Editorial

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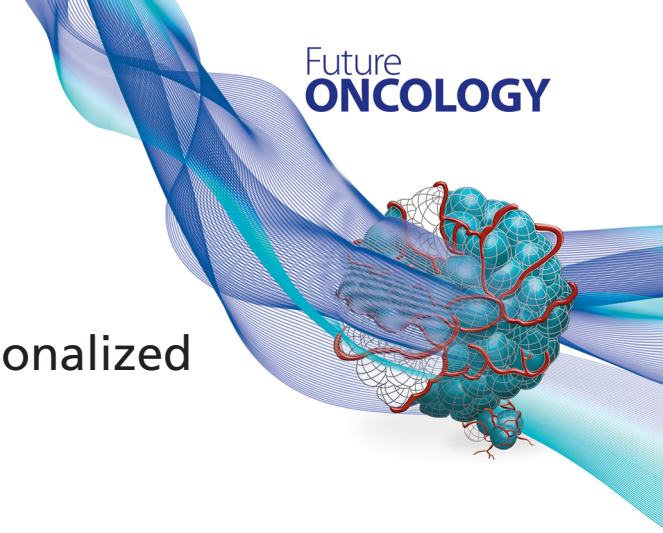

Challenges and innovations in personalized medicine care

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> "medicine is moving rapidly forward to new precision patient profiling to identify unique genetic aspects in order to break barriers for prevention, diagnosis and treatment"

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From evidence-based to precision medicine

In the last decade, we have witnessed the change of medicine: from the classic ideal of evidence-based medicine, to precision medicine, focused on a single subject with particular characteristics. As recently described by Liu and colleagues [1], application of precision medicine's modern technology, together with electronic medical record analysis, allow to achieve accurate diagnosis and treatments. The concept of precision medicine was conceived with three principal aims: to optimize and improve healthcare, discover and understand a pathologies mechanism, and obtain effective and accurate therapy [2]. This remarkable shift to patient focusing medicine was endorsed by technological and scientific improvement that has driven the explosive increase of information obtainable from a single patient's analysis.

The advances made in diagnostic and therapeutic approaches have emphasized differences among patients, such as biology, lifestyle, predisposition and environmental influences. These already known factors impact on different oncological and nononcological conditions in addition to the genetic variability of the pathology that can respond to treatments differently, although categorized as being the same histological type.

Indeed, patient classification into several subdivided groups have helped to tailor a more effective medical approach. Moreover, precision medicine that assesses patient genotype and phenotype before choosing the best options can expedite patient treatment avoiding the slow and dangerous process of trial-and-error prescribing before finding the most suitable one [3]. A striking example is the area of the mutated tumor: genetic alteration detectable by sequencing approaches can direct toward a targeted therapy and avoid multiple lines of treatment.

These innovative medical procedures have enhanced patient's survival and given a chance to subjects not responding to classic treatments, and have allowed researchers to gain a better understanding of several disease mechanisms [4]. Moreover, this conception has been applied to innovative cure (e.g., a molecular target for therapy) which has shown to increase overall survival and disease-free survival period. Clinical investigations so far have also enlightened that a tailor made approach improves quality of life [5,6]. Quality of life still misses indicators that are useful to compare worldwide; thus, an implementation of standard instruments (e.g., the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire for oncological patients) needs to be a priority in future research.

On the other hand, the rapid development of advanced technologies and the generation of large amounts of big data constantly raise the challenges to reach the short-term goal (i.e., patient treatment) and the long-term goal (i.e., discovery of disease etiology) of precision medicine [7]. Indeed, big data are characterized not only by large constant increasing volume, generated by real-time analysis but also with a variety of data obtained and its interpretation.

Precision medicine consists of more than classical medical record information: different levels of data associated with the disease are essential for analysis, starting from precise prevention to public health [8]. One of the youngest concepts of precision medicine with the greatest need of future developments is precise public health, which represents the right intervention in the population at need at the correct time [7]. Ideally, analyzing and stratifying

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disease information gathered from a large cohort of subjects could allow stratifying outcome and prognosis developing efficient tailor-made approaches to emerging risks for population. It is also necessary to consider that gathering information about different groups of individuals will generate outcome disparities in terms of social categories (e.g., nationality or ethnicity) [9]. Genetic differences between populations have been identified before, which can often raise important ethical issues in data manipulation and interpretation [10].

Patient empowerment

Analogously to the shift of precision medicine, another Copernican revolution has accursed: the patient has moved from a passive to an active role, placed in the core of the medical decision. This process started less than 20 years ago and the WHO defined it as patient empowerment, 'process through which people gain greater control over decisions and actions affecting their health'. Aspects of empowerment include self-efficacy, self-awareness, confidence, coping skills and health literacy [11].

Nowadays, the empowerment process has become the starting point of clinical medicine: the patient is fully educated about his/her own healthcare clinical condition with access to all the relevant information and treatment outcomes, and is encouraged to participate, acting as the main role in the healthcare team. This new aspect of medical interaction increases medical adherence to both treatment and clinical controls, deeply important for positive clinical outcomes [12]. Patient organizations around the world can play an educational role in improving health literacy and fostering dialogue with patients, ensuring also a dialogue with health bodies [13]. Nevertheless, patient autonomy has raised another ethical issue that needs to be addressed.

First, precision medicine generates a large amount of data with unknown medical impact. One example is genomic sequencing for the detection of useful targeted rearrangements could highlight unrelated or unknown mutations [6]. Moreover, genetic alterations that have incomplete penetrance could also be found, which creates other ethical dilemmas. This is heightened by the lack of standardization, different testing procedure and data analysis, technology immaturity or incomplete libraries that must be improved.

Second, the process of informed consent and privacy linked to electronic medical records must be considered as the base of novel medical processes. Transparency, fully informed choices, conscious of risk-benefit ratio to collateral effects and informed knowledge of medical options have become the solid foundation of healthcare practitioners-patient relationship [4]. Only if aware, the full-informed patient can have the complete ability to make choices consciously.

Ethical issues

Nowadays, we are facing the era of social diffusion of information and any material can reach a large number of people in less than a minute. Considering that digital tools are able to connect the patient and healthy subject to medical information and this phenomenon is expanding, patient empowerment by a specialist is essential and required to be discussed in a medical environment in order to block any uninformed and unsafe influence. Related to this, new emphasis has to gather on how ethics review boards or research ethics committees work, organs responsible for monitoring compliance with transparency, informed consent process and patient empowerment. Their coparticipation in innovating the medical process should also be performed by ethics education and training of healthcare professions.

It must be noted that health inequality is a reality worldwide that must be addressed. As reported by Abernethy and colleagues [14], new technologies and treatment approaches are more expensive, thus not equally translated in clinical practice in some countries (due to comparative effectiveness research, cost–effectiveness analysis and technology assessments). In order to reduce the differences, worldwide collaboration (i.e., clinical trials, translational projects and biobanks) must be encouraged allowing the same level of treatment everywhere [15].

Furthermore, imagining the long-range result (i.e., the results that will be achieved into 50 years), precision medicine could help to reduce healthcare cost, by for instance, reducing error dosing, drug reactions to unnecessary treatments and late diagnoses [16]. One of the most famous examples is the reduction of genome sequencing costs, thanks to the development of next-generation sequencing and its integration into clinical practice: from the $1 billion cost of the first draft of the human genome to the $1000 cost of nowadays sequencing comparable with other clinical test performed routinely [17].

Conclusion

All keys issue must be considered to assure translational utility of all material collected by various techniques (e.g., genomic, transcriptomic, proteomic, metabolomic, etc.) together with clinical data. The intersection of all data obtained from the different approaches, called panomics, could help to unravel pathological conditions complexity and guide patient care with clinical guidelines, potentially expediting precision medicine progress and successfulness [18,19]. Issues related to these approaches range from experimental (e.g., sample preparation and handling, study design, and reproducibility) to interpretation challenges (e.g., data analysis, false positives interpretation, results from validation and for prediction) [20].

Moreover, to promote new discoveries and improvements, it is essential that information collected in a dedicated database can be accessible worldwide to rapidly process and interpret the growing volumes of data [3]. Sharing data helps exploit the potential and push forward research supporting the shift toward patient-centered care in oncology.

In conclusion, medicine is moving rapidly forward to new precision patient profiling to identify unique genetic aspects in order to break barriers for prevention, diagnosis and treatment. The chance of a revolutionized healthcare system by personalized medicine will require a great effort by researchers, clinicians, industries, regulators and, most of all, patients [4]. The transition from a conception of reactive to a pro-active medicine, associated with the innovation and the ethical issues that is inextricably linked to it, must be considered as a primary goal in the health system and scientific community.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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