Prognostic significance of comorbidities in patients with diffuse peritonitis

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Summary

Background Diffuse peritonitis is a severe disease with high mortality and morbidity rates. Therapy is fundamentally surgical. It is important to identify patients with a significantly worse prognosis and patients who may benefit from more aggressive surgical and post-surgical care such as NPWT (Negative Pressure Wound Therapy) prior to surgery. We tried to identify a determining factor for higher morbidity and mortality rates resulting in a worse prognosis among initial data and patient comorbidities in order to focus therapy towards more aggressive surgical management.

Methods In a group of 274 patients with diffuse peritonitis, we evaluated the type of peritonitis according to effusion, origin, surgery type, and the age, gender, and present comorbidities of the patients, and compared it with the overall mortality, morbidity rate, and duration of hospitalization.

Results Patients without comorbidities had a significantly lower burden in both morbidity and mortality. We recorded the highest difference in mortality in patients with two or more comorbidities, with pulmonary and cardiovascular diseases, with malignancy and hypertension. Morbidity was found to be significantly exacerbated by the presence of two or more severe diseases, cardiovascular disease, malignancy, and hypertension.

Conclusion We identified age, effusion type, and the presence of comorbidities as key factors for the prognosis of our patients—the morbidity and mortality rates were substantially increased in patients with two or more comorbidities, as well as by the presence of cardiovascular disease, malignancy, and hypertension. A more aggressive approach should be considered to improve the prognosis in these patients.

Keywords Peritonitis · Type of effusion · Comorbidity · Narrow pressure wound therapy · Vacuum assisted closure

Abbreviations

- APACHE: Acute Physiology and Chronic Health Evaluation
- ASA: American Society of Anesthesiologists
- CD: Clavien–Dindo
- HPB: Hepatopancreatobiliary
- MPI: Mannheim Peritonitis Index
- NPWT: Negative Pressure Wound Therapy
- POSSUM: The Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity
- qSOFA: Quick Sepsis Organ Failure Assessment
- V.A.C.: Vacuum-Assisted Closure

Main novel aspects

- Age, type of effusion, and presence of severe comorbidities at the time of diffuse secondary peritonitis development are completely essential in determining patients’ prognosis, and the presence of two or more severe comorbidities seems to be more important than the presence of a specific severe disease at the time of the surgery.
- We propose classifying peritonitis according to the type of effusion rather than its origin, since this pre-
dictor correlates better with therapeutic outcomes and the prognosis of patients.

- Patients with a worse prognosis should be offered more aggressive treatment, e.g., intensified ATB therapy, complex resuscitation care, or a more appropriate surgical procedure, e.g., NPWT.

**Introduction**

Diffuse peritonitis is a severe disease with high morbidity and mortality rates and is often life threatening. Prognosis largely depends on the general condition of the patient. The mortality and morbidity percentage in these patients is still high, and the presence of severe comorbidities at the onset of diffuse peritonitis increases the risk of a severe disease course. These are often elderly patients with numerous comorbidities. The treatment is multidisciplinary, with primary treatment always surgical, subsequently continuing at intensive care units with comprehensive resuscitation care and targeted antibiotic therapy.

Surgical therapy of peritonitis is still essential. It is necessary to treat the cause of peritonitis and decontaminate the abdominal cavity. In principle, we may continue with two courses: 1) surgical revision of the abdominal cavity and temporary abdominal closure within 24–72 h, most often closed using NPWT or non-woven fabric (“COM”); or 2) potential primary closure with abdominal drainage and possible postsurgical lavage [1, 2]. Continuous postsurgical abdominal lavage was quite frequently used to treat diffuse peritonitis in the last decades of the 20th century, mainly in German-speaking countries in cases of advanced stercoral peritonitis. However, the effect of lavage has been questioned over time [3, 4]. Negative pressure wound therapy (NPWT, V.A.C.) has been increasingly used in severe forms of peritonitis of the past decade. It seems to be more beneficial than simple lavage during the surgery [5].

High mortality and morbidity rates are still a severe medical and social problem. Peritonitis risk can be estimated based on a number of scoring systems, e.g., MPI (Mannheim Peritonitis Index), POSSUM, qSOFA, APACHE, etc. These scoring systems are very well developed and also valid, but they suffer particularly from extensive complexity. Therefore, our aim was to provide at least a gross patient’s prognosis upon his/her admission to hospital based on the simplest initial data, possibly only based on medical history and evaluation of the patient's common demographic data. The objective of our study was to identify initial data and comorbidities of patients, which could be used to grossly estimate the mortality and morbidity rate. Afterwards, we focused on a more intensive and aggressive surgical as well as postsurgical treatment.

**Materials and methods**

Data collection started in January 2015 and ended in December 2019. 274 patients with a diagnosis of diffuse peritonitis who underwent surgery were enrolled in the study. We identified and classified patients based on their gender and age. Furthermore, based on their history and available data, we identified severe comorbidities and classified them into groups—these included cardiovascular disease, malignancy, hypertension, diabetes mellitus, chronic pulmonary disease, chronic renal disease, and other severe diseases; also patients without baseline comorbidities and finally patients with two or more comorbidities. Based on our experience, we subclassified patients into 4 groups according to the type of effusion in the abdominal cavity: 1) serous, chemical, and other peritonitis; 2) biliary peritonitis; 3) purulent peritonitis; and 4) stercoral peritonitis. We also classified patients into groups based on the peritonitis origin and location of the peritonitis, specifically right-sided colon and transverse colon (1), left-sided colon (2), rectum (3), small intestine (4), hepatopancreatobiliary origin (5), upper GI tract (6), and others (7; Fig. 1a,b).

Patients presented with symptoms of acute abdomen and underwent surgery. Peritonitis treatment was selected after treatment of the primary cause of peritonitis and lavage of the abdominal cavity. Negative pressure wound therapy (NPWT, V.A.C.) was applied in 66 patients; a relaparotomy was scheduled in 18 patients, non-woven fabric was implanted below the fascia to temporarily close the abdomen. In these procedures, we expected further planned revision within 24–48 h. In 84 patients, our aim was definitive closure of the abdominal cavity with postsurgical continuous lavage (usually four drains in each quadrant of the abdominal cavity, followed by continuous irrigation with antiseptic solution). In
106 patients, the abdominal cavity was closed only with gravity drainage. None of the two procedures expected further abdominal revision.

We evaluated the 30-day mortality and morbidity rate according to the Clavien–Dindo classification II and also the duration of hospitalization of patients. Level II of the CD classification was strictly used to evaluate morbidity, to obtain the most critical information and therapy of patients and their complications.

The obtained data were then statistically evaluated. IBM SPSS Statistics for Windows version 23.0 was used for statistical processing (IBM Corp., Armonk, NY, USA). All tests were performed at a significance level of 0.05. Differences in qualitative data were verified using Fisher's exact test. Differences in quantitative parameters (duration of hospitalization with non-normal distribution as verified by the Shapiro–Wilk normality test) were verified using the Mann–Whitney U test.

**Results**

Between 01.2015 and 12.2019, 274 patients with a diagnosis of secondary diffuse peritonitis underwent surgery at our workplace. We diagnosed and treated serous, chemical, and other peritonitis (1) in 35 patients; biliary peritonitis (2) was diagnosed in 16 patients; purulent peritonitis (3) was demonstrated in 162 patients; and stercoral peritonitis (4) was treated in 61 patients. Negative pressure wound therapy (NPWT, V.A.C.) was applied in 66 patients; non-woven fabric (“COM”) was implanted in 18 patients as preparation for further planned surgical revisions, 84 patients underwent abdominal closure with post-surgical continuous lavage and primary closure of the abdominal cavity, and 106 patients had only gravity drainage (Fig. 2 and 3).

The gender distribution in our cohort was symmetric: there were 56.2% men, 43.8% women, with no statistical difference between the two groups ($p = 0.670)$. The age distribution was also symmetric, the average age of patients was 61.9 ± 16.6 years.

The total 30-day mortality in our group was 22.6%, without statistical significance between the years 2015–2019 ($p = 0.820)$. The total morbidity rate in our cohort was 73.4%, also without statistically significant differences between individual years ($p = 0.166)$. The duration of hospitalization was 25.2 ± 22.5 days ($p = 0.651)$. We classified patients into nine groups according to identified comorbidities (see Fig. 2). The graph shows that the largest number of patients ($n = 168) had two or more comorbidities. The most common comorbidity was hypertension ($n = 154$), followed by a malignant disease ($n = 107$), severe cardiovascular disease, e.g., IHD, s/p MI, arrhythmias, etc. ($n = 85$), and comorbidities other than those stated ($n = 81$). There were 36 patients without comorbidities in our cohort. Of the total number of malignancies present ($n = 107$), the most common were colorectal cancer ($n = 32$), gynecological tumors ($n = 15$), upper GIT tumors ($n = 12$), urological tumors ($n = 10$), hepatopancreatobiliary tumors ($n = 8$), or hemato-oncological malignancies ($n = 9$). Others, such as breast and lung...
Individual comorbidities present in our cohort of patients with diffuse peritonitis

![Bar chart showing comorbidities in treated peritonitis cases (n = 274)](chart.png)

Obturing perforated tumor of the sigmoid colon with accompanying early stercoral peritonitis

Cross-section of the small bowel in the patient from Fig. 6 with structures of partially dissociating carcinoma with syncytial growth infiltrating surrounding tissues. In many sections, the tumor has grown into the bowel wall and spread to the peritoneum

Metastasis of colorectal cancer to the small bowel with accompanying serous peritonitis without perforation

Tumors, pseudomyxoma peritonei, etc., were less represented in our patient group (Fig. 4, 5, 6, 7, 8, and 9).

We related comorbidities to the overall mortality and morbidity rate and also to the duration of hospitalization. As seen in Table 1, patients without comorbidities had a significantly lower morbidity and mortality rate \((p = 0.031, <0.0001)\), and both examined variables significantly increased in the presence of comorbidities.

The highest difference in mortality was recorded in patients with pulmonary comorbidities, where the total 30-day mortality rate was 44% \((p < 0.0001)\), followed by patients with two or more comorbidities (81%, \(p = 0.0003\)), patients with cardiovascular disease (48%, \(p = 0.002\)), malignancy (53%, \(p = 0.012\)), and hypertension (69%, \(p = 0.021\)). Contrarily, diabetes mellitus did not have a negative effect on mortality (24%, \(p = 0.370\)), similarly to renal, HPB, or other comorbidities (\(p = 0.096, p = 0.116, p = 875\)).
As for morbidity, the absence of any other severe disease was associated with positive clinical outcomes, with a total morbidity rate in this group of patients of 6.5% ($p<0.0001$). On the contrary, the morbidity rate was significantly deteriorated by the presence of two or more severe diseases (68.7%, $p<0.0001$), the presence of a cardiovascular disease (37.3%, $p=0.0001$), malignancy (44.3%, $p=0.003$), and hypertension (63.2%, $p=0.0002$). Chronic pulmonary disease did not worsen the overall morbidity rate compared to the mortality rate (24.9%, $p=0.419$), similarly to diabetes mellitus (21.9%, $p=0.237$), HPB, renal, or other comorbidities ($p=0.455$, $p=0.368$, $p=0.053$; Table 1).

We further compared the mortality and morbidity rate with the age of the patients. We demonstrated a clear dependence of both the mortality rate and the presence of postsurgical complications on the age in our cohort—both values increased significantly with an increasing age ($p<0.0001$; Table 2).

We evaluated the mortality and morbidity rate with regard to the gender of patients. While previous variables yielded statistical significance for morbidity and mortality, the gender of patients in our cohort played no role in the 30-day mortality rate, 90-day mortality

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**Table 1** Dependence of the mortality and morbidity rates on the presence of comorbidities

| Comorbidity                  | Death within 30 days | Morbidity |
|------------------------------|----------------------|-----------|
|                              | Yes (n = 62)         | No (n = 212) | Yes (n = 76) | No (n = 198) | Yes (n = 201) | No (n = 73) |
|------------------------------|----------------------|-------------|-------------|-------------|-------------|-------------|
| No comorbidity               | %                    | %           | %           | %           | %           | %           |
| Yes                          | 5                    | 15.6        | 3.9         | 16.7        | 0.005*      | 6.5         | 31.5        | <0.0001*    |
| No                           | 95                   | 84.4        | 96.1        | 83.3        | 93.5        | 68.5        |
| Pulmonary                    | %                    | %           | %           | %           | %           | %           |
| Yes                          | 44                   | 17.5        | 43.4        | 15.7        | <0.0001*    | 24.9        | 19.2        | 0.419       |
| No                           | 56                   | 82.5        | 56.6        | 84.3        | 75.1        | 80.8        |
| Two or more comorbidities    | %                    | %           | %           | %           | %           | %           |
| Yes                          | 81                   | 55.7        | 80.3        | 54.0        | <0.0001*    | 68.7        | 41.1        | <0.0001*    |
| No                           | 19                   | 44.3        | 19.7        | 46.0        | 31.3        | 58.9        |
| Cardiovascular               | %                    | %           | %           | %           | %           | %           |
| Yes                          | 48                   | 25.9        | 46.1        | 25.3        | 0.001*      | 37.3        | 13.7        | 0.0001*     |
| No                           | 52                   | 74.1        | 53.9        | 74.7        | 62.7        | 86.3        |
| Malignancy                   | %                    | %           | %           | %           | %           | %           |
| Yes                          | 53                   | 34.9        | 51.3        | 34.3        | 0.012*      | 44.3        | 24.7        | 0.003*      |
| No                           | 47                   | 65.1        | 48.7        | 65.7        | 55.7        | 75.3        |
| Hypertension                 | %                    | %           | %           | %           | %           | %           |
| Yes                          | 69                   | 52.4        | 65.8        | 52.5        | 0.021*      | 63.2        | 37.0        | 0.0002*     |
| No                           | 31                   | 47.6        | 34.2        | 47.5        | 36.8        | 63.0        |
| Diabetes                     | %                    | %           | %           | %           | %           | %           |
| Yes                          | 24                   | 18.9        | 25.0        | 18.2        | 0.370       | 21.9        | 15.1        | 0.237       |
| No                           | 76                   | 81.1        | 75.0        | 81.8        | 78.1        | 84.9        |
| HPB                          | %                    | %           | %           | %           | %           | %           |
| Yes                          | 13                   | 6.6         | 11.8        | 6.6         | 0.116       | 9.0         | 5.5         | 0.455       |
| No                           | 87                   | 93.4        | 88.2        | 93.4        | 91.0        | 94.5        |
| Renal                        | %                    | %           | %           | %           | %           | %           |
| Yes                          | 16                   | 8.5         | 14.5        | 8.6         | 0.096       | 11.4        | 6.8         | 0.368       |
| No                           | 84                   | 91.5        | 85.5        | 91.4        | 88.6        | 93.2        |
| Others                       | %                    | %           | %           | %           | %           | %           |
| Yes                          | 31                   | 29.2        | 38.2        | 26.3        | 0.875       | 32.8        | 20.5        | 0.053       |
| No                           | 69                   | 70.8        | 61.8        | 73.7        | 67.2        | 79.5        |

*Statistically significant p-value
Table 2 Dependence of morbidity and mortality on age

| Age       | Death within 30 days | p-value |
|-----------|----------------------|---------|
|           | Yes (n = 62)         |         |
|           | Median | Min  | Max  | Mean | SD | Median | Min  | Max  | Mean | SD |
|           | 69.0   | 45.0 | 92.0 | 70.1 | 11.4 | 62.0 | 1.5  | 95.0 | 59.5 | 17.2 | <0.0001* |
|           | No (n = 212)        |         |
|           | Median | Min  | Max  | Mean | SD | Median | Min  | Max  | Mean | SD |
|           | 66.0   | 9.0  | 95.0 | 64.4 | 14.9 | 59.0 | 1.5  | 91.0 | 55.1 | 19.3 | 0.001* |

*Statistically significant p-value

Table 3 Dependence of morbidity and mortality rates on the gender of patients

| Gender of the patient | p-value |
|-----------------------|---------|
|                       | Male (n = 154) | Female (n = 120) |
| Death within 30 days  | Count | %    | Count | %    |
|                       | 33    | 21.4 | 29    | 24.2 |
| Death within 90 days  | 43    | 27.9 | 33    | 27.5 |
| Total morbidity       | 115   | 74.7 | 86    | 71.7 |

Table 4 Dependence of the mortality and morbidity rate on the type of effusion in peritonitis: serous, chemical, and other (1); purulent (2); stercoral (3); and biliary (4)

| Type of peritonitis according to effusion | p-value |
|------------------------------------------|---------|
| 1 (n = 35)                              |         |
| Death within 30 days                     | Count | %    | Count | %    | Count | %    | Count | %    | Count | %    |
|                                         | 8     | 23   | 25    | 15   | 24   | 39   | 5     | 31    |
| Death within 90 days                     | 9     | 26   | 32    | 20   | 29   | 48   | 6     | 38    |
| Total morbidity                          | 20    | 57   | 116   | 72   | 54   | 89   | 11    | 69    |
| Groups that differ based on the adjusted residue method are highlighted in bold. Group 2 has the lowest mortality rate, while group 3 has the highest mortality rate. The morbidity rate is lowest in group 1, and the highest in group 3 |

*Statistically significant p-value

Table 5 Dependence of the morbidity and mortality rate on etiology of peritonitis: right colon and transverse colon (1), left colon (2), rectum (3), small intestine (4), hepatopancreatobiliary origin (5), upper GI tract (6), and others (7)

| Type of peritonitis according to origin | p-value |
|----------------------------------------|---------|
| 1 (n = 40)                             |         |
| Death within 30 days                    | Count | %    | Count | %    | Count | %    | Count | %    | Count | %    |
|                                         | 10    | 25   | 11    | 19   | 3     | 18   | 15    | 27   | 8     | 28   |
| Death within 90 days                    | 10    | 25   | 14    | 24   | 4     | 24   | 20    | 36   | 12    | 41   |
| Total morbidity                         | 27    | 68   | 43    | 74   | 15    | 88   | 39    | 70   | 22    | 76   |
|                                         | 10    | 20   | 20    | 50   |

We evaluated morbidity and mortality in individual types of peritonitis based on effusion and also according to their etiology and origin. While the type of effusion showed a clear effect on morbidity and mortality according to its character ($p < 0.05$), the locality at which peritonitis developed (colon, small intestine, HPB, etc.) demonstrated no statistical significance ($p > 0.05$). Interestingly, the lowest mortality rate in our group was in the group of purulent peritonitis. On the contrary, in accordance with expectations and the literature, the highest mortality rate was demonstrated in the group of stercoral peritonitis. Morbidity is lowest in serous, chemical, and other peritonitis, and highest in the group of stercoral peritonitis (Tables 4 and 5).

Discussion

Diffuse peritonitis is a disease with high morbidity and mortality rates. The 30-day mortality rate ranges from 14.5 to 19.4%, its level significantly depends on the presence of severe comorbidities [6–10]. The general medical condition of the patient plays an essential role in the further prognosis of the patient. Scoring systems have been developed to determine the prognosis of patients. However, they suffer from significant complexity, with a number of monitored parameters. In a similar study carried out at our workplace, we used the ASA scoring system and compared it with
commonly used MPI and qSOFA systems: the results of these scoring systems correlated well with mortality and data reported in the literature. Even a simple ASA system seemed to be, at least according to our data, applicable in this indication [2]. However, scoring systems are complicated and are intended mainly for intensive care specialists for further management of diffuse peritonitis on a monitored bed. However, surgeons require information regarding a higher risk of a severe to fatal course prior to or during the surgery, and the surgical procedure is often urgent, without the necessary time to calculate complex scoring systems. The prognosis of patients often directly determines the surgical procedure. There is a differentiated procedure for extremely high-risk patients available, with rapid decontamination of the abdomen in combination with an NPWT technique, and subsequent elective revision after stabilization of the patient seems to be an optimal procedure for extremely high-risk patients. This procedure seems to be more effective in such patients according to our experience and the available world literature. Therefore, we tried to identify simple risk factors from the initial data which are associated with increased mortality and morbidity of patients. The Charlson Comorbidity Index is widely used in clinical practice. It estimates the 10-year survival rate of patients based on comorbidities [11]. This predictor may also be used in patients with peritonitis to estimate the course of the disease and short-term prognosis. However, our study focused on identification of individual comorbidities or initial data associated with a significantly worse disease course, i.e., cases where the open abdomen method with an NPWT technique could be used to improve the patient’s prognosis [12]. The use of NPWT in the therapy of diffuse secondary peritonitis is still a topical issue, and results remain dubious. However, it may lead to an improved prognosis in carefully selected patients [13].

The most frequently stated comorbidities which significantly worsen the prognosis of patients are age, gender, malignancy, presurgical organ failure, chronic renal disease, cardiovascular disease, and diabetes mellitus [6, 14–16].

In our cohort, we found the presence of two or more severe comorbidities to be a major negative prognostic factor significantly worsening both mortality and morbidity. In addition, two or more severe comorbidities were present in 61% of all patients with diffuse peritonitis in our cohort, which also corresponds to the age structure of the patients. It is clear that elderly and/or polymorbid patients are more likely to suffer from peritonitis, i.e., there is a presumption of impaired healing abilities in these groups of patients. Mortality and morbidity rates in our cohort were further significantly increased in the presence of a severe cardiovascular disease or a malignancy, which is in accordance with the literature. The mortality rate was significantly worsened in patients with chronic pulmonary disease, which, however, did not seem to worsen the morbidity rate of patients in our study. Contrarily, diabetes mellitus did not worsen the prognosis of patients or increase the morbidity rate. Similarly, we did not find chronic renal disease to be a negative prognostic factor, contrary to the literature.

An interesting additional finding of our study was that morbidity and mortality were clearly dependent on the character of effusion when classifying the peritonitis based on this factor. However, no statistical dependence was demonstrated for the origin of the peritonitis. It therefore seems to be more meaningful and, moreover, easier to evaluate peritonitis according to the type of effusion rather than its origin.

**Conclusion**

Our study demonstrated that the age, type of effusion, and the presence of severe comorbidities—cardiovascular disease, malignancy, and hypertension—at the time of diffuse secondary peritonitis development are completely essential in determining its prognosis. The presence of two or more severe comorbidities seems to be more important than the presence of a specific severe disease at the time of surgery according to our multivariate analysis and subsequent comparison with the literature. We did not identify comorbidities commonly stated in the literature, such as gender, chronic renal disease, or diabetes, as risk factors of mortality in our cohort. Our monocentric study found that the presence of cardiovascular disease, malignancy, hypertension, and the presence of two or more serious comorbidities significantly worsens the mortality and morbidity rates of patients, in correlation with the recent literature. In our study cohort, pulmonary disease worsened the mortality rate, but not the morbidity rate.

Our results show that the most important factor for the patient’s prognosis is thorough staging of the patient as early as during the diagnosis of suspected peritonitis, including their medical history as well as a comprehensive paraclinical examination, based on which we can determine the probability of a more severe disease course in certain patients and offer them a more aggressive method of treatment, such as escalated ATB therapy, comprehensive resuscitation care, or a more suitable surgical procedure, e.g., NPWT, as shown by the available results of our prospective study. Further prospective multicentric studies will be needed to verify our postulate.

Another very important outcome of our study for clinical practices is the need to classify peritonitis according to the type of effusion rather than its origin, since this predictor correlates better with treatment outcomes and the prognosis of patients.

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Declarations

Conflict of interest P Špička, J. Chudáček, T. Řezáč, K. Vomáčková, R. Ambrož, J. Molnár, D. Klos, and R. Vrbá declare that they have no competing interests.

Ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

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