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EDITORIAL COMMENT

Mitral annular function in acromegaly: Still a lot to learn

Função do anel mitral na acromegalia: muito para aprender...

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Acromegaly is a rare endocrine disorder associated with various systemic complications, cardiovascular (CV) disease being one of the most critical and responsible for about 60% of deaths.[1,2] Hence the importance of increasing cardiologists' knowledge about this disease.

The main feature of its CV manifestations is acromegalic cardiomyopathy, which usually begins with left ventricular (LV) hypertrophy and diastolic dysfunction, and can progress to systolic dysfunction in advanced stages. Valvular heart disease, coronary artery disease and arrhythmias are other common CV manifestations in acromegaly, and these patients also frequently develop CV risk factors such as hypertension, diabetes and sleep apnea syndrome.[1,2] It is important to note that early recognition and appropriate treatment can reverse some of these abnormalities, like LV hypertrophy.

For all these reasons there is an undeniable need for cardiologists to be involved in the surveillance and management of these patients. Studies are therefore needed to increase our knowledge of acromegalic cardiomyopathy, particularly regarding valvulopathy, its morphological and functional impact, frequency of echocardiographic follow-up and possible therapeutic implications.

The study by Nemes et al. published in this issue of the *Journal*[3] included 27 acromegalic patients and 38 matched healthy controls and assessed mitral annular (MA) size and function by three-dimensional speckle-tracking echocardiography (3D-STE). Their main finding was significant MA dilation with no functional impairment in acromegalic patients, regardless of disease activity. It should be noted that MA dimensions were based on measured end-diastolic MA diameter, area and perimeter, and MA functional properties were calculated based on MA fractional shortening (MAFS) and MA fractional area change (MAFAC), with only a brief and qualitative assessment of mitral regurgitation (MR), which was reported as insignificant and unrelated to disease activity.[3]

While this study adds some important information regarding mitral valve involvement in acromegaly, it also raises some questions. First, MA size and function were assessed through a 3D-STE-derived technique, which although already in use and confirmed to be capable of reproducible assessment of MA dimensions,[4] is still under investigation and has some technical limitations, including temporal and spatial resolution. Also, 3D-STE-derived MA dimensions showed somewhat lower values than full-volume real-time 3D echocardiography (RT-3DE), which has been validated by magnetic resonance imaging and is able to analyze the complex saddle-shaped configuration of the mitral annulus.[5]

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Secondly, although MA function was considered preserved despite MA dilation, this was assessed through MAFS and MAFAC. It would be interesting to put it into a more clinical perspective by relating it to valvular regurgitation.

There are several published studies reporting a high prevalence of mitral and aortic valve abnormalities in acromegaly, with a statistically significant higher prevalence of aortic and mitral regurgitation than in matched controls. However, this higher reported prevalence ranged widely, from 5% to 86% of acromegalic patients and from only trace to moderate severity, but was mainly asymptomatic and rarely clinically significant. Valvular heart disease appears to be definitely correlated with the duration of active disease, with a calculated 19% increase in odds ratio with every year of excess growth hormone (GH) duration, but irrespective of disease activity, meaning that valvular damage is irreversible even with successful treatment of acromegaly, in contrast to the observed regression of LV hypertrophy.[2,6–8] These studies also demonstrated that long-term exposure to excess GH leads to accelerated degenerative valvular changes, including myxomatous degeneration and calcifications of leaflets and annuli, suggesting that replacement valve surgery should be considered rather than valvuloplasty if therapeutic intervention is needed.[6–8]

In the study by Nemes et al., MR was reported as insignificant, with controls apparently showing no MR at all and only 25% of acromegalic patients showing trace or mild severity (grade $\leq$2). There was only a statistically significant predominance of MR in acromegalic individuals over controls in grade 1 severity (trace) and in inactive disease.[3]

The issue at stake is why MA dilation occurs without significant functional impairment or mitral regurgitation, in contrast to what is demonstrated in other cardiomyopathies, such as dilated or hypertrophic cardiomyopathy.[5]

The authors explain this phenomenon through a compensatory increase in LV and left atrial contractility owing to an increase in LV radial strains, as demonstrated in acromegaly by Kormányos et al.,[9] enabling adequate MA contraction and function despite dilation of the annulus. However, this is only seen in active disease, while patients with inactive disease show no radial strain gain compared to controls. But based on this argument, more MR would be expected than was actually reported, particularly in inactive disease. On the other hand, this is probably the reason for the tendency towards a slightly higher grade of MR in inactive acromegalic patients than in controls, although still at a very low grade of severity.

The authors also found preserved MA function independent of disease activity. Although this may be due to the early stage of acromegaly at which the assessment was performed, this cannot be confirmed since the stage of the disease in which patients were assessed was not identified. It can at least be presumed that it was not at a very advanced stage, given the low grade of LV hypertrophy and the preserved ejection fraction in these acromegalic patients, but this is not certain.

Besides this, the study lacks information on mitral valve structural abnormalities and the pathophysiological mechanisms responsible for MR in these patients, probably due to the low spatial resolution of 3D-STE. MR appears to have been an undervalued issue in this study, which soon became clear once the authors stated that MR severity was qualitatively rather than quantitatively graded (not following the latest guidelines of the European Association of Cardiovascular Imaging and the American Society of Echocardiography).

In conclusion, this study contrasts with previous ones by giving a clearer insight into acromegalic cardiomyopathy, since it demonstrates preserved MA function without significant MR despite MA dilation, highlighting a possible new mechanism for this to happen (increase in LV radial strain). Although it has some technical issues, including the small number of patients analyzed with an echocardiographic technique that has limited resolution, the authors should be congratulated for their effort to increase our knowledge of a rare but clinically significant disease.

I believe a more clinical approach with more emphasis on MR would be welcome, and the question remains whether these findings are related to an early or late stage of the disease. Therefore, more confirmatory studies are needed. But the importance of careful and continuous cardiological follow-up and echocardiographic monitoring in this disease remains unquestioned.

Conflicts of interest

The authors have no conflicts of interest to declare.

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