

# Malignant obstruction of the GI tract

How can we overcome the obstacles to conduct clinical studies and what are the most burning questions to answer?

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Hartwig Kørner MD, PhD  
*Professor of Surgery*

Dept. of GI Surgery  
Stavanger University Hospital, Norway

Regional Centre of Excellence of Palliative Care  
Haukeland University Hospital, Bergen

Dept. of Clinical Medicine  
University of Bergen, Norway



**7th International Seminar  
of the PRC and EAPC RN**

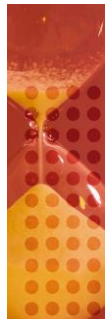
# No disclosures



# Malignant obstructions of the GI tract – the "Big Four"

- Esophagus
- Gastric outlet
- Biliary obstruction
- Malignant bowel obstruction

Self expanding metal stent (SEMS)  
High degree of consensus



# Malignant bowel obstruction – most complex, most burning condition!

- MBO - definition

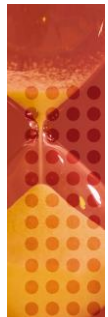
- Gross infiltration of the abdominal cavity by malignant tumor
- Irresectable, incurable
- Broad spectre of clinical presentation
- Severe condition – great symptom burden
- Remaining life time often short – but not always

## Treatment – highly controversial

- Medical?
- Surgery?
- When to operate
- Who to be offered surgery?
- Beneficial?

# What do we know

- 50% of patients – ovarian cancer
- 40% of patients – GI malignancies
- 10% of patients – extra-abdominal cancer with intra-abdominal spread
  - Breast cancer
  - Malignant melanoma



# Literature on MBO

- Mostly retrospective case series with limited sample sizes
  - selection bias
- Heterogenous end points, large variations reported
  - resolution of obstruction
  - complications & survival
  - definitions & terminology: "palliative"  $\approx$  "non-curative"
- Lack of patient-reported outcomes
- Absence of RCT's
- **Cochrane: no firm conclusions possible**

Cousins et al. Cochrane Database Syst Rev 2016

# What we do not know ...

- The true incidence figures
  - Important basic knowledge
- Clinical key knowledge
  - Benefits & harms of treatment
  - Currently personal experience & empiric knowledge
- How to measure treatment outcomes

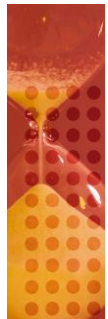
*Most burning research questions*



# Symptoms & signs of MBO

- Gradually impaired bowel transit
  - Nausea, vomiting, constipation, diarrhea
- Gradually extended abdomen
- Colicky and/or constant pain
- Nutritional failure
  - Loss of weight
  - Loss of appetite
  - Dehydration
- Fatigue
- Loss of function
- Depression ...

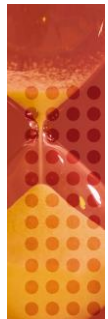
*Patient & surrogates:  
"You are surgeon,  
you've got to do something!"*



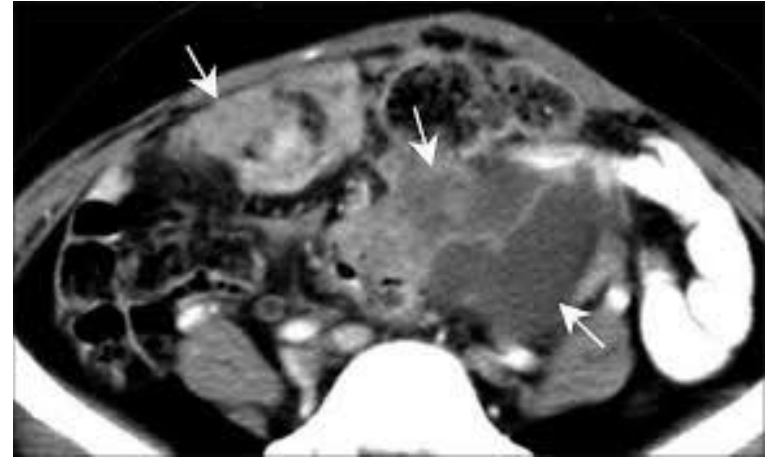


# Clinical presentation

- Localised disease
  - E.g. pelvis, colon, small bowels
  - Single vs. several bowel loops involved
  - proximal vs distal obstruction
- Minimal vs multiple gross infiltration of abdominal cavity
- Large variations – need of highly individual approach



# Diagnostic challenges



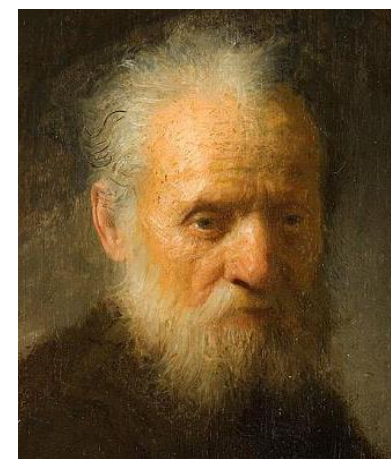
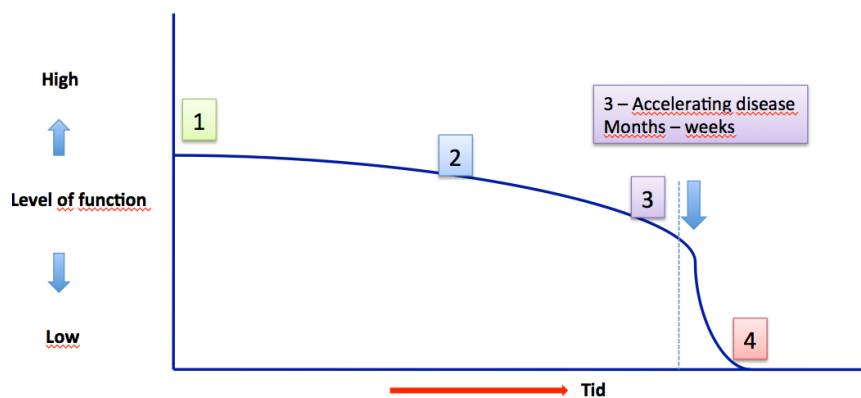
# Treatment options

- Surgery
  - Stoma, bypass, resection
- Minimal invasive interventions
  - Self expanding metal stent (SEMS)
  - PEG – gastric venting tube
- Conservative treatment
  - Bowel secretion
  - Bowel motility
  - Anti-inflammatory
  - Antiemetics, analgetics
- Combinations



# Treatment decisions

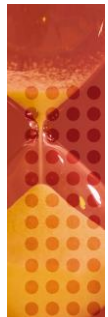
- Surgical intervention - feasible vs. useful
  - "The feasibility of an operation is not an indication alone"
- Individual treatment goal?
- Where is the patient in the disease trajectory?
- Where is the patient in trajectory of her/his life?



Rembrandt – Self portraits

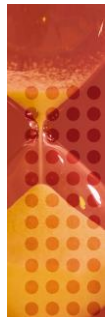
# Core research questions

- What is the true incidence of MBO?
- How to predict the benefit or harm of various treatment options
  - intervention vs conservative vs combinations
  - over- vs undertreatment
- How to measure the individual treatment goal



# Incidence of MBO

- Retrospective single institution studies:
  - Large variations – <10-30%
- Population-based figures from national registries
  - Problem: no specific ICD-kode
  - how to identify patients with MBO?



# True incidence of MBO?

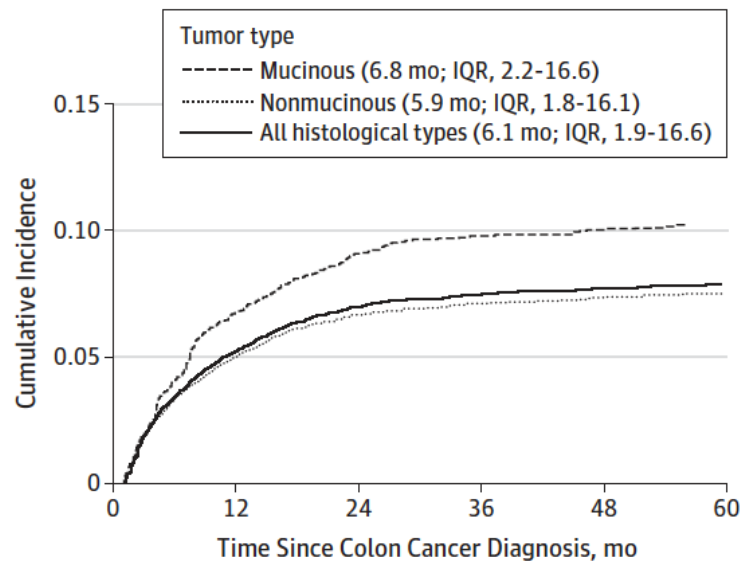
- SEER-Medicare database 1991-2005
  - 26% of US population
  - Patients with stage IV CRC,  $\geq 65$  years
  - Bowel obstruction  $\geq 30$  days after primary diagnose
- Selection of study cohort – exclude benign obstruction
  - based on assumptions and combinations of ICD codes and claims from health care providers



Winner et al. *JAMA Surg.* 2013

# 8% incidence of MBO – true?

Figure. Cumulative Incidence of Hospitalization for Bowel Obstruction Over Time

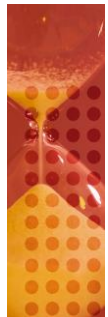


No. Still Alive						
Mucinous	10811	3311	1400	705	393	226
Nonmucinous	1742	523	217	115	72	50



# Questions

- The real true incidence?
  - limited to CRC stage IV at diagnosis, age  $\geq 65$  yrs ...
  - Gynecological cancer not accounted for
- Need for prospectively maintained population-based registry?
- Norwegian Patient Registry
  - Tailored cohort
  - Bowel obstruction and specific ICD10 codes and specific treatment codes ... ?



# Benefits and harms of treatment

- Surgery or not?
  - Over- vs. undertreatment
  - Equipoise of treatment options?
  - Net health effect – do the burdens of treatment annihilate the intended effect?
- Presently no RCT conducted!



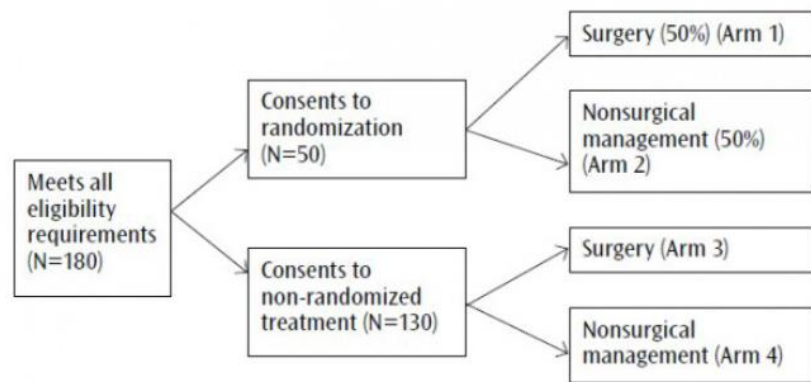
# Prospective comparative effectiveness trial for malignant bowel obstruction: SWOG S1316 trial

- Are there differences in H-QoL outcomes for patients with MBO who receive surgical vs nonsurgical intervention?
- Are there clinical factors that predict better health-related QoL outcomes for patients with MBO who receive surgical or nonsurgical intervention?
- Primary outcome: H-QoL of "good days"
  - days alive and outside of hospital during the first 91 days

Krouse. Bull Am Coll Surg 2015

# Design

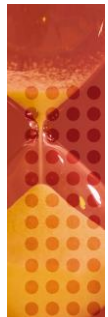
- Eligibility
  - candidate for surgery
  - indication for operation
  - agreement on non-surgical treatment as reasonable
  - no emergency
  - no primary diagnosis of bowel obstruction



All patients will be followed for 53 weeks.

# How to measure outcomes of MBO

- Procedure-related morbidity & morbidity
- Survival
- The ultimate outcome – individual treatment goal
  - relief of specific symptoms –pain, vomiting ...
  - performance & activities
  - achieve specific goals for remaining life time



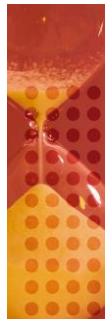
# Double-Blind, Placebo-Controlled, Randomized Trial of Octreotide in Malignant Bowel Obstruction

- Aim: Effect of octreotide added to standard conservative treatment
- Primary outcome: Patient-reported number of days free of vomiting at 72 hours
- Main outcomes
  - 87 participants
  - 17 (octreotide) vs 14 (conventional),  $p=0.67$
  - reduced # of vomiting episodes ( $p=0.019$ )
  - more likely to receive butylhyoscamine for colicky pain

Currow et al. J Pain Symptom Management 2015

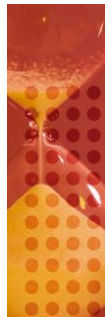
# Outcome measure – who's perspective?

- Primary outcome: Patient-reported number of days free of vomiting at 72 hours
- Individual treatment goal
  - reduced vs free of vomiting?
- Who defined this treatment goal?



# How to measure the individual treatment goal?

- Challenge:
  - General measurability of relief of specific individual symptom
  - Infra-additive effect of morbidity caused by treatment
  - Irreversibility of interventions as compared to conservative treatment





# EORTC – validated H-QoL tools

- Well established tools – Gold standard
- Well differentiated moduls
  - Various diagnoses
  - Palliative patients
- BUT
  - Who made the questions?
  - Do they really measure the individual treatment goal?



# Proposed solutions

- PSOS<sup>1</sup> – Palliative surgical outcome score

$$\text{PSOS} = \frac{\text{Number of hospitalised days}}{\text{Number of symptom-free non-hospitalised days (max. 180)}} (\%)$$

- $\geq 75\%$  outside hospital is considered as satisfactory
- H-QoL of "good days"<sup>2</sup>
  - days alive and outside of hospital during the first 91 days

<sup>1</sup> McCahill et al. Ann Surg Oncol 2003

<sup>2</sup> Krouse. Bull Am Coll Surg 2015

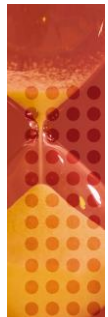
# PROMs

- PROM recently recognised as highly important outcome measure
    - research
    - Quality of modern health care systems
  - PROM to be incorporated in Norwegian Cancer quality registries
    - Prostate cancer – established pilot project
    - Breast
    - Colorectal
- } Work in progress



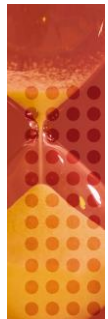
# Obstacles to research (1)

- Establishment of clinical databases
  - How to identify patients
    - MBO is not a defined entity
    - ICD-10: K56.6 – mechanical bowel obstruction
    - National registries: Neither CRN nor NPR
  - Prospective population based dataset
    - Infrequent occurrence
    - Multi centre – national approach
    - Need of dedicated health personnel



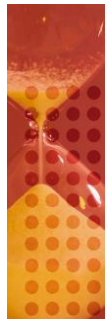
# Obstacles to research (2)

- Study design
  - Observational vs RCT?
- RCT:
  - Equipoise – individual preference?
    - Resection vs stoma ?
    - Surgery vs non-surgical?
  - Sample size and recruitment
  - Outcome measures



# Obstacles to research (3)

- General bias towards curative treatment
- Consensus
  - How to define MBO
  - How to diagnose MBO
  - How to select patients who might profit from surgery
  - How to minimize adverse outcomes of surgery
- Adequate PROM



# Conclusion

- Obstacles to research on MBO
  - lack of unselected databases
  - related to research methods and treatment options
  - bias towards curative treatment
- Central research questions
  - True incidence of MBO
  - True benefits & harms of surgery vs. non-surgical treatment
    - selection to either options or combination
  - Outcome measures for the individual treatment goal

