www.bdd.rdplf.org Volume 3, n° 4, Décembre 2020
https://doi.org/10.25796/bdd.v3i4.59643
ISSN 2607-9917

Bulletin de la Dialyse à Domicile

Symptomatic SARS-CoV2 infections in patients undergoing dialysis treatment in France either by hemodialysis in an establishment or at home, or by peritoneal dialysis: Data from the REIN and RDPLF registries.

(Infections symptomatiques à SARS-CoV2 des patients traités en France par hémodialyse en établissement, à domicile ou par dialyse péritonéale : Données des registres REIN et RDPLF)

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Note : ce texte est disponible en Français à la même adresse url : https://doi.org/10.25796/bdd.v3i4.59643

Résumé

L'ensemble des insuffisants rénaux traités par dialyse en France sont suivis par le registre REIN (Réseau Épidémiologie et Information en Néphrologie), en complément le registre RDPLF (Registre de Dialyse Péritonéale de Langue Française) suit en temps réel les patients traités à domicile dans les régions et pays de langue Française. En excluant de l'étude les patients asymptomatiques ayant un test de contamination SARS-CoV2 positif, l'étude a porté uniquement chez les patients avec la maladie COVID-19 symptomatique. Les données de REIN et du RDPLF ont été utilisées.
Au total, 3541 patients ont été déclarés symptomatiques avec COVID-19. La proportion de malades atteint de COVID-19 symptomatique était de 4.9% chez les patients traités à domicile par dialyse péritonéale ou hémodialyse et de 8.0% chez ceux traités par hémodialyse hors domicile. Après ajustement sur l'âge et les comorbidités, les patients symptomatiques traités à domicile étaient associés à un risque plus élevé de mortalité.

En conclusion, les traitements à domicile pourraient représenter une solution de prévention du risque de contamination lors de circulation du virus. En revanche, le risque de mortalité chez les patients symptomatiques à domicile pourrait être lié à un retard de prise en charge : une organisation rigoureuse à distance doit être mise en place afin de ne pas retarder la prise en charge des patients en cas d'infection.

Summary

In France all patients treated with dialysis are registered in the REIN registry (Epidemiology and Information Network in Nephrology) ; in addition the RDPLF (French Language Peritoneal Dialysis Registry) monitors patients treated at home in French-speaking regions and countries.

Asymptomatic patients with a positive SARS-CoV2 test were excluded : the study focused only on patients with symptomatic COVID-19 disease. Data from REIN and RDPLF were used. In total, 3,541 patients were declared symptomatic with COVID-19. The proportion of patients with symptomatic SAR-coV2 infection was 4.9% in patients treated at home by peritoneal dialysis or hemodialysis and 8.0% in those treated in a dialysis unit. After adjustment for age and comorbidities, being treated at home was associated with a higher risk of mortality. In conclusion, home treatments could represent a solution for preventing the risk of contamination during the circulation of the virus. On the other hand, the risk of mortality in symptomatic patients at home could be linked to a delay in treatment: rigorous remote organization must be implemented so as not to delay the treatment of patients in the event of infection.

Mots clés : SARS-CoV2, COVID-19 , Dialyse péritonéale, hémodialyse, mortalité, létalité

Key words : SARS-CoV2, COVID-19, peritoneal dialysis, hemodialysis, lethality

Abbreviations :
REIN: Epidemiology and Information Network in Nephrology
RDPLF: French-Language Peritoneal Dialysis Register A
RC: Clinical researcher associate
COVID +: Patients with clinically symptomatic COVID-19
COVID -: Patients without clinical signs of COVID-19, tested positive or not.

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www.bdd.rdplf.org Volume 3, n° 4, Décembre 2020
https://doi.org/10.25796/bdd.v3i4.59643
ISSN 2607-9917

INTRODUCTION

Patients undergoing dialysis for chronic renal disease represent a population at high risk of severe forms of SARS-CoV2 infection due to their fragility and the need for frequent care in a hospital environment. Home dialysis, which makes it possible to avoid travel and contact with other patients or several caregivers, could represent an interesting treatment modality in this context.1,2

The objective of the present study is to describe the morbidity and mortality of patients with clinical symptoms of SARS-CoV2 infection in France according to their dialysis modality.

METHODS

Population and information collected

All adult patients over 18 years treated with dialysis in mainland France in 2020 were included. Their latest clinical status and treatment modalities were used as described on the date of diagnosis of COVID-19, upon death, or at the end of November 2020.

All dialysis patients infected with SARS-CoV2 were reported to the ARCs of the REIN registry and entered into the Biomedicine Agency's DIADEM application, whether or not these patients presented with clinical symptoms. All the centers participating in the RDPLF registry were asked to register all patients infected with SARS-CoV2 with clinical manifestation.

The strong point of the REIN registry3 is its national coverage of all dialysis patients, whatever the treatment modality. On the other hand, the collection of cases and events and the quality control of the data collected require a certain amount of time and therefore do not make it possible to provide information in real time. Conversely, the RDPLF registry4 has nearly exhaustive and up-to-date data for patients on peritoneal dialysis. These two registries were used within the framework of this study. Information from the RDPLF registry was used for peritoneal dialysis patients.

Patients were classified into 6 groups, depending on whether they were COVID-19 positive or negative and whether they were being treated with peritoneal dialysis or home hemodialysis, or in hemodialysis units. Only symptomatic patients were selected.

The clinical characteristics of the patients were presented by group, in the form of frequency and median and interquartile range for continuous variables. Factors associated with the likelihood of exhibiting symptoms of COVID-19 were explored using generalized logistic regression, including treatment at home or not.

The causes of death were classified into 2 groups depending on whether or not COVID-19 was the cause of death. Factors associated with the likelihood of death in patients with symptomatic COVID-19 were explored using generalized logistic regression, taking into account the cause of death. In this section, all home patients were classified according to whether or not they received assistance, knowing that hemodialysis patients at home were considered independent.

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www.bdd.rdplf.org Volume 3, n° 4, Décembre 2020
https://doi.org/10.25796/bdd.v3i4.59643
ISSN 2607-9917

Temporal evolution: To assess whether the percentage of lethality (death rate from COVID-19 in infected patients) had varied among those undergoing peritoneal dialysis in the RDPLF, we calculated this percentage of deaths due to SARS-CoV2 before and after July 1, 2020.

Ethics: The REIN and RDPLF registers are declared to the National Commission for Computing and Liberties (CNIL). The databases of the REIN and RDPLF registries are independent and joint studies are carried out using previously anonymized data grouped together in an independent file unrelated to their origin.

RESULTS

Among the 41,128 adults in mainland France treated with hemodialysis between March and December 2020, a total of 3,843 COVID-19-positive dialysis patients were declared in the REIN registry, i.e., 9% of dialysis patients. Of these, 228 (6%) remained asymptomatic although they had tested positive for SARS-CoV2 infection during a systematic screening.

Over the same period, 149 adult patients were declared as having symptomatic COVID-19 among the 3,621 patients treated with peritoneal dialysis according to the RDPLF registry. In total, this study considered 3,764 symptomatic COVID-19 patients among 44,526 dialysis patients, or 8.45%. Figure 1 shows the cumulative incidence of these 3,746 symptomatic cases reported in the 2 registries.

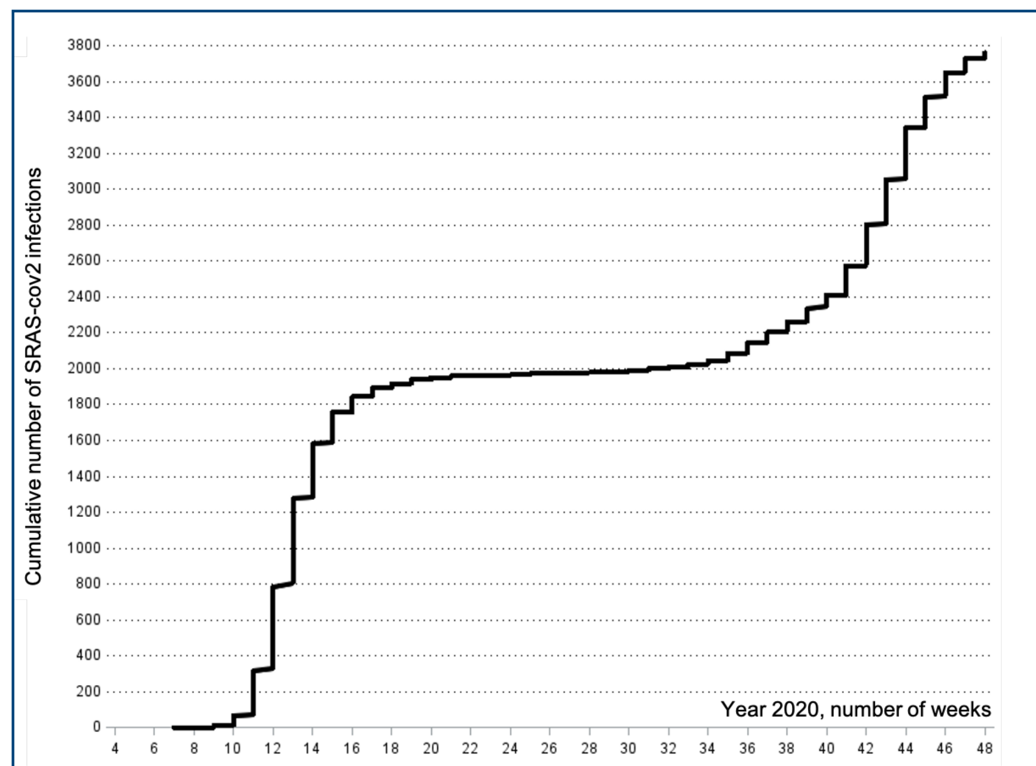

Figure 1. Cumulative incidence of dialysis patients with symptoms of SARS-CoV2

The proportion of patients with symptomatic COVID-19 was 3.9% in patients treated at home by peritoneal dialysis or hemodialysis and 8.9% in those treated by out-of-home hemodialysis (Table I).

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Table I. Number and percentage by age group of symptomatic COVID-19 patients

			18-44	45-64	65-74	75-84	85+
	Total number	Patients COVID-19 +	Proportion of patients COVID-19 + (%)				
Peritoneal dialysis	3621	149	2.9	3.2	3.9	4.4	5.9
Home hemodialysis	535	13	2.2	1.8	2.1	14.3	0.0
Total home dialysis patients	4156	162	2.7	2.9	3.8	4.7	5.9
Hemodialysis out of home	40370	3602	9.3	8.7	8.3	9.1	9.9

The clinical characteristics of the patients are shown in Table II. Home hemodialysis patients are approximately 20 years younger. Patients on peritoneal dialysis, taken as a whole, are of a similar age to patients on out-of-home hemodialysis and fewer comorbidities. It should be noted, however, that patients on peritoneal dialysis constitute a heterogeneous population made up of young, healthy, and autonomous patients (median age 64.8, IIQ 52.7-73.5) and very elderly patients with comorbidities and assisted for their treatment (median age 80.0, IQ 72.0-86.1).

In multivariate analysis, treatment at home was associated with a lower risk of COVID-19 infection, whether assisted (OR 0.6, 95% CI 0.5-0.7) or autonomous (OR 0.3, 95% CI 0.3-0.4). Only diabetes was associated with a 30% increase in probability of infection (OR 1.3, 95% CI 1.2-1.4), while a history of myocardial infarction was associated with a reduced risk (OR 0.9, 95% CI 0.8-1.0). Age and other comorbidities were not associated with the risk.

Table II. Clinical characteristics of patients with symptomatic COVID-19

	Home HD COVID-19 -	Home HD COVID-19 +	HD COVID-19 -	HD COVID-19 +	PD COVID-19 - (RDPLF)	PD COVID-19 + (RDPLF)
Number(N)	522	13	36768	3602	3472	149
Age median (IIQ)	53.5(44.5-63.5)	60.3(45.6-66.9)	72.2(62.1-81.1)	72.9(62.1-81.7)	72.2(60.4-81.6)	75.1(65.1-84.3)
	%					
Age >= 75 years	3.6	23.1	40.8	43.0	40.9	50.3
Pulmonary desease	9.7	7.7	16.9	17.0	7.5	8.4
Cancer	13.8	15.4	11.6	10.0	7.7	8.4
Arteritis	10.0	38.5	24.2	24.1	14.3	14.0
Cerebral vascular event	5.6	7.7	12.6	13.0	9.5	9.1
Myocardial infarction	7.9	7.7	11.2	10.1	12.2	13.3
Cardiac insuffiiency	10.8	23.1	25.0	24.1	18.2	22.4
Diabetes	16.5	38.5	44.2	50.2	34.2	49.7
Obesity	18.6	0.0	25.0	27.5	22.2	20.8

COVID-19 - (asymptomatic patients, tests positive or not), COVID-19 +: patients with clinically symptomatic COVID-19; HD DOM: home hemodialysis. HD: out-of-home hemodialysis.

Among the 3,764 patients with symptoms related to COVID-19, 785 patients (21%) died, inclu-

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www.bdd.rdplf.org Volume 3, n° 4, Décembre 2020
https://doi.org/10.25796/bdd.v3i4.59643
ISSN 2607-9917

ding 524 as a result of COVID-19 (67% of deaths). The case fatality (proportion of disease-related deaths compared to the total number of cases affected by the disease) was 13.9%. Mortality by cause of death, by age group, and by degree of independence at home are shown in Table III.

Table III. Mortality rate (%) by age group and cause of death

	18-44	45-64	65-74	75-84	85+
	Dialysis in an instutional unit n=3602				
Death not due to COVID-19	0.8	3.1	6.0	9.5	10.6
Death due to COVID-19	1.2	6.4	13.2	16.6	23.7
	Dialysis at home n=162				
Death not due to COVID-19	0.0	24.2	15.4	9.1	14.7
Death due to COVID-19	8.3	12.1	15.4	40.9	41.2
	of which assisted : n=87				
Death not due to COVID-19	0.0	25.0	15.0	6.9	10.3
Death due to COVID-19	0.0	37.5	20.0	48.3	44.8
	Of which autonomous : n=75				
Death not due to COVID-19	0.0	24.0	15.8	13.3	40.0
Death due to COVID-19	9.1	4.0	10.5	26.7	20.0

The characteristics of these patients according to their vital status and the cause of death are shown in Table IV. Patients who died from COVID-19 were younger, with fewer comorbidities, and were more often assisted than other patients who died during the period. On the other hand, these two groups of deceased patients were, as expected, older and more comorbid than the surviving patients.

Table IV. Patient characteristics according to vital status and cause of death

	Alive	Death due to COVID-19	Death not due to COVID-19
Number (N)	2979	261	524
Age, median (IIQ)	71 (59.9-79.9)	79.5 (70.1-85.1)	78.6 (71.3-85.9)
Age ≥ 75 years	38.0	62.1	63.0
Pulmonary disease	15.2	24.1	21.1
Cancer	9.2	15.4	11.8
Arteritis	22.0	33.1	29.1
Cerebral vascular event	12.0	17.6	15.6
Myocardial infarction	9.2	14.1	14.0
Cardiac insufficiency	22.2	36.5	28.5
Diabetes	49.0	54.7	54.3
Obesity	28.0	24.1	23.4
Assisted home dialysis	1.4	3.8	6.5
Autonomous home dialysis	1.8	5.0	1.7

In a multivariate analysis, despite taking these risk factors into account, home dialysis is associated with a threefold higher probability of death in patients with symptomatic COVID-19 regardless of the cause. Cause of death, age, respiratory disease, and history of stroke are associated with higher probabilities of death, of similar magnitude in the 2 groups (Table V). The presence of cancer, arteritis of the lower limbs, and history of myocardial infarction are not risk factors

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www.bdd.rdplf.org Volume 3, n° 4, Décembre 2020
https://doi.org/10.25796/bdd.v3i4.59643
ISSN 2607-9917

for death from COVID-19. Heart failure, obesity, and diabetes were not associated with the risk of death in the 2 groups. Independent home dialysis was more closely associated with the risk of death unrelated to COVID-19 (OR = 4.1 vs. 2.3 for death not associated with COVID-19), whereas assisted home dialysis was more often associated with death related to COVID-19 (OR = 5.7 vs. 2.3).

Table V. Relative to surviving patients, factors associated with the probability of death, by cause of death

	OR death not due to COVID-19 vs alive	OR death due to COVID-19 vs alive
Age 18-44 years	1	1
45-64 years	4.4(1-18.6)	3.3(1.2-9.2)
65-74 years	6.3(1.5-26.6)	7.4(2.7-20.4)
75-84 years	10.8(2.6-45.2)	10.6(3.9-29.2)
>= 85 years	14.5(3.5-60.8)	15.8(5.7-43.8)
Pulmonary desease	1.5(1.1-2.1)	1.3(1-1.7)
Cancer	1.7(1.2-2.5)	1.2(0.9-1.7)
Arteritis	1.4(1-1.9)	1.1(0.9-1.4)
Cerebral vascular event	1.2(0.8-1.9)	1.3(1-1.8)
Myocardia infarction	1.6(1.2-2.2)	1.1(0.8-1.3)
Cardiac insufficiency	1.1(0.9-1.5)	1.2(0.9-1.4)
Diabetes	0.9(0.6-1.2)	0.9(0.7-1.1)
Obesity	1.2(0.8-1.8)	1(0.8-1.4)
Assisted home dialysis	2.3(1.1-4.9)	4.1(2.5-6.6)
Autonomous home dialysis	5.7(2.9-11.2)	1.6(0.7-3.4)

Of the 149 PD patients, 83% of those who died from COVID-19 were assisted with their treatment. In patients who died from other causes and in patients who survived, the attendance rates were 46% and 50% respectively.

The peritoneal dialysis death rate in RDPLF in mainland France has evolved over time. From March 1 to June 30, the percentage of deaths: The percentage of deaths from COVID-19 in symptomatic COVID-19 patients was 31.7%.; from July 1 to November 30: the percentage of deaths from COVID-19 in symptomatic COVID-19 patients was 19.3%.

DISCUSSION

Peritoneal dialysis was recently recommended for patients hospitalized in intensive care for SARS-CoV2 infection.5 This study shows that the risk of developing COVID-19 was much lower in patients treated at home. However, despite taking age and associated comorbidities into account, the risk of death was 3 times higher in people treated at home. These results confirm the preliminary results published during the first phase of the epidemic.[1,3]

When the virus is circulating, at-home treatment to reduce contact with the hospital system may be a protective factor.6 Diabetes as a factor associated with a higher probability of contamination

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could be explained by 2 factors: the choice made to consider only symptomatic patients and the fact that the first phase of the epidemic especially affected the northeast of France, where the prevalence of diabetes among dialysis patients is high.

The higher mortality in patients at home could be due to several factors: patient reluctance to consult, delayed diagnosis,7 and preferential referral to home PD treatment for the most fragile patients, especially the elderly. The large proportion of patients who were assisted with their PD treatment and died of COVID-19 may be related to the higher case fatality in those at greatest risk or to the increased risk of contamination due to the intervention of an external person. Home isolation during a pandemic period can be a source of serious somatic and psychological complications, and it is important for these patients to develop all means of remote monitoring to ensure their safety at home [8].

These results should be interpreted with caution as the pandemic is still evolving. The data used in this study has not yet been consolidated in the REIN registry. Furthermore, it is necessary to take into account the differences in the case mix according to the dialysis modalities, which may not be fully considered in multivariate models despite the introduction of age and the main comorbidities. In addition, the epidemic has had a variable evolution over time and on French territory. The decrease in case fatalities in the second period may be partly linked to a lack of sufficient follow-up to observe deaths in recently infected patients, but also to a different geographical distribution; nonetheless, a better knowledge of the therapeutic approach and changes in resuscitation techniques certainly played a role. It is not excluded that the risks have also evolved.

CONCLUSION

At-home treatments could represent a solution to prevent the risk of contamination during the circulation of the virus. On the other hand, rigorous remote organization must occur to prevent delayed patient care in the event of infection.

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CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

received 2020/12/3 accepted after revision2020/12/09, published 2020/12/15

REMERCIEMENTS

Thanks to all the professionals contributing to the RDPLF registry and the REIN registry and in particular to all the centers whose names appear in the REIN annual report available on the website of the Biomedicine Agency: https://www.agence- biomedecine.fr/Les-chiffres-du-REIN , and thanks to all the nursing and medical teams who send information to the RDPLF in real time: https://www.rdplf.org/listecentres.html and https://www.rdplf.org/accueil-hdd/113-hdd /791-centres-hdd.html

1) Nephrologists participating to the REIN registry

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www.bdd.rdplf.org Volume 3, n° 4, Décembre 2020
https://doi.org/10.25796/bdd.v3i4.59643
ISSN 2607-9917

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