

Implications of genetics and major risk factors on platelet morphology, platelet aggregation and their relationship with coronary atherosclerosis

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Valorization

In this thesis we aimed to explore some crucial aspects related to platelets, that act as main actor in the atherothrombotic process, with specific regard to coronary artery disease. Our investigations have been focused to better characterize the platelet morphology and aggregation in patients referring for coronary angiography, in the search of new, user-friendly and cheap prognostic parameters for daily practice.

Given the central role of platelet in almost all the steps of atherosclerosis, from endothelial dysfunction to plaque promotion and rupture, any intervention on them has potential benefit on detrimental consequences of the disease. Considering the leading position in mortality and morbidity burden of ischemic heart disease, improvements in that field play a crucial role not only from the scientific side of knowledge advances but also could impact on life expectancy.

Laboratory values on platelets are easy to be obtained, during a routine blood test and provide a lot of information contributing to define patients' risk profile. The additional data should be interpreted according to individual features because platelet indexes should be considered as an addendum to traditional risk factors but not as a substitute. Moreover, specific measurement of platelet aggregation must be taken together with the platelet regimen that is ongoing, in order to maximize the info on platelet reactivity in the clinical management of antiplatelet therapy.

More in details, morphologic information on platelets have found related to coronary artery disease, but they do not represent independent predictor of atherosclerotic process

including its severity. Platelet volume and immature fraction remain attractive items of research even if their contribution should be still defined.

We also inquired the reactivity of platelets during dual antiplatelet therapy, the cornerstone of treatment in patients undergoing percutaneous coronary intervention. The selection of optimal antiplatelet regimen is crucial to avoid adverse events and re-intervention and to prevent harmful bleeding. Inappropriate platelet reactivity under antiplatelet treatment is related to detrimental consequences and the evaluation of adequate platelet inhibition is crucial, but contrasting results were reported into the application of platelet test- guided strategies. Therefore, the identification of the determinants of enhanced platelet aggregation may upgrade the expertise to choose the best antiplatelet drug regimen for each specific patient.

The emerging role of genetics results always more important as magnitude in contribution to regulation of atherosclerosis progression and it must be part of all further investigations: both pharmacological and non-pharmacological interventions might be favored or hampered by different patients' genetic profile.

The medicine tailored as much as possible will provide not only the best individualized treatment for every patient, but also will avoid to waste resources from several point of view, including the economic one. An increased ability to finely stratify the risk, that every patient presents, allows to schedule the appropriate treatment during the hospitalization and after the discharge. Moreover, the ability to early recognize factors that precipitate atherosclerosis may provide the opportunity to plan intervention to contrast them.

Of course, the complexity of atherosclerotic disease is a huge obstacle to achieve a comprehensive understanding of the underlying mechanisms, but all studies, even if little, might be a piece of puzzle to solve the picture.

The Constitution of the World Health Organization includes several crucial principles to guide our actions, and the first sentence is represented by the definition of health: “it is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” (**Figure 1**). The vast majority of research projects conducted so far in all fields, including the cardiovascular branch, have been focused to reduce and limit the incidence and impact of the diseases. They have been efficacious. Now we must consider in our future investigations the well-being concept, because we do not have to limit our action to reduce the disease burden, but extend it to the health of our patients, who, out of the hospital, are persons we meet every day.

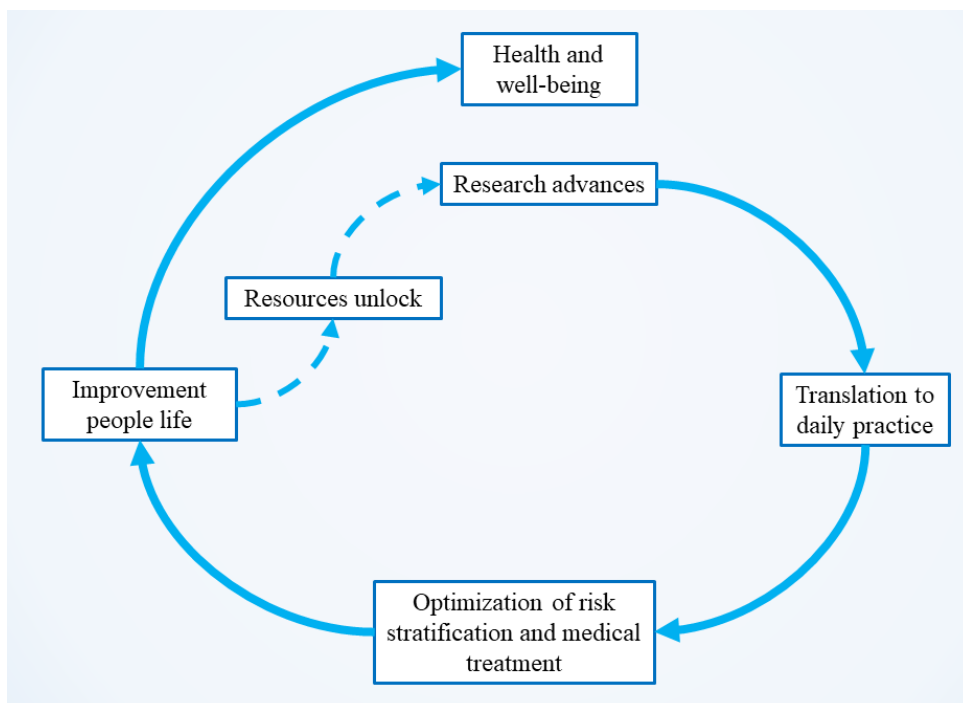


Figure 1. Vicious circle of medical research.

The findings of this thesis have been and will be shared with others in several ways. All except one chapters are published in international indexed scientific journal and are available online, the last has been submitted for publication. This thesis will be published online, to make it readable for everyone interested. Principal findings have been submitted as abstract to congress and general results of our research will be part of communication to scientific meeting.