Introduction. Dynamic intraventricular gradients (DIG) after valve replacement in severe aortic stenosis have been reported, although the incidence of DIG and clinical signs are still poorly understood.

Aim. To evaluate the incidence of DIG and determine risk factors and associated morbimortality.

Patients and method. One hundred nine consecutive patients with severe aortic valve stenosis undergoing valve replacement were studied prospectively by echocardiography to detect the postoperative appearance of DIG, defined as a maximum flow velocity ≥ 2.5 m/s.

Results. Sixteen patients (14.9%) developed postoperative DIG. Significant differences between the patients with or without DIG were found for ventricular diameter (left end-diastolic ventricular diameter (LEDVD) 43.2 vs. 47.7 mm, respectively, P<.001; left end-systolic ventricular diameter (LESVD) 21 vs. 29 mm, P<.001); left ventricular mass index (165 vs. 193 g/m², P<.05); mean aortic valve gradient (68 vs. 59 mmHg, P<.01); ejection fraction (73 vs. 61%, P<.001). No significant differences were found with respect to ventricular wall thicknesses (septal 16.3 vs. 15.7; posterior 14.37 vs. 14.62), the presence of aortic insufficiency, or other postoperative factors (anemia, inotropic agents, etc.).

Conclusions. DIG after aortic valve replacement to treat severe stenosis is not unusual (15%). DIG is usually found at a midventricular location, close to the septum. In patients with postoperative DIG the most common associated factors were small LEDVD, high ejection fractions and ratios of intraventricular septal to posterior wall ratios, high valve gradients and small left ventricular masses. Preoperative echocardiography can identify patients with a higher risk of developing DIG after aortic valve replacement.

Key words: Aortic stenosis. Cardiac surgery. Dynamic gradient. Echocardiography.

Introduction. Se conoce la existencia de un gradiente dinámico intraventricular (GDI) en el postoperatorio de recambio valvular aórtico, aunque se desconoce la incidencia del mismo, así como los factores determinantes de su presentación.

Objetivos. Determinar la incidencia de aparición de GDI, así como los posibles factores predictivos y la existencia de morbimortalidad asociada a este proceso.

Pacientes y método. Se ha realizado un estudio prospectivo mediante ecocardiografía-Doppler en 109 pacientes con estenosis aórtica valvular severa sometidos consecutivamente a recambio valvular y se ha valorado la aparición durante el período postoperatorio de GDI, definido por una velocidad máxima superior a 2.5 m/s.

Resultados. Se observó la aparición de GDI durante el postoperatorio en 16 pacientes (14,9% del total). Se encontraron diferencias significativas entre los pacientes que desarrollaron o no GDI con respecto a los diámetros ventriculares: diámetro telediástolico del ventrículo izquierdo (DTDVI) de 43,2 frente a 47,7 mm, respectivamente; p < 0,001; diámetro telesistólico del ventrículo izquierdo (DTSVI) de 21 frente a 29 mm; p < 0,01; el índice de masa del VI de 165 frente a 193 g/m²; p < 0,05; el gradiente medio transvalvular de 68 frente a 59 mmHg; p < 0,01; y la fracción de eyecisión de 73 frente a 61%; p < 0,001. No se encontraron diferencias significativas en cuanto al grosor de las paredes ventriculares (TIV de 16,3 frente a 15,7; PP de 14,37 frente a 14,62), ni en la existencia de insuficiencia aórtica, ni en otros factores clínicos postoperatorios (anemia, fármacos inotrópicos, etc.).

Conclusiones. Durante el postoperatorio del recambio valvular por estenosis aórtica severa aparece GDI en un número no despreciable de pacientes (15%).
INTRODUCTION

It is known that an obstructive dynamic intraventricular gradient (DIG) exists in hypertrophic cardiomyopathy and in patients with concentric ventricular hypertrophy secondary to arterial hypertension or aortic stenosis. DIG is also detected, in the absence of ventricular hypertrophy, in patients with increased contractility due to the administration of drugs or sympathomimetic hormones during severe hypovolemia or cardiac tamponade.

The development of DIG in patients with severe aortic stenosis (AS) is a finding that was reported in 1969. Since then, several articles have confirmed the association of the two diseases, as well as a greater incidence of DIG after aortic valve replacement. What is not clear is the frequency with which this gradient occurs, since there is a large difference in the baseline incidence, which ranges from 4.6% to 52%, the factors with which it is associated, and its clinical relevance. This could be because only a small number of cases have been compiled in different studies (25 to 100 patients, according to the studies). In these studies it has been shown that this gradient can be induced by the hypovolemic situation of postoperative patients, as well as by the use of vasoactive drugs in this situation. Recently, a higher mortality and morbidity have been described in the presence of DIG.

The present study was developed to determine the incidence of DIG in patients undergoing aortic valve replacement and to identify the factors predisposing to its appearance, its evolution, and the associated morbidity and mortality.

PATIENTS AND METHOD

Patients

A study was made of 124 patients with severe AS or a double aortic lesion with predominance of severe stenosis (valve area 0.75 cm or less) who consecutively underwent to aortic valve replacement between March 1996 and January 1998 in our center. All patients met the criteria for surgery established by current clinical guidelines.14

The following exclusion criteria were applied: patients with another cardiac valve disease that required valve replacement, predominant aortic insufficiency (AI), or patients not in sinus rhythm at the time of the baseline study.

Of a total of 124 patients hospitalized for aortic valve replacement, 2 were excluded for congenital AS that had been treated surgically or percutaneously, and severe concomitant AI, 9 were excluded for baseline atrial fibrillation, 2 patients had predominant AI, and 1 patient for obstructive hypertrophic cardiomyopathy that required myectomy during surgery. One patient was excluded for intraoperative death.

Echocardiographic study

The study was made with Vingmed® model CFM 750 and CFM 800 echographs with 3.5-MHz probes and a 2.0-MHz Doppler blank.

Preoperative echocardiographic study

A baseline study was made of the patient’s parameters: height, weight, body surface area (BSA), baseline hematocrit, and baseline blood pressure. An echocardiographic study was made to measure ventricular diameters and valvular and intraventricular flow. In the first study, M-mode echocardiography was used to determine the end-diastolic diameter of the left ventricle (LV) in mm (LVEDD), left ventricular end-systolic diameter (LVESD), LV shortening fraction (LVSF), thickness of the interventricular septum in diastole (IVS), the LV posterior wall thickness in diastole (PW), LV outflow tract (LVOT), and other...
cardiac cavities. Ventricular mass was determined with the Deveraux formula modified by the ASE: 0.8 (1.05.[LVEDD+IVS+PW] /LVEDD). In bidimensional echography, the ejection fraction was measured with the Simpson method for four chambers. Doppler echography was used to determine transmitral flow: maximum speed of the E wave (E), maximum speed of the A wave (A), and E/A ratio. The maximum and mean transaortic flow gradients were determined and the valvular area was calculated using the continuity equation. The morphology and maximum gradient were assessed in LVOT and mesocavitary flow. The presence of AI and mitral insufficiency were determined and quantified. All measures were made according to the recommendations of the American Society of Echocardiography. Significant DIG was interpreted as an intraventricular flow with a dynamic morphology and flow rate of more than 2.5 m/s (the most commonly used maximum value of normality in different series).

Early postoperative echocardiographic study

A second study was made within 6 h of the intervention to measure hemodynamic parameters, including systemic blood pressure, heart rate, central venous pressure (CVP), left atrial pressure (LAP), hematocrit (Hct), to note the association or not of inotropic drugs, and by means of echocardiography, to measure the intraventricular flow (mesocavitary and LVOT), transprosthetic gradient, and transmitral flow.

Late postoperative echocardiographic study

A third study was made 7±0.5 days after the intervention to measure the hemodynamic parameters measured at baseline and to record pharmacological treatment and, by means of Doppler echocardiography, the transprosthetic and intraventricular gradients.

A fourth study was made in the patients who presented DIG in the third study, 3 to 6 months after the intervention, to confirm the persistence of DIG.

Statistical analysis

The results of the continuous quantitative variables are expressed as mean and standard deviation. A Shapiro Wilk test was made to confirm the normal distribution of the variables. The comparison of mean values in both groups was carried out with the Student t test for independent data, after performing a Levene test to confirm the homogeneity of variances. The chi-square test was used for categorical variables. A value of \( P<.05 \) was considered significant. Statistical analyses were made with the SPSS package for Windows, version 9.0.

RESULTS

Descriptive study

Patients

Finally, 109 patients were included (45 women and 64 men; mean age of 64±10 years; range 36 to 79 years; body surface area 1.76±0.17 m). The overall data of the patients are shown in Table 1. The number of patients with concomitant coronary disease that required revascularization was 6/109 (5.5%). The comparative analysis of the patients finally included and excluded is shown in Table 1.

Preoperative study

A preoperative study was made of all patients included in the protocol. With respect to the echocardiographic parameters, LVOT was 20.52 mm, IVS 15.78 mm, PW 14.59 mm, and IVS/PW ratio 1.08. The EDD was 47.11 mm and the ESD, 28.59 mm. The shortening fraction was 39.73%, and the ejection fraction was 62.75%. The mean ventricular mass was 333 g. The mean E/A ratio was 0.89. The mean gradient of all patients was very high (61 mm Hg). The mean valve area was 0.61 cm.

Of the 109 patients included, in baseline conditions 4 patients had a significant DIG (maximum flow rate more than 2.5 m/s) and 2 patients had a flow rate of

\[
\text{TABLE 1. Comparison of the preoperative and postoperative echocardiographic and clinical parameters of the patients included and the patients excluded}
\]

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Included</th>
<th>Excluded</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>109</td>
<td>15</td>
<td>–</td>
</tr>
<tr>
<td>Age</td>
<td>64.28±10</td>
<td>57.27±18</td>
<td>NS</td>
</tr>
<tr>
<td>Sex</td>
<td>64 W/45 M</td>
<td>12 W/3 M</td>
<td>NS</td>
</tr>
<tr>
<td>BSA</td>
<td>1.76±0.17</td>
<td>1.85±0.25</td>
<td>NS</td>
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<td>LV mass</td>
<td>333±99</td>
<td>379.78±116</td>
<td>NS</td>
</tr>
<tr>
<td>LVM index</td>
<td>189±57</td>
<td>205±64</td>
<td>NS</td>
</tr>
<tr>
<td>IVS/PW</td>
<td>1.08±0.12</td>
<td>1.0±0.08</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDD</td>
<td>47.12±6.7</td>
<td>49.0±8.9</td>
<td>NS</td>
</tr>
<tr>
<td>EDD/BSA</td>
<td>26.92±4.5</td>
<td>26.0±4.8</td>
<td>NS</td>
</tr>
<tr>
<td>LVESD</td>
<td>28.59±7.7</td>
<td>29.8±9.6</td>
<td>NS</td>
</tr>
<tr>
<td>LVOT</td>
<td>20.52±2.2</td>
<td>21.84±2.4</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>62.75±13</td>
<td>68.5±10.8</td>
<td>NS</td>
</tr>
<tr>
<td>Maximum aortic gradient</td>
<td>90.94±23</td>
<td>79.8±19.76</td>
<td>NS</td>
</tr>
<tr>
<td>Mean aortic gradient</td>
<td>61.15±17</td>
<td>54.2±15.43</td>
<td>NS</td>
</tr>
<tr>
<td>AI (1-4)</td>
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<td>2.13±1.18</td>
<td>NS</td>
</tr>
<tr>
<td>Postoperative data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of prostheses</td>
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<td>0/5/10/0</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Postoperative hematocrit</td>
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<td>33±3.7</td>
<td>NS</td>
</tr>
<tr>
<td>Inotropic drugs</td>
<td>14</td>
<td>5</td>
<td>NS</td>
</tr>
<tr>
<td>CVP</td>
<td>8.23±3.0</td>
<td>7.69±2.9</td>
<td>NS</td>
</tr>
<tr>
<td>LAP</td>
<td>9.35±3.2</td>
<td>10.16±2.5</td>
<td>NS</td>
</tr>
<tr>
<td>Postoperative mortality</td>
<td>4/109</td>
<td>1/15</td>
<td>NS</td>
</tr>
</tbody>
</table>
more than 3 m/s. The rest had a normal intraventricular flow rate (Figure 1).

**Early postoperative study**

Prostheses were implanted in all the patients: 3 biological prostheses and 106 mechanical prostheses. Of the mechanical prostheses, 12 were single-disk and 94 were double-disk. The study could only be made in 103 cases (94.5% of the total). In the rest of the patients, a recording of sufficient quality for evaluation was not obtained, which was due to the poor echocardiographic window of the patients in the immediate postoperative period. Of all these patients, DIG was observed in 11 of them (Figure 2).

**Late postoperative study**

A late postoperative study was made in 105 patients (96.3% of the total). The study could not be made in the patients who died between the second and third studies. In all these patients, an acceptable recording was obtained. DIG was detected in 10 cases. Of these cases, 5 had not presented a significant gradient previously and an important DIG developed in the third study (Figure 3).

**Fourth study (3-6 months)**

This study was made only in the patients who evidenced DIG in the second or third study (16 patients altogether). In the fourth study, only one patient had a flow rate of more than 2.5 m/s. The rest of patients did not present a significant flow rate or dynamic morphology.

**Comparison of patients with and without an intraventricular gradient**

A total of 16 patients presented DIG in one of the echocardiographic studies, 1, 2, or 3. These patients constituted group A. The other 93 patients that did not present DIG constituted group B. The preoperative echocardiographic characteristics of both groups were analyzed. Likewise, the clinical evolution of patients and postoperative morbidity and mortality were also assessed.

**Differences in preoperative study**

The differential analysis of preoperative echocardiographic factors in the two groups (Table 2) reveals significant differences. The group with DIG had smaller ventricular diameters (LVEDD and LVESD), a larger IVS/PW ratio, greater ejection fraction, and a tendency (not significant) to a smaller LV outflow tract. In addition, the group with DIG had significantly higher aor-
tic valve gradients than the group that did not develop DIG.

On the other hand, there were no significant differences in ventricular wall thickness between the two groups. The ventricular mass and ventricular mass index were smaller in patients who developed DIG than in patients that did not.

Site of gradient

The site of the DIG is described in Table 3. In our series, 16 patients presented DIG, but only 7 had LVOT obstruction. The other 9 had mesocavitary obstruction, just between the pillars of the papillary muscles.

Evolution of gradient

By three months, the postoperative DIG had resolved in 94% of the patients who developed DIG, although a dynamic morphology persisted in some of them (Table 3).

Associated hemodynamic factors

There were apparently no differences between the two groups in the use of vasodilator or inotropic drugs, the presence of associated pericardial effusion, or a significant development of anemia that could explain the development of the gradient (Table 2).

Mortality

Two patients died in the group that developed DIG (Table 4). The first patient died on postoperative day 3.
due to a low output situation and constrictive pericarditis before the intervention. Pericardectomy had been performed in this patient. The second patient died on postoperative day 10 of sepsis of respiratory origin. Three deaths occurred in the group that did not present DIG. One of these patients had early prosthetic endocarditis with a severe periprosthetic leak as well as stroke, and died later of a septic condition. The second patient had sepsis of respiratory origin after prolonged intubation. The third patient presented an extensive acute perioperative myocardial infarction with LV systolic dysfunction that required prolonged mechanical ventilation. This patient finally died of sepsis of respiratory origin. In the group of patients who were excluded, one intraoperative death occurred.

**Morbidity**

Of the group with DIG, none of the patients showed a decrease in atrial fibrillation during admission. However, in the control group there was a reduction in atrial fibrillation in 11 patients (11% of total), which remitted during admission (Table 4). One patient in the group that developed DIG presented significant pericardial effusion; and 3 patients in group B presented pericardial effusion. No patient in the gradient group presented sternal dehiscence and only 2 patients in the control group developed infection of the sternal wound. One patient presented mediastinitis that made reintervention necessary. In 1 patient of the gradient group (who later died) and 4 patients of the control group (2 of which died), prolonged mechanical ventilation was required for respiratory superinfection. There were no significant differences in the mean postoperative stay: 14 days in DIG group and 13 days in the non-DIG group.

**DISCUSSION**

**Prevalence of DIG**

We must first establish the maximum flow rate at which DIG is considered significant. According to Hatle Angelsen, this value should be established at 2.5 m/s because in their experience the maximum flow rate is rarely reached by normal subjects, even in situations of hypovolemia or sympathetic stimulation. Clinically, this maximum limit of normality is debated, since a flow rate of 2.5 m/s (which correlates with a maximum gradient of 25 mm Hg) is not likely to have clinical implications. However, if a limit of 3 m/s is used, there is a greater correlation with clinical manifestations (it correlates with a maximum gradient of 36 mm Hg). The limit of 2.5 m/s was ultimately chosen because it is the value used in the literature.

<table>
<thead>
<tr>
<th>TABLE 4. Patients with and without an intraventricular dynamic gradient: comparison of morbidity and mortality in both groups</th>
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</thead>
<tbody>
<tr>
<td>Morbidity and mortality</td>
</tr>
<tr>
<td>Mortality</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
</tr>
<tr>
<td>Pericardial effusion</td>
</tr>
<tr>
<td>Sternal dehiscence</td>
</tr>
<tr>
<td>Respiratory infection</td>
</tr>
</tbody>
</table>

with aortic prostheses. Laurent et al. in 1991 found that 12% (5 of 41 patients) of the series developed DIG in the postoperative period of valve replacement surgery. This figure reached 21% when inhaled amyl nitrite was administered. In all of them, the baseline gradient disappeared in 3 months. Aurigemma in 1991 reported the appearance of DIG in 13 of 53 patients (24.5%), but used 1.5 m/s as the limit of normal flow rate. After reviewing this series, we observed that when a flow rate of 2.5 m/s was used, only 9 patients were found (17%). Again, Laurent at al. in 1993 found at baseline (before aortic valve replacement) 1 patient with dynamic gradient out of a total of 51. After the intervention, 8 of the 51 patients developed baseline DIG and 7 more after the administration of inhaled amyl nitrite (baseline prevalence 15.7%). The DIG disappeared after treatment with beta-blockers or correction of the factor that had induced it; it disappeared spontaneously in only one case. In 1993, Wiseth et al. reported that half of the patients in their series (13 of 25) developed DIG spontaneously in the first week after surgery. We must report that this author also established flow rates of 2 m/s or higher as significant. However, we were not able to determine the incidence of flow rates of 2.5 m/s or more in this series. In this series, most gradients disappeared spontaneously, except in 2 patients, who had significant gradients in spite of verapamil treatment at 3 months. Bartunek et al., in 1996, found 14% of cases at baseline in a total of 100 consecutive patients. After the administration of nipride and dobutamine, they found 30% and 48% of cases, respectively. After a one-year follow-up, DIG had disappeared in all the patients in the series.

In all the classic series, at baseline and using a limit of normal maximum flow rate of 2.5 m/s, incidences ranging from 5% to 50% were obtained.

In our series, if we used a limit of 2.5 m/s, we obtained a cumulative incidence of 14.7% (16 of 109 patients) and with a limit of 3 m/s we obtained an incidence of 12%. In addition, 3 months after the intervention only 1 patient of 16 that presented a dynamic gradient continued to have a dynamic DIG at baseline.
We should note that only the series of Bartunek et al. and our series had an acceptable number of patients (100 and 109 patients), and that both series showed an almost identical baseline incidence of dynamic gradient (14% versus 14.7%, respectively). In addition, the different series were similar in demonstrating that the appearance of a DIG is transitory and only occasionally persists after the surgical intervention.

Predictive preoperative echocardiographic factors

After analysis of the preoperative echocardiographic data of the 2 groups (Table 2), certain characteristics of the ventricles that present DIG can be established. The ventricles are smaller and tended to present asymmetrical hypertrophy. They also had more contractility and higher aortic valve gradients. In contrast with what seemed to be the case at first, the ventricular mass index was smaller in patients that developed DIG. This is because the calculation of ventricular mass is influenced more by the end-diastolic ventricular diameter than by wall thickness. These findings coincide with those of other series.

Site of gradient

The dynamic gradient was mesoventricular, as noted, related with concentric hypertrophy and apical hypertrophic cardiomyopathy. Unlike dynamic obstruction in obstructive hypertrophic cardiomyopathy, which is located preferentially in the LVOT, it has been mentioned that the systolic obstruction in patients with concentric hypertrophy could be located in the mesocavitary zone, in the ventricular papillary muscles. The series that have detected the appearance of DIG in the postoperative period of aortic valve replacement indicate a mesoventricular site of DIG in more than 50% of cases. In our series, only 7 of the patients with DIG had LVOT obstruction, while the others (9 patients) had mesocavitary obstruction. This site was related with ventricles of small ventricular diameter and a large ejection fraction. In the postoperative period of valve surgery, when the postload had been reduced by eliminating the aortic obstruction, the volume of the ventricular cavity, already small in some cases, decreased. To this was added the reduction in blood volume due to extracorporeal circulation and the possible use of inotropic, diuretic, or vasodilator drugs, which reduce preload still more.

Clinical implications

In various articles published in the literature, an association between the appearance of DIG and the existence of more morbidity and mortality has been communicated. Aurigemma et al. found a higher mortality at 3 months in the group that developed a dynamic gradient than in the group that did not (38% versus 12%). In contrast, Bartunek et al. found a lower one-year mortality in the group that developed a dynamic gradient than in the group that did not develop it (0/14 versus 3/86), although the hospital morbidity was greater, with a significantly higher incidence of dyspnea or hypotension (64% versus 21%) and more prolonged hospital stay. Wishet et al. also found a higher rate of dyspnea, asthenia, and difficulty in postoperative mobilization, but did not draw significant conclusions due to the study design.

Unlike other published series, in our series there was no significant variation in morbidity and mortality (Tables 2 and 3), although it probably cannot be excluded that this is due to the small number of patients with a dynamic gradient, which does not allow significant conclusions to be drawn. In spite of this, in other series it has been recommended that these patients be treated with beta-blockers or verapamil to lower the intraventricular gradient and reduce ventricular hypertrophy. In our series we doubt if the use of beta-blockers is indicated, since this is a transitory situation and we have not been able to demonstrate that the gradient indicates that the prognosis is worse. We think that if the persistence of the dynamic gradient for more than 3 months were confirmed, treatment with beta-blockers could be indicated. Another approach to consider would be prophylactic myectomy during surgery for patients with DIG in LVOT or marked IVS hypertrophy.

Limitations

Among the limitations of the study was the difficulty of making recordings in the immediate postoperative period, due to the fact that patients were intubated and mechanically ventilated. In these cases of poor visualization, echocardiographic contrast agents could be used to improve the definition of the endocardial margin, as has been communicated previously. Another limitation described is the difficulty of determining the diameter of LV outflow tract in patients with massive calcification of the aortic valve. In addition, in patients with a dynamic morphology in the LVOT in baseline conditions, this originated artifacts in the determination of the aortic valve area with the continuity equation.

CONCLUSIONS

The incidence of DIG during the postoperative period of aortic valve replacement for severe AS is not unappreciable (15% in our series).

The preoperative echocardiographic factors associated with the development of DIG were small ventricular diameters, high transvalvular gradient, good overall
contractility, discrete asymmetric hypertrophy, and tendency to a small LV outflow tract.

In the patients with severe AS, there are two sites where accelerated intraventricular flow rate can exist, the LVOT and mesocavitary area. In our series, the mesocavitary site of DIG was predominant (56%).

No differences were found in this series in the morbidity and mortality of patients, which can be due to the small number of patients, since the opposite had been communicated previously.

In order to avoid the appearance of DIG during the postoperative period, the use of arterial and venous vasodilator substances, diuretics, and inotropic agents should be avoided.

After the postoperative period, DIG and the dynamic morphology disappear progressively. Only a small percentage of patients had a dynamic gradient after a year (6% in our series).

ACKNOWLEDGMENTS

We would like to acknowledge the facilities that the Cardiac Surgery Department and Cardiac Postoperative Care Unit of Hospital Vall d’Hebron provided us, and thank the nurses of these units, particularly Ms. Olga Merino, nurse of the Echocardiography Laboratory.

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