Coronary flow reserve in dilated cardiomyopathy: an important pathophysiological tool to be considered among, but not instead of, other well-established prognostic factors

I read with great interest the article by Rigo et al. on coronary flow reserve (CFR) in patients with non-ischaeamic dilated cardiomyopathy (DC), recently published in the journal (2006;27:1319–1323), and the comments to the authors by Tona (2006;27:1884).

The study is original, well designed, and performed. Because their results are of clinical concern, further explanation needs to be provided in order to avoid potential misunderstanding.

In my opinion, and in agreement with Tona, the cut-off of 2.0 is not completely appropriate to identify normal CFR response. Recent studies and a peer review by the same Rigo et al. recommend at least 2.5 for normal CFR, whereas borderline values (2.0–2.4) should be carefully read in various clinical contests.

As noted by Tona, the value of 2 is taken on loan from patients with left anterior descending coronary artery stenosis. To date, there are no large studies that established the absolute CFR cut-off in patients with microcirculatory disease, in the lack of significant epicardial stenosis.

A couple of years ago, Canetti et al. reported an invasive CFR response to adenosine of 2.2 ± 0.5 in a group of patients with idiopathic DC and severe left ventricular (LV) systolic dysfunction, in comparison with 3.3 ± 0.8 in controls. More recently, Neishi et al. showed restricted CFR response after clinical improvement of chronic heart failure (1.5 ± 0.2 before and 2.0 ± 0.3 after optimal treatment). Their conclusions were that variables such as heart rate, basal peak and mean coronary velocity, LV preload, and/or volume overload, can affect CFR response in these patients.

In contrast, it is almost well definite that microcirculatory (microvessels and capillaries) impairment is identifiable in almost all patients with heart failure, with or without epicardial coronary stenosis. In addition, abnormal CFR response may be also due to impaired blood flow perfusion through intramyocardial arterioles, which cannot be easily assessed by echocardiography in DC. Blood flow in this compartment can be significantly rearranged by arteriolar wall thickening and narrowing, interstitial fibrosis, and/or myocardial bridges as demonstrated in patients with chronic myocardial ischaemia, hypertrophic cardiomyopathy, hypertensive heart, or myocarditis.

Therefore, it would be interesting to know how many patients in the study presented by Rigo et al. had CFR response ≥2.5, as long as the final message strongly points to treat aggressively only those with CFR ≥2.0. This may disregard some other patients with better CFR but poor prognosis anyway.

Unfortunately, conventional (and newest) risk predictors are able to discriminate only a proportion of patients at a risk for cardiac events. In daily patient management, clinicians are used to consider well-known cofactors, including C-reactive protein for myocarditis and, more recently, interventricular synchrony, to warrant the most suitable patient treatment. Actually, Rigo et al. appropriately show the univariate (but multivariate would have been better) analysis of some of these variables in Table 3. Even if not enough remarked in the final message of the article, taking into account the aforementioned cut-off limitations, we do agree with the authors that CFR is an important pathophysiological tool and should be considered among, but not instead of, several well-established risk predictors, which our decision-making is usually based on.

References

Cesare de Gregorio
Department of Medicine and Pharmacology
Cardiology and Cardiac Rehabilitation Unit
Cardiovascular Ultrasound Laboratory
University of Messina
Messina 98123
Italy
Tel/fax: +39 090 221 3531
E-mail address: cesaredegregorio@alice.it

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We thank Dr De Gregorio for the interest in our work. The cut-off value employed, 2, is a widely accepted criterion of normality as extensively discussed with review of the existing literature. Different cut-off values could have been employed and a receiver operating characteristic analysis was performed but was not considered an appropriate approach by the statistical reviewer because of the censored nature of the endpoint. The cut-off value that best related to the occurrence of spontaneous events was 1.8 and consistent with our previous reports addressing the value of prognostic power of coronary flow reserve (CFR). These observations should be put into a wider framework of test use and interpretation. In fact, the presence/absence of disease applied to diagnostic

Rosa Sicari
CNR
Institute of Clinical Physiology
Via G. Moruzzi, 1
Pisa 56124
Italy
Tel/fax: +39 050 315 2374
E-mail address: rosas@icf.cnr.it

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