IJCP THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

EDITORIAL

Transition

It is difficult to believe that I have been editing IJCP since the issue of Spring 1991. When my publisher (Chris Graf) did a search it appears that I have written over 150 editorials – do I qualify for the Guinness Book of Records? If not, a Guinness will do – preferably very cold. As I write this editorial, scheduled to begin 2013, interviews are being held to appoint my replacement at the end of 2013, with us working side by side during 2013 to ensure a smooth transition. So at the end of the new year, after 22 years, I will hang up my pen and metaphorically ride off into the editors' sunset.

During 2013 I will continue my monthly contribution, and thoughts of a mellowing will not automatically be realised. Of course I will look back and reflect but that is one of the few benefits of age. I remain deeply concerned about decisions that have little or no evidence to support them with the internet fanning the flames of vindictiveness. Anger is a powerfully destructive emotion – if you are right about an issue there is no need to be angry with others who adopt a different view, and if you are wrong you cannot afford to be angry. The abuse of anyone, but especially the innocent and trusting child, rightly concerns and emotionally charges us all, but let us be sure of the facts before accusing individuals. To be wrongly named as an abuser is in itself an abuse, and the damage often irreparable no matter the apology or financial settlement. Responsible journalism is the key to press freedom and sadly that has been lacking during 2012.

One of my colleagues on retirement said that the major benefit was spending the time with his grandchildren that he had neglected to do with his own children - the price of a medical career, which I assume is replicated in professions where long hours is the norm. As I have found myself, his observations are only too true. The retrospectoscope remains the "if only" view and a platform for despair, so it is important to use it positively – repair not despair.

There is more to life than work and using time constructively is an essential component of the work/life balance. So I have time this year to employ perspective and realise thoughts rather than dreams, though life without dreams would be dreadfully dull. Correctly I am not involved in the appointment of the new Editor-in-Chief, but look forward to the injection of different ideas – a painless transition which reminds us all that the concept (in this case IJCP) always is bigger than the individual.

A painless transition

Disclosures

None.

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The challenge of cardiovascular diseases in HIV-positive patients: it's time for redrawing the maps of cardiovascular risk?

Linked Comment: Kakinami *et al*. *Int J Clin Pract* 2013; 67: 6–13.

Although the combined antiretroviral therapy (cART) has improved the length and quality of life of HIV-infected patients, the survival of these patients is always decreased compared with the general population. This is the consequence of non-infectious illnesses including cardiovascular diseases. In fact, large studies have indicated an increased risk associated with a marked rise in the frequency of vasculopathy, coronary atherosclerotic disease and myocardial infarction in this population (1). Therefore, the increased incidence and the early presentation of cardiovascular complication observed make

prevention very important in HIV-positive population. In this sense, the use of cardiovascular risk stratification tools, borrowed from the experience in the general population, has been an important resource in clinical practice (2).

In the general population, cardiovascular risk scores are useful tools for estimating the probability of cardiovascular disease for individuals who have not already developed major atherosclerotic disease. Moreover, they are an aid for cardiologists and practitioners in making clinical decisions about how intensively to intervene on lifestyle and whether to use antihypertensive, lipid-lowering medication and anti-aggregant drugs. For this reason, the Framingham score was used in most studies, on HIV-positive patients also, to estimate the risk for coronary heart disease; however, it showed some limitations for detecting risk among these individuals. The problem is that the Framingham system fails to explain a part of heart disease morbidity and mortality in HIV-positive patients. In the same way, also other scores (PROCAM, SCORE) failed to predict the cardiovascular risk in HIV-positive population (3). Therefore, the cardiovascular risk assessment based on conventional risk prediction models does not offer a good predictive value for the HIV-positive population. Considering these difficulties, new methods of risk assessment have been explored. For example, utilising coronary artery calcium (CAC) score as an alternative coronary artery disease risk score and an indicator of subclinical atherosclerosis among individuals with HIV is a relatively new method (4,5). Moreover, initial studies investigate whether carotid intima-media thickness and brachial-ankle pulse wave velocity add value to the conventional risk prediction models in predicting the development of cardiovascular diseases in type HIV-positive patients with a negative history of major atherosclerotic disease.

While many cardiovascular risk scores show promise, the ideal method of assessment of cardiovascular health in HIV positive patients remains the hidden treasure

Even the currently available guidelines on the management of HIV infection reflect the present difficulty of finding ways to estimate the correct risk of cardiovascular disease. For example, the current version of the European AIDS Clinical Society (EACS) Guidelines recommends that risk assessment is performed by Framingham score; moreover, it indicates the possible use of a new risk equation developed from HIV populations, actually under evaluation (available at web site http://www.cphiv.dk/tools.aspx). The risk assessment by Framingham score is suggested: (i) in all HIV-positive men > 40 and women > 50 years without CVD, (ii) at HIV diagnosis and (iii) prior to starting cART and after with an annual follow-up frequency (6).

On the other hand, in the current version of Italian Guidelines for the use of antiretroviral drugs and the diagnostic-clinical management of people with HIV-1 infection, the assessment of overall risk of cardiovascular disease is performed using algorithms such as Framingham, PROCAM, Raynolds, SHAPE or DAD 5 year estimated risk calculator (7–9).

The reason why the tools of risk stratification tend to underestimate the cardiovascular risk is to be found in the fact that HIV-positive patients are a population in which the probability of experiencing coronary events depends not on traditional risk factors alone (10,11). Several factors may contribute to the pathogenesis of cardiovascular problems in the course of HIV infection: lifestyle, metabolic parameters, genetic predisposition, viral factors, immune activation, chronic inflammation and side effects of antiretroviral therapy. If traditional risk factors for cardiovascular diseases have a basic importance and are the same as described in general populations (smoking status, blood pressure, age, gender, race and menopausal status), also the other factors specific for HIV-positive population play a important role. For example, untreated HIV infection can increase cardiovascular risk in several ways and these effects are at least partially reversible with durable successful antiretroviral treatment: an active replication of HIV can cause proatherogenic elevations in serum lipids, increases in systemic inflammation, hypercoagulation and reductions in endovascular reactivity (12,13). On the other hand, HIV-infected patients receiving cART may experience metabolic complications (i.e. dyslipidaemia, impaired glucose metabolism and abnormal body fat distribution), potentially increasing their risk of cardiovascular disease. Moreover, the use of some specific antiretroviral drugs can impact cardiovascular risk by a direct and indirect cardiovascular toxicity linked to their action on the endothelium and platelets (11). If traditional risk factors and adverse effects of antiretroviral therapy justify much of the cardiovascular risk, remains to be considered an additional factor that that could be called the ‚occult filmmaker' of the increase in cardiovascular risk in HIV-positive population. This factor is the systemic chronic activation of the immune system: several data suggest that a low level of chronic immune activation and inflammation persists even in course of effective cART, and it seems to be associated with the accelerated ageing of multiple body systems and increased incidence of atherosclerotic cardiovascular disease (14,15). Starting from the historical works of Brenchley and Douek on mucosal immune dysfunction and resultant microbial translocation identified as a fundamental cause of chronic immune activation, many pathogenetic mechanisms have been proposed, including low-level ongoing HIV replication, chronic infections

with other viruses such as cytomegalovirus and immunosenescence (16,17). Notwithstanding the fact that many data have been acquired on this topic, its aetiology remains obscure and persistent immune activation emerges as a major challenge to the modern HIV treatment era. Moreover, cardiovascular diseases and the rapidity of progression of atherosclerosis seem linked also to concomitant chronic inflammation and excess immune activation depending on comorbidities (chronic C hepatitis, irritable bowel syndrome, autoimmune diseases) not directly associated with HIV (18,19).

Therefore, on the basis of these considerations, ideally, it seems now time to redraw the map of cardiovascular risk in the HIV-positive population. In this sense, various attempts to develop new tools are currently in progress: these predictive systems should be able to estimate the risk taking into account the distinctive factors of patients with HIV infection (20,21). However, currently, the real challenge is in finding ways to integrate the assessment of cardiovascular risk even with the influence of process of immune activation.

Despite it being clear that the cardiovascular risk scores have some significant bias in the evaluation of patients with HIV infection, at the moment, we have no alternative validated score for this special population. Pending new validated methods that do not underestimate the risk, probably currently the most reasonable choice in clinical practice is to continue using traditional risk scores associated with tests that can provide additional information on the progression of the possible cardiovascular damage in a single patient.

Disclosures

None.

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