Determinants of treatment: Outcome measures

or how to read studies on diverticular disease

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Outcome: overview

• Problems
• Diagnostic criteria and Classification systems
• Natural course/complications of the disease
• Treatment-related morbidity
• Treatment-related mortality
• Recurrence, persistence
• Costs, quality of life
Outcome measures: problems

Definitions/Classification: Complicated vs. uncomplicated

Reliability of diagnosis/Diagnostic criteria

Studies on diverticulitis and diverticular bleeding

Study design
- retrospective case series
- reviews and guidelines
- prospective open label studies
- prospective observational studies
- decision analysis model (Markov)

Costs

Cause of complications: Disease or treatment-related
Overview

- Problems
- **Diagnostic criteria and Classification systems**
- Natural course/complications of the disease
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### Diagnostic criteria: Examples

<table>
<thead>
<tr>
<th>Author</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horner (1952)</td>
<td>Required symptoms: constipation/diarrhea, cramping, tenderness, fever, leucocytosis</td>
</tr>
<tr>
<td>Zollinger (1968)</td>
<td>„adequate past history tabulated in the hospital records“</td>
</tr>
<tr>
<td>Parks (1969)</td>
<td>„clinical features, together with a) radiological …or b)... pathological evidence“</td>
</tr>
<tr>
<td>Elliot et al (1997)</td>
<td>ICD 9 diagnosis</td>
</tr>
</tbody>
</table>
## Classifications

<table>
<thead>
<tr>
<th>Author</th>
<th>Basis of the classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hughes et al (1963)</td>
<td>Clinical and intraoperative</td>
</tr>
<tr>
<td>Hinchey et al (1978)</td>
<td>Intraoperative or Pathology</td>
</tr>
<tr>
<td></td>
<td>N. b.: Multiple modifications</td>
</tr>
<tr>
<td>Hanson and Stock (1999)</td>
<td>Preoperative (physical, CT, colonoscopy)</td>
</tr>
</tbody>
</table>
## Classifications

<table>
<thead>
<tr>
<th>Finding</th>
<th>Hansen &amp; Stock</th>
<th>Siewert</th>
<th>Hinchey</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Diverticulosis (asymptomatic)</em></td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Acute uncomplicated diverticulitis</em></td>
<td>I</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Acute complicated diverticulitis</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peridiverticulitis, phlegmon (mesocolic)</td>
<td>IIa</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>Abscess (pericolic, mesocolic)</td>
<td>IIa</td>
<td></td>
<td>I</td>
</tr>
<tr>
<td>Pelvic abscess, sealed perforation</td>
<td>IIb</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Free perforation, purulent peritonitis</td>
<td>IIc</td>
<td>III</td>
<td>III</td>
</tr>
<tr>
<td>Free perforation, fecal peritonitis</td>
<td>IIc</td>
<td></td>
<td>IV</td>
</tr>
<tr>
<td>Recurrent diverticulitis, fistula</td>
<td>III</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

mod. Hoffmann, Kruis 2005
## Alternative classifications

<table>
<thead>
<tr>
<th>Finding</th>
<th>Ambrosetti</th>
<th>Hughes</th>
<th>Sher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diverticulosis (asymptomatic)</td>
<td>mild</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute uncomplicated diverticulitis</td>
<td>mild</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>Peridiverticulitis, phlegmon (mesocolic)</td>
<td>mild</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>Acute complicated diverticulitis</td>
<td>severe</td>
<td>II</td>
<td>I</td>
</tr>
<tr>
<td>Abscess (pericolic, mesocolic)</td>
<td>severe</td>
<td>II</td>
<td>I</td>
</tr>
<tr>
<td>Pelvic abscess</td>
<td>severe</td>
<td>II</td>
<td>IIa</td>
</tr>
<tr>
<td>Free perforation, purulent peritonitis</td>
<td>severe</td>
<td>III</td>
<td>III</td>
</tr>
<tr>
<td>Free perforation, fecal peritonitis</td>
<td>severe</td>
<td>IV</td>
<td>IV</td>
</tr>
<tr>
<td>Fistula</td>
<td></td>
<td>IIb</td>
<td></td>
</tr>
</tbody>
</table>
Overview

• Problems
• Classification systems
• **Natural course/complications of the disease**
• Treatment-related morbidity
• Treatment-related mortality
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Natural course/complications

„The prognosis of patients admitted to hospital with DD is uncertain, owing to poor quality data“ (Janes et al 2004)

• the data are retrospective
• insufficient follow up
• diagnostic criteria of earlier studies were mostly symptom-based or contrast enema-based
• assumption in older studies that admissions for abdominal pain were related to diverticulitis
Recommendation: Operation after 2nd attack, because

- Multiple reviews: Recurrent attacks are less likely to respond to medical therapy (response 6% vs 70%)
- High mortality rate during recurrence
- 60% risk of complications during recurrence
Natural course/complications
Parks, 1969

• **Multiple reviews: Recurrent attacks are less likely to respond to medical therapy (response 6% vs 70%)**
  - 1st recurrence: 25%, 2nd: 4%, 3rd: 1.6%
  - recurrence and outcome: symptom-based: „medical treatment was less rewarding, and more than half continued to have symptoms“

• **High mortality rate during recurrence**
  - mortality rate: initially 4.7%; 1st recurrence: 7.6%
  - what was the reason to treat medically initially?
Natural course/complications
Faramakis, 1994

• 60 % risk of complications during recurrence to respond to medical therapy (response 6% vs 70%)
- 120 patients with „complicated“ diverticulitis (1/3 acute phlegmon) over 5 years
- 39 patients developed severe complications, 10 died from diverticulitis (GP), 29 died from other disorders, 14/39 same complication, e.g. 3 purulent diverticulitis
- study design: 300 patients entered, 176 over 5 years, 30 centres, questionnaire return 120 (recall bias ?). Answers from GPs
Outcome: overview

- Problems
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- **Treatment-related morbidity**
- Treatment-related mortality
- Recurrence, persistence
- Costs, quality of life
Treatment-related morbidity

- Conservative treatment
  - Antibiotic-associated complications (e.g. pseudomembranous colitis)
  - General complications: DVT, PE, pneumonia, catheter sepsis, pneu etc.
  - Recurrence in high risk groups (e.g. immunosuppression)
  - Sepsis

- Operative treatment: Anesthesia-related
  - Respiratory failure, pneumonia
  - General complications: DVT, PE, pneumonia, catheter sepsis, pneu etc.

- Operative treatment: Surgery-related
  - Anastomotic leakage
  - Uncontrolled sepsis
  - Bleeding, wound infections, incisional hernia
  - Fistula
  - Abscess
Outcome: overview

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Treatment-related mortality

• Conservative treatment
  ➢ Uncontrolled sepsis
  ➢ General complications: PE, pneumonia, catheter sepsis, pneu, heart failure, etc.
  ➢ Recurrence in high risk groups (e.g. young age or immunosuppression)

• Operative treatment: Anesthesia-related
  ➢ Respiratory failure, pneumonia
  ➢ General complications: PE, pneumonia, catheter sepsis, pneu, MI, renal failure etc.

• Operative treatment: Surgery-related
  ➢ Uncontrolled sepsis
  ➢ Hemorrhage
Outcome overview

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Costs

• Direct costs:
  - inpatient (medication, drainage, operation)
  - outpatient care (medication, support)

• Indirect costs:
  - time off work
  - early retirement
Direct inpatient costs

- Ward + HDU: 45%
- ICU: 25%
- Surgery: 19%
- Outpatients: 5%
- Investigations: 6%
Inpatient costs

- Colorectal: $1,731,172
- Vascular: $952,643
- Breast: $166,212
- Upper G.I.: $821,576
- Diverticular disease: $465,263

Source: Papgrigoriadis, 2004
## Impact of diverticular disease on health care costs in Europe

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population in Europe (15 EU countries)</td>
<td>376 Million</td>
</tr>
<tr>
<td>% population with colonic diverticula (median of available data in Table 2)</td>
<td>27.3%</td>
</tr>
<tr>
<td>Estimation population with colonic diverticula</td>
<td>102 Million</td>
</tr>
<tr>
<td>Annual incidence of colonic perforation from diverticula</td>
<td>16/100 000</td>
</tr>
<tr>
<td>Number of perforation cases/year</td>
<td>60,237</td>
</tr>
<tr>
<td>Annual rate of hospital admissions for diverticular disease</td>
<td>209/100 000</td>
</tr>
<tr>
<td>Number of hospital admissions/year</td>
<td>786,846</td>
</tr>
<tr>
<td>Mortality rate of patients admitted for diverticular disease</td>
<td>3%</td>
</tr>
<tr>
<td>Number of deaths from diverticular disease/year</td>
<td>23,605</td>
</tr>
</tbody>
</table>

Delvaux et al, 2003
Impact of diverticular disease on health care costs in Europe

Estimated total cost for inpatient health care for DD 2.5 billion €/year

- 25% operation for $5,000 = 200,000 x $5,000 = 1.0 billion €/year
- 75% medical treatment for $2500 = 600,000 x $2500 = 1.5 billion €/year

Calculated from Delvaux et al, 2003
## Base-case results with different management strategies for diverticulitis (in $)

**Method:** model decision analysis (Markov model)

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Age</th>
<th>Cost/p.</th>
<th>QALY/p.</th>
<th>cost/QALY</th>
<th>Colostomies</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective colectomy after 1st</td>
<td>50</td>
<td>10,829</td>
<td>18.3</td>
<td>591.9</td>
<td>5.7%</td>
<td>2.93%</td>
</tr>
<tr>
<td>Elective colectomy after 2nd</td>
<td>50</td>
<td>5,230</td>
<td>18.7</td>
<td>279.6</td>
<td>3.1%</td>
<td>2.07%</td>
</tr>
<tr>
<td>Elective colectomy after 3rd</td>
<td>50</td>
<td>4,272</td>
<td>18.8</td>
<td>227.4</td>
<td>2.4%</td>
<td>1.65%</td>
</tr>
<tr>
<td>Elective colectomy after 4th</td>
<td>50</td>
<td>4,195</td>
<td>18.8</td>
<td>223.3</td>
<td>2.4%</td>
<td>1.57%</td>
</tr>
</tbody>
</table>

Salem et al., 2004
Outcome measures: summary

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