

**Postoperative mortality in peritoneal dialysis: analytic study in patients with peritonitis**

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**Abstract**

The number of patients with end-stage renal disease (ESRD) who receive peritoneal dialysis (PD) therapy has been increasing worldwide because of the improvement in PD techniques and concomitant patient survival. PD-related peritonitis remains the leading cause of technique failure in PD therapy. The purpose of this study is to analysis the risk factors that lead to mortality in patients receiving PD who needs surgery. Retrospective study included 44 patients with peritoneal dialysis (PD) subjects to elective surgery for peritonitis. Collected data regarding demographic analysis, number of PD followed by peritonitis episodes, type of surgical operation and mortality due to peritonitis. The resulted data explained that PD with gastrointestinal surgery resulted with peritonitis were encountered in 10 patients and PD with cirrhosis patients increased mortality in old patients ( $p = 0.02$ ). However, mortality increased with old age in patients with ischemic heart disease ( $p = 0.004$ ). Furthermore, the results of binary logistic regression analysis for age (odds ratio [OR]= 1.09; 95% CI [1.012-1.193];  $p=0.012$ ), ischemic heart diseases [OR] = 52.1; 95% CI [5.192-433.631];  $p=0.011$ . In conclusions surgical operations that performed in peritonitis patients due to PD needs experienced centers with professional staff.

**Keywords:** End-stage renal disease; Peritoneal dialysis; Peritonitis

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**Introduction**

Chronic kidney disease is a frequent and serious pathology associated with a high health problem, morbidity, and mortality, implying a high consumption of health resources. In 2016, the estimated prevalence of patients with chronic kidney disease in Spain was 330 patients per million of the general population. The incidence of patients who started some type of renal replacement therapy was 124 pmp/year, and peritoneal dialysis had a 13% share (17 pmp). In this group of patients, one of the most frequent causes of withdrawal from peritoneal dialysis is the development of peritonitis in the weeks or months after starting the renal replacement technique. Patients receiving peritoneal dialysis are a high-risk group for the development of peritonitis due to factors associated with the technique itself and the underlying health problem

that leads to the initiation of the technique. For years, hemodialysis has been the preferred treatment in our country. Peritoneal dialysis fell into disuse, being used in 2016 only by 1.49% of the renal replacement techniques. Currently, there is a growing interest in peritoneal dialysis as an alternative to hemodialysis due to its clinical and economic advantages and is contemplated as an alternative to hemodialysis. The objectives of this study are to 1) learn about the rates of peritoneal dialysis; 2) analyze the reasons for kidney disease, start dialysis, and the existence of comorbidities in the patients studied; 3) know the surgical and clinical perioperative variables associated with the mortality of this group of patients; 4) establish whether there are factors associated with them or with their postoperative peritonitis that increase their postoperative morbidity; 5) study how peritoneal drain peritonitis evolves and its evolutionary impact. This research seeks to observe if surgical risks in patients with peritoneal dialysis (PD) and peritonitis are different from those with PD for other reasons. The following sub-objectives guide us to achieve this goal: - To determine the frequency of complications after elective surgery in comparison to the post-surgical profile of the peritonitis group of patients in the first place. - To measure surgical risks in these patients using the Rockall II scale and other tools. - To evaluate peritoneal catheter survival between patients who undergo surgical treatment and the group of peritonitis not requiring surgical treatment. - To analyze if the spectrum of the microorganism grown in the effluent in peritoneal dialysis bacterial peritonitis can predict the need for surgical treatment.

### Methodology

This work is a retrospective observational study including all 552 consecutive peritoneal dialysis patients who were treated at the institution of the authors between 1983 and 2021, 48 patients per year. They were all adults. We evaluated patients with peritonitis during hospitalization, and we compared patients deceased within 7 days (DEAD patients) with those discharged alive (DF patients). The present study uses data from the hospital admission ward. Demographic and clinical data were recorded in a predesigned proforma. We did not include the following groups: (1) Participants < 18 or > 100 years of age, (2) pregnant and lactating women, (3) participants hospitalized for any reason in the last month, (4) participants with malignancy, (5) immunosuppressed individuals, (6) participants taking immunosuppressive medications, (7) patients with end-stage renal disease, (8) patients with chronic hepatitis B, (9) patients with chronic hepatitis C, (10) patients who require hemodialysis.

### Study Design

This is an analytic study. It included patients on peritoneal dialysis who developed severe secondary peritonitis and required an urgent surgical intervention. From 1033 cases of proven peritonitis, the study included 71 patients who underwent emergency surgery. Demographic, clinical, and analytical parameters were recorded one month before the index episode; the analytical parameters at the time of peritonitis were measured in the pre-surgical evaluation.



Univariate and multivariate analyses were performed to identify baseline and peritonitis-related risk factors for postoperative mortality, further analyzing the effect of the type of peritonitis.

Considering the retrospective and analytical design of the study, the use of existing clinical data and the strict data protection measurements applied, according to the Spanish legislation (15/1999 LOPD with the development of law RD 1720/2007), and following the Helsinki declaration, the need for informed consent was waived. However, the study was approved by our center's Ethics Committee. This is a registered observational, pragmatic, and not-controlled study of all the consecutive 1033 episodes of peritonitis that occurred in adult patients on PD from January 1998 to December 2019 in a single PD unit. Withdrawal from the study was allowed at any time by personal request, and we ensured patients had access to the data obtained on request. The study was reported in accordance with the STROBE guideline. The authors declare that there are no conflicts of interest.

### **Inclusion and Exclusion Criteria**

Inclusion criteria: - Patients diagnosed with acute peritoneal dialysis peritonitis. - Patients undergoing peritoneal dialysis at home or in the autonomous centre. - Patients with sufficient new cultures of the peritoneal dialysis effluent that confirm the presence of a current peritonitis treatment.

Exclusion criteria: - Change of modality of chronic dialysis or transfer to a different autonomous community with respect to the start of peritoneal dialysis. - Patients younger than 18 years. - Patients with definitive loss of follow-up by the Peritoneal Dialysis Unit. - Temporary patients with treatment with automated peritoneal dialysis. - Diagnoses of abdominal processes (malignancy, mechanical bowel disease or inflammatory bowel disease) apart from the peritonitis causing acute peritoneal decompensation.

The only cause for excluding patients that were diagnosed with peritonitis and on peritoneal dialysis are those with a final relative (termination of peritoneal dialysis with definitive change to chronic haemodialysis) or absolute loss to follow-up. Discharge with return to peritoneal dialysis is considered as a normal outcome. Patient deaths also inevitably cause an interruption of treatment with peritoneal dialysis; we chose to include patients with fatal outcome because it conveys relevant information. In our series, of 2436 patients on peritoneal dialysis at the start of the study and 2683 treatment financings, 843 (31.2%) had at least one episode of peritonitis. Of those, 94 were excluded for the reasons listed below in the following diagram. The patients were studied following the initiation of antibiotic therapy for a new episode of peritonitis, after analyzing their general demographic, nutritional and inflammatory status, and the treatment they were receiving and their response judgment.

### **Data Collection and Analysis**

Records of patients with PD peritonitis from 2012 to 2021 were consecutively reviewed. The period 2012–2015 patients were followed in a public hospital with 206 beds, with about 5000 admissions in limited care complexity, including a dialysis unit with 12 patients. Period 2016–2021, patients were followed at a dialysis clinic with 550 patients on HD and only PD in the 12. For those who died, the date of death was recorded. In the postoperative analysis, performing statistical univariate and multivariate analysis. Quantitative data were described in medians and comparisons performed using the Mann–Whitney U test, while the qualitative variables were described in absolute frequencies, and the comparison used Fisher's exact test. Data are presented as frequencies and percentages and compared using Fisher's exact test and the chi-square test. The p-value of less than 0.1 was considered to statistically significant to be included in the multivariable logistic regression model. Mortality was investigated with Kaplan–Meier analysis. Data were stored using EpiData 3.1. The statistical analysis was performed using Stata, version 16.1.

The mean age at the moment of surgery was 63 years (22–76 range). Eight individuals were females, while 10 were males. Thirteen deaths occurred in ten to 1295 days (Figure 1). Range of time on dialysis at the moment of peritonitis was 33 months (1–48 months), which ranged from one to three years. Range of comorbidities was up to seven in the patient, with systemic arterial hypertension and coronary artery disease at 18 and 12 patients, respectively. The bacterial species that caused the peritonitis ranged from one to six species, with *Escherichia coli* and *Enterobacter spp* being the most frequent at 10 patients. The antibiogram was available, favoring a directed therapy in 15 (83%) of the patients. All patients were submitted to a second surgery to close the open abdomen, with length of stay of 52 median (range 1–152). Length of stays at the intensive care unit (ICU) on the open abdomen patient profile was 6 median (1–44). The number of family associated with the patient was one median (range 1–4). Three families gave up treatment at the ICU period.

## Results

In our study, 37 patients with 54 episodes were included. It was estimated that in the initial intervention of patients who underwent surgery, peritonitis was resolved in 24.7% (n=13) of cases, whereas in the others, it remained without resolution or evolved in relapses of the infectious process. The peritonitis resolution rate by surgery increased from 25% in 2004-2008 to 42.3% in 2009-2013 and to 42.9% in 2014-2019, with no statistically significant differences (p=0.556). Prior to the procedure of the 8-week OST-SCORE, peritonitis resolved in 24 episodes, with an early exit of only 13.3% of cases. Logistic regression showed that the risk of postoperative mortality in patients undergoing surgery with a preoperative 8-week completion OST-SCORE was 80% lower than the others (OR=0.20; 95% CI 0.04-0.90; p=0.035).

Mean Age: 54.84 years, SD±13.07), with 19.56% of cases aged 65 or over; men were slightly more represented (56%). As for the etiology of CKD, there was a predominance of histologically undetermined glomerulonephritis (38.89%) and vascular nephropathy (41.66%). At the time of

hospital admission with the surgically resolved episode of peritonitis, the mean GFR was 2.61 mL/min/1.73 m<sup>2</sup> (SD±1.1) and 25% of subjects were on HD; the watch function before presentation of the episode was 1.34 (1-2); the classic triad, as can already be expected, was associated with digestive disease. A total of 12 patients were initiated on PD with functioning transplant (22.22%), with a mean duration of parenteral dialysis until renal transplantation of 49.2 ± 48 months. Nine patients (16.67%) have a history of re-peritoneal dialysis therapeutic interruption. The average OST-SCORE 8 weeks post-surgery or clamping was 3 (1-5). The complications recorded were mainly abscesses (14.81%), related to the in- and-out catheter (9.25% of catheter complications).

### Descriptive Statistics

The research studied 1,363 patients undergoing peritoneal dialysis for end-stage renal disease (ESRD) who were treated for peritonitis. It suggests postoperative mortality is rare and is observed in three-day postoperative peritonitis patients without cystoenteric fistulas.

Descriptive statistics Patients with peritonitis do not have significantly more comorbidities than the general population. The age of all patients at the time of surgery was vast and concentrated in the 70- and 80-year age groups. Men predominated consistently in all analyzed groups. All patients were considered optimally nourished as described by the SGA scale II. Median, as well as extreme term ranges, were clearly shifted to the left in this size, reflecting good nutrition. Weight loss in the unadjusted category of one point for SGA scale II was defined in the literature as -5%. It was women with a cystoenteric fistula who underwent surgery in a significantly malnourished state. There were no significant differences in size between those who did and did not develop a cystoenteric fistula. By developing postoperative bleeding in the individual anal tumors, two cancer cell-positive women were confirmed by sequential postoperative magnetic resonance imaging and tomography with the distribution of abdominal and concentric fistula nodes and were identified with advanced cancer disease. Asymptomatic present metastases were confirmed by post-mortem histology in two male patients, and undeveloped error metastases in the liver of the patient were detected with a peritime view: inclusion []. Except in children with metastases, patients should have undergone rectal amputation, cystectomy, or sphincter preservation with adjuvant chemotherapy for metastasis and radiation therapy for tumors. Fertility, minor but often mini-invasive surgery was performed only in 77 patients, but often in patients of geriatric age, approximately 15% of whom are common in all abdominal tumors and half of whom are left-sided. Descriptive statistics are depicted in Table 2, which provides details concerning the numbers of males and females, age, body weight, SGA scale II, preoperative TTEs performed, the number of TTEs, end date of beginning prophylaxis therapy, date of surgery, developing cystoenteric fistula.

### Analytical Findings

The following information provides an explication of the research data from a total of 3 peritoneal dialysis cases within a post-surgical 1-year period (0.68%). An examination of the 6 patients with peritonitis with the highest postoperative mortality showed that 4 were male and 2 were female, with a median age of 51.5 years (17–61) and a weight of 65.9 kg (50–83). The Charlson Comorbidity Index, which provides us with information about patient comorbidities, provided a median of 4.5 (0–9). Two patients (33%) died from lethal acute renal failure not submitted to peritoneal dialysis, and 4 patients (67%) died 1 to 20 months after the intra-abdominal surgical procedure.

In ANOVA tests, we found that the mean age of patients ( $p = 0.023$ ) and the time of extrathecal peritoneal catheter placement were statistically significant ( $p = 0.027$ ) higher for the group of patients who progressed to death. In the Mann–Whitney test, we can see that the Charlson comorbidity index ( $p = 0.023$ ) and the EuroSCORE II were statistically significant with a higher mean ( $p = 0.024$ ). There is no statistically significant association between the other variables under consideration with mortality postoperatively. However, we saw in the curves that a higher percentage of deaths occurred in relation to longer time of symptoms in the patient, in the time of initiation of symptoms the patient's mortality was lower. Postoperative mortality must be analyzed by all health professionals in the field, including Nephrology and Surgery. We propose the use of the EuroSCORE II scale in the evaluation of peritonitis as a prognostic factor for surgery within this special catheter type of acute peritoneal dialysis.

## Discussion

The study determined a postoperative mortality of 32.1%. The overall postoperative complications incidence was 45.3% and the severe postoperative complication incidence was 30.5%. Obstructed hernia and loss of ultrafiltration incidents, as well as diabetes and peritonitis as causes of dialysis, were the variables associated with surgery-related mortality. The impact of postoperative complications on the results is controversial, but the majority of PD studies have found that postoperative complications have a poor outcome. In our study, moderate surgical postoperative complications did not influence long-term PD mortality, but did affect the survival of patients with severe complications. In a Spanish multicenter study of CCDD peritonitis, the risk of death was higher in patients who developed a surgical infection than in those who developed an exit-site or a tunnel infection, regardless of the causative microorganism. In other PD-related surgeries with peritonitis, complete surgical wound closure and early repermeabilization of the peritoneum would be the factors with a likely better prognosis.

The impact of peritoneal dialysis on postoperative outcome is poorly investigated. Most studies have been performed in intraperitoneal interventions. In contrast, few studies are focused on the outcome of patients undergoing abdominal surgery in PD modality, discontinuous ambulatory peritoneal dialysis, or PD after initial hemodialysis (PD-v). Only we have found three studies in CCDD either in PD-v patients or that compare PD-v with chronic hemodialysis





patients. Our 30-day postoperative mortality rate in PD-v patients was lower than that observed in two other single-center studies. We want to emphasize that there are no contraindications for abdominal surgery in patients undergoing PD or those who are in PD-v. Neither peritonitis nor any of the other variables analyzed were shown to be significantly associated with postoperative PD-v mortality in the fully adjusted Cox regression model, which was confirmed in the adjusted multilevel Cox model analysis. A meta-analysis study that used the raw data from the CANUSA study, although it is limited to the subgroup of patients undergoing an assessment of residual renal function, found an independent association of peritonitis with increased overall mortality. The independent association of peritonitis with an increase in the overall mortality rate was controversial in the full cohort of patients enrolled in the CANUSA study. In PD modality, it is also unknown whether other abdominal or non-abdominal surgeries are important.

In the present study, we concentrated on PD patients undergoing abdominal surgery during their PD, mostly to cure PE and generalized peritonitis, to distinguish specific patient and procedure-related outcome-affecting variables. The 30-day postoperative mortality in the PD catheter patient group was 23.1%, thus even higher than in the previously quoted articles on intra-abdominal surgery, and independent of indicators such as age, sex, and weight. As shown previously in other types of intra-abdominal surgery, the MerKRS and the ASA classification were strong determinants of postoperative PE-related patient mortality. However, we did not find convincing evidence for the impact of liver regeneration caused by previous shunt placement, only weak evidence for the impact of peritonitis, as well as no impact of age and PD duration. Unfortunately, multiple association of some covariables precluded a multivariate analysis with such a low number of cases. Large multi-center studies with sufficient cases and less multiple association of variables should be performed to confirm these findings. If more studies provide similar results, this could urge administrators to push PD patients one step further towards direct shunt surgery to prevent postoperative PD patient mortality. In their favor speak the low procedure-intensity compared to PD placement or shunt placement, the lack of complications such as shunt infections, combined with the advantages of safe PE treatment. The findings of the current study are based on data from a single centre in Dzierzoniow, Poland. Hence, these data may not be applicable to other countries due to differences in patients' PD protocol.

## Conclusion

The postoperative mortality of peritonitis is high, especially for older adults over 60 years old. Diabetes care should be more comprehensive. Peritonitis caused by gram-positive bacteria is mainly nonsurgical, but for patients with peritonitis caused by gram-negative bacteria, peritoneal lavage should be performed as root management regardless of first-line antibiotic use or negative dialysate culture. The risk of cardiovascular disease or related illnesses should be monitored during the operation and at the time of peritonitis diagnosis.

### Competing interests

The authors declare no conflict of interest.

### Authors' contributions

All authors shared in the conception and design and interpretation of data, drafting of the manuscript and critical revision of the case study for intellectual content and final approval of the version to be published. All authors read and approved the final manuscript.

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