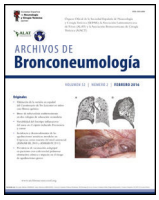
Arch Bronconeumol. 2016;52(9):455–456

Sociedad Española de Neumología y Cirugía Torácica SEPAR

ARCHIVOS DE Bronconeumología

www.archbronconeumol.org



Editorial

Precision Medicine: A Modern Odyssey☆

Medicina de precisión: un viaje a Ítaca

Gerard Torres,[a,b] Manuel Sánchez-de-la-Torre,[a,b] Ferran Barbé[a,b,*]

[a] Servicio de Neumología, Hospital Universitari Arnau de Vilanova y Santa Maria, IRBLleida, Lleida, Spain
[b] Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Madrid, Spain

Precision medicine is defined as prevention or applied treatment, tailored to each patient's individual needs, as determined by the genetic profile, biomarkers, phenotype or psychosocial characteristics that distinguish some patients from others, despite a similar clinical presentation.[1] This concept introduces new dimensions into the diagnosis and treatment of disease. On the one hand, new, more complex diagnostic classifications will be required, based on the factors that differentiate patient subgroups among a population with a specific disease. On the other, new personalized treatments will be developed that are applicable only to certain subgroups within a population presenting the same disease. These new treatments will be more specific, more effective, and less toxic. Thus, treatments will not be administered to patients who will not respond to them, generating significant savings in healthcare costs. In respiratory medicine, we can already cite examples of personalized medicine applied to lung cancer, infections, and more recently, sleep apnea. In the case of cancer, the determination of genetic markers in patients has transformed standard histological classification, permitting the identification of specific subgroups of patients who will respond to certain treatments. We know now, for example, that subjects with non-small cell carcinomas who have the Echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase (EML4-ALK) fusion gene respond well to crizotinib.[2] In respiratory infections, the recently described role of immunologically integrated microorganisms in our respiratory tract, known as the microbiome, has acquired significance in patients who develop exacerbations in chronic respiratory diseases. In chronic obstructive pulmonary disease and other diseases such as cystic fibrosis (CF), the composition of the microbiome varies depending on disease progression and modulates the virulence of the pathogens involved in exacerbations. Thus, if the host microbiome is characterized, the severity of the disease can be better defined and new, more personalized approaches can be designed for the treatment of exacerbations. This will reduce the risk of side effects.[3] Furthermore, the use of genetic and epigenetic analytical tools has improved characterization of patients and their response to treatment. For example, in patients with sleep apnea–hypopnea syndrome (SAHS), the effect of CPAP on blood pressure can be predicted by analyzing microRNA (HIPARCO score).[4] The use of the HIPARCO score, then, may optimize the indication of CPAP, reducing the adverse effects derived from the use of ineffective drugs or from CPAP itself, in addition to reducing costs.

These changes in medicine are being driven by our expanding knowledge of genetics, epigenetics, and the identification of biomarkers in most diseases, along with the technological capacity for analyzing large amounts of data. Thanks to these technological advances, registries and clinical and biological databases have been developed, allowing the analysis of large numbers of patients (big data). This will lead to the identification of patient clusters with common, but still unknown, characteristics in terms of prognosis or therapeutic sensitivity. These advances will also require healthcare personnel to embrace radical changes, and these approaches must be implemented in both undergraduate and postgraduate training, to give medical professionals the skills they need to manage diseases from the new perspective of precision medicine.

Precision medicine, by improving prognostic and therapeutic efficacy, is beneficial for patients, administrative staff and healthcare personnel. However, this enthusiastic vision of precision medicine as a ground-breaking innovation must be tempered and contrasted with a series of questions.[5] To date, attempts to predict the risk of disease based on genetic characteristics have produced very modest results, with very limited applications. Drugs that have been developed on the basis of gene targets are very often applicable only to a small proportion of the affected patients, and as such do not provide any improved overall prognosis among individuals with that disease. This is the case, for example, with lumacaftor and ivacaftor in the treatment of CF, which benefit only a very small number of patients with specific mutations.[6] Moreover, the reduced size of these target populations increases the cost of drug development. Situations have also been documented in which the use of genetic testing to guide treatment has not improved efficacy or safety.[7] Finally, problems arise as evidence of the heterogeneity and poor quality of the information stored in databases and registries come to light.

All diagnostic or therapeutic innovations have to be backed up by studies supporting their benefits in the overall prognosis or clinical course of patients, that is to say, reduced morbidity and/or mortality. Standards must be equally high when

☆ Please cite this article as: Torres G, Sánchez-de-la-Torre M, Barbé F. Medicina de precisión: un viaje a Ítaca. Arch Bronconeumol. 2016;52:455–456.

* Corresponding author.
E-mail address: febarbe.lleida.ics@gencat.cat (F. Barbé).

introducing strategies based on precision medicine, since all healthcare systems must implement innovations on the basis of these criteria and on considerations of cost-effectiveness. Evaluation of precision medicine from a pragmatic viewpoint of scientific rigor and social interest presents a considerable methodological challenge. How can benefits demonstrated in a single subject (trials with *N*=1) be extrapolated to a certain population? Is it useful to establish associations based on analyses of large databases (with no previous hypothesis)? These questions remain unanswered. Some authors have suggested that precision medicine targeted at prevention, rather than treatment, may be more realistic, generalizable, and cost-effective.[8] In conclusion, on the road leading to the introduction of precision medicine we will have to categorize patients according to factors that go beyond our current perception of disease, to acquire skills in new areas and learn new concepts, to assimilate hitherto unimaginable associations and interactions, and to develop new analytical methodologies. Only at the end of the odyssey will we realize the importance of the journey.

References

1. Jameson JL, Longo DL. Precision medicine-personalized, problematic and promising. N Engl J Med. 2015;372:2229–34.
2. Kwak EL, Bang YL, Camidge DR, Shaw AT, Solomon B, Maki RG, et al. Anaplasic lymphoma kinase inhibition in non small-cell lung cancer. N Engl J Med. 2010;363:1693–703.
3. Rogers GB, Wesselingh S. Precision respiratory medicine and the microbiome. Lancet Respir Med. 2015;4:73–82.
4. Sánchez-de-la-Torre M, Khalyfa A, Sánchez-de-la-Torre A, Martínez-Alonso M, Martínez-García MÁ, Barceló A, et al. Precision medicine in patients with resistant hypertension and obstructive sleep apnea: blood pressure response to continuous positive airway pressure treatment. J Am Coll Cardiol. 2015;66:1023–32.
5. Joyner MJ, Paneth N. Seven questions for personalized medicine. JAMA. 2015;314:999–1000.
6. Wainwright CE, Elborn JS, Ramsey BW, Marigowda G, Huang X, Cipolli M, et al. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del CFRT. N Engl J Med. 2015;373:220–31.
7. Stegiopoulos K, Brown DL. Genotipe-guided vs clinical dosing of warfarine and its analogues: meta-analysis of randomized controlled trials. JAMA Intern Med. 2014;174:1330–8.
8. Dzau VJ, Ginsburg GS, van Nuys K, Agus D, Goldman D. Aligning incentives to fulfil the promise of personalized medicine. Lancet. 2015;385:2118–9.