unclear whether these patients had ACPO or CIPO

➔ **Important.. But still remains unknown**

Chronic disease and pharmacologic factors

- Many ACPO patients are **elderly and have chronic disease**

  → occurring further acute physiologic insult

- The ENS and its extrinsic regulation are affected in several conditions commonly associated with **DM, Parkinson's disease, Alzheimer's disease**
- ENS, ICC degenerated **with age**

- Patients with chronic condition are also more likely to be on multiple medication affecting colonic motility
  - including anticholinergics, opiates, CCB, psychotropic drugs,
- clonidine & amitraz (a2 agonist) associated with ACPO

Elderly
Chronic disease
Drugs
Nerve degeneration

Obstetric causes

- The OP most commonly resulting in ACPO = **C/sec**
- Also after normal **delivery** and instrumental delivery
- **Preeclampsia, multiple pregnancy, antepartum hemorrhage, placenta previa**

- However, it remains unclear how..
  - ? Compression of parasympathetic plexuses by gravid uterus
  - ? Uterus may fall back into pelvis causing mechanical obstruction at RS colon

- Pregnancy (↑ progesterone, glucagon) → diminish the tone of large bowel
- Prostaglandin (involved in parturition) as a possible contributors to ACPO

Metabolic factors

- A disrupted "***milieu interieur***" is common in ACPO
  → precipitate or exacerbate the effect of altered autonomic functions or other mechanisms

- Renal failure, **Electrolyte** disturbances often accompany ACPO
  - whether this is a cause or effect of the pseudo-obstruction
  - Alteration of "K" or other ion → alter ICC pacemaker or smooth muscle activity
  - E' imbalance has been identified as a predictor of a poor response to neostigmine

- Prostaglandin, cytokines (TNF-a, IL-6, IL-8, IL-1b)
  - not yet been investigated in ACPO

- PG have been implicated in post-op ileus, CIPO, acute small bowel dysmotility, affect ICC function ➔ no study about ACPO

Viral enteroneuropathy

- Several viral infection
  - Herpes zoster reactivation in low thoracic or lumbar distribution
  - Disseminated zoster
  - Acute CMV
  - Severe dengue

- Mechanism
  - Virus in enteric ganglia may result in a sympathetic autonomic neuritis
  - Local inflammation with afferent stimuli to the sacral nerve roots and blockage of parasympathetic supply
  - Viral spread from dorsal root ganglia may interrupt sacral parasympathetic pathways
  - post-viral dysautonomia

Other hypothesis

- ? Compromised vascular supply to the colon (in early reports)
  →now thought to represent an exacerbating complication rather than cause
- ? "Hinge-kinking" at the transition
  →intra-op, radiological findings generally suggesting a "gradual" transition in colonic caliber
- "air-fluid lock syndrome" and colonic distension d/t aerophagy in chronic respiratory disease

Table 2 Prevalent medical and surgical risk factors for acute colonic pseudo-obstruction

Category	Risk factors
Surgical	Cardiac surgery, solid organ transplantation, major orthopaedic surgery, spine surgery
Cardiorespiratory	Shock, myocardial infarction, congestive heart failure, chronic obstructive pulmonary disease
Neurological	Dementia, Parkinson's disease, Alzheimer's disease, stroke, spinal cord injury
Metabolic	Electrolyte imbalance, diabetes, renal failure, hepatic failure
Medications	Opiates, anti-Parkinson agents, anticholinergics, antipsychotics, cytotoxic chemotherapy, clonidine
Obstetric/ gynaecological	Caesarean section, normal vaginal delivery, instrumental delivery, preeclampsia, normal pregnancy, pelvic surgery
Infectious	Varicella-zoster virus, herpes virus, cytomegalovirus
Miscellaneous	Major burns/trauma, severe sepsis, idiopathic

Wells CI *et al*. Mechanisms of acute colonic pseudo-obstruction

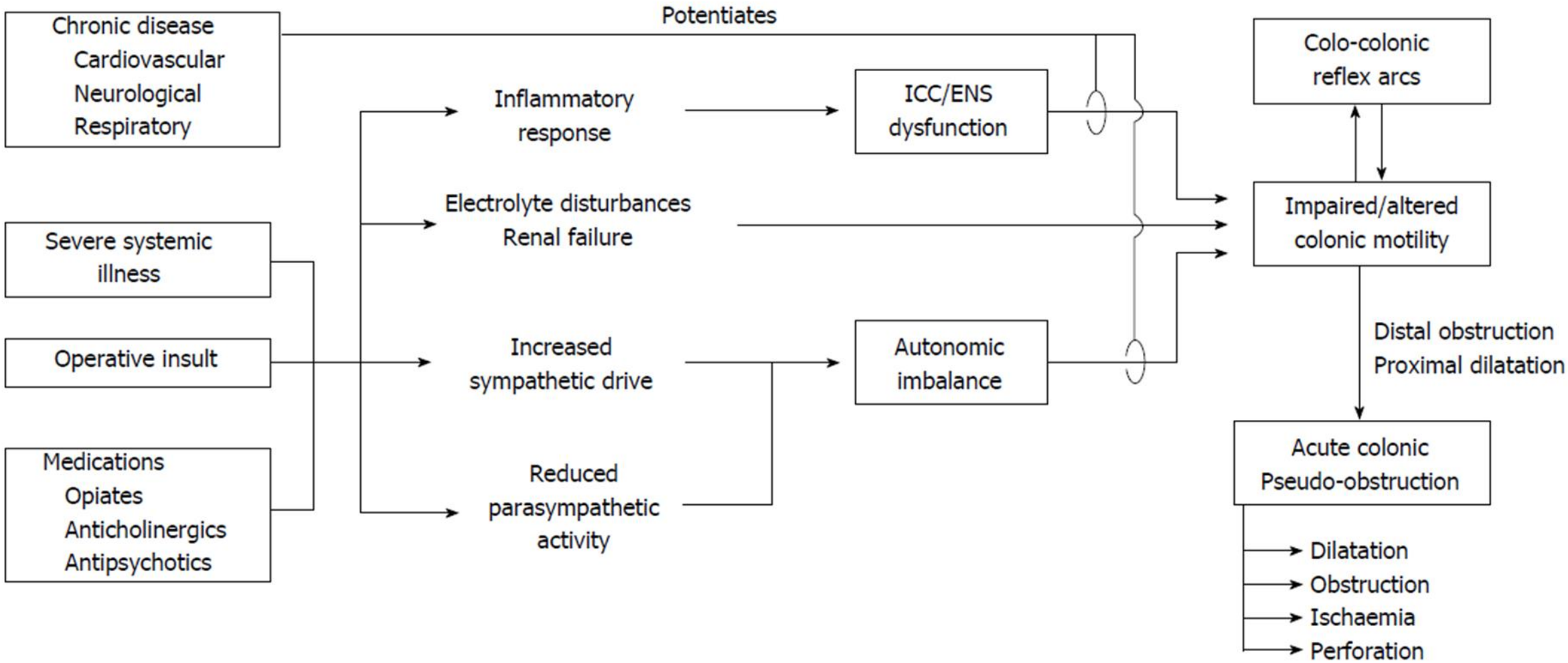


Figure 1 Pathophysiological factors that have been implicated in the development of acute colonic pseudo-obstruction. ICC: Interstitial cells of Cajal; ENS: Enteric nervous system.

Wells CI *et al*. Mechanisms of acute colonic pseudo-obstruction

Clinical presentation

- **Eldery + multiple comorbidity + recent Op Hx**

- Sx
  - Abdominal pain, distention, N/V
  - Inability to pass flatus and stool (common but not invariably present)
  - Diarrhea (hypersecretion of water)
  - Fever in 78% pt. with ischemic perforated bowel, 31% pts with viable bowel

- P/Ex
  - Significant abdominal distention with tympany, high-pitched sound or absent sound
  - Abdominal Td (ischemic bowel or perforation)

Diagnosis

- Dx of exclusion, **rule out any mechanical obstruction**
- Lab test : WBC, CRP, E' . . .
- Diagnostic colonoscopy : NOT advised, not helpful
- Radiologic study : X-ray, CT
  - rule out cecal or sigmoid volvulus, other obstructing lesion
  - perforation, small bowel obstruction
  - cecal diameter (9-12cm) → impending perforation
  - **CT : ESSENTIAL in assuring no source of mechanical obstruction**
- Typical CT finding
  - **proximal colonic dilatation with a transition point at the level of the splenic flexure**
- Gastrograffin (water-soluble contrast agent)

Complication and Maximal cecal diameter

- **Colonic perforation 15-20%, Mortality 40-50%**

- CT : pneumoperitoneum, free peritoneal fluid, pneumatosis intestinalis
  → strong suspicion of colon perforation, urgent laparotomy
- Maximal tolerable diameter of cecum : 9cm-12cm

- **Poor prognosis factor**
  - Age, ischemia, Cecal perforation, delay of more than six days in colonic decompression

Treatment

1. Conservative treatment
2. Medical therapy
3. Endoscopic therapy
4. Surgical therapy

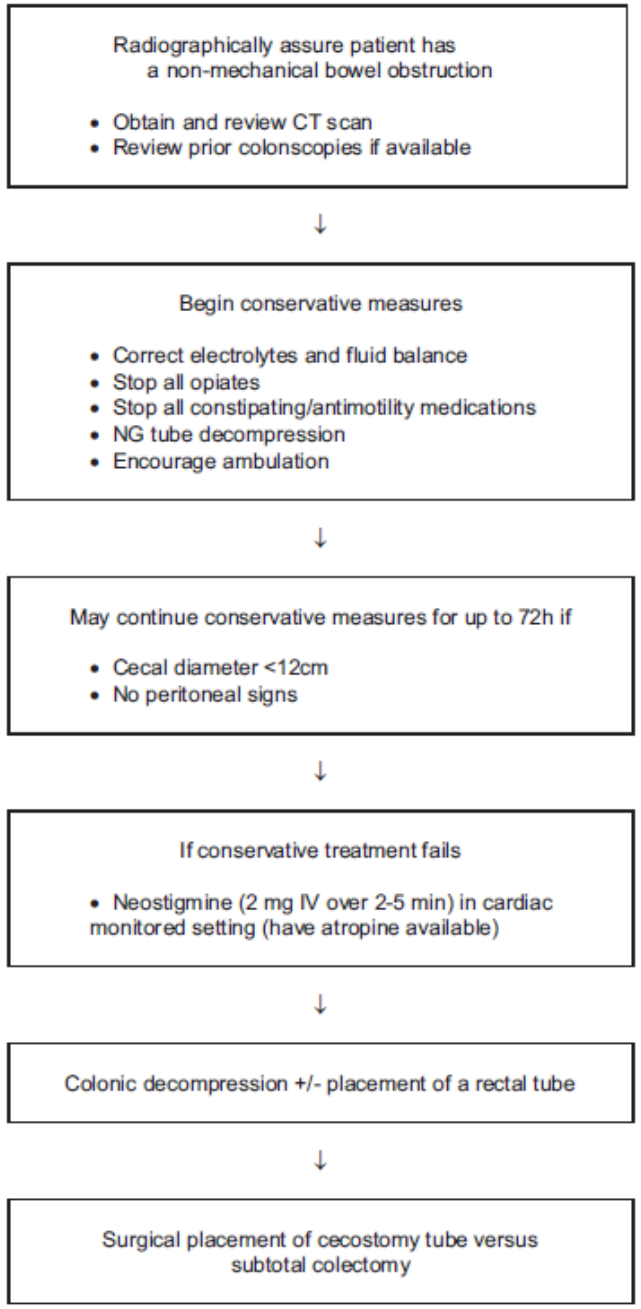


Fig. 2 An evidence-based treatment algorithm for acute colonic pseudoobstruction.

Conservative treatment

- **Decompression : fasting, NG tube, Rectal tube**
- **IV fluid**, **Electrolyte correction** (K, Mg)
- **Discontinuation of medication**
  anticholinergics, atrophinics, antihypertensive, anti-Parkinson med, antidepressant, neuroleptics, opiates, clonidine
- Osmotic laxative : contra-indicatied (fermentation, gas distention↑)
- **Position** : Ambulation, Knee-chest position or Rt/Lt decubitus

- Successful in **70**% (by Wegner)
- Should **not** be continued beyond **3 days**
  - Beyond a delay of six days → increased risk of perforation

- Effectiveness : Abdominal distention↓, Gas passing/stool passing, Cecal diameter↓

Pharmacologic treatment

- **Neostigmine, Statistically significant more effective than placebo (3 RCT)**
  - Reversible cholinesterase inhibitor
  - 91% responded to a single IV neostigmine 2mg (Ponec et al)

- Administration
  - 2-2.5mg IV bolus over 3-5min
    → colonic motility within 20-30min, success rate 80%
  - 2^{nd}/3^{rd} bolus can be administered
  - infusion pump : 0.4-0.8mg/h over 24hr

- Effectiveness of neostigmine
  - 64~91% after 1^{st} dose
  - 40%~100% after 2^{nd} dose
- Recurrence
  - up to 38%

Pharmacologic treatment

- **Contraindication of neostigmine**
  - acute urinary retention
  - gastro-duodenal ulcer
  - acute coronary syndrome
  - Acidosis
  - asthma, bronchospasm
  - bradycardia, b-blockage therapy
  - renal insufficiency
  - mechanical bowel obstruction, colonic perforation

Pharmacologic treatment (기타)

- **Oral administration of PEG : to prevent recurrent ACPO**
- **Grastrografin** enema : hyperosmotic water-soluble contrast agent, laxative properties
  - Effective in 78%; mean decrease of 4.6cm in cecal diameter

- Stimulant of motility : cannot e recommended
  - Erythromycin, success rate is only 40%/recurrence 50%
- Tegaserod, nicotine patches, metoclopramide, indomethacin, ibuprofen – cannot be recommended

Epidural anesthesia

- **Sympathetic hypertonia** is partly responsible for the onsetb and persistence of megacolon
- Sympathetic nerve blockage creates splanchnic vasodilatation, interrupt the neural flow of inhibitory pain receptors

Colonoscopic exsufflation

- First performed in 1977
- Difficult (lumen is filled with stool, residue of contrast)
- Risk of insufflation required to insert the colonoscopy → perforation risk
- To detect ischemia (requiring surgical treatment)

- **No preparation is required**
- **Sedated with benzodiazepine but narcotics should be avoided**
- **The colonoscope can be passed Rt colon in 85%, but not absolutely necessary to reach the cecum**
  - ✓ **If the hepatic flexure cannot be turned, exsufflation starting in the transverse colon is often sufficient**
- **Demonstration of ischemic colonic mucosa requires that endosopy be terminated and converted to surgery**

Colonoscopic exsufflation

- Effectiveness (in retrospective study)
  - **Decreased cecal diameter** : 12.8cm → 8.7cm (strodel et al) (P<0.01)
  - **immediate success varied fro 61% ~ 95%**
  - recurrence ACPO may be as high as 40%
  - perforation 2%, mortality 1%

- Definition of successful endoscopic exsufflation
  - Reduction of the cecal diameter by at least 3cm

- Placement of a long multi-perforated large-bore drainage tube
  - to prevent recurrence, flushed every 4-6 hr
- Instillation of PEG also useful in preventing recurrence

Percutaneous cecostomy

NOT recommended

- Percutaneous cecostomy guided by either radiology or colooscopy has been reported in literature but cannot be recommended for general usage at this time
  - percutaneous endoscopic cecostomy(PEG) has a complication rate of 40% (abscess, bleeding, hematoma, perforation, stomal retractuion)

Surgery

- Surgery is the treatment of **last** resort
  - Only when above-mentioned therapies have **failed**
  - or there are clinical or radiological indications of **perforation**

- Colonic ischemic and perforation occurs in 3-10% pts
  - who have risk factors including cecal diameter > 12cm, duration of dilatation > 6 days

- Tube cecostomy, cecostomy, colostomy
  - determined on a case-by-case basis

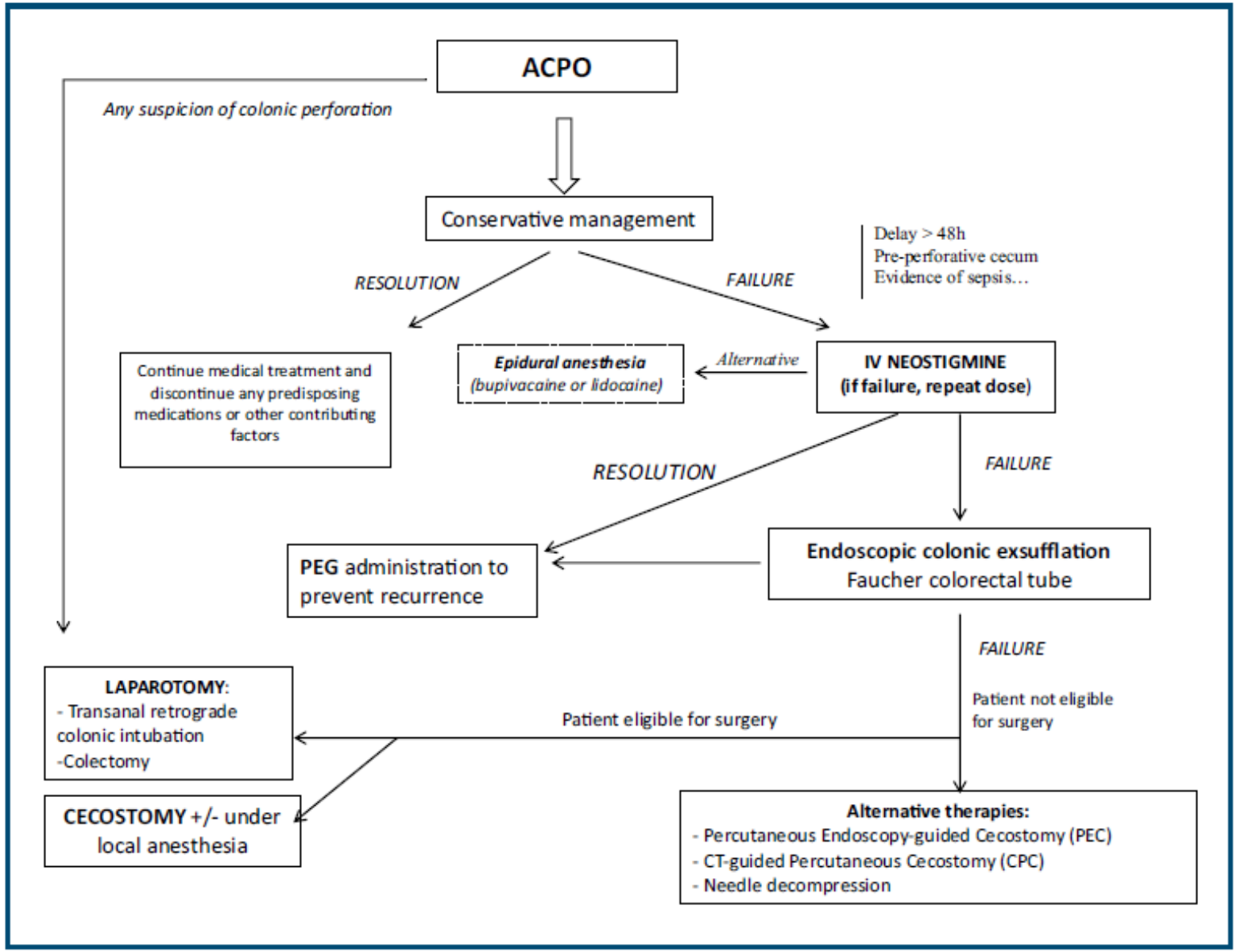


Figure 3. Decisional algorithm for management of acute colonic pseudo-obstruction (ACPO). PEG: polyethylene glycol.

Reference

1. Wells, C. I., et al. (2017). "Acute colonic pseudo-obstruction: A systematic review of aetiology and mechanisms." World J Gastroenterol **23**(30): 5634-5644.
2. Pereira, P., et al. (2015). "Ogilvie's syndrome-acute colonic pseudo-obstruction." J Visc Surg **152**(2): 99-105.
3. Vogel, J. D., et al. (2016). "Clinical Practice Guidelines for Colon Volvulus and Acute Colonic Pseudo-Obstruction." Dis Colon Rectum **59**(7): 589-600.
4. Chudzinski, A. P., et al. (2015). "Acute colonic pseudoobstruction." Clin Colon Rectal Surg **28**(2): 112-117.