OPINION

The COPD control panel: towards personalised medicine in COPD

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ABSTRACT

Background Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease whose assessment and management have traditionally been based on the severity of airflow limitation (forced expiratory volume in 1 s (FEV1)). Yet, it is now clear that FEV1 alone cannot describe the complexity of the disease. In fact, the recently released Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2011 revision has proposed a new combined assessment method using three variables (symptoms, airflow limitation and exacerbations). Methods Here, we go one step further and propose that in the near future physicians will need a ‘control panel’ for the assessment and optimal management of individual patients with complex diseases, including COPD, that provides a path towards personalised medicine. Results We propose that such a ‘COPD control panel’ should include at least three different domains of the disease: severity, activity and impact. Each of these domains presents information on different ‘elements’ of the disease with potential prognostic value and/or with specific therapeutic requirements. All this information can be easily incorporated into an ‘app’ for daily use in clinical practice. Conclusion We recognise that this preliminary proposal needs debate, validation and evolution (eg, including ‘omics’ and molecular imaging information in the future), but we hope that it may stimulate debate and research in the field.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease with pulmonary and extrapulmonary manifestations.1 Until very recently its diagnosis and assessment was based on the presence and severity of chronic airflow limitation (forced expiratory volume in 1 s (FEV1)).2 Yet, the relationship between FEV1 and clinically relevant domains of the disease, such as symptoms, exercise capacity, frequency of exacerbations or the presence of comorbidity, is poor or non-existent.1 Importantly, each of these domains is clinically relevant because they can influence outcomes, such as prognosis, significantly and independently3 and may deserve specific therapeutic interventions. Hence, proper clinical assessment of patients with COPD must include domains other than FEV1.4 The recently released Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy recognises these limitations and proposes to combine FEV1, the level of symptoms and the past history of exacerbations to assess and manage patients with COPD more comprehensively.5 This is an important step forward but it should not be viewed as the final one because it is largely based on expert opinion, and therefore, likely to be modified by future research.

Here, we hypothesise that the future assessment and management of patients with COPD will have to consider other domains of the disease to properly capture its complexity and to provide the best possible care to individual patients, hence moving the field towards personalised medicine in COPD. To do so, we propose that a ‘COPD control panel’ will have to be designed and validated. In this paper, we present the theoretical basis of this approach; propose an initial version of such a ‘control panel’ that considers three domains of the disease (severity, activity and impact of the disease); and explore its potential application in two hypothetical individual patients.

COPD AS A COMPLEX SYSTEM

A complex system is a collection of linked individual elements with so-called emerging properties that cannot be attributed to each element considered separately.6,7 A plane (figure 1A) is a complex system since it is formed by numerous linked elements (engines, wings, fuselage, tires, others) and has one emerging property: flying. Yet, none of the individual elements of a plane can fly it on its own. Life, health and disease are emerging properties of an extremely complex system: the human body. In this context, the emerging discipline of systems/network medicine states that diseases should be viewed (diagnosed and treated) as the consequence of one or more biological networks in the relevant organ that become disease perturbed through genetic and/or environmental pathogenic changes.8,9

To fly the plane safely, pilots need a ‘control panel’ (figure 1B) that allows them to visualise the status of the relevant elements of the plane (instruments) and the environmental conditions that surround it to make the appropriate decisions. We propose that, similarly to pilots, doctors caring for patients with COPD (and likely other complex diseases)8 should have a ‘COPD control panel’ that allows them to visualise the status of the relevant domains of the disease (and the environment) to make the appropriate therapeutic decisions. This is exactly what a good clinician does: to integrate information coming from diverse sources (clinical, biological, radiological, etc) to make a proper diagnosis and determine the best therapy in each patient. Thus, medicine has been ‘personalised’ since its very beginnings. The challenge today is...
that the volume and complexity of information that the clinician
has to integrate has increased in proportion to the complexity
of the disease and will increase exponentially in the future as a
result of high throughput technologies that will provide data on
proteomics, metabolomics and genomics, and others such as
molecular imaging. Thus a ‘COPD control panel’ is likely to be
important in the individualised management of this and other
complex diseases.

THE COPD CONTROL PANEL: A THREE-DOMAIN PROPOSAL
We propose that a COPD control panel could be constructed
using three disease domains (severity, activity and impact). Each
of these domains contains information on a number of elements
of the system (COPD) that provide complementary and relevant
information for the proper management of the individual
patient, either because of its prognostic implications and/or
requirement for specific therapeutic intervention (figure 2).

The severity of a given disease (including COPD) is inversely
proportional to the functional reserve left in the target organ.10
In COPD, FEV1 is a good estimate of that functional reserve,
although other physiological measurements such as the inspira-
tory to total lung capacity ratio (IC/TLC),11 arterial blood
gases5 and exercise capacity11 provide complementary informa-
tion that also reflect the severity of COPD, and importantly,
may require specific therapeutic interventions (bronchodilator
treatment/lung volume reduction surgery, oxygen therapy or
rehabilitation, respectively). Hence, we propose that the ‘sever-
ity’ module of the COPD control panel includes information on
FEV1, IC/TLC, arterial oxygenation and exercise capacity. We
also propose to include the number and severity of the
comorbidities because of their well known prognostic impact
and need for specific therapy.5 The Charlson index12 may be a
good indicator of comorbidities to be included in the severity
domain, but individual comorbidities present in COPD (cardio-
vascular disease, metabolic syndrome, and depression, etc)
would be an alternative.13

The activity of a disease reflects the intensity of the biological
mechanisms that cause it.10 14 The concept of ‘activity of
COPD’ has been ignored until now.15 Importantly activity and
severity do not always run in parallel. For instance, activity may
be high in the early stages of COPD but severity is mild. By con-
trast, advanced disease may be severe but may have low disease
activity due to the spontaneous and/or therapeutically induced
downregulation of the biological mechanisms that caused it.
The most appropriate marker of activity in COPD is an unre-
solved issue15 but several clinical and biological candidates may
be considered. Among the former, the rate of decline of FEV1 is
an obvious one since recent research has shown that the rate of

Figure 1  A plane (A) is a complex
system and flying is an emerging
property of the system. To fly the
plane, the pilot in the cockpit (B) uses
a control panel formed by different
modules that inform them of the
functioning of the system and the
environment.

Figure 2  Proposal for a chronic obstructive pulmonary disease control panel. For further explanation, see text. 6MWD, 6 min walk distance; CAT,
Chronic Obstructive Pulmonary Disease Assessment Test; FEV1, forced expiratory volume in 1 s; IC/TLC, inspiratory to total lung capacity ratio;
mMRC, modified Medical Research Council Dyspnea Scale; PaO2, arterial oxygen pressure.
change in FEV1 among patients with COPD is highly vari-
able.16–18 Given that smoking is the major pathogenic me-
chanism in the development of COPD, continued smoking may also be
considered a marker of disease activity. Another potential
clinical marker of disease activity may be the frequency of
smoking.20 Hence we propose that the activity domain of the COPD
control panel includes information on smoking status, FEV1
decline, annual rate of exacerbation, BMI and selected systemic
biomarkers.

The impact of any disease depends on how the patient per-
ceives the disease and modifies his/her activities of daily living.
This perception is likely to vary substantially between indi-
viduals, as it is well established in asthma.23 In COPD, we have
traditionally assumed that mild disease (as assessed by FEV1) has
a minor impact on the patient, whereas the impact is much
greater in severe disease. Yet, instruments that measure such an
impact, like the St George’s Respiratory Questionnaire24 and
the COPD Assessment Test (CAT),25 have shown that the rela-
tionship between FEV1 and health status is poor and individual
variability is enormous.1 In fact, as discussed above, the new
GOLD 2011 recommendations recognise this variability and
propose to determine the level of symptoms as a key component
of the assessment of these patients.5 Similar arguments can be
applied to other domains of the disease, such as exacerbations,26
since a number of patients suffer ‘unreported exacerbations’ and
lung function is severely impaired in a subgroup of patients who
had never required hospitalisation because of exacer-
batation.27 These observations suggest that, as described in
asthma,23 28 there may be poor symptom perceptions among
patients with COPD. Finally, it is of note that daily activities are
impaired in some, but not all, patients with COPD,29 and that
objectively measured physical activity is the strongest predictor
of all-cause mortality in patients with COPD.30 Hence, we
propose that the impact domain of the COPD control panel
includes some symptom measures (modified Medical Research
Council Dyspnea Scale (mMRC) and/or CAT) as well as the
level of daily activity.

In summary, we propose that such a ‘COPD control panel’
provides a way to visualise the complexity of COPD, and that
the combined assessment of the severity, impact and activity can
best inform the physician on the most appropriate management
strategies for an individual patient.5 Yet, we acknowledge that
our proposal has limitations. For instance, the type of measures
included in each domain needs to be discussed and validated,
and how to link this type of holistic information to specific
therapeutic interventions needs to be determined.

TOWARDS PERSONALISED MEDICINE IN COPD
The practice of medicine was originally based largely on per-
sonal experience. It was only in the late 1980s when evidence-
based medicine (EBM) was introduced.31 EBM has facilitated
the development and refinement of clinical practice guidelines32
but has well recognised limitations. The clearest one is that ran-
domised clinical trials, the cornerstone of EBM, study a subset
of the whole population of patients, and as a result, a significant
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degree of extrapolation is needed. Besides, they do not take into
account the individual phenotypic variation that occurs inevi-
tably in any disease. Thus only recommendations for the general
population of patients can be formulated. As a result of these
limitations, there is increasing interest in studying well identified
subgroups, so-called ‘clinical phenotypes’ of patients who are
associated with different outcomes and/or deserve specific therapeu-
tic interventions.33 This is not yet ‘personalised’ medicine
(perhaps ‘stratified’ medicine), but it is clearly a step forward in this
direction.14 In this setting, two hypothetical patients may
illustrate the potential practical use of the COPD control panel.

Patient A has mild disease (GOLD grade II, no hyperinflation,
normal arterial oxygen pressure, normal exercise tolerance and
no comorbidities), low impact (normal mMRC and CAT scores,
normal daily activity) but a high level of disease activity (current
smoker, increased FEV1 decline with two exacerbations over the
past 8 months plus raised levels of a potential biomarker of
disease activity). Despite the ‘mild’ clinical presentation, the evi-
dence of increased disease activity may indicate the need for a
therapeutic intervention (anti-inflammatory therapy?) that pre-
vents future progression of the disease. By contrast, patient B is
characterised by severe disease (FEV1<50% predicted, hyperin-
flation, low exercise capacity, comorbidities (cardiovascular
disease and obesity)) and high impact (high mMRC, low CAT,
house bound). Yet, there is little evidence of disease activity
(ex-smoker, constant FEV1, no frequent exacerbations, stable
BMI and normal levels of potential biomarker(s) of disease
activity). In this case, the physician may need to optimise bron-
chodilator treatment, treat comorbidities, and provide rehabilita-
ition but may question the need for anti-inflammatory therapy.

CONCLUSIONS
We propose an integrated way to address the complexity of
COPD: the ‘COPD control panel’. This proposal should be con-
sidered the starting point of a debate that we hope, might result
in better clinical care of patients with COPD. We predict that, in
the near future, the availability of quick and cheap ‘omic’ anal-
yses will add to the ‘control panel’, and that new user-friendly
bioinformatic technologies (so-called clinical decision support
systems, which will be easily downloadable as ‘apps’) will allow
the clinician to integrate this vast amount of information for the
benefit of a single patient, hence fulfilling the goal of ‘persona-
lised’ medicine in COPD.

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