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Peritoneal catheter infections : data from the French peritoneal dialysis registry (RDPLF) and risk factors

Infections du cathéter de dialyse péritonéale : résultats du Registre de Dialyse Péritonéale de
Langue Française (RDPLF), facteurs de risque.

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Résumé

Depuis 1997 le Registre de Dialyse Péritonéale de Langue Française (RDPLF) enregistre les différents aspects liés à la pose des cathéters de dialyse péritonéale et leur suivi. Le but de notre étude a été d'analyser les infections de 10801 cathéters de 124 centres entre janvier 1997 et décembre 2018.

Les infections sont plus fréquentes dans le premier mois et 50% surviennent avant le dixième mois. Le risque d'infection augmente en cas d'hématome de paroi et/ou de fuite initiale de dialysat, et en cas de surpoids. Il diminue avec l'antibioprophylaxie pré-opératoire, surtout avec la vancomycine, si l'implantation du cathéter est réalisée par un opérateur fidélisé, si un délai de 7 jours est respecté avant le premier pansement, et avec l'application de mupirocine à l'orifice de sortie.

Le pourcentage d'infections à Staphylocoque aureus reste prédominant mais diminue au cours des années au profit des Pseudomonas, Corynebacterium et autres cocci Gram positifs.

L'incidence des infections de cathéter est plus faible que dans la littérature : 0,16 épisode par an en 2013-2017.

L'ISPD recommandait en 2018 de pratiquer une antibioprophylaxie pré-opératoire, puis locale et de dépister le portage nasal de Staphylocoque aureus ; ces recommandations ne sont suivies dans le RDPLF respectivement que dans 70,7 %, 15,6 % et 42 % des cas.

Notre étude confirme une grande variabilité dans le respect des recommandations de l'ISPD, globalement et entre centres. Mais la participation au module Cathéter permet de suivre les modifications de l'écologie bactérienne, l'évolution des pratiques de soins dans les centres francophones, et la fréquence des infections de cathéter sur plus de 20 ans.

Mots clés : Dialyse péritonéale, cathéter, infection, recommandations

Summary

The French Language Peritoneal Dialysis Registry (RDPLF) record since 1997 all data dealing with peritoneal catheter insertion and follow up. The aim of this study is to analyze catheter infections on 10801 catheters in 144 centres from January 1, 1997 and December 31, 2018.

Infections are more common in the first month and 50% occur before the tenth month. The risk of infection increases in case of wall hematoma, initial fluid leakage, and obesity. It decreases with the use of prophylactic antibiotics at the time of catheter insertion, with experienced operator, if the first dressing is delayed for 7 days, and with mupirocin as exit-site prophylaxis.

During last two decades the percentage of Staphylococcus aureus infections has decreased, whereas the proportion of Pseudomonas, Corynebacterium and other Gram + cocci increased.

The incidence of catheter infections is low compared to literature data: it decreased to 0.16 episodes per year for the 2013-2017 period.

Adherence to ISPD guidelines: preoperative antibioprophylaxis is the most followed guideline (70.7% of catheter implantations in 2018). Local antibioprophylaxis concerns only 15.6% of catheters, and remains concentrated in a few centres ; mupirocin is the most frequently used agent. Screening for nasal carriage of S. aureus is performed in only 42% of cases.

The catheter section of the RDPLF has allowed the follow-up of clinical practices incidence of infections and ecology for 20 years, both at the national and center level. Our study confirms a wide variability in clinical practices, compared to ISPD guidelines.

Keywords : peritoneal dialysis, catheter, infection, guidelines

The French Language Peritoneal Dialysis Registry (RDPLF) was created in 1987 with the first, or main, module "Survival and infections". Subsequently, seven optional modules were developed, including the Catheter module, initiated in 1997. It allows the study of infections on all the catheters included in the database, as well as the identification and analysis of these infections, and their consequences in each dialysis center.

PATIENTS AND METHODS

This work is based on a retrospective study of data from the RDPLF Catheter module from January 1, 1997 to December 31, 2018. Of the 293 French-language dialysis centers participating in the RDPLF, 144 reported catheters in the module and 135 were still active at the end of 2018.

Study population

The study concerned 10801 catheters implanted in 10180 patients aged over 18, reported by 144 centers (121 French centers, 13 Belgian centers, 1 Swiss center, 1 Luxembourg center, 5 Moroccan centers and 3 Tunisian centers).

Variables

The variables studied are extracted from the data of the Catheter module: presence of wall hematoma and / or initial leakage of dialysate, loyal and experienced operator or not, date of catheter insertion, delay between catheter implantation, first dressing of the exit site and early use of the catheter, risk factors related to the patient (diabetes, obesity), nasal carriage of *Staphylococcus aureus* and its treatment, immediate externalization of the external end of the catheter or buried catheter (Moncrief technique), prescription of preoperative antibiotic prophylaxis and / or emergence of the catheter, date of infection (defined by the presence of a purulent flow at the outlet), type of germs involved.

Since 2011, the new version of the Catheter module makes it possible to specify the use of vancomycin for antibiotic prophylaxis during catheter implantation. Of the 10801 catheters included in the study, 6221 were reported in this new release.

The information has been entered online since 2013. The results of each center are accessible at any time.

Statistics

It is essentially a descriptive study, categorical variables are described according to their frequency and percentage. Chi2 and Fisher tests were used to compare the distribution of these variables.

RESULTS

Frequency of infections

The frequency of catheter infections is 1 episode every 78.13 months x patient (0.15 episodes per year). It has decreased over the years, from 1 episode every 68.25 months x patient between 1997 and 2001 (0.17 episodes per year), to 1 episode every 74.81 months x patient between 2013 and 2017 (0.16 episodes a year).

The risk of catheter infection decreases over time, both during the life of the catheters and during the follow-up years in the registry (Fig.1).

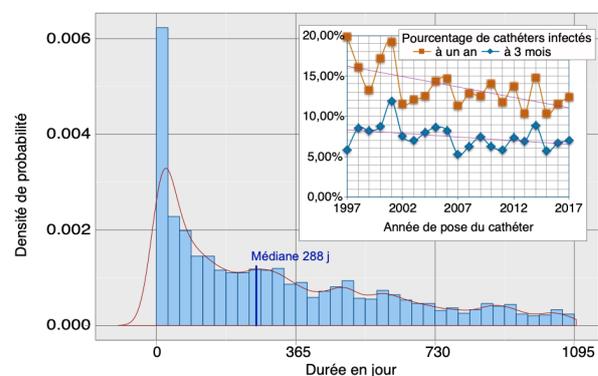


Figure 1. Probability of catheter infection after implantation represented by the histogram of monthly probability of infection and the probability density curve: median at 288 days. Superimposed, graph of the evolution of the percentage of catheters infected at 3 months and 1 year over a period of 20 years.

Infections are more common in the first month after catheter implantation (or externalization for buried catheters) and the risk is decreasing; 50% of infections occur before the tenth month.

On all catheters included since 1997, the percentage of catheters infected at 3 months and at 1 year decreases steadily, this decrease is more sensitive for infections at 1 year; in 2017, the percentage of infected catheters is 7% at 3 months and 12.38% at 1 year.

Factors Influencing the Occurrence of Infections

The risk of catheter infection increases with wall hematoma (RR 2.3 [1.98 - 3.4] 95% CI, $p < 0.001$) and / or initial dialysate leak (RR 2.6 [1.9 - 3.7] 95% CI, $p < 0.001$), and in the presence of obesity in the overweight stage (BMI ≥ 25 kg / m², RR 1.8 [1.4 - 2.3] 95% CI, $p < 0.001$); obesity is an independent risk factor for diabetes.

Of all catheters, the percentage of infected catheters

is no different whether the catheters are buried or not (buried catheters: 6.5% at 3 months and 12.9% at 1 year, immediate externalization: 7.33 % at 3 months and 12.67% at 1 year, NS). The results do not change if one considers only centers that practice both techniques.

We did not find any significant difference in terms of catheter infection according to the person performing the local care: patient, family or nurse.

The risk of infection in the first year decreases significantly if the implantation of the catheter is performed by a loyal operator (RR 1,42 [1,13 - 1,88] 95% CI, p <0,001), and if a delay of 7 days was observed between the implantation of the catheter and the first exit site dressing (RR 1.48 [1.29 - 1.7] 95% CI, p <0.001). Preoperative antibiotic prophylaxis decreases the risk of early infection; the protective effect is maximum in the first month and remains significant at 3 months. Antibiotic prophylaxis with vancomycin is almost 2 times more effective than other antibiotics in preventing early infections. This protective effect decreases but remains significant at 3 months (Table 1).

The proportion of catheters placed under pre-operative antibiotic prophylaxis has increased since 2011 and especially the last 2 years to reach 70.7% of implantations (Fig.2). Antibiotic prophylaxis was based on vancomycin in 33.2 to 36.6% of cases from 2012 to

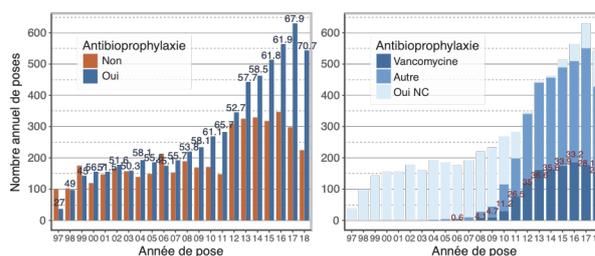


Figure 2. Left, histogram of the number of catheter placements per year, with preoperative antibiotic prophylaxis (in blue) or without pre-operative prophylaxis (in red), indication of the percentage of implantations with antibiotic prophylaxis above each column. On the right, histogram according to the type of antibioprophyllaxis (NC = not known); the collection of this data was possible only secondarily, following the modification of the Catheter module.

2016, and this proportion seems to decrease in 2017 and 2018 around 28% (result to be qualified given the large proportion of antibioprophyllaxis unspecified).

Antibiotic prophylaxis at the catheter exit site is still not widespread in centers participating in the catheter module since it concerns only 1691 catheters / 10801 (15.6%), of which 1344 under mupirocin (79.5%). The application of mupirocin to the exit site is a practice concentrated in 13 centers that prescribe it in more than 80% of cases, 4 of which are 100%. For the 347 catheters (20.5%) under different local antibioprophyllaxis, the alternative to mupirocine is represented almost exclusively by fucidine, and largely concentrated in 2 centers (250 catheters / 347).

The application of mupirocin to the emergence of the catheter has a protective effect against infections early and even more clearly at 1 year (Table II). Other local antibiotic prophylaxis did not differ significantly from abstention.

Nasal carriage of Staphylococcus aureus is a factor favoring catheter infections. Its screening before implantation of the catheter involved 4536 catheters or 42% of all catheters (Fig.3). The practice of this screening has been-decreasing in the last 5 years (35.7% of cases).

Table II Protective effect of mupirocin on catheter infections at 3 months and 1 year.

Local antibioprophyllaxy	Cathéters infectés (%)	
	at 3 month	at 1 year
Mupirocin	5,2	8,8
nothing	7,7	13,6
	RR = 1,47 [1,16 - 1,88] IC 95% p < 0,001	RR = 1,52 [1,27 - 1,82] IC 95% p < 0,001

Table I. Effect of preoperative antibioprophyllaxis on the risk of early catheter infection: top, efficacy of antibioprophyllaxis on all catheters since 1997; bottom, efficacy of vancomycin versus other antibioprophyllaxis on the catheters declared in the new version of the module (catheters placed from 01/01/2012 to 31/12/2018).

Pre-operative antibioprophyllaxy	infected month 1	Healthy month 1	Infected month 3	Healthy month 3
Yes (n = 6183)	251	5932	420	5763
No (n = 4450)	242	4208	357	4093
	RR = 1,34 [1,13 - 1,6] IC 95% p < 0,001		RR = 1,18 [1,04 - 1,36] IC 95% p < 0,02	

Antibioprophyllaxis informations are missing for 168 catheters out of 10801 and have been excluded

pre-operative Vancomycin	infected month 1	Healthy month 1	infected month 3	Healthy month 3
Oui (n=1141)	29	1112	61	1080
Autre (n=2077)	106	1971	160	1917
	RR = 2,0 [1,34 - 3,0] IC 95% p < 0,001		RR = 1,39 [1,06 - 1,83] IC 95% p = 0,01	

The type of antibioprophyllaxis is not available in 286 catheters and have been excluded from the analysis.

Nasal carriage is positive in 807/4536 cases (17.8%), and this result is very stable during the study. In the 807 positives, the risk of catheter infection is significantly higher at 3 months ($p = 0.04$, RR = 1.31 [1.02 - 1.68] 95% CI) and at 1 year ($p = 0.03$, RR = 1.22 [1.02 - 1.47] 95% CI).

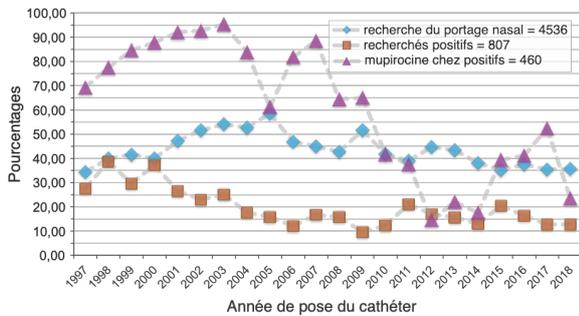


Figure 3. Percent change of catheter implantations preceded by *S. aureus* nasal carriage research, percentage of patients found positive, and percent of mupirocin nasal treated patients per year over a 20-year period.

The eradication of the nasal carriage of *Staphylococcus aureus* by mupirocine is carried out only in 57% of all positive patients and this prescription decreases from 2010. We did not find any significant difference in terms of occurrence of infections between mupirocin-treated nasal-carrying patients and untreated positive-test patients in centers performing nasal-carriage search before at least 50% of catheter implantations, a result which should be viewed with caution because of the small sample size.

Bacterial ecology

Bacterial ecology has evolved over time (Table III). *Staphylococcus aureus* remains predominant in percentage of infections, but its frequency decreases over the years, from 68% between 1999 and 2000, to 40% between 2017 and 2018. In the last 2 years, the percentage of *Pseudomonas* infections has increased as well as infections with *Corynebacterium* and other Gram + Cocci, and negative cultures and multiple germs infections decreased.

Completeness of data collection

The completeness of the data collection was established by comparing the number of patients included in the mandatory core module and the number of catheters reported over the same period. The completeness concerning the Catheter module is variable (Fig.4) but in marked progression for the past 2 years.

Seventy-six centers (54%) are more than 70% complete, and 37 centers are between 90% and 100%. However, if we look at the number of catheters seized, the more we increase the requirement of completeness, the more we lose; thus, if we want to work on the data of the centers with an exhaustiveness of more than 90%, there remains only 4219/10801 usable catheters ie 39% of all the catheters declared.

Respect of the recommendations of the International Society of Peritoneal Dialysis (2017) for the prevention of catheter infections. Where are we in 2018?

Antibiotic prophylaxis should be given immediately before insertion of the catheter (1A): preoperative antibiotic prophylaxis implantations in our series increased to 70.7% of the total number.

The daily local application of antibiotic cream to the

Table III Germs responsible for catheter infections from 1999 to 2018, every 2 years, expressed as a percentage of infections per organism.

	99-00	01-02	03-04	05-06	07-08	09-10	11-12	13-14	15-16	17-18
<i>Staph. Aureus</i>	68,0	62,9	57,0	52,4	45,4	45,2	42,1	39,9	31,8	40,0
Staph. others	10,2	10,8	11,6	15,0	16,8	12,1	13,6	15,7	22,6	13,8
Other Cocci Gram+	0,7	0,6	2,9	1,0	0,9	1,5	1,3	3,2	2,0	4,3
<i>Pseudomonas</i>	6,1	5,1	8,2	5,4	11,8	14,6	9,7	11,8	18,5	16,0
Other Gram-negatives	8,2	9,7	2,3	6,3	10,0	9,5	7,1	6,2	11,3	8,5
<i>Corynebacterium</i>	2,7	4,6	6,4	6,3	2,3	4,0	8,4	7,3	7,0	11,9
Other Gram-positives	0,7	0	0	0	0,5	0	0,3	0,9	0,7	0,4
Multiple organisms	2,0	2,9	8,1	7,8	5,5	5,0	11,7	10,3	2,8	1,7
Yeast or fungi	0	0	0	1,0	2,3	0,5	1,0	1,1	0,7	0,7
Negative culture	1,4	3,4	3,5	4,8	4,5	7,6	4,8	3,6	1,5	2,4

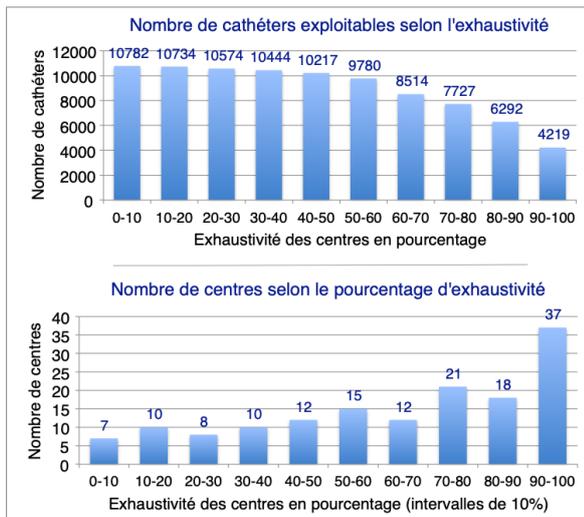


Figure 4. At the top, each column represents the number of exploitable catheters according to the minimum requirement of completeness requested. At the bottom, each column corresponds to the number of centers according to the percentage of completeness of the catheter declarations. catheter outlet is recommended (1A): the application of antibiotic prophylaxis to emergence increases but still only affects 15.6% of catheters and mainly uses the mupirocin.

Cleaning of the exit site must be done at least twice a week (1C): this recommendation is applied by all centers.

Nasal carriage of *S. aureus* should be investigated prior to catheter implantation (2D), and if positive, nasal and topical application of mupirocin is recommended (1B): Nasal carriage of *S. aureus* experienced a 35.7% drop in catheter implantations, and positive patients were treated with nasal mupirocin in only 23% of cases. Each dialysis department studies, at least annually, the incidence of catheter (1C) infections: 49% of centers reporting patients to the RDPLF main module participate in the Catheter module and therefore have an annual report of catheter infections .

DISCUSSION

Peritoneal dialysis catheter infections can cause catheter loss, technical failure and even peritonitis mortality in peritoneal dialysis patients (1-4).

The incidence of reported catheter infections in the literature is highly variable, from 0.05 to 1.02 episodes per patient-year. Our results are among the low incidences and the decrease in catheter infections continues over the years.

The evolution of the bacterial ecology of catheter

infections shows a decrease in the proportion of Gram-positive cocci and an increase in the proportion of Gram-negative bacilli, including *Pseudomonas*; these results are consistent with published results for peritonitis (5) and for peritoneal dialysis catheter infections (6).

The first recommendations of the International Society of Peritoneal Dialysis (ISPD) concerning the prevention and treatment of infectious complications were published in 1983 and were the subject of successive revisions including two recent updates: in 2017, devoted to catheter infections (7), and in 2019, concerning the creation and maintenance of an optimal peritoneal approach (8). These recommendations are based on GRADE (Grading of Recommendations, Assessment, Development and Evaluation). They are based on concrete evidence obtained from literature data, but the authors specify that they must be adapted by each center according to the reality of the field.

The main prevention factors for catheter infections recognized by these recommendations are: preoperative antibiotic prophylaxis for catheter implantation, antibiotic application at the exit site, care of the latter at least twice per week, screening and eradication of nasal carriage of *Staphylococcus aureus* prior to catheter placement, and annual monitoring of catheter infections in each dialysis center.

Despite the existence of the recommendations of the ISPD, the great variability of care practices has been reported in all published studies (9-12). Motivated by a higher frequency of infections and a lower technical survival compared to those observed in other countries (13), the Australian and New Zealand teams have been very active in gathering information about the practices of the centers and studying the barriers to the implementation of international recommendations.); in 2016, despite a marked improvement in the results, their peritonitis rate remained above the threshold of less than 0.36 episodes per year x patient suggested by the ISPD. New practical recommendations have been published, emphasizing the value of a structured quality improvement process focused on catheter infections (14).

Campbell et al's 2017 study of Australian and New Zealand nephrologist practices was based on a questionnaire sent to all nephrologists (15); 39.9% responded to the survey; 95.5% reported that catheter implantations were performed under preoperative antibiotic prophylaxis using a cephalosporin (88.7%) or vancomycin (22.6%); 63.9% were looking for nasal

carriage of *S. aureus*, but in case of positivity, only 88.4% of them reported treating patients; finally, 59.4% educated their patients with the application of mupirocin at the exit site.

The variability of practices is found at the national level but also between the dialysis centers of the same region, evoking the role of a center-effect. Thus, a previous retrospective study published in 2016 based on data from the RDPLF Catheter module (16) has demonstrated the effectiveness of preoperative antibioprohylaxis for the prevention of early peritonitis, on all of the included catheters; but if the center-effect is taken into account, preoperative antibioprohylaxis is effective only in some centers. These results are in agreement with those of Nadeau-Fredette et al, based on data from the ANZDATA registry, identifying the characteristics of centers associated with low or high rates of peritonitis (17,18). The impact on catheter infections has not been studied.

A second study in 2018 based on data from the RDPLF Catheter module explored the effect center-effect in metropolitan France. The centers have been grouped into clusters of practices with a certain geographical coherence evoking the existence of centers of influence; this approach remains theoretical for the moment because of the anonymisation of the data during the study (19).

The first results of the prospective cohort study PDOPPS (10) including 11389 patients from 6 countries (no francophone center) confirm the great international variability of practices; By referring to ISPD's high-level recommendations for the prevention and treatment of infections, they find, as in our study, significant differences in practice with respect to these recommendations, whether at the country level or at that of the dialysis centers.

The main limitations of all these studies as of ours, are the participation bias (selection of nephrologists more motivated by peritoneal dialysis and in our case, by the problems related to peritoneal access, who may therefore have different care practices) and lack of completeness of data collection.

The RDPLF Catheter Module is 21 years old and participation in this module as well as the completeness of the data collection increase over time, allowing to follow changes in bacterial ecology, changing care practices in francophone centers, and results in terms of frequency and risk factors for catheter infections.

CONCLUSION

Results from the RDPLF Catheter Module identify risk factors for infection: wall hematoma, initial dialysate leakage, obesity, nasal carriage of *Staphylococcus aureus*; and protective factors: implantation by a loyal operator, delay of 7 days before the first catheter dressing, preoperative antibiotic prophylaxis, application of mupirocin to the outlet.

Despite their wide dissemination, the ISPD recommendations still have a limited effect on the evolution of practices. Interventions targeting a certain number of practices within each center appear to be more effective, and participation in the French Language Peritoneal Dialysis Registry is part of a process of continuous improvement of the quality of care: the individual statistics of a center allow it to compare its results with those of all the centers; they serve as a support for the annual report of infectious complications recommended by the recommendations, and make it possible to review the protocols of care.

DISCLOSURE

The authors declare that they have no conflict of interest for this article.

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