Impact of a rare respiratory diseases reference centre set-up on primary ciliary dyskinesia care pathway

Received: 04 Sept 2021
Accepted: 14 Oct 2021

To the Editor:

Rare diseases have such a low prevalence that special organisation of the patient care pathway is required to address them. In France, the implementation of specific cystic fibrosis (CF) centres [1] has improved the care pathway of CF patients. Indeed, early diagnosis and progress in usual routine treatment might have contributed to improving the prognosis of CF [2]. In the light of this success, rare respiratory diseases reference centres (CRMR: "centre de Références des Maladies Respiratoires Rares") were created from 2007 under the framework of the national plan for rare diseases. The ear, nose and throat (ENT), pneumology and paediatrics departments at our hospital (CHIC: "Centre hospitalier intercommunal de Créteil") have a long-standing expertise in the diagnosis and treatment of primary ciliary dyskinesia (PCD) [3, 4]. A reference centre for rare respiratory diseases (CRMR-RESPIRARE-Site Créteil) was accredited in 2017.

In the present study, we aimed to assess the impact of the opening of the CRMR on the care of PCD patients and their lung function.

This is a retrospective cohort study from one academic tertiary centre. Adult and paediatric PCD patients with a confirmed diagnosis [5] were included. The analysis of the patients' hospital pathways was carried out based on an administrative database, the "Programme De Médicalisation des Systèmes d'Information" (PMSI), for the period 2010–2018. The collected data contains information such as date of admission, patient age, medical act codes using French common classification of medical acts (CCAM 14) or diagnosis (ICD-10). All personal data were either discarded or anonymised using one-way encryption prior to being transmitted and used for analysis. Data processing was carried out using Python version 3.7 and SQL. The study conforms to the Declaration of Helsinki and was approved by the institutional review board of the French Learned Society for Respiratory Medicine – Société de Pneumologie de Langue Française (IRB#, 2021–030).

Patient care pathways were reconstructed using a unique anonymised patient identifier [6]. The hospitalisation database was linked with the outpatient database to obtain the sequence of patient visits. The care pathway thus constituted includes consultations with pneumologists (child or adult), ENT physician and physiotherapists, as well as day hospital and admissions in the emergency department (ED). Annual visit frequencies were calculated over the period 2015–2016 *versus* 2017–2019 and compared using one-sided Wilcoxon rank test [7]. Differences were considered significant when p-values were <0.05.

Forced expiratory volume in 1 s (FEV_1) expressed in litres and as a percentage of the predicted value, coming from the outpatient clinic visits only, were recorded between 2015 and 2019 to monitor respiratory function, according to European Respiratory Society/American Thoracic Society recommendations [8]. Respiratory trajectories were assessed by longitudinal FEV_1 measurements for patients with at least two pulmonary function tests (PFTs). Random effects models were used to estimate the rate of decline of FEV_1 over the period 2015–2016 *versus* 2017–2019.

Between 2010 and 2018, there were 536 664 patients admitted to the CHIC for a consultation or for a hospitalisation, including 118 patients with PCD. Only the 90 patients whose last visit was less than

Shareable abstract (@ERSpublications)
This study shows that the creation of the Rare Lung Diseases Centre impacted the PCD patient care pathway with an increase in physiotherapist and paediatric pulmonology consultations, and a decrease of emergency department visits https://bit.ly/3BfsVWr

Cite this article as: Epaud S, Epaud R, Salaün-Penquer N, *et al*. Impact of a rare respiratory diseases reference centre set-up on primary ciliary dyskinesia care pathway. *Eur Respir J* 2022; 59: 2102413 [DOI: 10.1183/13993003.02413-2021].

18 months before the end of the study period were selected. Among them, 74 patients (31 children and 43 adults) had at least one ENT visit and one pulmonologist (adult or paediatric) visit. There were nine patients with only pulmonologist visits, two with only ENT visits and five without a pulmonologist or ENT visit. The sex ratio was 49.6% (0.96:1). The mean±SD age at first visit was 21.5±17.8 years, whereas

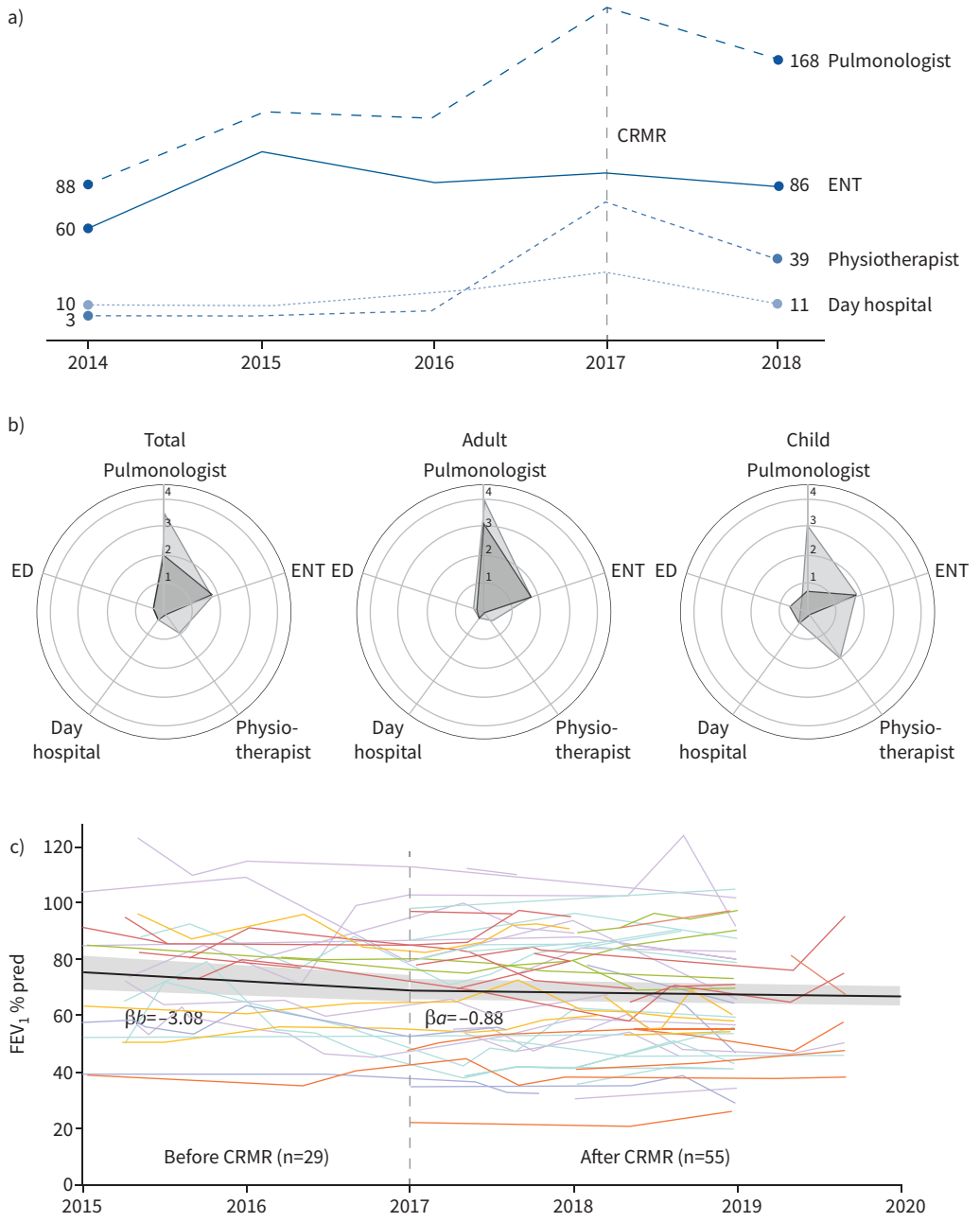

FIGURE 1 a) Evolution of the number of visits of primary ciliary dyskinesia (PCD) patients treated in the Creteil centre. The vertical dotted line indicates the creation of the reference centre for rare respiratory diseases (CRMR) in 2017. b) Comparison of the number of visits per year of PCD patients before and after the CRMR designation. Each vertex of the polygon represents the average number of visits per year of the group studied. A vertex contained in the circle of radius 1 indicates that there is, on average less than one visit per year for this specialty. The study period is 2010–2016 for the label "Before CRMR" and 2017–2018 for the label "After CRMR". c) Estimated rate of decline of forced expiratory volume in 1 s (FEV_1) for PCD subjects before and after CRMR designation. Rate of decline of FEV_1 % predicted estimated by random effects models over the periods 2015–2016 (in 29 patients) and 2017–2019 (in 55 patients). The shaded areas represent the 95% confidence intervals of each estimate. ENT: ear, nose and throat; ED: emergency department.

the mean±SD duration of follow up was 5.5±2.7 years. The mean±SD number of new patients was 7.4±7.1 per year, with 80% living in the CHIC area.

The number of visits for PCD has grown steadily since 2014 to reach a peak in 2017 (figure 1a). As represented in figure 1b, the use of physiotherapy (with sputum analysis) significantly improved following the CRMR opening, from 0.1 to 1.0 visits per year ($p<0.001$). For children, the frequency of pulmonologist visits increased sharply from 0.8 to 3.0 per year ($p<0.001$) but not for adults ($p=0.596$). Meanwhile, ED admissions decreased for children from 0.6 to 0.2 admissions per year ($p=0.033$). ENT follow-up was similar for both children and adults with 1.89 visits per year in adults *versus* 1.79 per year in children ($p=0.874$) and remained stable following the CRMR creation (1.86 per year in adults and 1.81 in children; $p=0.858$). After the creation of this specialised centre, the median number of PFTs per year and per patient significantly increased from 0.5 to 1 ($p=0.019$). The mean±SD FEV_1 over 2017–2019 was similar to 2015–2016 (68±21% pred *versus* 73±19% pred; $p=0.292$). FEV_1 was analysed for patients with at least two PFTs over the period 2015–2019 (n=55), including 16 children (29%) and 39 adults (71%). Between 2015 and 2016, FEV_1 decreased by 3.1% (95% CI −6.1, −0.1%) per year ($p=0.046$), while it decreased by 0.9% (95% CI −2.2, 0.5%) per year between 2017 and 2019 ($p=0.193$) (figure 1c).

Unlike CF, PCD diagnosis is difficult, particularly for children, resulting in a delay of patient care delivery [5]. Thus, it is crucial to ensure rigorous follow-up and prevent recurrent airway infections due to impaired mucociliary clearance leading to progressive lung destruction [9, 10]. In this light, it is likely that the set-up of dedicated centres will contribute to improve the management of PCD. However, studies on the impact of rare lung disease centre establishment are scarce. The present study shows that the care pathway of PCD patients has significantly improved with the setting of the CRMR. In CF, beyond therapeutic advances, the organisation of care is particularly important to improve care pathways and quality of life of patients [11–13]. The main specialists involved in the care pathway of these two diseases are pulmonologists, ENT specialists and physiotherapists; ENT follow-up being more extensive for PCD patients [14, 15]. Prior to 2017, the care pathway for PCD patients at the CHIC had several pitfalls compared to that of CF patients, such as irregular physiotherapy follow-up and little use of day hospitals. Thanks to the creation of the CRMR, PCD patients have benefited from more regular follow-up in pneumology and physiotherapy, especially for children. As a result, more than half of the patients have improved their lung function and there has been a reduction in ED admissions for children, suggesting less frequent relapses. The accreditation of the CRMR did not lead to an increase in ENT visits and the use of day hospitals. The number of ENT visits was already in accord with French recommendations, which may explain this stability. In Creteil, ENT, adult and paediatric pulmonologist are not located in the same building, but there is an ongoing project to bring together the different specialists within a single building, which will likely improve organisation of day hospital and patient care pathways.

Although more studies are needed to confirm our results and other cofactors may have contributed to this outcome, such as improvement of overall care, we think that the creation of a geographically unified rare lung disease centre may significantly improve the care pathway, health, and quality of life for PCD patients.

Salome Epaud[1,9], Ralph Epaud[2,3,4,5,9], Noemie Salaün-Penquer[1], Ekaterina Belozertseva[4,6], Natascha Remus[2,4], Benoit Douvry[4,7], Emilie Bequignon[4,8], Andre Coste[3,4,8], Virginie Prulière-Escabasse[3,4,8], Frédéric Schlemmer[3,4,5,7], Camille Jung[6], Matthieu Ortala[1], Bernard Maitre[3,4,5,7,9] and Céline Delestrain[2,3,4,5,9]

[1]Kaduceo SAS, Toulouse, France. [2]Centre Hospitalier Intercommunal de Créteil, Service de Pédiatrie Générale, Créteil, France. [3]University Paris Est Créteil, INSERM, IMRB, Créteil, France. [4]Centre des Maladies Respiratoires Rares (RESPIRARE), Créteil, France. [5]FHU SENEC, Créteil, France. [6]Clinical Research Centre, Intercommunal Hospital of Créteil, Créteil, France. [7]Centre Hospitalier Intercommunal de Créteil, Service de Pneumologie, Créteil, France. [8]Centre Hospitalier Intercommunal de Créteil, Service d'ORL, Créteil, France. [9]Equal contributors.

Corresponding author: Ralph Epaud (ralph.epaud@chicreteil.fr)

Acknowledgement: We are very grateful to the patients who accepted to participate to this study and RespiRare and RADICO-PCD for their valuable help in collecting the data used in this study. We thank the Filière RespiFil together with BEAT-PCD for their support and assistance and Samuel Kerr for English editing assistance. This

study was supported by the REMEDIA project funded by the European Union's Horizon 2020 Research and Innovation Program under grant agreement number 874753.

Conflict of interest: The authors declare they have no conflicts of interest regarding this paper.

References

1 Rault G, Roussey M, Desrues B, *et al.* Mucoviscidose: recommandations pour l'organisation des centres et réseaux de soins. *Arch Pediatr Organe Off Soc Francaise Pediatr* 2001; 8: Suppl. 5, 802s–817s.
2 Bellis G, Cazes M-H, Parant A, *et al.* Cystic fibrosis mortality trends in France. *J Cyst Fibros* 2007; 6: 179–186.
3 Frija-Masson J, Bassinet L, Honoré I, *et al.* Clinical characteristics, functional respiratory decline and follow-up in adult patients with primary ciliary dyskinesia. *Thorax* 2017; 72: 154–160.
4 Bequignon E, Dupuy L, Escabasse V, *et al.* Follow-up and management of chronic rhinosinusitis in adults with primary ciliary dyskinesia: review and experience of our reference centers. *J Clin Med* 2019; 8: E1495.
5 Lucas JS, Barbato A, Collins SA, *et al.* European Respiratory Society guidelines for the diagnosis of primary ciliary dyskinesia. *Eur Respir J* 2017; 49: 1601090.
6 Blein C, Chamoux C, Reynaud D, *et al.* Diversité des prises en charge des patients atteints de sclérose en plaques entre régions françaises. *Rev DÉpidémiologie Santé Publique* 2018; 66: 385–394.
7 Ward MM. Rheumatology visit frequency and changes in functional disability and pain in patients with rheumatoid arthritis. *J Rheumatol* 1997; 24: 35–42.
8 Miller MR, Hankinson J, Brusasco V, *et al.* Standardisation of spirometry. *Eur Respir J* 2005; 26: 319–338.
9 Strippoli M-PF, Frischer T, Barbato A, *et al.* Management of primary ciliary dyskinesia in European children: recommendations and clinical practice. *Eur Respir J* 2012; 39: 1482–1491.
10 Marthin JK, Lucas JS, Boon M, *et al.* International BEAT-PCD consensus statement for infection prevention and control for primary ciliary dyskinesia in collaboration with ERN-LUNG PCD Core Network and patient representatives. *ERJ Open Res* 2021; 7: 00301-2021.
11 Stevens DP, Marshall BC. A decade of healthcare improvement in cystic fibrosis: lessons for other chronic diseases. *BMJ Qual Saf* 2014; 23: Suppl. 1, i1–i2.
12 Schrijvers G, van Hoorn A, Huiskes N. The care pathway: concepts and theories: an introduction. *Int J Integr Care* 2012; 12: e192.
13 Bertrand D P, Nowak E, Dehillotte C, *et al.* Quality of care in cystic fibrosis: assessment protocol of the French QIP PHARE-M. *Orphanet J Rare Dis* 2018; 13: Suppl. 1, 10.
14 Noone PG, Leigh MW, Sannuti A, *et al.* Primary ciliary dyskinesia: diagnostic and phenotypic features. *Am J Respir Crit Care Med* 2004; 169: 459–467.
15 Shapiro AJ, Zariwala MA, Ferkol T, *et al.* Diagnosis, monitoring, and treatment of primary ciliary dyskinesia: PCD foundation consensus recommendations based on state of the art review. *Pediatr Pulmonol* 2016; 51: 115–132.