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IS PERITONITIS RISK INCREASED IN ELDERLY PATIENTS ON PERITONEAL DIALYSIS? REPORT FROM THE FRENCH LANGUAGE PERITONEAL DIALYSIS REGISTRY (RDPLF)

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♦ ***Introduction:*** **This study was carried out to examine whether or not elderly patients on peritoneal dialysis (PD) had an increased risk of peritonitis.**

♦ ***Methods:*** **This was a retrospective cohort study based on data from the French Language Peritoneal Dialysis Registry. We analyzed 8,396 incident patients starting PD between January 2003 and December 2010. The end of the observation period was 31 December 2012. Patients were separated into 2 age groups: up to 75 and over of 75 years old.**

♦ ***Results:*** **Among 8,396 patients starting dialysis there were 3,173 patients older than 75. When using a Cox model, no association was found between age greater than 75 years and increased risk of peritonitis (hazard ratio [HR]: 0.97 [0.88 – 1.07]). Diabetes (HR: 1.14 [1.01 – 1.28] and continuous ambulatory PD (HR: 1.13 [1.04 – 1.23]) were significantly associated with a higher risk of peritoneal infection whereas nurse-assisted PD was associated with a lower risk of peritonitis (HR: 0.85 [0.78 – 0.94]. In the analysis restricted to the 3,840 self-care PD patients, there was no association between age older than 75 years and risk of peritonitis.**

♦ ***Conclusion:*** **The risk of peritonitis is not increased in elderly patients on PD in a country where assisted PD is available.**

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KEY WORDS: Peritoneal dialysis; peritonitis; elderly.

An important proportion of subjects starting dialysis are older patients (1,2). In addition, as life expectancy on dialysis is improving and because elderly patients have a lower priority access to the waiting list for renal transplantation, the number of elderly patients on renal replacement therapy is increasing (3,4). One report from the Renal Epidemiology and Information Network (REIN) registry showed that peritoneal dialysis (PD) seemed to be the preferred dialysis modality for elderly patients starting renal replacement therapy (5). At the same time, compared with hemodialysis, PD was associated with a higher risk of mortality in the elderly population in France (6). It is possible that these elderly patients were overexposed to the complications of PD, which may have affected the outcome on dialysis. Visual deficiency, functional impairment, and cognitive dysfunction are common problems in elderly patients and may increase the risk of peritoneal infection linked to errors occurring during manipulation of the device. In addition, diverticulosis, which is more frequent in elderly patients, could increase the risk of enteric peritonitis. Peritoneal infection affects patient survival on dialysis as well as quality of life under treatment. In most of the studies already published, older age was not associated with a higher risk of peritoneal infection (7,8,9). However, these results must be confirmed in a country where disabilities, comorbidities, and functional impairment do not represent contraindications for PD.

This study was carried out to evaluate whether or not elderly patients treated with PD had a higher risk of peritoneal infection.

STUDY POPULATION AND METHODS

STUDY POPULATION

This was a retrospective study using data from the French Peritoneal Dialysis Registry (RDPLF). All adults (older than 18 years) starting PD in France between 1 January 2003 and 31 December 2010 were included. The end of the observation period was 31 December 2012. We excluded patients who had had primary PD failure, defined as PD duration of less than 2 days, and patients previously treated with PD. We also excluded patients treated with hemodialysis for more than 3 months before PD initiation, considering them not to be incident dialysis patients. A subset of self-care PD patients was extracted from the dataset.

DEFINITION OF THE EVENTS

We examined the occurrence of peritoneal infection during PD. The time from PD start and the first peritonitis were calculated. The number of peritoneal infections during PD was determined for each patient. In addition, the number of peritonitis episodes due to *Staphylococcus epidermidis* was evaluated, *S. epidermidis* peritonitis being considered an indicator of peritonitis linked to errors in manipulation of the equipment.

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DEFINITION OF THE VARIABLES

The main objective of the study was to assess whether elderly patients had a greater risk of peritonitis than other patients. Several definitions of elderly population have been used in the nephrology literature. Here, the elderly population was arbitrarily defined by an age greater than 75 years, corresponding to the criteria used in 2 previous studies from France (6,10). Others covariates were gender, comorbidities, diabetes mellitus, underlying nephropathy, PD modality 3 months after dialysis start (automated PD or continuous ambulatory PD [CAPD]), assisted PD (family assistance, nurse assistance), starting PD after transplantation failure, center size, and center category. For center size evaluation, we calculated the number of incident PD patients per center and per year of participation during the study period. Centers were divided into 4 groups (non-profit center, community center, academic hospital, and private hospital). To assess patients' comorbidities we extracted the Charlson comorbidity score (CCI) from the database. In an attempt to evaluate the role of comorbidities independently of patient age, we calculated a modified CCI by subtracting the age sub-score. The causes of transfer to hemodialysis and the causes of the first peritonitis episode were also extracted. The cause of peritonitis is a declarative covariate recorded in the registry.

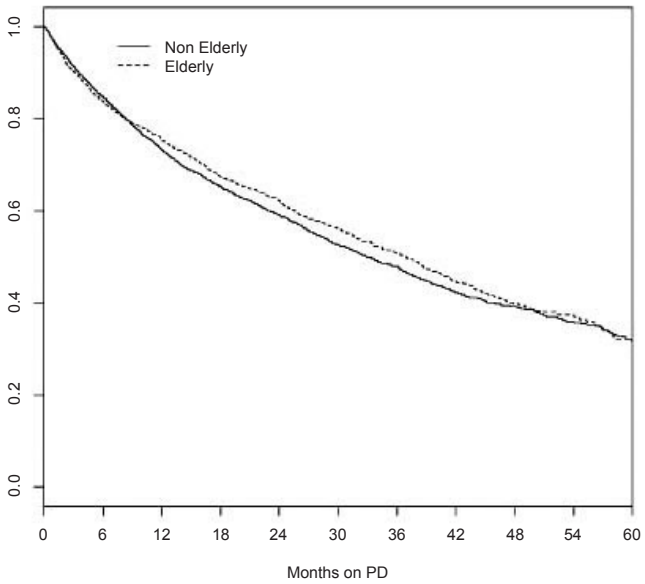
STATISTICAL ANALYSIS

Continuous variables were recorded as the median value, with the first and third quartile; categorical variables were recorded as frequencies and percentage. To avoid multiple testing issues, no statistical tests were performed for the group description. A Cox model was used for the time-to-event analysis. The event of interest was the occurrence of the first peritonitis episode. Only 95% confidence intervals (CIs) were used for statistical inference and to represent the uncertainty of both hazard ratios (HRs).

A Kaplan-Meier curve of survival free of peritonitis was drawn for the elderly and patients younger than 75 (Figure 1). We explored the relationship between variables and the time to first peritoneal infection episode using a bivariate Cox regression model. Regression spline was used to explore the functional form of the relationship between patient age and the risk of peritonitis (Figure 2). Proportional hazard assumptions were tested with Schoenfeld residual plots. Multivariate analysis was performed with a Cox regression model. Patient age (older or younger than 75 years) was entered in the model based on *a priori* consideration. Covariates were included in the multivariate analysis when they were associated with peritonitis risk in the bivariate analysis. The interaction between patient age and assisted PD was tested in the multivariate analysis with a Cox model.

MISSING DATA

Five percent of the data were missing for the CCI. We, therefore performed 5 sets of imputation for the missing



Number at risk

Months	6	12	18	24	30	36	42	48	54	60
Elderly	2,119	1,580	1,197	913	637	442	293	179	134	75
Others	3,829	2,688	1,951	1,398	960	660	447	311	210	135

Figure 1 — Survival free of peritonitis (Kaplan-Meier survival curve). PD = peritoneal dialysis.

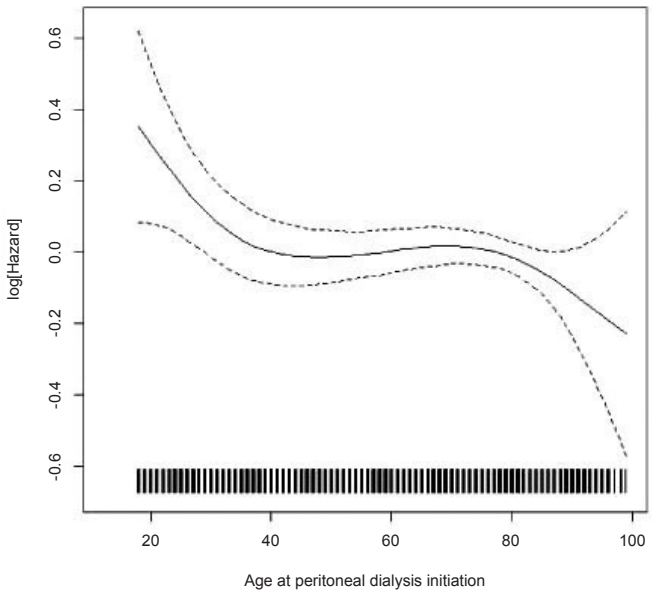


Figure 2 — Relation between patient age and peritonitis risk (smoothing penalized spline).

CCI values. The set of imputed CCI values was chosen based on a graphic representation of the imputed value and the observed value. Modified CCI was calculated using the imputed CCI value.

Statistical analyses were done using R 2.15.1 (R Foundation for Statistical Computing), including the package survival, and MICE (multiple imputation by chained equations).

The RDPLF has the approval of the French national ethics committee, *Commission nationale de l'informatique et des libertés*. This study took place within the framework of this authorization.

RESULTS

PATIENT CHARACTERISTICS

Of the 8,396 patients included in the study, 3,173 were older than 75 years. The median ages at dialysis initiation were respectively 82 and 59 years for the elderly group and the other patients. Elderly patients had a higher modified Charlson score than the other patients. Elderly patients were more frequently treated using CAPD and assisted PD than patients under 75. Detailed information about patient characteristics by dialysis initiation is provided in Table 1. Among the 8,396 patients there were 3,840 self-care PD patients. The 2-year actuarial patient survival was 36% (95% CI: 34 – 38) for the elderly patients and 70% (95% CI: 68 – 71) for the other patients. The 2-year technique survival of the elderly patients was 73% (95% CI: 0.71 – 0.75) compared with 59% (95% CI: 0.58 – 0.61) for the younger patients.

PERITONEAL INFECTION

The median PD duration of the cohort was 12.68 months (interquartile range: 5.15 – 26.15). There were 5,958 peritonitis episodes for a total exposure time of 145,811 months on PD (1/25 patient months). The peritonitis rate was 1/27 patient months and 1/24 patients months for the elderly and younger patients, respectively. The incidence rate ratio of peritonitis was 0.86 (95% CI: 0.81 – 0.91, elderly as reference group). In addition, for infections specifically due to *S. epidermidis* the incidence ratio was 0.82 (0.69 – 0.98, elderly as reference group). The 2-year actuarial survival free of peritonitis was 62% (95% CI: 60 – 64) and 59% (95% CI: 57 – 61) for the elderly and other patients, respectively. Among the elderly patients, peritonitis was responsible for 109/637 (17%) of transfers to hemodialysis whereas peritonitis was a cause of PD cessation for 333/1,760 (19%) of the younger patients. There was no difference between the 2 groups regarding the causative agent of the peritonitis episode except for peritoneal infection due to the category of miscellaneous microorganisms (Table 2).

RISK OF PERITONITIS

The Cox regression model showed that nurse-assisted PD was associated with a lower risk of peritoneal infection (Table 3). Nurse-assisted PD had a protective effect for elderly patients but had no significant effect on the peritonitis risk for younger patients (data not shown). Male patients, diabetic patients, and CAPD were associated with an increased risk of peritonitis. There was a significant relationship between patient age and assisted PD. In the multivariate analysis, there was no significant relationship between age greater than 75 years and peritonitis risk (Table 4). In the multivariate analysis restricted to the non-assisted PD patients, there was no significant association between age over 75 and risk of peritoneal infection (Table 5). Figure 2 represents the relationship between patient age and peritonitis risk.

TABLE 1
Patient Characteristics According to Patient Age

Covariate	Elderly (*N*=3,173) Median (IQR) *N*	%	Others (*N*=5,223) Median (IQR) *N*	%
Age at PD initiation	82 (79–85)		59 (46–69)	
Modified CCI	4 (3–5)		3 (2–5)	
Sex (male)	1,733	56	3,099	56
Diabetes	1,132	35	1,642	31
Nephropathy				
Unknown	470	15	508	10
Interstitial nephritis	140	4	321	17
Glomerulonephritis	190	6	1,040	20
Diabetic	595	19	1,134	22
Polycystic kidney disease	51	2	432	8
Miscellaneous	106	4	441	9
Uropathy	96	3	213	4
Vascular	1,358	43	904	18
Systemic disease	37	1	171	3
Missing	130	—	26	—
PD modality (CAPD)	2,357	85	2,502	52
Assisted peritoneal dialysis	2,768	87	1,788	34
Modality of assistance				
Self-care PD	401	13	3,424	66
Family-assisted PD	379	12	504	10
Nurse-assisted PD	2,389	75	1,284	25
Treatment before PD				
Hemodialysis	387	12	764	15
Not on dialysis	2,778	88	4,340	83
Renal transplantation	1	0	103	2
Missing	7	—	16	—
Centre size (new patients per year)				
<10	2,120	67	3,157	60
10–20	951	30	1,902	36
>20	102	3	164	3
Type of center				
Non profit	611	19	1,113	21
Community hospital	1,731	55	2,649	51
Academic hospital	554	17	1,194	23
Private hospital	277	9	267	5

IQR = inter-quartile range; PD = peritoneal dialysis; CCI = Charlson Comorbidity Index; CAPD = continuous ambulatory PD.

DISCUSSION

The results of this report are in line with the findings of our previous study about PD in elderly patients (10). In this new analysis, in an attempt to assess the risk of peritonitis linked to patient age, older individuals were compared with

TABLE 2
Cause of Peritonitis According to Patient Age

Micro-organisms	Elderly patients (1,621) *N*	%	Others (3,234) *N*	%
Gram-positive	939	57.10	1,845	57.90
Gram-negative	454	28.00	918	28.40
Multiple	170	10.50	275	8.50
Miscellaneous	31	1.91	140	4.33
Fungal	27	1.67	56	1.73
Sterile	392	—	695	—

TABLE 3
Association Between Each Covariate and Peritonitis (Bivariate Analysis with Cox Model)

Covariate	Cox model cs-HR (95%CI)
Age > 75 years	0.94 (0.88–1.05)
Age by decade	0.98 (0.96–1.00)
Age by quartiles	
Q1 (18–55)	ref
Q2 (55–71)	0.98 (0.89–1.08)
Q3 (71–80)	0.96 (0.87–1.06)
Q4 (80–99)	0.93 (0.85–1.04)
Gender (male)	1.09 (1.02–1.18)
Underlying nephropathy	
Polycystic kidney disease	ref
Interstitial nephritis	1.17 (0.95–1.44)
Glomerulonephritis	1.21 (1.01–1.45)
Diabetes	1.21 (1.02–1.44)
Unknown	1.19 (0.99–1.43)
Miscellaneous	1.24 (1.00–1.55)
Urologic	1.18 (0.92–1.50)
Vascular	1.11 (0.94–1.31)
Systemic disease	1.34 (1.03–1.76)
Diabetes	1.10 (1.02–1.18)
Modified CCI (per unit)	1.02 (1.00–1.04)
HD prior to PD	1.13 (1.02–1.25)
Assisted PD	0.93 (0.86–0.99)
Modality of assistance	
Self-PD	ref
Family-assisted	1.03 (0.92–1.58)
Nurse-assisted	0.90 (0.83–0.97)
Centre size by category	
<10 new patients per year	ref
10–20	1.09 (1.02–1.18)
>20	0.90 (0.73–1.12)
Type of center	
Non profit	ref
Community hospital	1.02 (0.94–1.12)
Academic hospital	1.01 (0.90–1.12)
Private hospital	0.96 (0.82–1.37)
First PD modality (CAPD)	1.06 (098–1.15)

cs-HR = cause specific hazard ratio; CI = confidence interval; CCI = Charlson comorbidity index; HD = hemodialysis; PD = peritoneal dialysis; CAPD = continuous ambulatory PD.

younger ones. There was no relationship between patient age and risk of peritonitis in the Cox model in our study. However, there was a bias due to the association between assisted PD, risk of peritonitis, and age greater than 75. Thus, it cannot be excluded that younger age *per se* is associated with a greater risk of infection.

There are few large-scale studies regarding the role of patient age on peritonitis risk. Li *et al.* compared PD outcomes between patients older than 65 years and younger patients (7). There was no significant difference between the 2 groups in peritonitis-free survival. In one study from Canada, age above 70 was not associated with an increased risk of peritonitis (9). In this study, 2 periods of PD initiation were separated (1996 to 2000 and 2001 to 2005). The authors found that older age was associated with a higher risk of infection during the first period but not during the second period of PD initiation. The authors hypothesized that the lack of association between increased age and peritonitis during the recent period could reflect the use of the flush-before-fill technique and of topical antibiotics. The results observed in the second period could also be partially explained by better selection of elderly patients for PD. Recently, Lim *et al.* found that patients older than 65 years and those 65 and under had similar rates of peritonitis-free survival (11). In this study, however, elderly patients had a higher risk of peritonitis-related and all-cause mortality. In a recent study from Brazil, the only factor associated with death during peritoneal infection was older age (12). This emphasizes the notion that, even if the risk of peritonitis is not higher in the older population, the consequences could be more severe because older subjects have more comorbidities. Colonic diverticular disease, highly prevalent in the older population, may increase peritonitis risk. Surprisingly, there was no difference in the rate of peritoneal infection due to gram-negative microorganisms between elderly and younger patients. Older patients presenting diverticulosis may have been contra-indicated for PD. Nevertheless, it has recently been observed that asymptomatic diverticulosis was not a risk factor for enteric peritonitis in PD patients (13).

It should be noted that more than 85% of the elderly patients in our study were treated with assisted PD, which could cause a co-linearity in the regression modeling. However, when the multivariate analysis was restricted to the subset of individuals on self-care PD, age over 75 was not associated with a higher risk of peritoneal infection. One limitation of our study is that nurse-assisted PD is fully covered by public healthcare insurance in France, and this assistance is therefore widely used by the elderly population. Consequently, the results of our study must be interpreted with caution, especially if applying them to a country where nurse-assisted PD is not available. Indeed, nurse-assisted PD could have a protective effect in elderly patients who have difficulties in manipulating the equipment. One may also argue that self-care elderly patients on PD could have been selected based on their ability

TABLE 4
Multivariate Analysis of Peritoneal Infection (Cox Model)

Covariate	Cox model cs-HR (95%CI)
Age greater than 75 years	0.97 (0.88–1.07)
Gender (male)	1.10 (1.02–1.19)
Diabetes	1.14 (1.01–1.28)
Charlson modified (unit)	1.01 (0.98–1.04)
Underlying nephropathy	
Polycystic kidney disease	ref
Interstitial nephritis	1.18 (0.98–1.43)
Glomerulonephritis	1.19 (0.99–1.43)
Diabetes	1.07 (0.87–1.31)
Unknown	1.18 (0.98–1.43)
Miscellaneous	1.21 (0.99–1.49)
Urologic	1.20 (0.94–1.54)
Vascular	1.08 (0.90–1.29)
Systemic disease	1.37 (1.04–1.80)
First PD modality (CAPD)	1.13 (1.04–1.23)
Modality of assistance	
Self-PD	ref
Family-assisted	0.98 (0.87-1.11)
Nurse-assisted	0.85 (0.78-0.94)
Centre size by category	
<10 new patients per year	ref
10–20	1.09 (1.00-1.17)
>20	0.95 (0.76-1.18)

cs-HR = cause specific hazard ratio; CI = confidence interval; PD = peritoneal dialysis, CAPD = continuous ambulatory PD.

TABLE 5
Multivariate Analysis or Peritoneal Infection Restricted to Self-Care Peritoneal Dialysis Patients (Cox Model)

Covariate	Cox model cs-HR (95%CI)
Age greater than 75 years	1.10 (0.94–1.29)
Gender (male)	1.17 (1.05–1.31)
Diabetes	1.24 (1.01–1.50)
Charlson modified (unit)	1.02 (0.98–1.05)
Underlying nephropathy	
Polycystic kidney disease	ref
Interstitial nephritis	1.17 (0.90–1.52)
Glomerulonephritis	1.16 (0.94–1.42)
Diabetes	1.02 (0.77–1.35)
Unknown	1.16 (0.92–1.46)
Miscellaneous	1.23 (0.96–1.57)
Urologic	1.55 (1.14–2.09)
Vascular	1.03 (0.83–1.27)
Systemic disease	1.22 (0.87–1.72)
First PD modality (CAPD)	1.14 (1.03–1.27)
Centre size by category	
<10 new patients per year	ref
10–20	1.06 (0.95–1.18)
>20	1.14 (0.82–1.60)

cs-HR = cause specific hazard ratio; CI = confidence interval; PD = peritoneal dialysis; CAPD = continuous ambulatory PD.

to manipulate the catheter connection without the support of a nurse. On the contrary, in 2004, Verger *et al.* showed that, in patients treated with automated PD, nurse assistance was associated with a higher risk of peritonitis (14). However, when regular nurse visits from the PD center were organized, assisted PD was not associated with a higher risk of peritoneal infection. The differences between our findings and the results of Verger *et al.* could be explained by the effect of nurse assistance possibly varying from one PD modality to another, as most of the elderly patients included in our study were treated with CAPD. In addition, following the report of Verger *et al.*, and because there were financial incentives to promote PD, more than 50% of PD centers in France had implemented nurse home visits by 2010.

Both diabetes and PD were associated with peritonitis risk in our study. In 2 studies from Australia, increased rate of peritonitis in PD patients was associated with diabetes (15,16). Possible reasons for an association between diabetes and peritonitis may have been visual impairment or immune function of diabetic patients. The role of PD modality on peritonitis risk remains controversial. A meta-analysis concluded that automated PD reduced the peritonitis rate compared with CAPD, whereas in a recent large scale study, PD modality was not associated with a higher peritonitis risk (16,17). It is difficult to draw any conclusion regarding the link between PD modality and peritonitis risk because of the indication bias.

Although it offers advantages in terms of quality of life, PD is underused in elderly patients (18). Our study confirms that, at least in select self-care elderly patients, the risk of peritonitis is similar to the risk observed in younger patients. In addition, our results support the idea that assisted PD may protect non-autonomous elderly patients from peritonitis. Further studies are needed to confirm this finding. We believe, like others, that older age should not be considered a risk factor for peritoneal infection.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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