Diagnosis in acute abdominal pain and ongoing abdominal sepsis
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Citation for published version (APA):
Kiewiet, J. J. S. (2016). Diagnosis in acute abdominal pain and ongoing abdominal sepsis

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Chapter 6

SURGICAL APPROACHES TO PERITONITIS

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PERITONITIS

Terminology
Peritonitis has a widespread aetiological background. Primary peritonitis is discerned from secondary peritonitis on aetiological ground. In primary peritonitis the infectious route is commonly unknown and the gastrointestinal tract is intact. Pivot in the treatment of primary peritonitis is antibiotic therapy. \(^1\) In secondary peritonitis an abdominal infection is manifest due to a breach in the continuity of the gastrointestinal tract caused by perforation, infection, inflammation, ischemia or as a consequence of a postoperative complication. \(^2,3\) ‘Tertiary peritonitis’ is a frequently encountered term. \(^1,3,4\) However, the validity of this term can be questioned since the given definitions are far from uniform. Furthermore, primary and secondary peritonitis are distinguished based on pathogenesis whereas ‘tertiary peritonitis’ is used for a clinical course of secondary peritonitis characterized by the perseverance of the infection caused by low pathogenic micro-organisms and the difficulty of treatment.

Incidence and impact
Secondary peritonitis is associated with high mortality rates (20-60%) which has barely decreased in the past few decades. In addition, associated morbidity is high (40-49%) and the hospital and intensive care unit (ICU) stay is long with respectively 27 to 52 days and 8 to 18 days. \(^3,5-8\) Precise numbers on the incidence are not available but it is a frequently encountered entity. An estimated one out of nine emergency admissions in the United States is due to secondary peritonitis. \(^9\) The cases of secondary peritonitis after elective surgery are supplementary to these numbers indicating that it is not desirable to centralize the treatment.

TREATMENT
The treatment of secondary peritonitis is outlined in the sustainment of organ function to provide adequate perfusion and oxygenation also known as resuscitation, antimicrobial therapy and surgery.

Resuscitation
Sepsis as a consequence of secondary peritonitis has a great impact on the cardiovascular state of the patient. Consequences are low peripheral resistance, high cardiac output, myocardial dysfunction and disturbance of the microcirculation resulting in inadequate tissue
perfusion and hypoxia. Functionality of several organ systems is disrupted and supportive therapy aimed at the circulation and cellular respiration is warranted to prevent further deterioration of specific organ function. Resuscitation comprises all measures taken to sustain adequate perfusion and oxygenation. Adequate resuscitation in the first six hours of a septic shock improves mortality significantly.\(^\text{10}\)

**Antimicrobial therapy**

Early administration of antibiotic therapy is of great importance. With every delay of 30 minutes after secondary peritonitis is suspected the mortality rate increases with an odds ratio of 1.021 (95% CI: 1.003 to 1.038).\(^\text{11}\) The importance of adequate and early administration of antibiotics is illustrated in a 33% relative risk reduction in patients with bacteraemia admitted to the intensive care unit.\(^\text{12}\) There is no preference for one of the available empiric antibiotic regimes since they prove to have similar results in a Cochrane review.\(^\text{13}\) The empiric antimicrobial therapy should be aimed at the expected strains. When the exact strains and their susceptibility become available from cultures the antibiotic regime should be adapted.

**Antifungal therapy**

A substantial part of the patients with secondary peritonitis will end up in the intensive care unit where colonisation with yeast and fungi is common, especially with *Candida spp.*\(^\text{14}\) A recent meta-analysis showed that antifungal prophylaxis is useful in reducing yeast infections in severely ill patients with either a single-drug antifungal prophylaxis (odds ratio; 0.54 95%CI: 0.39 to 0.75) or with selective bowel decontamination (odds ratio; 0.29 95%CI: 0.18 to 0.45). To prevent one yeast infection 20 patients had to be treated with single-drug prophylaxis or 18 patients had to be treated with selective bowel decontamination. Furthermore, mortality rates are lower with antifungal prophylaxis irrespective of single or multi-drug regimes with a combined odds ratio of 0.23 (95%CI: 0.09 to 0.60) and a number needed to treat of 41.\(^\text{15}\) In the light if the rising prevalence of fungal infections antifungal prophylaxis is advised in high risk patients. Known risk factors are previous surgery, nosocomial peritonitis, perforation of the upper gastrointestinal tract, immune deficiency, long term treatment with antibiotics, acute kidney failure and the presence of a central venous catheter.\(^\text{16,17}\)
SURGICAL STRATEGY

Surgery remains the cornerstone of the treatment of secondary peritonitis where elimination of the infectious focus and prevention of an ongoing infection are key features.

Elimination of the infectious focus

Elimination of the infectious focus is frequently characterized as ‘source control’. This comprehends not only surgical intervention but also additional measures such as a radiological intervention or the removal of an infected catheter. Source control can be achieved by direct repair of a breach in the continuity of the gastrointestinal tract, but also by performing a resection or exteriorisation of the infectious focus. The underlying condition and the anatomical site causing secondary peritonitis prescribe which procedure is appropriate. Specific surgical techniques used for each condition are not discussed here since the widespread underlying causes would need extensive description and is beyond the scope of this chapter. Effort must be made to achieve complete source control in an early phase of the disease and in one surgical procedure. Source control is of greater importance than restoration of normal function and/or anatomy.

Decrease of contamination of the abdominal cavity

Rinsing of the abdominal cavity with saline, antibiotics or antiseptic agents in case of an intra-abdominal infection is common practice in surgery. None of the used solutions prove to have any positive effect on the outcome of secondary peritonitis, whereas rinsing can damage mesothelial cells which play a key role in the immune reaction. The proverb ‘the solution to pollution is dilution’ therefore seems superseded for the abdominal cavity and can even prove to be harmful.

Surgical strategy after the initial operation

Despite adequate source control during the initial operation, a relaparotomy might be necessary in some cases of secondary peritonitis. It is generally accepted that in patients who are less severely ill at initial presentation (‘Acute physiology and chronic health evaluation’ (APACHE-II) score ≤ 10) the clinical course after the initial operation dictates whether a relaparotomy is necessary. Only in case of clinical deterioration or insufficient improvement in the first few days a relaparotomy is performed. This is called the ‘on-demand’ strategy.
Severely ill patients (APACHE-II score > 10) were submitted to more aggressive surgical strategies until recently, like radical peritoneal debridement, the ‘open abdomen’ treatment and planned relaparotomies. Fibrin deposition is removed from the entire abdominal cavity in radical peritoneal debridement, but high mortality and morbidity rates eliminated its use in current practice. In the open abdomen strategy the fascia is not closed after the initial operation. This approach has gone into abeyance since a randomised trial reported a significantly higher mortality in the open abdomen strategy group compared to a closed abdomen group (55% versus 30%; Odds ratio 2.85). In specific circumstances the open abdomen strategy can be used, for instance when the intra abdominal pressure is vigorously high or the viscera are extremely swollen. A relaparotomy is performed every two to three days after the initial operation in the planned relaparotomy strategy until there is no macroscopic sign of residual intra abdominal infection.

On-demand and planned relaparotomy are the most used strategies in current practice. The last few years there have been several indications that prefer the on-demand strategy above the planned relaparotomy strategy. A meta-analysis of observational studies showed a non-significant lower mortality in the on-demand strategy (combined odds ratio: 0.70, 95% CI; 0.27 to 1.80). Significantly lower mortality was seen in a retrospective cohort study where the mortality was 22% in the on-demand strategy versus 36% in the planned relaparotomy strategy \( (p = 0.016) \). The severity of disease was comparable for both strategies indicated with a mean APACHE-II score of 10.8 versus 11.7 respectively. In 2007 the only prospective randomised trial comparing the on-demand and planned strategy was published. For this trial 510 patients with secondary peritonitis were registered, of which more then half was excluded because of an APACHE-II score \( \leq 10 \). Two hundred and thirty two patients were included of who 116 were treated with the on-demand strategy and 116 with the planned relaparotomy strategy. The mortality in the on-demand group was 29% versus 36% in the planned relaparotomy group \( (p = 0.22) \). Even for the most severely ill patients with an APACHE-II score \( > 20 \) this pattern was observed (figure 1). This is an important finding against the often advanced proposition that especially the most severely ill patient benefit from the planned relaparotomy strategy. Another dogma that can be disputed with data from this trial and a retrospective cohort study is that a planned relaparotomy is indispensable in case of faecal contamination (figure 2). The on-demand strategy significantly decreases healthcare utilisation resulting in a cost reduction of USD 23.000 per patient.
Patients treated with the on-demand strategy are admitted shorter to the ICU and hospital. Less relaparotomies are performed in the on-demand group; 113 versus 233 in the planned relaparotomy group. Furthermore, the 31% rate of unnecessary relaparotomies was significantly lower in the on-demand group than in the planned relaparotomy group where the rate was 66%.

Figure 1.

Mortality of secondary peritonitis patients, divided based on the severity of disease expressed by the APACHE-II score. Two surgical strategies were compared per category, relaparotomy on-demand (□) and planned relaparotomy (■). A total of 510 patients were registered, patients with an APACHE-II score >10 were randomized between the on-demand and planned relaparotomy strategy.
Figure 2.

Comparison of mortality rates between the on-demand (square) and planned relaparotomy strategy (circle) in patients with secondary peritonitis that had either diffuse peritonitis, faecal peritonitis or a combination of both. The left panel represents the results of a retrospective cohort study (n=278), the right panel displays the results of a randomized trial (n=232).
Decision-making in the on-demand strategy
Results of two national surveys among Dutch surgeons, performed in 2002 and 2008, were compared. The percentage of surgeons exclusively using the planned relaparotomy strategy declined drastically from 23% in 2002 to 1% in 2008. However, the percentage of surgeons exclusively using the on-demand strategy stayed the same (39% in 2002 versus 41% in 2008). The remaining 58% of surgeons vary between the two strategies despite of the substantial leads that the on-demand strategy should be preferred. It is clear that implementing the safe and more efficient on-demand strategy requires additional effort. The main obstacle for exclusive use of the on-demand strategy lies in the timely and adequate identification of a patient needing a relaparotomy. There is no guideline available to support the decision whether or not to perform a relaparotomy and is currently based on a series of subjective variables. There are no reliable variables that predict which patients will have an ongoing intra abdominal infection requiring a relaparotomy, including the common parameters of infection such as fever, C-reactive protein and white blood cell count. The only lead there is suggests that clinical variables after the initial operation have the best predictive value.\textsuperscript{26,27} Therefore, intensive monitoring of the patient is an essential part of the on-demand strategy; round the clock capacity to re-evaluate the decision to perform a relaparotomy is required.

IMAGING
In patients suspected of having secondary peritonitis after elective abdominal surgery computed tomography (CT) plays an important role as diagnostic imaging modality. The positive predictive value of a CT scan to detect a abdominal source of sepsis is 71% (95% CI: 57% to 83%) leaving a margin of error. However, the predictive value for the absence of an abdominal source of sepsis is only 15% (95%CI: 6% to 32%) making it a reliable modality.\textsuperscript{28} CT is also demonstrated to play an important role in the evaluation of patients presenting with acute abdominal pain having secondary peritonitis. However, there is no data on the role of CT after the initial operation. In the prospective trial only 18% of on-demand patients received an abdominal CT scan in the first week after the initial laparotomy despite the fact that almost all of the relaparotomies in this group were performed in the first week. In current practice the use of CT seems to be limited in the selection of patients needing a relaparotomy, whereas increase would also increase effectiveness of the on-demand strategy. There are some drawbacks to the more liberal use of CT, such as the increase in costs, the transport of severely ill patients from the ICU to the CT-room and the radiation exposure.
CARE

Intensive care unit
About 40% of all patients with secondary peritonitis requires admission to the ICU. Of the 232 included patients of the prospective trial (APACHE-II score >10) more then 90% of patients were admitted to the ICU. The influence of ICU characteristics on mortality and morbidity is of growing interest. Higher treatment volume of an ICU is associated with lower mortality in patients with severe sepsis. A similar relation for secondary peritonitis is not established, but is plausible. As discussed, centralisation of care for secondary peritonitis is not desirable, but it is worth considering treating severely ill patients in higher level ICU’s.

Organisation of care
The treatment of secondary peritonitis requires a multidisciplinary setting, where surgeon, intensivist, radiologist and microbiologist work together closely. In the prospective trial there was a remarkable difference between the expected mortality based on the APACHE-II score and the observed mortality between different hospitals which is illustrated in figure 3. Partially these differences can be attributed to differences in the organisation of care, for instance the round the clock availability of a radiologist capable of performing interventions and the presence of an intensivist.

CONCLUSION
The treatment of secondary peritonitis is composed of several aspects. Therefore, it should not be expected that mortality would drop dramatically when a single aspect is improved. It seems more realistic to seek improvement in a multidisciplinary policy with extensive use of diagnostic support and aid in the decision-making process. Examples of advances in this policy are the administration of antifungal prophylaxis in high risk patients, the questioning of the benefit of extensive rinsing of the peritoneal cavity and the use of the on-demand strategy in severely ill patients. It is essential that the multidisciplinary team caring for patients with secondary peritonitis monitor the patients intensively and ensure that round the clock, seven days a week decision-making is possible just like the on-demand strategy requires.
Figure 3.

Differences in mortality ratio between participating hospitals in the randomized trial comparing the on-demand (■) and planned relaparotomy strategy (□) in patients with secondary peritonitis. The mortality ratio was calculated by dividing the observed mortality by the expected mortality calculated based on the average APACHE-II score. A ratio of > 1 indicates that the observed mortality is higher then would be expected. Besides the overall mortality ratio two of the seven participating hospitals are displayed to illustrate the great differences between the performances of hospitals in the on-demand strategy, whereas the mortality ratio in the planned relaparotomy strategy is almost exactly identical.
REFERENCES


