

EDITORIAL

Precision medicine and clinical relevance in older people

Precision medicine is not just about precise or accurate dosing. It is an emerging field that considers interindividual variability in genomics, demographics (age, sex), comorbidities (e.g. renal or hepatic impairment, cognitive impairment), background environment, and lifestyle in the management strategies. This approach not only allows for more accurate treatment and dose prescription, it also enables improvement in other aspects of patient management such as investigations or disease prevention in subgroups of patients (and eventually individuals) rather than the traditional one-size-fits-all approach. Therefore, it is especially relevant in older patients, where comorbidities and many individual variabilities such as age, environment, and genomics are the norm.

Geriatricians in some ways already practice some basic principles similar to precision medicine. For instance, the principle of “start low and go slow” when initiating drug therapy allows for better and safer dosing.¹ However, to be more systematic in patient management, it would be beneficial to understand how this emerging field is affecting the clinical care of older people.

Firstly, the in-depth knowledge we have with pharmacodynamics and pharmacokinetics sets a good foundation for precision medicine. The variability of age, sex, renal, and hepatic function are just some vital determinants we already know to take into account when prescribing for older people. Other factors such as environmental (e.g. various foods intake, alcohol, smoking) and drug–drug interactions are examples of basics that help refine the preciseness of prescription.

Secondly, the emerging field of liquid biopsy, using mRNA technology, has enabled more precise quantification of individual variability of hepatic cytochrome-P450 enzymes and transporters.² Similar application to the field of onco-medicine by using ctDNA has provided an alternative to tissue diagnosis and treatment.³ The mRNA technology has even been successfully used to develop mRNA vaccines in the fight against the COVID-19 pandemic.⁴ The applications, together with ever-improving treatments such as monoclonal antibodies, checkpoint inhibitors (PD-1, PD-L1, CTLA-4) are amongst the latest armamentarium geriatricians can access nowadays in managing older patients.

Thirdly, genotyping is becoming ever so widespread and affordable that it may be possible for geriatricians to test if patients may develop allergic and immune reactions that are associated with genotypes, such as HLA-related genes. Such examples include


hypersensitivities to allopurinol and carbamazepine that are HLA linked or genetic polymorphisms affecting dosages and risk of side effects caused by statins and warfarin. Genotyping will allow for polymorphisms to be tested accurately so the phenotypes such as fast or slow metabolizers or possibility of drug interactions or adverse reactions due to phenotypes can be predicted more accurately.

Finally, one of the main reasons to date why geriatric medicine still lacks preciseness is that many randomized controlled trials exclude the recruitment of older people with multiple comorbidities. Therefore, while the internal validity of the trials is good, the external validity or generalization is a problem, especially to the older age group. Hence, geriatricians often have to “guestimate” the likely efficacy and do a balancing act on harm and benefit. A more accurate means would be to include older people in the drug trials but safeguard them with individualizing the doses that they would need for treatment, using the knowledge of genotyping, liquid biopsy, as well as other traditional tools such as pharmacodynamics and pharmacokinetics. Thus, results obtained from trials can be more generalizable to our older population. This a priori (instead of a posteriori) approach would mean simulation or modeling of trial conditions required beforehand.

In conclusion, the speed of the advance in medicine is enormous and precision medicine is at hand for us to use to improve the health of older people who will benefit from this approach. Geriatricians should embrace it rather than shy away from it.

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