INTRODUCTION

Mortality from peritonitis remains high, especially in patients who develop severe septic complications. It varies significantly depending on the specific cause: from 0.25% for appendicitis to 45% for fecal peritonitis (Weigelt et al., 2007; Ross et al., 2018).

Already for ten years, the American Society of Infectious Diseases guidelines on complicated intra-abdominal infections and their treatment tactics in primary, secondary and tertiary peritonitis have existed (Eckmann et al., 2011). Also, European surgeons, oncologists, and internists struggle with high rates of morbidity and mortality from peritonitis. Improved diagnostics, treatment with antibiotics and other modern procedures like vacuum-assisted intraabdominal closure (Perrone et al., 2020; Skicko et al., 2021) have reduced the complications rate of peritonitis, but it remains high. Factors still exist that contribute to its adverse outcome. Authors from different countries have attempted...
to clarify the risk factors of mortality from peritonitis like old age, comorbidities, or sites of perforation (Heijkant et al., 2013; Khan et al., 2013; Taber et al., 2015; Ikeda et al., 2021).

Many investigations performed during recent years worldwide have shown that if not treated and diagnosed properly in time, peritonitis is still a surgical problem to be taken into consideration. It is a condition that may prove rapidly fatal in both old and young, which worldwide studies have proven (Malangoni and Inui, 2006; Tochie et al., 2020). In the western part of the world, elderly have a higher risk in developing severe sepsis in intraabdominal infections, which may become fatal since they have less physiological reserve and multiple comorbidities; common causes are surgical disorders like diverticulitis, cholecystitis, pancreatitis, malignancies as colon cancer and mesenteric ischaemia (Riche et al., 2009; Khan et al., 2013; Dimopoulos et al., 2017; Šapovalovs et al., 2021). However, elsewhere the age at which the patients are admitted to clinics due to peritonitis tend to be younger. In various studies, causes like appendicular perforation and ulcers related to typhoid and tuberculosis have been mentioned and contributing factors to the mortality are late presentation, site of perforation and aetiology (Bali et al., 2014; Ghosh et al., 2016; Meena et al., 2017; Jastaniah et al., 2018; Tantarattanapong and Arwae, 2018).

Questions remain on what may contribute to patients not receiving treatment in time and what makes peritonitis a diagnostic challenge in clinics. Most articles about fatal peritonitis are not fully detailed, which may lead to doctors misdiagnosing it, and other important factors that need to be investigated might be missed. Multiple comorbidities significantly increase the risk of developing intraabdominal sepsis with mortal outcome, but certain comorbidities like diabetes mellitus (DM) increase the risk more than others (Taber et al., 2015; Payá-Llorente et al., 2020). Does this signify that certain patient groups should be examined on a more regular basis by general practitioners? Therefore, further research needs to be conducted both ante- and post-mortem to find answers to these questions.

The aim of the study was to analyse the causes of fatal peritonitis, the contributing factors of its mortal outcome, and diagnostic discrepancies.

MATERIALS AND METHODS

Study material. This study was conducted at the Pathology Department of Riga Stradiņš University (RSU) and Pathology Centre at the Riga East University Hospital (RECUH). The research was conducted as a retrospective study where autopsy records for a three-year period were selected and analysed. Among 1350 records (years 2018–2020), 52 cases of peritonitis were found.

Each case considered appropriate for the study was carefully analysed and recorded in a originally designed table with multiple parameters: age, sex, length of hospital stay, clinical and pathological diagnosis, complications, comorbidities, and discrepancies between them. In cases where the patient was found dead at home, it was documented as a home case. Also, eventual family doctors’ notes, and laboratory markers were recorded.

Ethical compliance. This article does not contain any studies involving human participants or animals performed by any of the authors. Ethical approval was obtained from the Riga Stradiņš University Research Ethics Committee (No. 6-1/06/17).

Morphology. Specimens from autopsies were stained with the haematoxylin Eosin, examined and made images produced under a Leica microscope (Leitz, Wetzlar, Germany). Microscopically, the type of peritonitis was evaluated as serous, fibrinous, or purulent. For the diagnosis of some malignancies, immunohistochemistry was conducted with markers (CK7, CK5, CEA, NSA, p53, CD3, CD2, CD8, and CD138).

Statistical analysis. All data were entered into a computer-based data file in Excel-format. Statistical analysis was performed using IBM SPSS® Statistics version 26. There were six home cases, and these therefore had no hospitalisation time (in days). This was also one major reason why hospital and home cases were analysed separately. Our study results were tested using Spearman’s correlation test to compare correlation between hospitalisation time and patient age. A p-value less than 0.05 was considered as a statistically significant difference. Descriptive statistics (mean and median) were calculated for age and hospitalisation time.

RESULTS

Hospital cases. There were 46 hospital cases with fatal peritonitis. Median hospitalisation time was 2.0 days. The shortest time was 0.01 days and the longest stay was 42 days. In most cases the patient died within 1 day and some within a few hours. The youngest patient was 20 and the eldest 87 with a median age of 65 years. The majority of the patients were over 60 years of age and male — 61.4%.

A cross-tabulation test between the variables age and sex showed a tendency for males to die at a younger age than females. The Spearman’s test showed a statistically significant association between age and hospitalisation time: (r = 0.61; p = 0.036) — older patient died sooner.

Causes of peritonitis. The most common pathological diagnoses that had been confirmed by autopsy as the causes of the peritonitis were: non-oncological pathologies of the digestive system (42%), different malignancies (23%), HIV related (10%) and vascular diseases (7%) and other causes (18%) like chronic pyelonephritis and complications due to amputation after femoral fracture and sepsis (Fig. 1).

Organ perforation was one of the non-oncological gastrointestinal diagnoses. The most common cause of the perfora-
tions was gastric ulcer followed by diverticulitis and duodenal ulcers. One case involved obstipation with coprolite formation, which resulted in perforation of the bowel wall.

The most common oncological diagnoses were colon, gastric and haematological malignancies. Other diagnoses encountered were one case with metastatic lung cancer and one with cervical cancer in T4 stadium, which had led to growth into the urinary bladder with purulent nephritis and abscess at L4 vertebra as well as complications with perforation and vesicovaginal fistula.

All cases involving pancreatitis were found to be acute. At least three of them involved acute pancreatitis, which had caused total enzymatic peritonitis. Two in-hospital cases were diagnosed as chronic pancreatitis with exacerbation and fibrocystic degeneration, which had led to generalised peritonitis with multiple enzymatic steatonecrosis in adipose tissue (Fig. 2). We also found some fatal cases due to phlegmonous cholecystitis with dense inflammatory infiltrates around the vessels of adipose tissue containing septic thrombi (Fig. 3).

Among the patients with HIV, three were in advanced stage of CIII and one in stage BIII. In two of the cases with stage CIII, there had also been diagnosed bilateral pneumonia with a mixed flora of *P. jerovicii*, *C. albicans*, *S. aureus*, *Acinetobacter baumanii* and CMV. In the third advanced case, the patient had generalised tuberculosis that had spread to the kidneys, small intestines and meninges that was characterised by typical granulomatous inflammation with giant cells (Fig. 4). It was mentioned in the autopsy record that the patient had undergone surgery with resection of bowel and ileostomy.

Mesenteric ischaemia was the most frequently encountered diagnosis of cardioembolic origin, which had led to gangrene of small intestines.

Other diagnoses that were infrequent, but still accounted for 18% of the pathological diagnoses, were chronic pyelonephritis with calcaneus stones, decompensation of diabetes mellitus, benign prostate hyperplasia causing cystitis with rupture. In the reports it had been noted if the peritonitis had been complicated by becoming generalised. Among hospitalised cases (n = 46), generalised intra-abdominal infection accounted for 61.5% and localised for 38.5%. The reasons of death in local peritonitis cases were related to chronic comorbidities like coronary heart disease and chronic alcoholism, where pulmonary artery thromboembol-
lism, pulmonary oedema, and liver and kidney insufficiency developed accordingly. The Spearman’s test showed no statistically significant association between age and the extent of peritonitis ($p = 0.098$).

**Comorbidities.** The most common comorbidities of analysed cases were cardiovascular (31%) and liver disorders (26%), followed by gastrointestinal pathologies (15%) and alcoholism — 10% (Fig. 5). Common cardiovascular comorbidities were generalised atherosclerosis and coronary heart disease. Cirrhosis and hepatic steatosis were frequent liver disorders, and also cases of liver encephalopathy were diagnosed. In many cases alcoholism was mentioned together with the liver disorders. Among the most common adjacent diseases in the digestive tract should be noted gall-bladder stones, chronic pancreatitis, and cachexia.

However, the other diagnoses (18%) that could not be categorised included respiratory disorders like chronic obstructive bronchitis as well as neurological and muscular conditions, chronic kidney disease, and benign hyperplasia of prostate.

**Laboratory tests.** Laboratory reports were included in the autopsy records of hospital cases. Among these, leucocytosis, anaemia, and elevated CRP, creatinine and ESR were frequently reported. In some cases, cultures had been performed from blood, wound, sputum and oral smear, which reported bacteria like *S. aureus*, *Cryptococcus neoformans* and *Acinetobacter baumannii* been found. The only virus was CMV and the most frequently reported fungi was *Candida albicans*.

**Diagnostic discrepancies.** Misdiagnoses were found in eight of the hospital cases (17.4%), where the clinical diagnosis did not match the pathological. The most common situations where misdiagnoses had occurred, were when the patient had ischaemic disorder of the mesentery, perforations in the case of peptic ulcer and malignancies of various origins (Table 1).

The departments that had most correctly diagnosed peritonitis were surgery and emergency departments. These were also the departments with the most intra-abdominal infection cases.

**Home cases.** Out of the 52 cases, six patients had been found dead outside the hospital: five of them had been discovered by ambulance at home and one was homeless. These persons were four females and two males. 50% were between 44 to 65 years of age and the rest were between 66 to 88. The median age was 63.

Causes of the peritonitis varied in this group, but the majority had oncological (33%) and gastrointestinal origin (33%). The oncological cases had pathological diagnoses of caecal adenocarcinoma with dissemination (Fig. 6) and villous adenoma that rotated around its axis, necrotised, and caused gastric perforation. The gastrointestinal cases were peptic ulcer with perforation and exacerbation of chronic calculous cholecystitis. Other peritonitis cases had vascular aetiology and were caused by atherosclerosis of mesenteric arteries.

### Table 1. Diagnosis discrepancies in fatal peritonitis

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Clinical diagnosis</th>
<th>Pathologist’s diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>52</td>
<td>Urinary tract infection, sepsis and left-sided pneumonia.</td>
<td>Ulcerative Colitis-procto-sigmoiditis with perforation. Peritonitis. Sepsis</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>72</td>
<td>Mesenterial thrombosis and intestinal gangrene.</td>
<td>Peptic ulcer with perforation. Diffuse peritonitis.</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>66</td>
<td>Lung cancer (T3, N2, M1).</td>
<td>General atherosclerosis in mesenteric arteries and chronic active ischaemic colitis with microperforations. Diffuse peritonitis.</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>53</td>
<td>Acute abdomen.</td>
<td>Ileus. Diffuse fibrinous peritonitis.</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>60</td>
<td>Metastatic carcinoma with unknown primary location. Breast cancer in year 2003.</td>
<td>Gastric signet cell cancer (T3N1M1 G3) with perforation. Purulent peritonitis.</td>
</tr>
</tbody>
</table>

![Fig. 6. Peritonitis due to dissemination of adenocarcinoma (arrow) in mesentery with inflammatory infiltrates around its structures. Haematoxylin-eosin, OM 50x.](image-url)
Peritonitis was generalised in 83.3% of cases of persons who died at home. The most common comorbidities among the home cases were cardiovascular (66.7%) and gastrointestinal (33.3%). The rest were liver disorders (16.7%), alcoholism (16.7%) and others (33.3%). The cardiovascular comorbidities were atherosclerosis, coronary heart disease and cardiomyopathies. In two cases, chronic pancreatitis had been diagnosed, one was related to alcoholism. Among the liver disorders, one diagnosis was liver steatosis, where the patient also had a history of alcohol use. One patient had chronic kidney disease. Also, psychiatric disorders were noted, such as schizophrenia and neurological manifestations of alcoholism. In these cases, family doctors had supplied short information about the patients, but mainly they highlighted the fact that they had not visited a general practitioner for many years.

DISCUSSION

Treatment of peritonitis in the world and in Latvia has improved significantly in the last two decades (Perone et al., 2017; Skicko et al., 2021), but early management of peritonitis remains a challenge for physicians in a reception department, emergency medicine, surgery, and oncology (Beckman et al., 2016; Medford-Davis et al., 2016; Ikeda et al., 2021).

This study presents some perspectives not only on why peritonitis may lead to mortality but also to identify some factors that could have been prevented during the patient's lifetime.

In general, the causes for developing deadly peritonitis in our study did not differ significantly from those mentioned for elderly in other western studies (Patnos et al., 2002; Benjamin et al., 2016, pp. 692–702; Paya-Llorence et al., 2020). However, they were totally different from those in the eastern part of the world. No cases of appendicitis were found among our group of patients, which is a common cause of perforation and mortal outcomes in the East, especially among the younger population (Danish, 2022). However, we would like to highlight that of the 46 hospitalised patients, surgery was performed only in one case. One reason that surgery was never performed could have been that most of the patients died within short time after arriving at the hospital. Also, another factor that must be taken into consideration, which has been pointed out in several studies (Bali et al., 2014; Meena et al., 2017; Iritani et al., 2021), is that the patients were brought to the hospital with late stages of peritonitis, as in our study.

There are age differences of these surgical patients in different parts of the world. In the studies from the eastern countries (Malhotra et al., 2016; Jantani et al., 2017), the average age of the patients with fatal peritonitis was 34.2 years, while in the Riga hospital study it was 65 years. The above cited authors mention that generalised peritonitis is still a significant surgical problem in the East and West and various explanations exist. One is that in the eastern countries have higher incidence of infectious diseases like tuberculosis, typhoid fever and amebiasis. Further, there is mentioned that 14% of all jejunal perforations were caused by tuberculosis and 25% of them had mortal outcome. In our study only one case had tuberculosis diagnosis and it was HIV patient.

Our study found that multiple concomitant diseases worsen and accelerate the clinical course of peritonitis. In studies conducted by Western physicians, mainly liver-related disorders are mentioned, but in the Eastern countries respiratory disorders are highlighted.

In our study, liver pathologies as co-morbidities were proved in 26% of fatal cases. Microscopic analysis of these autopsy slides proved that in some of these persons, liver changes like steatosis and cirrhosis occurred together with neuropathological features of alcoholism and chronic pancreatitis. Therefore, we can argue that chronic alcoholism was more common in our analysed cases, than the 10% calculated from medical records of physicians. However, the most common co-morbidities in our study were cardiovascular diseases such as general atherosclerosis, hypertension, coronary heart disease and cardiomyopathies (31% in hospital cases and 66.7% — in home cases). These diseases can cause venous hyperaemia, hypoxia, and impaired regeneration in the affected hollow organs of the abdominal cavity. All this contributes to the progression of inflammation and necrosis in the primary place of injury; thus a normal anatomical barrier therefore is disrupted, and intraluminal bacteria invade peritoneal cavity or retroperitoneal space (Beckman et al., 2016).

Our statistical analysis proved that the higher the age of the patients, the shorter the hospitalisation time due to mortal outcome. As mentioned previously, elderly patients have higher incidence of comorbidities, which masks the symptoms of peritonitis. This is also highlighted in a study on elderly patients in the emergency department (Samaras et al., 2010; Ikada et al., 2021). Old people more often show atypical symptoms and are more likely to become misdiagnosed and discharged with untreated health issues. Furthermore, the authors emphasised that abdominal pain is a major complaint in 3–13% of elderly patients that visit the emergency department. However, 78% of emergency doctors report difficulties in management of abdominal pain in geriatric patients and the most often misdiagnosed disorders are gall-bladder disease, nonspecific abdominal pain, cancers, and diverticulitis (Samaras et al., 2010; Danish, 2022). Not all of these studies mentioned how often these misdiagnoses lead to mortal outcome in old patients, but it is obvious that these values vary from country to country and hospital and are still high.

In this study the most common diagnostic discrepancy that had led to patient death was mesenteric ischaemia. It has frequently been pointed out that mesenteric ischemia is a diagnostic challenge. In some clinical reviews (Oldenburg et al., 2004; Ghosh et al., 2016; Medford-Davis et al., 2016), this is explained by its nonspecific presentation and compli-
cations such as ileus and gastrointestinal bleedings that may mask the ischaemia. The authors further explain that there are four categories of acute mesenteric ischaemia 1) arterial embolism, 2) arterial thrombosis, 3) nonocclusive mesenteric ischemia and 4) mesenteric venous thrombosis, which all have different signs and symptoms as well as different mortality rates. For example, arterial embolism has a more abrupt and dramatic onset than arterial thrombosis, which is progressive in nature and has higher mortality rates ranging from 70 to 100 percent due to delay in diagnosis (Oldenburg et al., 2004). The key to treating mesenteric ischaemia properly is early diagnosis or it is rapidly fatal, but as the authors highlight, it has various and nonspecific presentation. If diagnosis occurs within 24 hours after onset of symptoms, the survival rate is 50 percent, but if later then the odds of survival are only 20 to 30% (Oldenburg et al., 2004; Adaba et al., 2015; Sapoovalovs et al., 2021).

Diagnostic discrepancies were found in 18% of our cases, and some departments had a higher incidence of misdiagnosing peritonitis than others. Departments such as emergency and surgery have most cases and therefore it could be concluded that they have more experience in diagnosing peritonitis than, for example, an oncology department. Emergency departments use a multidisciplinary approach, which increases the diagnostic rate. Abdominal pain is a frequent complaint in emergency departments in the US (Medford-Davis et al., 2016) and an area of high risk of misdiagnosis since a wide variety of conditions present with abdominal pain. In that study, the common sources of misdiagnosis in the emergency department were incomplete history taking, ordering insufficient tests and improper follow-up of test results. These results can be compared with those of another American study (Kachalia et al., 2007), which found breakdown points in the diagnostic process, such as failure to order appropriate tests, medical history and physical examination, interpretation of test results and ordering consultations. The authors of that study also found that 52% of the misdiagnoses had been made by emergency doctors.

In our study, six patients had been found dead outside the hospital. For various reasons, these patients or their relatives had not called for an ambulance. In some cases, it was mentioned in notes from the family doctor that the patient had not visited them for many years, which may have been a contributing factor to the development of peritonitis as a complication of other underlying disorders. Physicians have tried to describe the main reasons that people avoid medical care (Taber et al., 2015). That study that previous studies had only been focusing on specific populations and diseases and not on people in general. They found three main categories why people avoid seeking medical care when they are ill: 1) low perceived need to seek medical care, 2) traditional barriers to medical care, and 3) unfavourable evaluations of seeking care. The first category contained reasons such as that the problems “would improve over time” or “not being sick enough”, the second had reasons as “the cost is too high”, “not enough time/too busy”, or “lack of health insurance”, and the final category were further divided into factors such as physician, organizational, affective, and expected negative outcomes. Physician factors where the largest group, where issues were related to the relationship to the doctor such as “communication”, “low trust” etc. In their discussion the authors emphasised that these categories could be applicable on primary care, which in many cases is the first point where patients contact the health care system.

CONCLUSION

This study, which is based on autopsy cases, demonstrated that fatal peritonitis develops mainly in elderly at the 7th decade of life with multiple concomitant diseases, which could have been treated by general practitioners in a timely manner. Statistically significant association between older age and short hospitalisation time due to unfavourable outcome of intra-abdominal infection was found. An important contributing factor of fatal peritonitis in patients both at home and in hospital was lack of sharing the responsibility from persons themselves and their relatives, as most patients enrolled in clinics in the advanced stages of malignancies of the organs of the abdominal cavity, as well as during the period of exacerbation of untreated chronic diseases of the digestive system. Misdiaisons of peritonitis occurs in emergent situations, which also decreases the survival rate as physicians have lack of time to order to conduct an adequate examination of the patient with appropriate laboratory tests.

CONFLICT OF INTEREST

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES


