BÄSTA LIVSPLATSEN

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Somatostatin analogues for major symptom control in inoperable malignant bowel obstruction - A review

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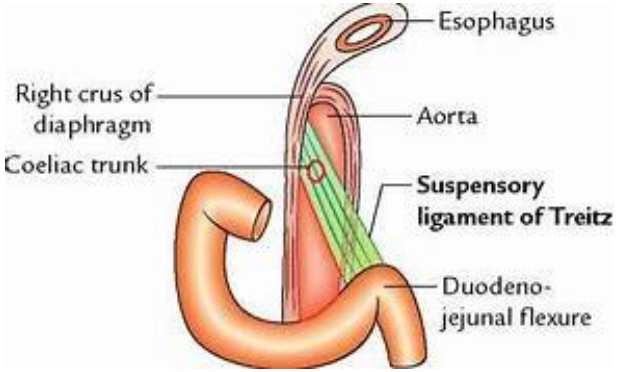
Background

- First specific definition of malignant bowel obstruction (MBO) was proposed in 2007

Major physical symptoms	**Prevalence**
▪ Continuous abdominal pain	>90% of patients
▪ Intermittent abdominal colicky pain	72-76%
▪ Nausea ± vomiting	60-70%



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Common treatments used in MBO

- Surgery or self expanding metallic stents (SEMS)
- Nasogastric tube (NGT) and percutaneous endoscopic gastrostomy (PEG)
- Medical symptom management:

SYMPTOM	STANDARD TREATMENT
Continuous abdominal pain	Opioids
Intermittent colicky abdominal pain	Hyoscine butylbromide, scopolamine butylbromide or glycopyrrolate
Nausea / Vomiting	Haloperidol, anticholinergics or **somatostatin analogues**
Other	Steroids, H2-blockers or proton pump inhibitors

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Human somatostatin and the analogues

- Human somatostatin
  - Reduction of intestinal secretion -> reduced hyperdistention
  - Reduction of intestinal spastic activity

- The first analogue was synthesized in 1979
- **Octreotide** is the most commonly studied (and used)
  - Same biological effects as somatostatin but with greater specificity, potency and a longer action
  - Onset 30 min, half-life 90 minutes, and duration 8 hours
- Other analogues: **Lanreotide** and **Pasireotide**

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Aims and objectives

- To evaluate the evidence of somatostatin analogues efficacy for major symptom control in adult patients with inoperable MBO

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Material and methods

- Systematic search in PubMed and Cochrane Library database (31th of March 2018)

- Separate searches made in EAPC, PCF, American Journal of Hospice and Palliative Medicine, Journal of Pain and Symptom Management , Supportive Care in Cancer and Palliative Medicine

- Hand search of reference list of all included articles, of 16 reviews and of 5 systematic reviews

- An additional search in PubMed was conducted on 30th of December 2018

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Inclusion and exclusion criteria

- Inclusion criteria
  - Randomized controlled studies (RCTs), or non-randomized controlled studies
  - Adults, aged 19+ years, with inoperable MBO
  - Studies evaluating change in major symptoms in MBO; abdominal pain, nausea or vomiting
- Exclusion criteria
  - Studies comparing somatostatin analogues with surgery, SEMS or PEG
  - Articles in other languages than English

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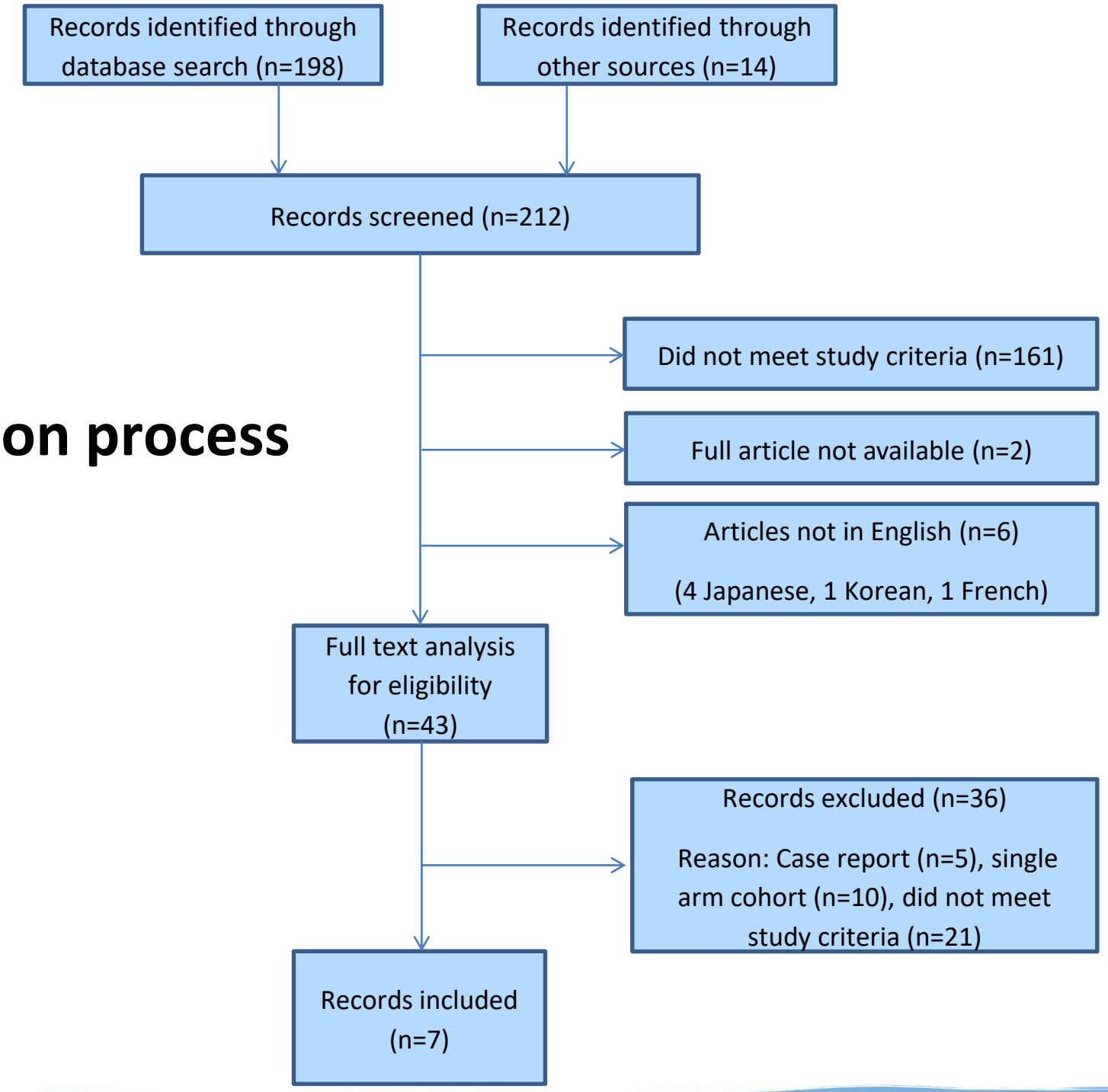
Study selection process



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Quality assessment

- **The Cochrane Risk of Bias tool** was used for assessment of each study. This tool evaluates 6 domains of the study design:
  - Random sequence generation
  - Allocation concealment
  - Performance
  - Detection
  - Attrition
  - Reporting
- Each study is classified as high, unclear or low risk of bias for each domain

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Results

- Seven RCTs (n=430)
  - Three RCTs compared **somatostatin analogues** with **placebo**
  - Four RCTs compared **octreotide** with **hyoscine butylbromide**

  - Primary endpoints: Either **vomiting** OR **volume of NGT-secretion**
  - Reduction of **nausea** and **pain scores** were secondary endpoints

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Somatostatin analogues vs placebo

Author, year, participants, substance, and time of follow up	Primary endpoint and main results	Comments	Risk of bias
Laval G, et al, 2012 Octreotide		Problems with recruitment and withdrawal No statistical analyses could be made	High
Mariani P, et al, 2012 (n=80) Lanreotide Follow up: 20 days	Vomiting episodes -> No statistical significance in intention-to-treat population	Significance was seen in the per-protocol analyses	High
Currow D, et al, 2015 (n=87) Octreotide Follow up: 3 days	Days free of vomiting -> No significance between the groups	Significance in reduction of total number of vomiting episodes	Low

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Octreotide vs Hyoscine Butylbromide

Author, year, participants, and time of follow up	Primary endpoint and main results	Comments	Risk of bias
Ripamonti C, et al, 2000 (n=10) Follow up: 3 days	Amount of NGT secretion -> Significant reduction	All patients with NGT	Unclear
Mercadante S, et al, 2000 (n=18) Follow up: 3 days	Vomiting episodes -> Significant reduction day 1-2	No patients with NGT	Unclear
Mystakidou K, et al, 2002 (n=68) Follow up: Until death	Vomiting episodes -> Significant reduction on day 3, but not later		Unclear
Peng X, et al, 2015 (n=96) Follow up: 3 days	Vomiting episodes OR amount of NGT secretion -> Significant effect day 1-3 OR day 1-2	Patients with or without NGT	Unclear

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Secondary endpoints and adverse effects

- Summary of secondary endpoints
  - Improvement of nausea
    - In all 4 studies comparing octreotide with hyoscine butylbromide
  - Effect on pain scores was investigated in 6 out of 7 studies
    - Improvement of *constant abdominal pain* in 2 studies
    - No improvement of *intermittent colicky pain* in any study

- Adverse effects
  - Generally mild
  - Minor skin reactions, local inflammation or erythema, mild arthralgia

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Conclusion

- The role of somatostatin analogues in the medical management of MBO is poorly investigated
- The RCTs are few, short, and mostly very small
- Lack of consensus which outcome should be considered as clinically relevant

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Conclusion

- Some low level evidence supporting the use of octreotide for symptom control in MBO:
  - Reduction of vomiting/NGT-secretion, nausea and continuous abdominal pain compared to hyoscine butylbromide

- The only placebo controlled study with low risk of bias showed no benefit in primary endpoint

- Somatostatin analogues are well tolerated

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THANK YOU FOR YOUR ATTENTION….!