New Concepts of Diverticular Disease

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Introduction

- Prevalence correlates with age
- 30% of the population has acquired diverticular change by age 60
- 60% of those aged 80 years and older are affected


Definitions

- “Diverticulosis” and “diverticular disease” describe the presence of uninfamed diverticula
- Diverticulitis is the inflammation of a diverticulum, which is commonly accompanied by gross or microscopic perforation

Questions

True/False
1. Diverticulosis is associated with chronic gastrointestinal symptoms in the absence of diverticulitis or overt colitis.
2. A very high-fiber diet may prevent development of diverticulitis.
3. Acute diverticulitis is an infection and must be treated with antibiotics.
4. Elective surgical resection of the affected colon should be advisable after a second attack of diverticulitis in older individuals and after a first attack in young adults.
5. Colonoscopy should be suggested after an episode of acute diverticulitis to exclude colon cancer.
6. Patients with a history of diverticulitis should avoid nuts and seeds to prevent further episodes.

Adapted: Peery AF, Sandler RS. Clin Gastroenterol & Hepatol 2013;11:1858-1867

PATHOPHYSIOLOGY

Pathophysiology of colon diverticulum

- Assumption – decreased dietary fiber intake, results in decreased intestinal contents and hence decreased size of the lumen.
- Results in the transmission of muscular contraction pressure to the wall of the colon rather than to the contents of the lumen.
- The result of increased force (pressure) on the wall is the formation of diverticula at the weakest point in the wall, which is the sites of penetration by blood vessels.

Prevention of diverticulitis

- Health Professionals Follow-up Study, which prospectively followed 51,529 US male health professionals
- A significant inverse association was found between insoluble dietary fiber intake (especially fruit and vegetable, e.g., cellulose fiber) and the risk of subsequently developing symptomatic diverticular disease (Relative Risk = 0.63, 95% CI 0.44 – 0.91)

Recommendations:
1. Diets high in fruit and vegetable fiber may decrease the development of colonic diverticulitis
2. Greatest benefit was seen in those individuals consuming an average of 32 g/day of total fiber


Role of fiber to prevent diverticulosis

Method
- Oxford cohort of European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford study)
- A cohort of 47,033 men and women followed for an average of 12 years
- The adjusted relative risk of hospitalization for diverticular disease was 0.59 in individuals in the highest category of fiber intake compared with those with the lowest fiber intake

Results:
- Patients in the EPIC study were hospitalized or died as a result of diverticular disease and were therefore likely to have had complicated disease

Conclusion: High fiber diet may prevent diverticular complications

Adapted: Strate LL. Gastroenterology 2012;142:205-210

Diet and risk of diverticular disease in Oxford cohort of European Prospective Investigation into Cancer and Nutrition (EPIC): prospective study of British vegetarians and non-vegetarians

Setting: The EPIC-Oxford study, a cohort of mainly health conscious participants recruited from around the UK

Method
- 47,000 men and women living in England or Scotland of whom 15,459 (33%) reported consuming a vegetarian diet

Results:
- 812 cases of diverticular disease over a mean follow-up time of 11.6 years
- Vegetarians had a 31% lower risk of diverticular disease compared with meat eaters
- Inverse association with dietary fiber intake; participants in the highest fifth had a 42% lower risk for both men and women
- The adjusted relative risk of hospitalization for diverticular disease was 0.59 in individuals in the highest category of fiber intake compared with those with the lowest fiber intake

Conclusion: High fiber may prevent diverticular complications

Adapted: Crowe FL, et al. BMJ 2011;343:i1-15
A high-fiber diet does not protect against asymptomatic diverticulosis

**Background:** Many physicians and patients believe that a high-fiber diet and frequent bowel movements prevent the development of diverticulosis

**Methods:**
- A cross-sectional study of 2104 participants, 30-80 years old, who underwent outpatient colonoscopy from 1998 to 2010
- Diet and physical activity were assessed in interviews using validated instruments

**Results:**
- The prevalence of diverticulosis increased with age
- High intake of fiber did not reduce the prevalence of diverticulosis
- The quartile with the highest fiber intake had a greater prevalence of diverticulosis than the lowest

Adapted: Peery AF, et al. Gastroenterology 2012;142(2):266-72

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**Results Cont.:**

**Methods:**
- Constipation was not a risk factor
- Compared to individuals with < 7 bowel movements per week, individuals with > 15 bowel movements per week had a 70% greater risk for diverticulosis (prevalence ratio = 1.70; 95% confidence interval 1.24 – 2.34)
- Neither physical inactivity nor intake of fat or red meat was associated with diverticulosis

Adapted: Peery AF, et al. Gastroenterology 2012;142(2):266-72

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Dietary restriction of nuts and seeds in patients with diverticulosis

- Dietary nuts, corn, and seeds were not associated with an increased risk of diverticulitis or diverticular bleeding in a prospective cohort of male health professionals

Obesity increases the risks of diverticulitis and diverticular bleeding

**Methods:** A prospective cohort study of 47,228 male health professionals that were free of diverticular disease in 1986

**Results:**
- 801 cases of diverticulitis and 383 cases of diverticular bleeding during 18 years of follow-up
- Men with BMI ≥ 30 kg/m² had a relative risk (RR) of 1.78 (95% confidence interval [CI]) for diverticulitis and a 4.19 for diverticular bleeding, compared to men with BMI < 2 kg/m²
- Waist-to-hip ratio was also associated with the risk of diverticular complications, when the highest and lowest quintiles were compared: multivariable RR 1.62 (95% CI; 1.23-2.14) for diverticulitis and multivariable RR 1.91 (95% CI; 1.26-2.90) for diverticular bleeding
- Adjustment for BMI did not change the associations seen for waist-to-hip ratio


Physical activity decreases diverticular complications

**Methods:** 47,230 US males in the Health Professionals Follow-up Study cohort who were aged 40 – 75 years and free of diverticular disease, gastrointestinal cancer and inflammatory bowel disease at baseline in 1986

**Results:**
- During 18 years of follow-up, 80 cases of diverticulitis and 383 cases of diverticular bleeding were identified
- Total cumulative physical activity was associated with a decreased risk of diverticulitis and diverticular bleeding
- After adjustment for potential confounders, the relative risk for men in the highest quintile of total activity (≥57.4) was 0.75 for diverticulitis, and 0.54 for bleeding
- Vigorous activity was inversely related to diverticulitis (multivariable RR 0.66) and bleeding (RR 0.61) in a high vs. low comparison, whereas non-vigorous activity was not


**SYMPTOMS**
Uncomplicated diverticular disease is not a common cause of colonic symptoms

Method
- Participants ≥50 years completed a locally validated Rome II questionnaire on colonic symptoms

Results:
- Among patients with and without diverticular disease, the frequency of Symptoms is not significantly different
  - Abdominal pain 123 (44%) and 226 (46%)
  - Diarrhea 44 (16%) and 80 (17%)
  - Constipation 38 (14%) and 80 (17%)
  - Irritable bowel syndrome 66 (25%) and 119 (25%)
- Patients with diverticulum have GI symptoms similar to those without diverticulum


Diarrhea-predominant irritable bowel syndrome is associated with diverticular disease: A population-based study

Aim: To evaluate whether IBS and diverticular disease are associated

Introduction:
- A subset of patients with colonic diverticular disease have chronic gastrointestinal symptoms and some have a clinical diagnosis of irritable bowel syndrome

Methods:
- A population-based, cross-sectional survey
- Subjects with at least one relevant test – colonoscopy, CT scan, or barium enema were included
- IBS was defined using ROME II criteria


Cont. Results
- 1,712 subjects who had undergone colon testing (76%): 919 women (54%); age 65 (±11 years)
- Colonic diverticular disease was identified in 44%
- IBS was reported by 8.8% (95% CI 6.9 – 11.0) of men and 17.0% (95% CI 14.6 – 19.6) of women
- Presence of IBS was associated with a ninefold higher odds for diverticulosis
- Conclusion: A significantly increased odds for colonic diverticulosis in patients with IBS

Clinical Features of Acute Diverticulitis

Pain
- Patients with redundant sigmoids may well manifest suprapubic or even right-sided pain.
- The pain may be intermittent or constant, and is frequently associated with a change in bowel habits, either diarrhea or constipation.

Hematochezia
- Dysuria and urinary frequency may be reported, reflecting a 'sympathetic cystitis' induced by bladder irritation.

Other Findings
- Fever is present in the majority of patients.
- WBC count is elevated (55%) of patients.


Diagnosis and Treatment

Imaging
- Computed tomography is recommended as the initial radiologic examination.
- Sensitivity (approximately 93% to 97%); specificity approaching 100% for the diagnosis.
- Allows delineation of the extent of the disease process.

Computed Tomographic Criteria to Assess Severity of Diverticulitis

<table>
<thead>
<tr>
<th>Mild Diverticulitis</th>
<th>Severe Diverticulitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized sigmoid wall thickening (&gt;5 mm) inflammation of pericolic fat</td>
<td>Same as mild diverticulitis plus one of the following:</td>
</tr>
<tr>
<td></td>
<td>• Abscess</td>
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<tr>
<td></td>
<td>• Extraluminal air</td>
</tr>
<tr>
<td></td>
<td>• Extraluminal contrast</td>
</tr>
</tbody>
</table>


An appropriate candidate for outpatient management

- Mild symptoms
- No peritoneal signs
- Ability to tolerate oral fluids
- Supportive home network
- Not the very elderly or immunosuppressed patients
- Those without severe comorbid disease
- Those without high fevers


Diverticulitis treatment: In-patient

- In-patient immunocompromised
  - Organ transplantation
  - HIV infection
  - Taking corticosteroids
- Elderly especially with comorbidities
- Significant leukocytes
- Reason – consequences of diverticulitis

Immunosuppression

- Associated with an increased incidence of perforated diverticulitis, i.e. chemotherapy, corticosteroid therapy, diabetics, renal failure and collagen-vascular disorders
- Immunosuppressed patients may present with minimal symptoms or signs even with frank peritonitis
- Surgery is necessary in almost all immunocompromised patients


Out-Patient:
Regimens Commonly Used to Treat Diverticulitis

<table>
<thead>
<tr>
<th>Drug Regimen</th>
<th>Dosage</th>
</tr>
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<tbody>
<tr>
<td>Intravenous regimens for inpatients</td>
<td></td>
</tr>
<tr>
<td>Metronidazole and a quinolone</td>
<td>Metronidazole – 500 mg every 6 to 8 hr</td>
</tr>
<tr>
<td>Metronidazole and a third-generation cephalosporin</td>
<td>Quinolone (e.g. ciprofloxacin – 400 every 12 hr)</td>
</tr>
<tr>
<td>Beta-lactam with a beta-lactamase inhibitor</td>
<td>Metronidazole – 500 mg every 6 to 8 hr</td>
</tr>
<tr>
<td></td>
<td>Third-generation cephalosporin (e.g., ceftriaxone – 1-2 g every 24 hr)</td>
</tr>
<tr>
<td>Beta-lactam with a beta-lactamase inhibitor</td>
<td>Beta-lactam with a beta-lactamase inhibitor (e.g., amoxicillin-sulbactam – 3 g every 6 hr)</td>
</tr>
</tbody>
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In-Patient:
Regimens Commonly Used to Treat Diverticulitis

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</tr>
<tr>
<td>Metronidazole and trimethoprim-sulfamethoxazole</td>
<td>Quinolone (e.g. ciprofloxacin – 500 – 750 mg every 12 hr)</td>
</tr>
<tr>
<td>Metronidazole and trimethoprim-sulfamethoxazole</td>
<td>Metronidazole – 500 mg every 6 to 8 hr</td>
</tr>
<tr>
<td></td>
<td>Trimethoprim – sulfamethoxazole – 160 mg trimethoprim and 800 mg sulfamethoxazole every 12 hr</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>Amoxicillin-clavulanate – 875 mg every 12 hr</td>
</tr>
</tbody>
</table>

Antibiotics may not improve short-term or long-term outcomes in acute uncomplicated diverticulitis

Aim: To evaluate whether or not antibiotic therapy for acute uncomplicated left-sided diverticulitis improves recovery

Methods:
- Non-blinded randomized trial comparing treatment of acute, uncomplicated left-sided diverticulitis with or without antibiotics was performed
- 623 patients with signs of acute diverticulitis, without sepsis, immunosuppressive and pregnancy, who had a raised white cell count and C-reactive protein and a corroborating CT scan

Adapted: Westwood DA, Elinton T. Evidence-Based Medicine 2013;18(1):32-33

Antibiotics may not improve short-term or long-term outcomes in acute uncomplicated diverticulitis

Cont.
Results:
- The rate of recurrent diverticulitis necessitating hospital readmission at 12 month follow-up was similar between the two groups (16%, p=0.881)
- The median duration of hospital stay was 3 days in both groups
- Rate of complications (sigmoid perforation or abscess formation) in patients who received no antibiotics was similar to that in patients who were treated with antibiotics (1.9% vs. 1.0%, p=0.302)

Adapted: Westwood DA, Elinton T. Evidence-Based Medicine 2013;18(1):32-33

SUMMARY
Medical treatment in patients with uncomplicated diverticulitis

- Selected patients for out-patient management
- Success rate ranges from 70 % to 100%
- May not need antibiotics
- Radiographic imaging with CT clarifies severity of disease
- Percutaneous drainage for diverticulitis complicated by a localized abscess >3 cm

Diverticulitis with abscess

- Small pericolic abscesses < 3 cm can frequently be managed conservatively
- Larger >3 cm abscesses require drainage
- CT-guided percutaneous drainage allows for rapid stabilization – 80%
- Initial surgical procedure is required in the 20-25% of patients in whom the abscess is multiloculated, anatomically inaccessible for drainage, or not responding to drainage


Indications for operative management for acute diverticulitis

Absolute
- Complications of diverticulitis
  - Peritonitis
  - Abscess (failed percutaneous drainage)
  - Fistula
  - Obstruction
- Clinical deterioration or failure to improve with medical therapy by 3rd to 5th day
- Intractable symptoms (exclude IBS)
- Inability to exclude carcinoma

Relative
- Symptomatic stricture
- Immunosuppression
- Right-sided diverticulitis – exclude appendicitis

Important clinical question after resolution of symptoms

Was colon cancer causing acute diverticulitis?

Diverticular disease and the risk of colon cancer – a population-based case-control study

Aim: To analyze the risk of colon cancer after hospitalization for diverticular disease

Method:
- 41,037 patients with colon cancer in a nationwide case-control study during 1992-2006
- Each case was matched with two control subjects

Results:
- Within 6 months after an admission due to diverticular disease, OR of having a colon cancer diagnosis were up to 31.49
- After 12 months, there was no increased risk

Conclusion:
- The increased risk of colon cancer within the first 12 months after diagnosing diverticular disease is most likely due to surveillance and misclassification


Is colonoscopy still mandatory after a CT diagnosis of left-sided diverticulitis: Can colorectal cancer be confidently excluded?

Aim: To determine whether colonoscopy is necessary and what additional information is gained from this procedure after diverticulitis

Method
- A retrospective cohort study of 2009 patients in whom left-sided diverticulitis was diagnosed on CT scan and matched with colonoscopy reports within 1 year from the date of CT

Results:
- Follow-up colonoscopy reports were available for 319 patients
- 82 (26%) patients had incidental findings of polyps (9 polyps > 1cm), and 9 patients (2.8%) were diagnosed with colorectal cancers on colonoscopy

Adapted: Dis Colon Rectum 2011;54:1265-1270
Results Cont.

- Inverse association with dietary fiber intake; participants in the highest fifth had a 41% lower risk for both men and women
- The odds of a diagnosis of colorectal cancer were 6.7 times in patients with an abscess reported on CT and 18 times in patients with fistula compared with patients with uncomplicated diverticulitis

Conclusion: The rate of occult carcinoma is substantial in this patient population

Adapted: Dis Colon Rectum 2011;54:1265-1270

Conclusions

- Colon cancer may present with symptoms suggestive of diverticulitis
- Patients should undergo colonoscopy after an episode of diverticulitis

Natural History of Diverticular Disease and Role of Elective Surgery
Patterns of recurrence in patients with acute diverticulitis

**Method**
- A retrospective chart review of patients with diverticulitis between June 1997 and June 2002

**POP:**
- 337 (67%) patients with uncomplicated and 165 (33%) with complicated diverticulitis
- Median follow-up was 101 months
- 320 (95%) patients with uncomplicated diverticulitis managed conservatively

Cont.

**Results:**
- 60 (18.8%) had one episode of recurrence, whereas 15 (4.7%) had two or more episodes
- After an initial attack of uncomplicated diverticulitis, only 5.0% developed complicated disease
- Complicated disease recurred in 24%, no difference from uncomplicated disease
- Recurrence usually occurred within 12 months of the initial episode

**Elective resection to prevent complications of diverticular disease**
- Mortality rate associated with emergency operation is 12% - 36%
- Operative mortality rate 17% among 48 patients undergoing emergency surgery for complicated diverticular disease
  - 96% of these patients had no history of diverticular disease suggesting that prophylactic resection would have had little impact in preventing severe complications

**Conclusion:**
- Offering elective resection would have little impact on the incidence of patients requiring emergency procedures
- For most patients, a complication of diverticular disease is the first manifestation of disease

Summary: Need for elective surgery

• Recurrent diverticulitis is relatively rare and further more often uncomplicated than previously assumed; therefore, the prognosis is better per se.

• The risk of relapse is estimated to 2% per year.

• 16% of cases with first-time diverticulitis were operated acutely compared to 6% of relapsed cases.

• The incidence of conservative treatment failure was similar in both groups (10%).


Summary: Need for elective surgery

Cont.

• A lower mortality of 2.5% was found for recurrences compared to 10% at the first episode of diverticulitis.

• The majority of patients presenting with severe diverticulitis lack a history of the disease.

• Observational study of 25,058 cases of which 80.3% had conservative treatment; of these 19% experienced relapse and 18% were treated by surgery.
  – Predicted relapse rate demanding surgery after a single case was as low as 5.5%.


Should patients younger than 50 years undergo elective surgery after first attack of uncomplicated diverticulitis?
Long-term follow-up after first acute episode of sigmoid diverticulitis: Is surgery mandatory?

Aim: To evaluate the long-term natural history of sigmoid diverticulitis in patients treated non-surgically after a first acute episode

Method:
• 144 patients between 1986 and 1991 admitted for acute diverticulitis diagnosed by abdominal CT

Results:
• 118 patients were followed for a median of 9.5 (range, 0.2 – 13.8) years
• 80 patients had no complications, and 38 had remote complications
• The incidence of remote complications was the highest (54% at 5 years) for young patients with severe diverticulitis on CT and lowest (13% at 5 years) for older patients with mild disease
• Young age and severe diverticulitis taken separately were both statistically significant factors of poor outcome (P = 0.007 and P = 0.003, respectively); although age was no longer significant after stratification for disease severity


Young patients (< 50 years) with diverticulitis

• 20% to 29%, male predominance, ranging from 2:1 to 4:1, the majority of patients are obese
• No significant difference for the rate of emergency surgery (26.1% vs. 23.9%) or failure of conservative treatment for the younger patients (3.4% vs. 4.9%)
• No convincing arguments to insist on resection after resolution of uncomplicated diverticulitis in a young patient


Diverticulitis: the effect of age and location on the course of disease

Aim: To follow-up the data on 119 patients with acute diverticulitis

Method:
• Follow-up 7-102 months, median 40
• Patients were divided by their age into two groups – 60 years or younger and age over 60
• Location of their disease (108 to the left of the middle transverse, 11 to the right)
• Symptoms & signs: Lower abdominal pain, abdominal tenderness and fever

Results:
• Younger patients had a significantly greater preponderance in the right colon (P = 0.02) than in older patients
• Abdominal abscesses and fistulas were more common in right-sided diverticulitis (P=0.01)

Management of < 50 year old with acute diverticulitis

- Manage non-operatively for uncomplicated disease
- Observe after resolution because of likely higher rate of recurrence
- If severe, (complicated) disease, evaluate for surgery
- If right-sided, exclude appendicitis and observe for complications

Barkin JS

THANK YOU