Abstract.—Objective. To identify septal hypokinesia (SH) with signs of right ventricular (RV) overload.

Materials and methods. Prospective study of consecutive patients divided into cases with SH (n = 39) and controls without SH (n = 27). Subjects with septal perfusion defects and alterations in conduction were excluded. Images were obtained after injection of 20 mCi (740 MBq) of technetium tracer. The perfusion and septal mobility, RV and left ventricle values were quantified and other clinical parameters were obtained. Multivariate non-parametric tests and Pearson’s correlation tests were applied.

Results. RV perfusion was higher in the case group (31.7 % vs 27.5 %, p = 0.012). 35.9 % of cases had undergone cardiac surgery (CS) in the past. A higher number of subjects with valve diseases (VD) was found in the case group (23.1 % vs 3.7 %, p = 0.031); the same occurred with smoking (46.2 % in cases vs. 11.1 % in controls, p = 0.05). Correlation was obtained between septal motion and RV perfusion (–0.374, p = 0.015 bilateral), and between septal and RV wall motion (0.299, p = 0.015 one-sided).

Discussion. This test has been scarcely applied in RV pathology; this entity has great repercussion on the prognosis of patients with heart failure. These findings may clarify certain aspects of its physiopathology.

Conclusions. According to our study, SH is associated with the degree of RV perfusion and wall motion, as well as the presence of history of CS, VD and smoking.

KEY WORDS: interventricular septum, hypokinesia, right ventricular overload, myocardial perfusion gated-SPECT.

INTRODUCTION

Alterations in myocardial wall motion have multiple and varied causes, the most common being the presence of an underlying perfusion defect. Alterations in left bundle branch block (LBBB) synchronisation1,2 and pacemaker implant3 make septal hypokinesia a frequent
finding in these patients. Other less common causes include: hypertrophic cardiomyopathy and its treatment by septal ablation4-6, cardiac surgery (HS)7, systemic diseases8,9, heart malformations10, blanket radiotherapy in mediastinic lymphomas11 and poisoning due to insect bites12.

Myocardial perfusion gated-SPECT studies allow visualisation of left ventricular (LV) wall motion, evaluation of end-systolic and diastolic volumes and calculation of the LV ejection fraction (LVEF). The values obtained for these parameters correlate significantly with the results of other reference techniques13-16.

There is little literature relating to the usefulness of this technique in the evaluation of the right ventricle (RV), despite the significant prognostic implications it entails in those patients with heart failure or previous myocardial infarction17-20. Echocardiographically, the RV overload is depicted by dilation, hypertrophy and hypocontractility of the RV, as well as flattening of the interventricular septum21-26. At present, 2-dimensional Doppler echocardiography is the most widely used method for the assessment of this entity27-30, but it offers a limited view through an anatomically limited window which may impede the correct evaluation of the RV. Some nuclear medicine studies have reported good correlation between the presence of high tracer uptake in the RV free wall and high pulmonary arterial pressure in subjects with congenital heart diseases31-33 or chronic lung disease34,35.

In our routine work, we observed an increasing tendency in the onset of SH in patients who did not have perfusion septal defects or conduction alterations. We decided then, to evaluate other radioisotopic findings and to analyse possible causes related with SH.

**OBJECTIVE**

To identify which factors determine SH and verify whether the SH is related with signs of RV overload.

**MATERIAL AND METHODS**

**Subject selection**

We conducted a prospective study with consecutive patients who had been referred for myocardial perfusion gated-SPECT, under indications of suspicion or follow-up of coronary artery disease between March 2006 and January 2007.

**Exclusion criteria**

The most common proven causes of SH were excluded. Others, which although indicated as possible causes, have not been sufficiently described in the literature were not excluded. To that end, we defined the exclusion criteria as patients with: septal perfusion defects (SP), alterations in cardiac conduction, LBBB, including left hemiblocks or pacemaker implant.

**Study groups**

Two groups were defined: one case group with SH (n = 39) and one control group without SH (n = 27). The study variables were: perfusion and wall motion of the septum and RV free wall, as well as the estimated end-systolic volume (EESV), the estimated end-diastolic volume (EEDV) and the LVEF, following the model by Nishijima et al35. The RV volumes and their ejection fraction were not included in the final analysis given their low reproducibility. We also gathered information from patients in relation to history of cardiovascular risk factors: hypertension, diabetes mellitus, dyslipidaemia, obesity and smoking, as well as previous history of lung disease confirmed spirometrically, valvular disease (VD) diagnosed by echocardiography, CS, history of percutaneous coronary intervention and the presence of perfusion defects found in the isotopic study, without extension of the septal wall.

**Myocardial perfusion imaging**

The studies were assessed exclusively at rest, after the injection of 20 mCi (740 MBq) of Tc-99m Tetrofosmin® or Tc-99m Sestamibi®. Images were acquired 20-90 minutes after the injection (depending on the radiotracer used) in a dual head gamma camera (ADAC Vertex V60®) using a low energy, high resolution collimator. The acquisition was performed over a 180° circumference (from 45° right anterior oblique to 45° left posterior oblique) with the patient in supine position and the arm raised above the head. A window centred at 140KeV ± 20 % was used, with 30 seconds per image, 8 segments per cycle. All images were reconstructed using the software Autoquant
Cedars Sinai® (AutoSpect plus and Autoquant). Filtered back-projection was applied on a 64 × 64 matrix and then a Butterworth filter (cut-off 0.50, order 5.0) was used on all.

Image interpretation

All the images were reviewed by two nuclear medicine specialists and semi-quantitative values were obtained for the primary variables. The regions of interest applicable to the study were defined (septal wall and RV free wall) and values were obtained for the variables described. Those patients who had SP less than 59 % of the maximum were excluded from the study (exclusion criterion). The presence of SH was defined as a septal wall motion (SWM) value ≤ 4.8 mm out of a maximum of 10 mm and the absence of SH was determined by a SWM with a value of ≥ 5.3 mm (fig. 1).

Statistical analysis

The descriptors of the quantitative variables are represented by the medians (minimum-maximum). The differences between the two groups studied were analysed by applying the Chi-squared test; in the event of insufficient sample, non-parametric tests were applied (Fisher’s or Mann-Whitney U test).

The differences between the variables of both groups were examined by applying Mann-Whitney tests for the continuous variables and Chi-squared tests for the qualitative.

A possible correlation between the SWM and RV perfusion (RVP) was also investigated, as was the correlation between the SWM and the RV wall motion, by applying Pearson’s correlation tests.

Finally, non-parametric tests (Mann Whitney U test) were applied to evaluate the possible influence of the different risk factors on the primary study variables (RV perfusion and wall motion) independently in each group.

All tests had two-sided statistical significance and the statistical significance value was set at p < 0.05 in all cases.

RESULTS

Descriptive analysis of the study populations

The results are summarised in table 1. Statistically significant differences were observed in the SWM of both groups, as was expected, given the nature of the study. There were a significantly higher percentage of males in the case group compared with the control group. For reasons mentioned above, this finding was not considered capable of altering the results of the final statistical analysis. The variables age and SP did not show statistically significant differences between groups.

Study variables

The results are summarised in table 2. Significantly higher RVP values were found in the SH group. Likewise, the SH group had notably lesser RV wall motion (RVWM) compared to the group without.

![Fig. 1.—Increase in the visualisation of the right ventricle (RV) in the horizontal long axis. “Bulls eye” view of normal septal perfusion with associated septal hypokinesia (SH).](image)

Table 1

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<th>Description of the Study Populations</th>
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hypokinesia; although a statistically significant value was not obtained (p = 0.054), these differences were close to the significance value.

In relation to the various clinical variables, a significant percentage of the population with previous CS were included in the hypokinesia group, whilst in the control group, none of the patients had such history. Similarly, more patients with history of VD were found in the SH group. There were more smokers in the case group than in the control group, with a p value at the limit of statistical significance.

The EESV and EEDV in the case group were significantly higher than those found in the control group, with a significantly higher LVEF value in the latter group. There were no statistically significant differences found in the proportion of patients with a pathological SPECT result between both groups.

No other statistically significant differences were observed in the other variables studied.

Correlation tests

The results are shown in figures 2 and 3. We obtained a negative correlation between SWM and RVP, with a value of -0.374, statistically significant (p = 0.002 two-sided). A correlation was also found, in this case positive, between the SWM and RV wall motion, with a value of 0.299 (p = 0.015 one-sided).

Stratified analysis

When the different variables relating to the patient clinical data were evaluated independently, no statistically significant differences were found within the control group.

In the case group, those patients with previous CS had a SH value higher than those who had not undergone surgery in the past (SWM = 1.95 compared to SWM = 2.9 respectively, p = 0.045).

No statistically significant differences were found between those patients who had negative SPECT results compared to those with pathological results.

DISCUSSION

RV evaluation is not a usual indication for myocardial perfusion SPECT. Even so, there are scintigraphic findings indicative of the presence of RV overload that have been published, mainly in studies related with paediatric patients with congenital heart diseases or patients with elevated pulmonary arterial pressure. High tracer uptake by the RV free wall, as well as a RV uptake: LV uptake ratio greater than 1.0.
than 0.45 have been postulated as markers of RV overload\textsuperscript{31,32,36}.

In this respect, Movahed et al were the first to describe a triad of scintigraphic findings associated with the presence of RV overload in patients with documented pulmonary hypertension: flattening of the interventricular septum (D-shaped LV), dilation of the RV and increased uptake by the RV\textsuperscript{37}. In our study, SH was used instead of the septal flattening described by Movahed et al, since both hypomotility and paradoxical septal motion are the result of the tendency of the septum to invade the left cardiac cavities in the presence of right heart overload\textsuperscript{38,39}.

Our study agrees with that of Movahed et al in that we observed that SH accompanies other signs suggestive of RV overload such as greater uptake in the right free wall and greater dilation of the RV. Aepfelbacher et al\textsuperscript{40} conducted a study with 194 patients and described a significant correlation between the tricuspid regurgitant velocity and the presence of greater tracer uptake by the RV in myocardial perfusion SPECT studies\textsuperscript{40}. We also established a correlation between the degree of SWM and visualisation of the RV semi-quantitatively. In their work on animal models, Wackers et al observed that there was higher tracer uptake in the RV after banding the pulmonary artery, and that this was due to two mechanisms: the first and most immediate associated with greater initial ventricular flow, and the second, in a more chronic phase, was due to compensatory hypertrophy; they also observed that the product of both remained stable over time\textsuperscript{34}. It was assumed that the highest uptake intensity visualised in the RD of our SH patients was mainly due to this second hypertrophy mechanism, as the temporary increase in the cardiac flow is only observed in acute events like pulmonary thromboembolism\textsuperscript{41} or massive acute myocardial infarction\textsuperscript{42}; none of the patients had these clinical conditions during the study period.

In their study, Aepfelbacher et al\textsuperscript{40} observed a poor correlation between the RV volume data obtained by the calculation with SPECT and the calculation with echocardiography. This problem derives mainly from the morphological variability as well as from the partial volume effect and poor scintigraphic resolution in the cardiac apical segment. Despite not having included the results of the RV volumes in the final analysis, we consider it worth mentioning the fact that the values obtained for RV EESV and EEDV in the SH group were significantly higher than those in the group without SH (EESV-RV = 28.2 ml compared to 17.8 ml, \( p = 0.007 \); EEDV-RV: 31.3 ml compared to 18.7 ml, \( p = 0.002 \)). Although it may be bold to extract conclusions from these data, the fact that they coincide to a large degree with findings described in previous studies of a similar nature, with respect to the pathology of SWM and dilation of right cavities, can be appreciated.

Our study showed a positive, significant correlation between SWM and RVWM, another indirect sign of overloading of that ventricle. It should be noted that the SH group had a higher number of patients with LV pathological parameters (lower LVEF and dilated volumes) compared with the control group. The SH group, therefore, may be representing a patient group which, although they did not show statistically significant differences as regards pathological SPECT results with the control group, a certain tendency to have a larger extension in ischaemic/necrotic lesions was observed and, therefore, they may be indirectly conditioning poorer RV function.

In our study, the variable most directly related with the presence of SH was previous CS. Of the patients who had undergone CS in the past (14 in total), 12 had undergone coronary by-pass surgery, 1 had mitral valve replacement and the other had both surgeries. There is evidence that supports the presence of contractibility defects and systolic thickening in the septal region which appear early after coronary by-
pass surgery. Although these defects normally improve 6 months after surgery, there are a percentage of patients in which these alterations remain indefinitely\textsuperscript{43,44}. It is advisable to reflect in turn on the fact that patients who undergo CS may show underlying irreversible necrotic lesions, of a considerable area, which condition fibrosis and worsening of the global contractibility. Moreover, two of the patients had also undergone valve replacement surgery, so the worsening of the SWM may be related not only with the post-surgical alterations described, but also with the effect of right overload implicit in the physiopathology of the mitral disease. In this respect, our study agrees with the fact that greater retrograde pressure from the mitral valve lesion could give rise to scintigraphic findings related with right ventricular overload, such as SH (all the valvular disease patients had aortic or mitral pathology). No statistically significant differences were found in any of the RV parameters when stratified by the variable VD, a fact which may be related with small sample size, as well as by the interaction of other risk factors, as we are dealing with a patient population which is essentially multi-pathological.

Although a significantly higher percentage of patients with pulmonary pathology was not found in the SH group, a greater tendency to have this type of pathology was observed in this group. We also observed a higher percentage of smokers in patients with SH compared with the control group, and although the difference was within the limit of statistical significance, the following may be taken into account; smoking is directly related with the development of chronic obstructive pulmonary disease (COPD), so we may be dealing with a population with a defined risk of developing the aforementioned condition. In contrast, there were many patients who, despite not having spirometric confirmation of COPD, had clinical symptoms compatible with this process, so their incorporation in the variable “lung disease” could have been avoided. Furthermore, smoking in our study population, the median age of which was in their seventies, corresponded primarily to men, a fact which may justify the higher percentage of males in the case group with respect to the control group. The sex difference between both groups is not, from our perspective, a source of error for performing the statistical analysis; there is no clinical evidence of a higher risk of SH in men, and the only thing that could have influenced is the higher number of male smokers among the 70 year old population, as well as a possible randomised error in relation to the small sample size.

**LIMITATIONS**

Although the main objective of our study was centred on the scintigraphic findings, based on the evidence published on similar findings in echocardiographic studies, the lack of complementary diagnostic tests to verify the existence of RV overload (echocardiography, nuclear magnetic resonance, measurement of pulmonary artery pressure) is a clear limitation when it comes to establishing a relationship with this condition. The application of other diagnostic techniques would then be an evident starting point for future studies in this field.

The image processing, although it was carried out semi-quantitatively using our equipment software, may be a possible source of systematic error; the degree of RV visualisation is characterised not only by the relative intensity of the LV (which in turn is affected by the absolute tracer uptake by the LV, as well as by the selection of the colour scale) but also depends on the apparent thickening of the LV (which in turn also depends on the type of filter applied). It would have been more helpful to work with RV:LV ratios to obtain more extrapolable values. This would be another possible future starting point.

Finally, a larger population size, as well as performing paired case-control comparison, would have provided our analysis with more statistical power.

**CONCLUSIONS**

Evaluation of the RV has not been sufficiently studied in nuclear cardiology, in spite of the implications that it has on the prognosis of a considerable group of patients. Our results, consistent with other similar echocardiographic and scintigraphic studies based in this field, support the presence of correlation between the degree of SWM and tracer uptake in the RV free wall. We also found a correlation between the degree of SWM and the degree of RV wall motion. SH appears more frequently in those patients with history of CS or VD and, to a lesser extent, in those patients with a history of smoking.
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