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A Pulmonary Fibrosis Research Contact Registry

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Abstract

Background: Pulmonary fibrosis (PF) is a chronic, progressive disease that causes dyspnea-induced limitations in physical activity and impaired quality of life. PF has several etiologies that can be used to generate subgroups under the PF umbrella. One of the largest subgroups is composed of patients with idiopathic pulmonary fibrosis (IPF)-a specific diagnosis rendered when a particular pattern of scarring is identified on high-resolution computed tomography images or in surgical lung biopsy specimens. The majority of PF research has focused on patients with IPF, and drug trials enroll only select IPF patients who meet certain inclusion criteria.

Objective: To describe a PF contact registry designed as a recruitment tool for interested investigators to use in prospective research.

Methods: In our patient-centered research program, the P3F or Participation Program for Pulmonary Fibrosis, we have designed a secure, nationwide registry to store contact information of PF patients and their informal caregivers who wish to be made aware of research studies for which they may qualify.

Results: In the first four months, 102 people have enrolled in the registry. The majority are patients with PF, but 12 informal caregivers have registered as well.

Conclusions: Our registry holds a database of contact information for PF patients and their caregivers who wish to participate in research. It serves as an excellent recruitment tool for prospective studies, and we invite other investigators to contact us if they would like to take advantage of this resource.

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease; HRCT: High-resolution Computed Tomography; IC: Informal Caregiver; IPF: Idiopathic Pulmonary Fibrosis; P3F: Participation Program for Pulmonary Fibrosis; P4F: Patient Participation Program for Pulmonary Fibrosis; PCORI: Patient Centered Outcomes Research Institute; PF: Pulmonary Fibrosis

Introduction

Pulmonary fibrosis (PF) refers to a condition in which the lung parenchyma is diffusely scarred. This scarring leaves the lungs stiff and malfunctioning, restricted from filling to capacity and unable to transfer normal amounts of oxygen into the bloodstream. There are a number of known causes of PF, including connective tissue diseases (e.g., rheumatoid arthritis) and environmental or occupational exposures (e.g., asbestos); however, most commonly, the cause of PF is unknown. And, among all PF cases whose causes are unknown, the most common entity is idiopathic pulmonary fibrosis (IPF), a specific diagnosis, rendered only when a particular pattern of scarring is identified on high-resolution computed tomography (HRCT) images or in surgical lung biopsy specimens [1].

In 2014, PF, regardless of its cause, is not curable, and universally reliably effective therapeutic agents are lacking. Over the last ten years, amazing progress has been made in deciphering the pathogenesis of PF and thus pinpointing a number of promising targets at which to take aim with novel therapies. The enthusiasm that these discoveries have conjured is tempered somewhat by the vexing observation that the incidence of PF (at least in the U.S.) appears to be on the rise [2,3].

Whatever its cause, PF is a potentially life-shortening and, inarguably, a life-altering condition, insinuating itself into patients' lives with activity-limiting shortness of breath, nagging cough and relentless fatigue [4,5]. Most patients with PF will need supplemental oxygen at some point in the course of their disease. It is not surprising that quality of life among patients with PF is poor compared with people in the general population [6,7]. Despite the practice of prescribing supplemental oxygen for many patients with PF, very little is known about whether and how supplemental oxygen benefits them [8]; justification lies in scientific rationale and extension of limited and often surprisingly conflicting data from the Chronic Obstructive Pulmonary Disease (COPD) literature. Clearly, this is a topic ripe for additional research.

Our team-the P_3F or Participation Program for Pulmonary Fibrosis (www.pulmonaryfibrosisresearch.org)-was recently awarded funding from PCORI (the Patient-Centered Outcomes Research Institute) to take aim at this issue. In an effort to capture potential subjects, we have created and maintain a secure contact registry of PF patients and informal caregivers (ICs) of PF patients who are willing to be contacted about our-and other investigators'-research opportunities. Here, we describe the registry and the first 102 enrollees.

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Methods

Approval for the P3F Contact Registry was granted by the National Jewish Health Institutional Review Board (HS#2789), and it is registered on ClinicalTrials.gov (NCT01935726).

Any English literate PF patient (or IC of a PF patient) over the age of 18 may enroll. Consent and enrollment forms can be obtained, completed and submitted by enrollees in any of three ways: 1) Complete the forms (in PDF or HTML format) and submit online 8 at

https://dccweb.njhealth.org/sec/P3F_Swigris/Forms/PF_Registry_PDF_Sept_2013.pdf or

https://dccweb.njhealth.org/sec/P3F_Swigris/Forms/PF_Registry_HTML_Sept_2013.html respectively;

2) Download a PDF file of the forms at

https://dccweb.njhealth.org/sec/P3F_Swigris/Forms/PF_Registry_Paper_Sept_2013.pdf and mail the completed forms to the P3F Coordinating Center; or

3) Call or e-mail the P3F (contact information at www.pulmonaryfibrosisresearch.org) and request to have a hardcopy of the forms mailed to them in a packet that includes a pre-paid/-addressed envelope for returning the completed forms.

The enrollment form asks for the following information (all self-report): demographic data, contact information, data on when and how the PF diagnosis was made, supplemental oxygen use, and whether the enrollee authorizes the P3F to contact them about future research studies for which they may qualify. Registrants must sign the form either electronically or by hand to have their data stored in the Registry database; without a signature, the form is not processed. Other than the signature field, any question on the form may be left blank. Forms submitted electronically, including HTML and PDF formats, are processed by Cardiff TeleForm™ Verification software with human verification. Those submitted in paper format are entered into the database manually by qualified P3F staff. The fidelity of submitted information is not checked (e.g., we do not collect data to confirm diagnosis or clinical status). The database is HIPPA-compliant and housed on a secure server managed by the Data Coordinating.

Center (DCC) at National Jewish Health. We have funding to maintain the registry for three years but anticipate it will long outlive our funding. We have developed a protocol to allow other investigators access to group-level, de-identified data from the registry upon request. In addition, we have devised procedures to make registrants aware of other investigators' studies after protocols for those studies have been vetted by the P3F review board. Once registrants are informed of such studies, they are free to contact these other investigators to learn more about their studies and to enroll if they so desire; the investigators would need to confirm the PF diagnosis themselves if they require greater robustness than self-report. For this manuscript, summary statistics for the first 102 enrollees were generated and tabulated. Student's t test was used to test for significant differences between continuous variables. We considered $p<0.05$ to represent statistical significance. All statistics were run using SAS, version 9.3 (SAS Institute, Inc.; Cary, NC).

Results

Twenty-three registrants mailed in hard copy consent/enrollment forms; the other 79 enrolled online. Among the 90 patient registrants, 22 mailed in hard copy forms, and 68 enrolled online. Patients who mailed in their forms were older than patients who enrolled online (68.6 ± 9.0 vs. 64.4 ± 8.4 years, t=2.05, p=0.04).

Characteristics of the 102 enrollees in the P3F contact registry are displayed in Table 1. Eighty-six patient enrollees gave their state of residence: they hail from 30 different states; 10 are from California, and six are from each of Colorado, Texas, Virginia and Washington. Among the 85 patients who gave their year of diagnosis, 67 were diagnosed in 2009 or later. The majority of patient enrollees report their PF as being idiopathic in etiology. Six of the IC enrollees are men and six are women.

Discussion

As part of our PCORI-funded project previously named P4F and recently re-titled P3F (The Participation Program for Pulmonary Fibrosis), we have developed and implemented a nationwide, (predominantly) online PF contact registry. The chief purpose of the registry is to serve as a recruitment vehicle for our prospective research; however, we invite other investigators to use it as well.

The P3F team includes physicians, support group leaders, patient advocacy group representatives and-consistent with PCORI's mission to include patients in all aspects of patient-centered research-patients with PF. Our patient informants were integral in shaping our research program; specifically, in identifying questions important to patients with PF and in helping to shape an investigational approach to answer these questions, including fine-tuning the registry and a currently

Caregivers	N=12
	8 Spouse/partner
	1 Child
	1 Parent
	1 Sibling
	1 Other
Patients	N=90
Female	39 (43%)
Age, years	65.4±8.7
Ethnicity	41 Not Hispanic
	1 Hispanic
	1 Refused
	1 Unknown
	46 Did not respond
Race	1 American Indian/Native Alaskan
	1 Asian
	5 Black or African American
	1 More than one race
	82 White
Years since dx*	4.0 (IQR=2.0-5.0, range=0.3-21.0)
Had surgical lung biopsy	48 (53%)
	7 Connective tissue disease
	1 Drug-related
	3 Familial
	4 Hypersensitivity pneumonitis
	69 Idiopathic
	6 Other or unknown
Uses supplemental O2	55 (62%)
	32 Continuous
*85 responded	

Table 1: First 102 enrollees in P3F contact registry.

enrolling study of the effects of supplemental oxygen on a range of outcomes important to PF patients.

There are a host of different types of registries, including population-based registries, genetic registries and rare disease registries [9,10]. The Pulmonary Fibrosis Foundation, the largest and most widely-recognized PF patient advocacy group in the U.S. recently announced the development of a PF registry (http://www.pulmonaryfibrosis.org/patientregistry, accessed Feb 18, 2014), designed to capture massive amounts of data from centers across the U.S. on PF epidemiology, as well as how patients with PF are diagnosed, treated and followed longitudinally; Pennsylvania has a state registry for IPF patients; in Canada, IPF patients who are prescribed the drug pirfenidone are given the opportunity to participate in a longitudinal registry; Germany has established a large IPF registry called INSIGHTS; and there are others.

A contact registry serves purposes different from these. We elected to create the contact registry because we believe it gave us the opportunity to reach out to the greatest number of PF patients and ICs across the USA. All too-often, patient-centered research requires participants to be seen at a research facility. For a condition like PF, the requirements for research participation can be even more restrictive and/or burdensome for patients: in this field, the majority of clinical research is focused on the specific disease idiopathic pulmonary fibrosis (or IPF) a condition confidently diagnosed only after expert multidisciplinary input, [1] and thus studies are conducted predominantly out of centers of excellence where such experts are found. If IPF patients wish to participate in such research, travel to one of these centers is usually required. Patients unwilling or unable to travel are thus excluded.

Equally frustrating for patients with PF of known cause (i.e., PF that does not meet diagnostic criteria for IPF) is the inclusion criterion, for nearly every drug trial, of a diagnosis of IPF and, due to other entry criteria, often a relatively narrow slice of the spectrum of IPF severity. Given the complexities of PF, the challenges in making confident diagnoses, and the potential for longitudinal disease behavior to differ substantially between IPF and non-IPF pulmonary fibrosis, these inclusion practices are understandable; however, they leave most non-IPF patients (and certain IPF patients) who are willing to participate in research without the option to do so.

We want to include a broad spectrum of people in our research: patients with PF of any cause (not just IPF) as well as their ICs. Based on work by our group and others, it is clear that ICs of PF patients are profoundly affected by living with a loved one with this disease. More research is needed to help ICs overcome the struggles they confront in caring for their patient-loved-ones, while they attempt to also maintain their own identities [11-13]. Thus, we believed it was important to include ICs as well as patients in our contact registry.

There are limitations to our registry. To date, the majority of registrants are patients; only 12 ICs have enrolled. This may be due to the culture of research in the U.S.: understandably, most research is directed at improving the lives of patients afflicted with disease, even though ICs can be profoundly affected by living through a loved-one's illness [14-16]. Indeed, in previous work from our group, we heard how ICs were forced to live in a "smaller world" because of their loved ones' PF. Although even in its infancy our registry includes patients from 30 states, the online format could be limiting our ability to reach PF patients and their ICs who are not connected to the Internet for whatever reason (e.g., no home computer, limited computer skills, etc.). However, the majority of our effective advertising has been through web-based outlets (our website, patient advocacy group websites and online patient and IC support groups, Facebook and Twitter), and the majority of registrants have enrolled directly through the online portal. Not surprisingly, to date, online enrollees are significantly younger than mail-in enrollees, suggesting that older patients and ICs may not have access to or be as proficient at using the Internet, or may (despite the security of the registry) have some trepidation about providing identifying information over the Internet.

Conclusions

What makes the P3F registry unique is its inextricable link to our website, which offers PF patients, ICs and providers a wealth of disease-related information that is at once trustworthy and patient-friendly, yet detailed enough to be useful to practitioners caring for PF patients. It also provides PF patients and ICs a safe online environment, where experiences are shared and practical, patient-to-patient information is exchanged. The registry, itself, is special, because it is inclusive: any patient with PF regardless of cause is welcome to enroll; ICs are also encouraged to enroll, so they can be contacted about planned future projects; enrollment is simple and can be accomplished by any one of several means; and it offers other PF researchers a database of potential subjects for their projects. We are acutely aware that many patients do not have access to a PF center of excellence and are uninformed about advances in the PF field and research opportunities. The P3F affords many of them the first opportunity to actively participate in their medical care by receiving immediate and accurate disease-related information, and the contact registry allows them the chance to play a role in elevating the PF field to a new level of understanding by participating in important research investigations.

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