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Repeat peritonitis in peritoneal dialysis : A cohort study

(Péritonite répétée en dialyse péritonéale : une étude de cohorte)

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Summary

Introduction: The understanding of the pathophysiological mechanisms of repeat peritonitis, defined as the occurrence of peritonitis more than 4 weeks after the end of appropriate antibiotic treatment for a previous episode involving the same germ, remains limited.

Methods: We studied the outcomes of 26 episodes of repeat peritonitis between 2006 and 2024 (Repeat Group) and compared them with 23 episodes of relapsing peritonitis (Relapse Group) and 84 episodes of peritonitis preceded by 4 weeks or more by another episode with a different organism (Control Group).

Results: The majority of cases of repeat peritonitis are caused by gram-positive organisms (65.5%), predominantly *Staphylococcus aureus* (38.5%), whereas most episodes of relapsing peritonitis are culture-negative (69.5%), followed by gram-negative bacilli episodes (17.4%).

Exit site infection is significantly associated with PD peritonitis. Gram-positive cocci are responsible for 95.5% of exit site infections, mainly due to *Staphylococcus aureus*.

In the Repeat Group, 14 (66%) patients achieved primary response, and 10 (47%) of them reached complete cure. After the first episode of repeat peritonitis, 3 (14%) patients had their catheter removed and were transferred to long-term hemodialysis; however, the risk of developing relapsing peritonitis was 4.7%, and recurrent peritonitis was 9.5%.

Conclusion: The definition of repeat peritonitis is clear. Despite a favorable outcome with antibiotic treatment, the risk of further episodes of peritonitis remains high, threatening the time on peritoneal dialysis therapy and the life of the patient.

Keywords: peritoneal dialysis, peritonitis, repeat peritonitis, catheter removal

Résumé

Introduction : La compréhension des mécanismes physiopathologiques des péritonites répétées, définies comme la survenue d'un nouvel épisode de péritonite plus de 4 semaines après l'arrêt d'une antibiothérapie adaptée pour un épisode précédent impliquant le même germe, reste limitée.

Méthodes : Nous avons étudié les résultats de 26 épisodes de péritonites répétées entre 2006 et 2024 (Groupe Répété) et les avons comparés à 23 épisodes de péritonites récidivantes (Groupe Récidive) et à 84 épisodes de péritonite survenant 4 semaines ou plus après un autre épisode avec un organisme différent (Groupe Témoin).

Résultats : La majorité des épisodes de péritonites répétées sont causés par des organismes à gram positif (65,5 %), principalement dus au *Staphylococcus aureus* (38,5 %), tandis que la plupart des épisodes de péritonites récidivantes sont à culture négative (69,5 %), suivis d'épisodes de péritonites à bacilles gram négatif (17,4 %). L'infection du site d'émergence est significativement associée à la survenue de péritonite. Les cocci gram positif sont responsables de 95,5 % des infections du site d'émergence principalement dues au *Staphylococcus aureus*.

Dans le Groupe Répété, 14 (66 %) patients ont obtenu une réponse primaire sous antibiotiques, tandis que la guérison complète a été atteinte chez 10 (47 %) patients, alors que le cathéter de dialyse péritonéale a été retiré chez 3 (14 %) patients dès le premier épisode de péritonite répétée; cependant, le risque de développer une péritonite récidivante était de 4,7 %, et une péritonite récurrente était de 9,5%.

Conclusion : La définition de la péritonite répétée est claire. Malgré un résultat favorable sous traitement antibiotique, le risque de développer de nouveaux épisodes de péritonite reste élevé, menaçant la survie de la technique et la vie du patient.

Mots-clés : dialyse péritonéale, péritonite, péritonite répétée, retrait du cathéter



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Introduction

Peritoneal dialysis (PD) associated-peritonitis is the most common and dreadful complication of PD.

Outcomes of peritonitis vary considerably from one country to another, ranging from cure with antibiotics (69.0-80.7%), catheter removal (10.8-20.4%), or mortality (1.8-6.0%). [1]

On the other hand, mortality related to peritonitis was defined and reported differently in 55% of studies, with a prevalence ranging from 10% to 20%. [1-4]

The International Society of Peritoneal Dialysis (ISPD) 2022 recommendations clearly define repeat peritonitis as an episode of peritonitis occurring more than 4 weeks after the end of antibiotic treatment for a previous episode with the same organism. In contrast, relapsing peritonitis is defined as an episode of peritonitis occurring within 4 weeks of the end of appropriate antibiotic treatment for a previous episode with the same organism, or a sterile episode, and a recurrent peritonitis as an episode that occurs within 4 weeks after completion of therapy but with a different organism. [5]

Regardless of the type of peritonitis, the occurrence of new episodes suggests persistence of infection and may be associated with an increased risk of infectious complications; the prognosis will depend on how quickly the cause is identified and treated.

The aim of this study is to identify patients at risk of developing repeat peritonitis, to understand the associated factors and to assess the outcomes in order to prolong the survival of the technique and to lower morbidity and mortality.

Materials and methods

Patient Selection

From the 2006 opening of our PD unit until January 2024, 235 patients were recruited in our unit. All episodes of PD peritonitis during this period were carefully considered. (*Figure 1*)

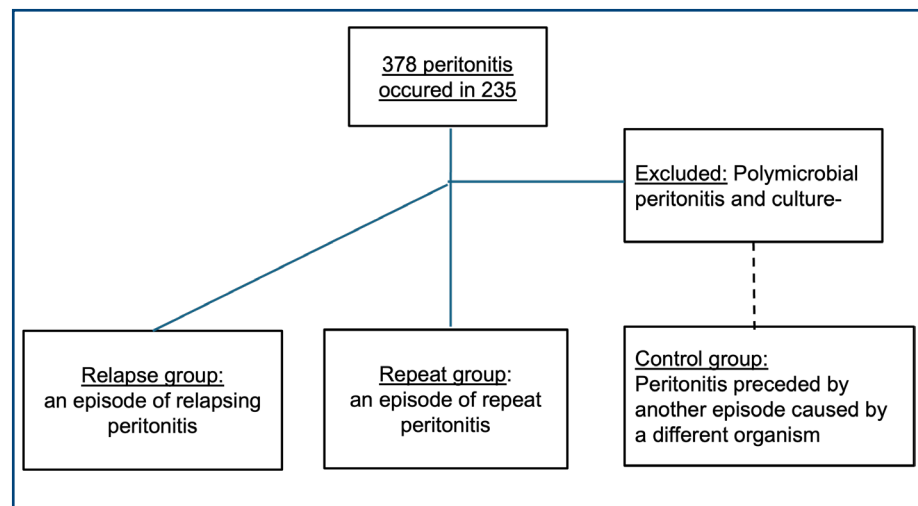
Data was collected by reviewing the French Language Peritoneal Dialysis Registry (RDPLF) database, as well as each patient's hospital records.

According to the ISPD guidelines [5], PD peritonitis was diagnosed when at least two of the following are present : 1) abdominal pain and/or cloudy dialysis effluent; 2) dialysis effluent white cell count $> 100/\mu\text{L}$ or $> 0.1 \times 10^9 /\text{L}$ (after a dwell time of at least 2 h), with $> 50\%$ polymorphonuclear leukocytes (PMN); 3) positive dialysis effluent culture.

In this study and according to ISPD guidelines , we defined repeat peritonitis as an episode that occurs more than 4 weeks after completion of therapy of a prior episode with the same organism. In the 18 years of the study period, 378 episodes of PD peritonitis (in 9 389 patient-months of treatment) were recorded in our unit. 26 episodes (6.8%) were repeat peritonitis. The result is compared with 23 episodes of relapsing peritonitis during the same period (the Relapse

Group), and 84 episodes of peritonitis which had been preceded by another episode caused by a different organism 4 weeks to 24 months (the Control Group). We excluded culture-negative and polymicrobial episodes while selecting the control episodes.

The demographic characteristics, underlying medical conditions, previous PD peritonitis, catheter removal, and clinical outcome were also examined.



↑ Figure 1. Study design

Microbiological investigation

Bacterial culture of the dialysate fluid was performed on Chapman and/or chocolate agar, and on Cystine–lactose–electrolyte-deficient (CLED) and blood agar.

Clinical management

PD peritonitis episodes were treated according to the standard antibiotic protocol of our center at the time, which was systematically modified over time.

We initially administer Ceftazidime and Cefazolin IP or IV, plus an aminoglycoside. Antibiotic regimens for individual patients were modified when culture results were available, and the peritoneal dialysis effluent was regularly inspected. Antibiotic therapy was continued for a total of 14 days for episodes caused by *Staphylococcus* coagulase negative and 21 days for episodes caused by gram negative bacillus or *Staphylococcus aureus*.

Primary response was defined clinically as the resolution of abdominal pain, clarification of dialysate on day 5 with antibiotics alone.

Complete cure was defined as complete resolution of PD peritonitis with antibiotics alone without relapse or recurrence within 4 weeks after completion of treatment. The Tenckhoff catheter was removed only after staff discussion. If the catheter is removed, antibiotics are maintained for an additional two weeks. If reinsertion of a new catheter was contraindicated, we consider it as a technique failure and the patient transferred to long term hemodialysis.

Statistical Analysis

Qualitative variables were expressed as numbers and percentages, and compared using the chi-square test. Quantitative variables were expressed either as the mean \pm standard deviation (SD) if the distribution of the variable was normal, and compared using the t student or ANOVA, or as the median with the interquartile range if the distribution of the variable was asymmetric. Statistical analyses were performed using Jamovi 2.3.21

Results

In our study, 96 patients were included, with a sex ratio of 1.4 (M/F), while the mean age was $50 \pm 17,3$ years.

While 79,2% of our patients were on Continuous ambulatory peritoneal dialysis (CAPD), 85.4% were autonomous.

↓ *Table I. Baseline characteristics of the patients at the time of PD peritonitis*

	Repeat Group	Relapse Group	Control Group	Comparing Repeat and Relapse Groups	Comparing Repeat and Control Groups
No. of patients	21	19	56	-	-
Sex (men:women)	15:6	8:11	34:22	0,123	0,632
Age (years)	44 \pm 18	42,6 \pm 16,8	51,1 \pm 16,8	0,692	0,149
Duration of dialysis (months)	39 \pm 33,7	26,3 \pm 23,3	36,3 \pm 27,9	0,179	0,718
Duration from last peritonitis episode (months)					
mean \pm SD	19,9 \pm 16,7	13,8 \pm 16,2	16,3 \pm 16,5	0,432	0,595
median (range)	19 (7,5-30,5)	6 (1-26)	12 (6-19)		
No. of previous peritonitis episode					
mean \pm SD	2,67 \pm 1,2	3,37 \pm 1,61	2,15 \pm 0,448	0,134	<u>0,024</u>
median (range)	2 (2-3)	2 (2-4)	2 (2-2,5)		
Diagnosis, no. of cases (%)					
glomerulonephritis	3 (14,3%)	6 (31,6%)	5 (8,9%)		
diabetes	4 (19%)	5 (26,3%)	7 (12,5%)		
hypertension	3 (14,3%)	0 (0%)	8 (14,3%)		
polycystic	2 (9,5%)	0 (0%)	7 (12,5%)		
others/unknown	6 (28,6%)	7 (36,8%)	18 (32,1%)		
Tubulointerstitial	3 (14,3%)	1 (5,3%)	11 (19,6%)		
Charlson's index score					
mean \pm SD	2,52 \pm 0,98	2,63 \pm 1,01	2,63 \pm 0,906	0,727	0,666
median (range)	2 (2-3)	2 (2-3,5)	2 (2-3)		

Of all our patients, 21 (Repeat Group) developed a repeat peritonitis, 19 patients (Relapse Group) developed relapsing peritonitis, and 56 patients (Control Group) had an episode of peritonitis which had been preceded 4 weeks to 24 months by another episode caused by a different organism.

The baseline clinical characteristics at the time of PD peritonitis of the patients are summarized in *Table I*. There is no significant difference in the baseline clinical characteristics between groups.

Causative Organism

The microbiological cause of the peritonitis is summarized in *Table II*.

There was a significant difference in the distribution of the causative organisms between groups. *Staphylococcus aureus* (38.5%) is significantly the germ most frequently involved in repeat peritonitis. Although not significant, *Escherichia coli* (15.5%) was less frequent in this group. However, no fungi or mycobacteria were identified.

↓ *Table II. Microbiological cause of the peritonitis episode*

	Repeat Group	Relapse Group	Control Group
Gram-positive Cocci (GPC)	17 (65.5%)	3 (13%)	45 (53.7%)
Staphylococcus aureus	10 (38.5%)	2 (8,7%)	19 (22%)
Coagulase Negative Staphylococcus	5 (19%)	0	6 (7%)
other Staphylococcus species	2 (8%)	1 (4,3%)	19 (22%)
other Streptococcus species	0	0	1 (1,2%)
Gram negative Bacilli (GNB)	9 (34.5%)	4 (17.4%)	31 (41%)
Escherichia coli	4 (15.5%)	0	8 (9,3%)
Pseudomonas aeruginosa	3 (11.5%)	2 (8,7%)	5 (6%)
Others	2 (7.5%)	2 (8,7%)	22 (25.5%)
Fungi	0	0	3 (3,5%)
Mycobacterium	0	0	3 (3,5%)
Culture-negative	0	16 (69.5%)	0
Total	26	23	86

Exit-Site Infection

The microbiological cause of exit site infections in the year preceding the occurrence of peritonitis is summarized in *Table III*.

Exit site infection is significantly associated with the occurrence of peritonitis ($p < 0.001$)

In the Repeat Group, GPC were responsible for 95.5% of exit site infections, mainly due to *S. aureus* (87% of cases), and only 38% of exit site infections were concomitant with peritonitis ($p = 0.769$).

Table III. Microbiological cause of the exit site infection

	Repeat Group	Relapse Group
Exit site infection per year	1 [0-2.5]	1 [0-4]
Gram-positive Cocci (GPC)	22 (95.5%)	13 (54%)
Staphylococcus aureus	20 (87%)	12 (50%)
Coagulase Negative Staphylococcus	2 (8.5%)	1 (4%)
other Staphylococcus species	0	0
other Streptococcus species	0	0
Gram negative Bacilli (GNB)	1 (4.3%)	11 (45%)
Pseudomonas aeruginosa	0	8 (33%)
Enterobacter cloacae	0	2 (8%)
Klebsiella pneumoniae	1 (4.3%)	1 (4%)

Outcome of repeat peritonitis under antibiotic therapy

The main clinical results are shown in *Figure 2*.

After a follow-up of 24 months, primary response was achieved in 14 (66%) patients, 11 of them had a GPC PD peritonitis, and a complete cure was reached in 10 (47%) patients.

We recorded one more episode of repeat peritonitis in 4 (19%) patients over an average period of 9 months, and 2 repeat episodes in one (4.7%) patient after two months of the first episode.

Relapsing peritonitis occurred in only one (4.7%) patient. Recurrent peritonitis occurred in 2 (9.5%) patients.

The PD catheter was removed at the first episode of repeat peritonitis in 3 (14%) patients, two of them because of fungal PD peritonitis co-infection, and one of them because of repeated and concomitant tunnel infection.

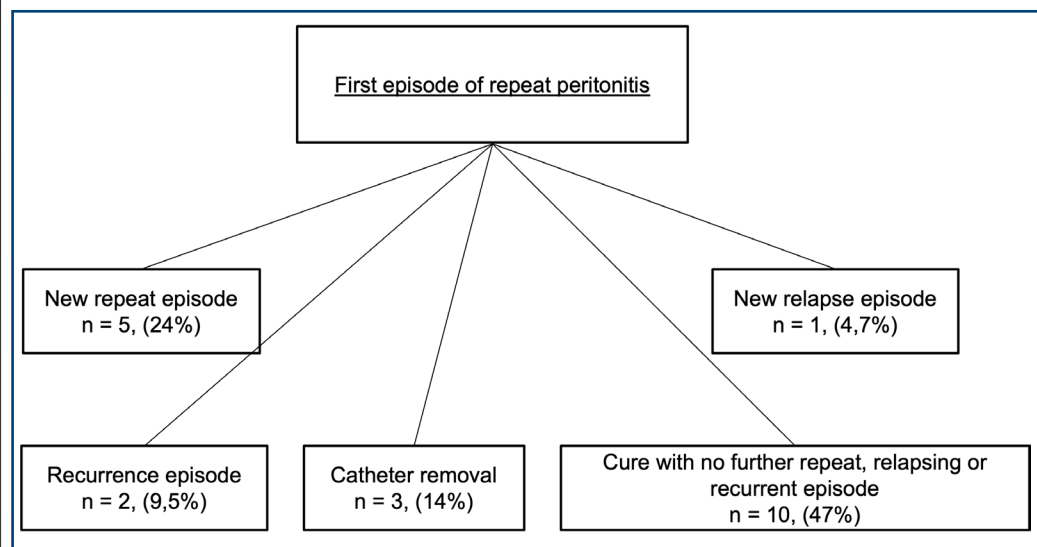


Figure 2. Outcome of repeat peritonitis

Discussion

In our study, only 6.8% of all episodes of PD peritonitis were followed by repeat peritonitis, a lower incidence compared to results reported by other studies. [1,6]

Our results showed that the rate of repeat peritonitis due to *S. aureus* and CNSs was approximately 65.5%, which is significantly higher than other reports. [7–9]

Unlike the time duration of PD and the time elapsed since the previous episode, the occurrence of an exit site infection in the previous year was significantly associated with the occurrence of peritonitis.

We observed a significant difference between the type of causative germ for repeat peritonitis and that responsible for relapsing peritonitis, suggesting the need for different therapeutic approaches.

Contrary to general expectations [10], we noted that episodes of repeat peritonitis had a higher initial response rate and a lower catheter removal rate, probably due to the generally good response to antibiotics of the causative germ, in contrast to other pathogens in the other groups, notably fungi and mycobacterial episodes, which have a high catheter withdrawal rate, which we have found in previous reports. [8]

From a practical perspective, our results highlight the importance of giving particular attention to episodes of repeat peritonitis. Although initial antibiotic therapy may be effective, there is a significant risk of further episodes, indicating subsequent catheter removal.

Nevertheless, risk factors associated with PD peritonitis, such as hypokalaemia [11], obesity, poor lifestyle, immunosuppression, should be investigated and treated, not forgetting treatment of nasal carriage of *Staphylococcus aureus* and exit site infections. [12,13]

Gastrointestinal disorders that can cause endogenous infections [14] must be detected and managed as well, such as diverticulosis. On the other hand, Gastrointestinal and gynecologic procedures carry also a risk of PD peritonitis and may be the source of repeat or relapsing peritonitis. For this reason, the ISPD guidelines recommend appropriate antibiotic prophylaxis before each procedure [5,15,16]. Surprisingly, there is no association between polycystic kidney disease and PD peritonitis according to several studies. [17–19]

Finally, as reported in a number of studies, increased vigilance and retraining of medical and nursing staff and patients are mandatory to prevent the occurrence of PD peritonitis. [20,21]

Conclusion

Repeat peritonitis is a specific clinical entity. Although they generally have a satisfactory primary response to antibiotic therapy, they present a substantial risk of developing relapsing, recurrent or even more episodes of repeat peritonitis. Therefore, a local cause must be identified and taken care of, and catheter removal should be considered.

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Declaration of interests

No conflict of interest to declare.

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