Original Article

Post-Extrasystolic Potentiation in Chronic Chagas' Heart Disease. A Radiologic Contrast Ventriculography Study

José Mário M. Brandão, Andrea Miziara, Geraldo Luiz de Figueiredo, Moysés O. Lima-Filho, Elias M. Ayres-Neto, José Antonio Marin-Neto
Ribeirão Preto, SP - Brazil

Objective

To determine the existence and frequency of the phenomenon of post-extrasystolic potentiation in dysynergic myocardial areas of patients with chronic Chagas' heart disease studied by use of radiologic contrast ventriculography.

Methods

This study is a semiquantitative retrospective analysis of radiologic contrast ventriculography in patients with chronic Chagas' disease, who were consecutively studied to assess the mechanisms of ventricular tachycardia.

Results

Of the 72 patients initially included, in only 20 patients was possible the ventriculographic analysis for the purposes of this study. The phenomenon of post-extrasystolic potentiation was observed in 11 (55%) of these patients, and a 15.31% improvement was observed in the contractility score from the baseline to the post-extrasystole condition (P=0.0001). That phenomenon occurred even in ventricular segments with an intense deficit in contractility.

Conclusion

The phenomenon of post-extrasystolic potentiation is observed in a significant proportion of patients with chronic Chagas' heart disease, in whom the phenomenon could be angiographically analyzed, indicating the existence of potentially recruitable contractile reserve in ventricular regions, showing marked dysynergy. Additional studies for clarifying the underlying mechanisms are required.

Key words

Chagas' heart disease; post-extrasystolic potentiation; contrast ventriculography

Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto - USP
Mailing address: José Antonio Marin-Neto - Rua Ângelo de Paschoal, 105 - Cep 14025-640 - Ribeiro Preto, SP, Brazil
E-mail: jamarin@cardiol.br
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The phenomenon of increased contractile force, which occurs in the beat following an extrasystole was observed more than 100 years ago by Langerdoff. Later, Cooper MW, 1993 [1] called it post-extrasystolic potentiation. Several studies followed in an attempt to physiologically explain the phenomenon, but its mechanism remains controversial [2-6]. The post-extrasystolic potentiation occurs both in healthy hearts and in those with contractility deficits [3,4]. Post-extrasystolic potentiation may be experimentally demonstrated, as in isolated myocytes of rats, and the several factors that influence it may be studied [5,6].

Post-extrasystolic potentiation was observed in patients with ischemic heart disease and regional contractile deficits during radiologic contrast ventriculography or echocardiography [7-9]. That observation showed that the myocardium could recruit its contractile reserve, and that, therefore, those akinetic or hypocontractile areas were essentially viable [7-9]. Later, the degree of post-extrasystolic potentiation was shown to be inversely proportional to the degree of ischemia in experimental studies using occlusion of the anterior descending artery in dogs [1], ie, more intensely ischemic myocardial segments could not show post-extrasystolic potentiation.

In chronic Chagas' heart disease, similarly to that which occurs in ischemic heart disease due to coronary heart disease, the early occurrence of regional ventricular dysynergy is characteristically observed [10,11]. However, unlike coronary heart disease, the subepicardial arteries in chronic Chagas' heart disease usually lack obstructive processes [12,13], and their pathophysiological peculiarities make the exploration of the phenomenon of post-extrasystolic potentiation in chagasic patients studied with radiologic contrast ventriculography attractive. This study aimed at analyzing the contrast ventriculograms of chronic chagasic patients with ventricular tachycardia undergoing correlative studies of ventricular electrophysiology and segmentary mobility [14].

Methods

This retrospective study comprised 72 consecutive patients with chronic Chagas' heart disease (minimum of 2 positive specific serologic tests: ELISA, indirect immunofluorescence, or hemaglutination) undergoing hemodynamic and cineangiocardiographic examinations after giving written consent, according to the research protocol approved by the committee on ethics in research at our institution. After selective right and left coronary angiography

through manual injection of contrast medium in each ostium, radiologic contrast ventriculography was performed always with automate injection of 20-35 mL of contrast medium inside the left ventricle with nominal flow velocity, ranging from 10 to 15 mL, depending on whether the catheter used was an 8F Sones (brachial approach) or a 6-8F pigtail (femoral approach). Two positions were always used: right anterior oblique (RAO) at approximately 30°, and left anterior oblique (LAO) at approximately 45°. That allowed the analysis of the diastolic-systolic excursion according to the following 10-segment model: 1) RAO view: anterobasal, anterolateral, anteroapical, apical, inferior, and inferobasal; and 2) LAO view: septal, low posterolateral, high posterolateral, and inferoapical.

Of the 72 patients selected, those who met the following 3 criteria during ventriculography were included in the study: a) "spontaneous" premature ectopic ventricular beat during ventricular contrast administration; b) at least one analyzable normal ventricular beat preceding the premature beat; c) at least one analyzable normal ventricular beat after the premature ectopic beat. Such criteria were present in only 20 of the 72 (37.8%) patients. In 34 (47.2%) patients, no premature extrasystolic beat occurred; 18 (25%) had nonsustained ventricular tachycardia or had no analyzable normal pre-extrasystolic beat.

In each segment, the diastolic-systolic excursion was assessed by using semiquantitative scores on 2 distinct occasions: 1) during the systole preceding the "spontaneous" extrasystole; 2) on the first beat following that of the extrasystole. The 5-point score scale attributed numerical values to different patterns of diastolic-systolic excursion: 0 (normal contractility), 1 (moderate hypokinesia), 2 (intense hypokinesia), 3 (akinesia), 4 (dyskinesia). Score attribution was always performed by comparing the pre- and post-extrasystolic beats. Score attribution was always performed by 2 researchers with experience in interpretation of radiologic contrast cineventriculography. The concordance index was elevated (kappa statistic = 0.96). In case of discordance, the score was reassessed by both researchers and a consensus was obtained.

In statistical analysis, the Wilcoxon test was used for comparison between the scores of ventricular contractility during normal systole and during the beat immediately after extrasystole.

Results

All 20 patients studied had angiographically normal subepicardial coronary arteries or minimum luminal alterations (obstructions < 30% luminal diameter reduction) in those arteries (fig. 1). Of the 20 patients, 11 (55%) had post-extrasystolic potentiation as follows: at least one dysynergic ventricular segment after the normal systole, which showed improvement in the systolic-diastolic excursion during the normal beat after the extrasystole (figs. 2 and 3). The other 9 patients had no post-extrasystolic potentiation in any segment. In the group with post-extrasystolic potentiation, the mean score of ventricular contractility ranged from 2.22 during normal systole to 1.88 during contractility with post-extrasystolic potentiation (-0.34 or overall contractile improvement of 15.31%; P = 0.0001, Wilcoxon test). The post-extrasystolic potentiation was detected in ventricular segments exhibiting, at baseline, ventricular dysynergy of variable intensity (range: from moderate hypokinesia to akinesia) (fig. 4), and it was not observed in segments with dyskinesia.

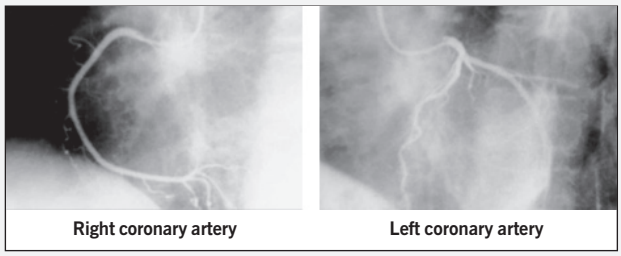

Fig. 1 - Examples of right and left cine coronary angiography pictures showing lack of significant obstructive lesions at the subepicardial level. This pattern was uniformly observed in all patients studied.

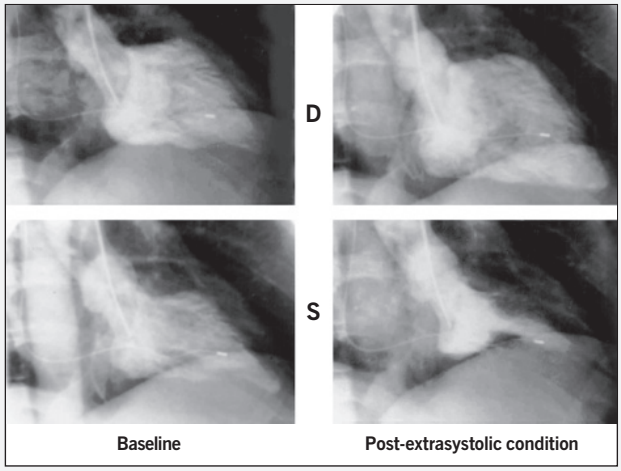

Fig. 2 - Example of radiologic contrast ventriculography pictures in the RAO view. At baseline, intense hypokinesia of the apical segment occurs, moderate hypokinesia of the anteroapical, anterolateral, and inferobasal segments occurs, and mild hypokinesia of the inferior segment. In the post-extrasystolic condition, a significant increase in ventricular contractility is observed in several segments, except for the apical and inferobasal. S - telesystolic pictures; D - telediastolic pictures.

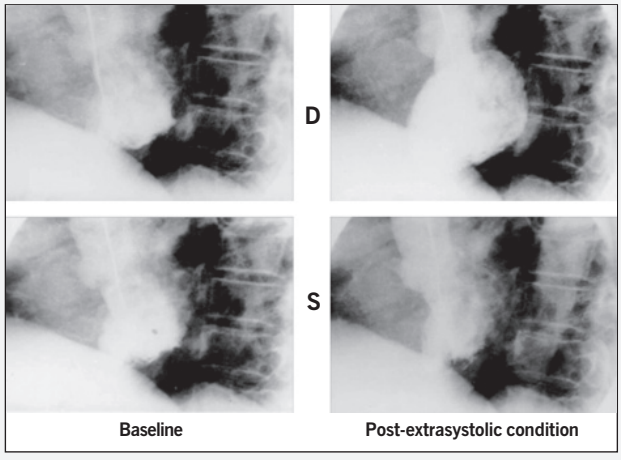

Fig. 3 - Example of radiologic contrast ventriculography pictures in the LAO view. At baseline, moderate hypokinesia of the high and low posterolateral segments occurs, and this dysynergy almost disappears in the post-extrasystolic condition. S - telesystolic pictures; D - telediastolic pictures.

Discussion

The phenomenon of post-extrasystolic potentiation, usually observed in patients with obstructive coronary heart disease at the subepicardial level, had not yet been reported in chronic Chagas' heart disease. Its existence was determined in this study, and it was confirmed as an extremely frequent phenomenon, including in ventricular areas with a marked degree of dysynergy. It should be stressed that, at least in the chagasic population with ventricular dysrhythmia,

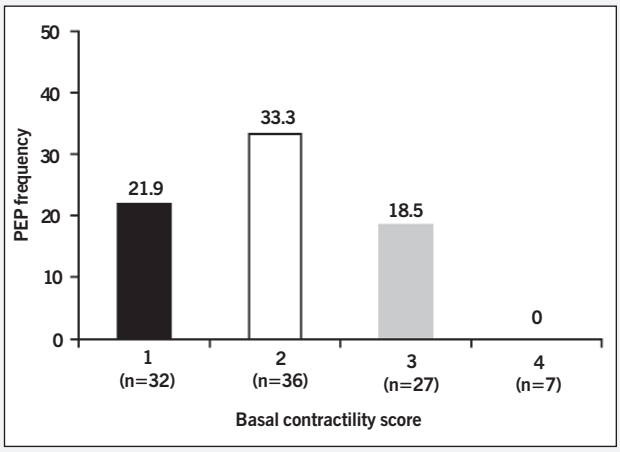

Fig. 4 - Frequency of dysynergic segments showing PEP in function of the basal contractility score in 20 patients with analyzable extrasystoles. The figures between parentheses represent the number of segments analyzed for each degree of contractile performance. Degrees of contractile performance assessed by use of the diastolic-systolic excursion: 0 (normal contractility), 1 (moderate hypokinesia), 2 (intense hypokinesia), 3 (akinesia), 4 (dyskinesia); PEP - post-extrasystolic potentiation.

the analysis of the contrast ventriculogram allowed the study of post-extrasystolic potentiation in only one third of the patients.

Considering that the post-extrasystolic period is usually longer, thereby allowing greater ventricular filling, it would be natural to interpret the phenomenon of post-extrasystolic potentiation as inserted in the context of cardiac heterometric autoregulation; more specifically, it could be linked to the Frank-Starling mechanism. However, in a review study [1], post-extrasystolic potentiation has been conceptualized as an intrinsic phenomenon of the myocardium, not exclusively dependent on preload (or ventricular filling), ie, the Frank-Starling mechanism would not be the major mechanism responsible for the increment in contractile force. The studies assessed have suggested that transient changes in calcium inflow involving the sarcoplasmic reticulum and the sodium and calcium channels are implicated in the appearance of post-extrasystolic potentiation [5,6], which progressively increases in a directly proportional manner to the reduction in the interval between the normal systole and extrasystole [2]. Although usually observed after ventricular extrasystole, post-extrasystolic potentiation may equally manifest after atrial extrasystole.

Similarly to that which occurs in atherosclerotic ischemic heart disease [7-9], post-extrasystolic potentiation demonstrated in chronic Chagas' heart disease indicates the occurrence of viable myocardium, although no systolic mobility is observed at rest in these dysynergic areas. Consequently, the existence of predominant fibrosis is ruled out in these dysynergic ventricular regions, in which post-extrasystolic potentiation is detected.

The assessment of post-extrasystolic potentiation in patients with ischemic heart disease due to atherosclerotic obstructive coronary artery disease, as performed by use of tests of inotropic stimulation with pharmacologic action [15-18], has proved to be useful for understanding the pathophysiological processes of myocardial hibernation and "stunning" [19,20]. Its meaning in patients with chronic Chagas' disease, however, is difficult to understand.

Some chagasic patients may have precordialgia atypical of coronary artery disease, but sufficiently intense and frequent to clinically require the performance of cine coronary angiography. Several studies carried out in such patients have shown the presence of disorders compatible with the occurrence of ischemia at the microvascular level[11-13], in association with virtual angiographic normality, but with anomalies in the subepicardial coronary circulation regulation[21,22]. Such alterations in human beings also correspond to microcirculatory disorders observed in experimental models of *T. cruzi* infection, attenuated by vasodilating agents[23-25]. Therefore, one may speculate about the occurrence of a phenomenon similar to that of myocardial hibernation detected in patients with obstructive coronary artery disease [17], which, in individuals with chronic Chagas' heart disease would be caused by a process of microvascular ischemia.

As already reported, the present study also confirmed that, in patients with typical manifestations of chronic Chagas' heart disease, the subepicardial coronary arteries usually have no hemodynamically significant obstruction. Thus, in dysynergic ventricular areas at rest and with post-extrasystolic potentiation, once transmural fibrosis is ruled out as a factor responsible for dysynergy, the mechanisms subjacent to contractile deficit in patients with chronic Chagas' heart disease may be varied in nature. One first possibility could involve microcirculatory disorders consequent to inflammatory processes caused by parasitic reaction or an immune-based reaction [26-28]. In the second possibility, the mechanical hypothesis, the coronary microcirculatory alterations could be consequent to the loss of autonomic control of the heart, an extremely frequent disorder in patients with chronic Chagas' heart disease[29,30]. In both pathophysiological possibilities, these disorders could be associated with the previously described reversible and paradoxical perfusion defects in patients with chronic Chagas' heart disease during myocardial scintigraphy performed during physical exercise or even at rest [12, 21]. Finally, one can consider the hypothesis that, instead of representing a real contractile recovery of the hypocontractile regions at rest, the reversion of that dysynergy elicited by post-extrasystolic potentiation in chronic Chagas' heart disease could result from masking the local defect during the most vigorous performance of the adjacent regions. Additional studies are required to explore those distinct pathophysiological possibilities that could explain the phenomenon of post-extrasystolic potentiation in patients with chronic Chagas' heart disease.

It has been well established that the radiologic contrast may induce chronotropism, and mainly negative inotropes. Such effects could theoretically mask the expression of post-extrasystolic potentiation in regions other than those reported in this study.

In addition, only chagasic patients with ventricular tachycardia undergoing investigation about the mechanisms responsible for sustainability or not of the arrhythmia have been studied. This does not allow the extrapolation of the present results to other population samples with Chagas' disease.

Finally, although the observation of post-extrasystolic potentiation in dysynergic ventricular areas suggests that no predominant (or transmural) fibrosis occurs in them, pulling of those regions by a more vigorous contractility of the adjacent segments may also contribute to the apparent contractile recovery that characterizes post-extrasystolic potentiation itself.

In conclusion, this study describes for the first time the phenomenon of post-extrasystolic potentiation in patients with chronic Chagas' heart disease. The existence of this phenomenon in chagasic patients suggests the occurrence of areas of viable myocardial tissue, and not of transmural fibrosis in dysynergic segments at baseline,

similarly to that which occurs in patients with heart disease due to subepicardial obstruction. The existence of this real contractile reserve may be useful for perfecting the understanding of the pathophysiology of chronic Chagas' heart disease and be relevant in the therapeutic choice to be used. However, the results of this study should first be confirmed by use of methods, such as perfusion myocardial scintigraphy, for the real appreciation of myocardial viability in the segments with post-extrasystolic potentiation.

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