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Early View

Research letter

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Impact of a Rare Respiratory Diseases Reference Centre Set-up on Primary Ciliary Dyskinesia Care Pathway

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Take home" message: 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.

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Rare diseases have such a low prevalence that a 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 improve the prognosis of CF[2]. In the light of this success, rare respiratory diseases reference centres (CRMR: "centre de Références des Maladies Respiratoires Rares" in French) were created from 2007 under the framework of the national plan for rare diseases. The ENT, pneumology and paediatrics departments at our centre 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.

Methods

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's 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 have been reconstructed using a unique anonymised patient identifier[6]. The hospitalisation database has been 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 *vs.* 2017-2019 and compared using one-sided Wilcoxon rank test[7]. Differences were considered significant when P values < 0.05.

Forced Expiratory Volume in one second (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 acknowledge for respiratory function, according to European Respiratory Society/American Thoracic Society (ERS/ATS) recommendations[8]. Respiratory trajectories were assessed by longitudinal FEV_1 measurements for patients with at least two PFTs. Random effects models were used to estimate the rate of decline of FEV_1 over the period 2015-2016 *vs.* 2017-2019.

Results

Characteristics of PCD Patients

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 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 9 patients with only pulmonologist visits, 2 with only ENT visits and 5 without a pulmonologist or ENT visit. The sex ratio was 49.6 % (0.96:1). The mean (SD) age at 1st visit was 21.5 (17.8), whereas 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)/ years with 80 % living in the CHIC area.

Impact of the CRMR establishment on the PCD Care pathway

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/year ($p<0.001$) but not for adults ($p = 0.596$). Meanwhile, ED admissions decreased for children from 0.6 to 0.2 admissions/ year; $p = 0.033$. ENT follow-up was similar for both children and adults with 1.89 visits/year in adults *vs.* 1.79/year in children ($p=0.874$) and remained stable following the CRMR creation (1.86/year in adults and 1.81 in children, $p=0.858$). After the creation of this specialised centre, the median number of PFT/ 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 Value *vs.* 73 (19) %Pred Value; $p=0.292$). FEV_1 was analysed for patients with at least 2 PFT over 2015-2019 (n=55) including 16 children (29%) and 39 adults (71%). Between 2015 and 2016, FEV_1 decreased by 3.1 (CI= [-6.1, -0.1]) %/year ($p= 0.046$) while it decreased by 0.9 (CI= [-2.2, 0.5]) %/year between 2017 and 2019 ($p=0.193$) (Figure 1C).

Discussion

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 centres 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 low 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 adequation with French recommendations which may explained this stability. In Creteil, ENT, adult and paediatric pulmonologist are not located in the same building, but there is the project of bringing together the different specialists within a single building which will likely improve organisation of day hospital and patients 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 diseases centre may significantly improve the care pathway, health, and quality of life for PCD patients.

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Figures

Figure 1

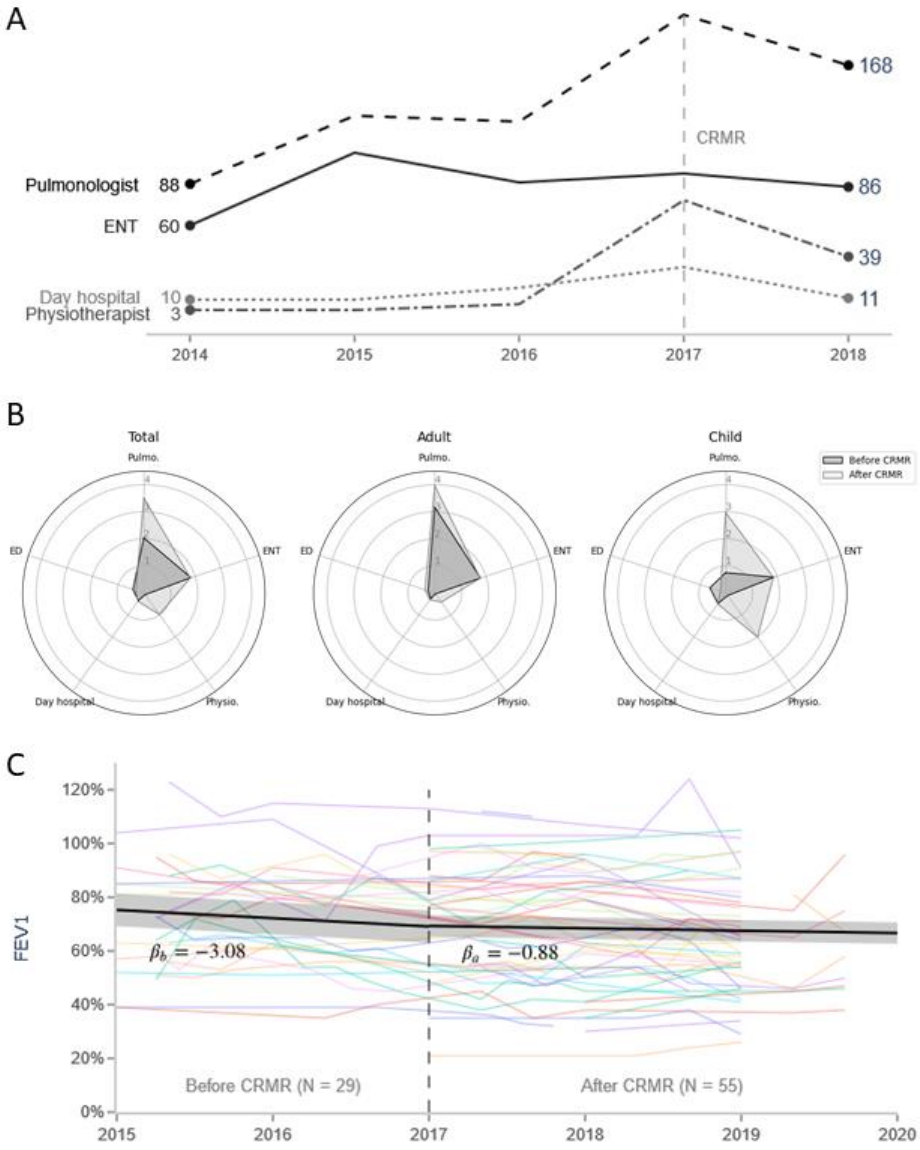

Figure 1A: **Evolution of the number of visits of PCD patients treated in Creteil Centre:** The vertical dotted line indicates the creation of the centre for rare respiratory diseases in 2017. CRMR: centre for rare respiratory diseases.

Figure 1B: **Comparison of the number of visits per year of PCD before and after the CRMR labelling.** 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". CRMR: Reference Centre for Rare Respiratory diseases; ED: emergency department.

Figure 1C: **Estimated rate of decline of FEV1 (%)** PCD subjects **before and after CRMR labelling:** Rate of decline of FEV1 percent predicted estimated by random effects models over 2015-2016 (among 29 patients) and over 2017-2019 (among 55 patients). The shaded areas represent the confidence intervals of each estimate. CRMR: Reference Centre for Rare Respiratory diseases; FEV1: forced expiratory volume in one second.