Experience with Percutaneous Aortic Valve Implantation in Patients with Severe Aortic Stenosis at High Surgical Risk in a Rural Community

Surgical aortic valve replacement is the treatment of choice for severe, symptomatic aortic stenosis. Occasionally, surgery is impossible due to old age and comorbidities. In these cases, percutaneous valve replacement is a safe and effective option for high risk patients.

The purpose of this article is to describe the experience of a consolidated working team on transcatheter aortic valve implantation (TAVI) carried out in a rural city center that admits patients from the same city or from neighboring rural towns after having systematized the technique, with follow-up until the study cutoff date.

This prospective registry was initiated after the initial experience carried out between 2013 and 2016, and after each one of the 4 interventional cardiologists obtained the certification to perform the procedure. Patients were assessed by a multidisciplinary team of clinical cardiologists, echocardiography specialists, electrophysiologists, interventional cardiologists, cardiac surgeons, and anesthesiologists. Fifty-one consecutive high-surgical risk patients with symptomatic severe aortic stenosis ruled out for conventional surgery, who underwent TAVI between 12/01/2016 and 04/30/2019 in a rural community clinic, were included.

Mean age was 78 6.1 years, and 37.2% were men. Mean-valve area measured by Doppler ultrasonography was 0.67 ± 0.27 cm2. In 92.2% of cases, patients were in functional class (FC) III, and in 7.8% in FC IV. The EuroSCORE was 15.4 ± 7.5 (Table 1). Table 1 shows patient characteristics. All the procedures were performed under deep sedation and local anesthesia. One patient required mechanical ventilation for 48 hours following the procedure due to respiratory depression. Dissection of the femoral artery was performed in all the procedures, and in 49 of the 51 cases an active fixation catheter was placed for the transient pacemaker and in the remaining 2 the stimulus was performed by the valve guidewire. In 50 cases (98%), self-expanding valves were implanted, while in the remaining case, a balloon-expandable valve was used. All the procedures were successful, resulting in a significant reduction of the aortic transvalvular peak gradient (71 ± 19 mm Hg to 5 ± 3 mm Hg; p <0.001), without development of moderate or severe post-procedure aortic regurgitation. The size of the implanted valves and the requirements of pre-or post-valve implantation valvuloplasty are described in Table 2.

Baseline ECG showed sinus rhythm in 46 patients. The remaining 5 patients presented with atrial fibrillation (9.8%). After the procedure, 21 patients presented with complete left bundle branch block (CLBBB) (41.2%) and 9 required implantation of a permanent pacemaker (17.6%) (8 due to intraprocedural complete atrioventricular block (CAVB), and 1 due to CLBBB with first-degree atrioventricular block (AVB) with prolonged HV interval). One patient required pericardial drainage due to signs of cardiac tamponade 24 hours after the procedure. Median length of hospital stay was 3 days (IQR 25-75: 2-5 days) (Table 2). No deaths occurred during the procedure or hospitalization. Follow-up after discharge was at 15 and 30 days, and at 6 months in the doctor's office, where a complete physical examination was performed and the evolution, symptoms, FC and control ECGs at 30 days and 6 months were evaluated. Follow-up during the evolution was coordinated with the primary cardiologist of the patient's home town. In addition to the scheduled visits, a telephone follow-up was carried out in which survival, hospitalization, intercurrences, and FC were recorded. Three deaths from non-cardiac cause occurred during follow-up. Median follow-up was 431 days (IQR 258-595 days). Six patients had to be hospitalized during follow-up: 3 for dyspnea, 1 for pseudoaneurysm at the site where the arterial introducer was placed (contralateral to the dissected artery), 1 for infection at the surgical site, and 1 for syncope.

Table 1. Baseline population characteristics

Age (years)	78 ± 6.1
Female sex % (n)	62.8% (32)
Logistic EuroSCORE	15.4 ± 7.5
NYHA III dyspnea % (n)	92.2 (47)
NYHA IV dyspnea % (n)	7.8 (4)
Coronary heart disease % (n)	62.7 (32)
Previous cardiac surgery % (n)	5.9 (3)
Diabetes % (n)	19.6 (10)
Peripheral vascular disease % (n)	82.3 (42)
COPD % (n)	29.4 (15)
Renal dysfunction % (n)	51 (26)
Pulmonary hypertension % (n)	52.9 (27)
History of thoracic radiation % (n)	5.9 (3)
History of aortic valve replacement	9.8 (5)
Atrial fibrillation % (n)	9.8 (5)
Ejection fraction	47.7 ± 18 %
Ejection fraction 30% - 50%	43.1 (22)
Ejection fraction <30%	9.8 (5)
Aortic valve area (cm2)	0.67 ± 0.27
Mean gradient (mmHg)	45 ± 16
Maximum gradient (mmHg)	71 ± 19

NYHA: New York Heart Association. COPD: Chronic obstructive pulmonary disease.

Table 2. Procedure and patient follow-up

PROCEDURE (N= 51)	
Anesthesia: Local anesthesia or conscious sedation, % (n)	100 (51)
Mortality, % (n)	0
Cardiac tamponade, % (n)	2% (1)
Stroke, % (n)	0
Vascular complications, % (n)	3.9% (2)
Hospitalization (days), median (IQR 25-75)	3 (2-5)
Post-TAVI maximum gradient (mmHg)	5 ± 3 mm
Aortic regurgitation	
0, % (n)	62.7 (32)
I, % (n)	35.3 (18)
II, % (n)	2 (1)
III-IV, % (n)	0
Permanent pacemaker implantation, % (n)	17.6 (9)
Requirement of valvuloplasty prior to valve replacement, % (n)	60.8 (31)
Requirement of valvuloplasty after valve replacement, % (n)	23.5 (12)
No requirement of valvuloplasty in valve implantation, % (n)	35.2 (18)
Prosthetic valve size	
#23, % (n)	2 (1)
#25/26, % (n)	39.2 (20)
#29, % (n)	50.9 (26)
#31, % (n)	5.9 (3)
#34, % (n)	2 (1)
Prosthetic valve type	
CORE-VALVE, % (n)	27.4 (14)
CORE-VALVE EVOLUT R, % (n)	60.8 (31)
SAPIEN XT, % (n)	2 (1)
ACURATE neo/TF, % (n)	7.8 (4)
PORTICO, % (n)	2 (1)
FOLLOW-UP	
Follow-up (days), median (IQR 25-75)	431; (258-595)
NYHA I, % (n)	90.2 (46)
Post-TAVI valve area (cm2)	1.82 ± 2
Post-TAVI mean gradient (mmHg)	8.3 ± 5
Mortality, % (n)	5.9 (3)
Hospitalizations, % (n)	11.8 (6)

NYHA: New York Heart Association. TAVI: Transcatheter aortic valve implantation

Improvement in FC was observed in all patients during follow-up, with progress to FC I in 90.2% of cases (Table 2). In our case, results were consistent with other national registries. (1) The absence of mortality, the success of all the procedures and the significant improvement in patient FC support our conclusion. The need to provide adequate medical care poses a dilemma to institutions in rural areas, which must assume greater challenges, with a demand for better results based on a historical perception of lower performance in procedures requiring more technology in these areas. These results were achieved due to the systematization of the procedure and the team expertise. In addition to a short hospital stay (median 3; IQR 2-5 days), the cost-benefit analysis of performing this type of procedure in the patient's town or in neighboring cities could also be considered favorable, since it allows patients to remain in their environment, in permanent contact with the attending physician in charge of their follow-up, and also prevents their family members travel expenses and higher costs for lodging and meals in larger cities. (2) Aortic valve replacement under local anesthesia or conscious sedation, avoidance of orotracheal intubation, procedure systematization and patient follow-up are also associated with the short hospital stay. (3)

Regarding the acute intercurrences derived from the procedure, 9 patients required implantation of a permanent pacemaker due to conduction disorders, and 1 patient required drainage due to cardiac tamponade. With the evolution of implantable devices, the trend for pacemaker use has been decreasing both in published registries and in our series, where pacemaker implantation was required in 3 of the last 25 patients (12%). (4) The use of premeasured chordal loops is a very important factor in preventing cardiac tamponade, an intercurrence observed in only one case of our series. In this regard, active fixation pacemaker leads or guidewires are also convenient.

A significant improvement in patient FC was detected during follow-up, with 3 deaths (5.9%) from non-cardiac cause. The information on long-term follow-up of patients undergoing percutaneous aortic valve implantation available in the literature is limited. Mortality rate at 5 years ranges between 50%-70%. (5, 6) According to published data, the highest mortality rate occurs in the first follow-up year, at the expense of the first month, due to complications derived from the procedure. (6) After hospital discharge, the main cause of death is non-cardiac, due to the comorbidities in this population. (5, 6) Since no mortality was associated with the procedure in our series, long-term follow-up of this population is important in order to quantify survival and determine the causes of death.

In conclusion, treatment of severe aortic stenosis with percutaneous valve replacement in high surgical risk patients – who were ruled out for conventional surgery –is a feasible alternative in patients from a rural community. The adequate selection of our patients, the systematization of the procedure technique, and a multidisciplinary approach increase its effectiveness and safety.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material).

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Intoxication with Psychotropic Drugs and Indication for ECMO

This is the case of a 25-year-old female patient with a history of several autolytic attempts due to drug intoxication, the latest resulting in hospitalization in the Critical Care Unit in December 2016.

On June 25, 2016, at 10 pm, the patient was taken by her mother to the Emergency Room; since she was admitted with Glasgow 4/15, orotracheal intubation (OTI) and mechanical ventilation were performed. A nasogastric tube was inserted and gastric lavage was performed, removing some tablets, and treatment by serial activated charcoal in combination with laxatives was initiated.

A friend of the patient mentioned that she had ingested a great number of tablets early in the morning.

A blister of medications was provided: alprazolam 30 mg, amitriptyline 1,250 mg, valproic acid 7,500 mg, and pregabalin 1,500 mg. ECG and lab tests on admission were normal. The plasma concentration of valproic acid was 309 μg/m, and chest x-ray showed an image consistent with bronchoaspiration.

On June 28, 2016, the patient presented with cardiopulmonary arrest due to ventricular fibrillation and cardiopulmonary resuscitation was performed for 20 minutes. The patient progressed with distributive and cardiogenic shock, requiring high doses of vasoactive drugs.

In view of shock refractoriness, A-V ECMO (Extracorporeal Membrane Oxygenation) for systemic assistance was indicated, reducing the inotropic support and showing slow improvement. On the third day of ECMO support, the patient showed improvement and was progressively weaned from ECMO, which was removed on day 4. Then, mechanical ventilation was removed on day 5, after a short weaning period.

EMCO is a standard technique for the treatment of refractory cardiogenic shock and cardiac arrest induced by drug intoxication. (1) Cardiac arrest may occur during the course of intoxication with psychotropic drugs. Awareness of the severity of a toxic cardiac arrest should allow shortening the times of ECMO indication and placement before the cardiac arrest occurs.

ECMO is a therapeutic tool in cardiotoxicity due to tricyclic antidepressants, since it is a short-term ventricular assist device with easy placement and weaning which provides hemodynamic and systemic support. (2) It also allows the reduction or discontinuation of inotropic agents that perpetuate cardiotoxicity.

The toxic dose of amitriptyline is >5mg/kg; a dose between 10 and 20 mg/kg results in severe toxicity, and >25 mg/kg is lethal. Amitriptyline causes sinus tachycardia, hypotension, ventricular tachycardia and

Fig. 1. ECMO used during patient treatment.

Fig. 2. ECMO machine connected to the patient.

fibrillation, and ECG alterations (widening and deformation of QRS and prolonged QT interval). (3)

Intoxication due to tricyclic antidepressants is a severe entity. Resuscitation should be rapid, with gastric lavage and serial activated charcoal; plasmapheresis on hemodialysis is recommended within the first hours, and ECMO should be considered in intoxicated patients experiencing cardiac arrest or severe shock.

ECMO is an ideal support in intoxication due to tricyclic antidepressants, because a short-term assistance provides hemodynamic and respiratory support until intoxication is overcome and inotropic agents are discontinued. (4)

Tricyclic antidepressants are used to treat a wide spectrum of conditions. The pharmacological group of antidepressants is the second most common cause of intoxication, and within this group, tricyclic antidepressants produce greater morbidity and mortality secondary to significant cardiovascular and neurological toxicity. (5) It is very important to keep in mind that, in case of tricycle antidepressant intoxication, referral to a center with ECMO availability should be considered. (6)

Conflicts of interest

None declared.

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Neonatal Aortic Coarctation

Coarctation of the aorta (CoA) refers to a narrowing of the artery that causes obstruction of blood flow. It is typically located at the insertion of the ductus arteriosus at the origin of the left subclavian artery. It accounts for 8 to 10% of all congenital heart defects with a reported prevalence of approximately 4 per 10,000 live births and a 2:1 male/female ratio. (1) The precise pathogenesis is unknown, but the two main theories for the development of congenital CoA are the reduction of antegrade intrauterine blood flow from the aortic arch causing its underdevelopment, or the migration or extension of ductal tissue into the wall of the fetal thoracic aorta. Pathological examination shows hypertrophy of the middle layer of the posterior wall of the vessel that protrudes into the interior and reduces the aortic lumen. (2) Clini-

cal manifestations vary according to patient age and severity of the lesion, and may range from asymptomatic patients to patients with acute circulatory shock.

We present the case of a 4-day-old male newborn. The 23-year-old primigravida mother underwent 10 prenatal check-ups and 3 obstetrical ultrasounds with normal results. The neonate was born by Cesarean section due to compromised fetal well-being, at full-term 38.2 weeks of gestation, APGAR: 8-9, and anthropometric measurements according to age. He was referred to the Department of Neonatology due to respiratory distress (Sat O2: 84% with Fi O2: 21%, nasal flaring, respiratory grunting, subcostal retraction and tachypnea (RR: 64 x min.), and hyperbilirubinemia (total bilirubin: 16.5 mg/dl). Physical examination revealed a grade IV/VI systolic murmur focusing at the base of the heart; no organomegaly was palpated, and pulses were positive and symmetrical. Complete blood count with acute phase reactants showed no alterations, and chest teleradiography showed a slight increase in cardiothoracic index. ECG on admission reported a 6.9 mm patent ductus arteriosus (PDA), moderate pulmonary hypertension, and global cardiac dilatation, so pharmacological closure of PDA with oral ibuprofen was indicated for 3 days, with fluid restriction and furosemide.
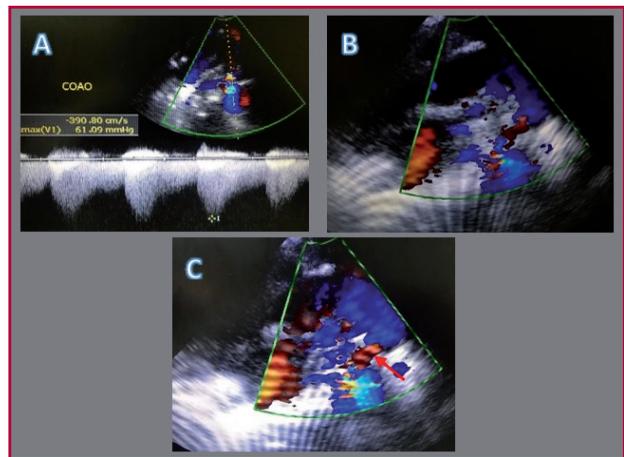
A cardiovascular control at 72 h reported a 4.4 mm PDA with hemodynamic repercussion, so a second course of oral ibuprofen was started with no positive response. Therefore, upon consultation, the Department of Cardiothoracic Surgery recommended surgical closure. On the 7th day of hospitalization, the ductus was ligated in the operating room with a titanium clip using a right posterolateral approach, without complications. The patient was transferred to the neonatal intensive care unit for 3 days under mechanical ventilation, on antibiotic therapy, and inotropic and nutritional support.

Extubation was then achieved, and the patient was transferred to the Intermediate Care Unit, where he was stable for about 8 hours. Suddenly, the patient presented with cardiovascular and respiratory deterioration (Downes score 8) that required mechanical ventilation with high parameters. Because of the abrupt onset of those symptoms, an ECG was requested, which reported a possible CoA due to pressure gradient of 61 mmHg, diastolic runoff and pulmonary pressure of 37 mmHg (Figure 1 A-C). A chest CT angiography with contrast revealed severe stenosis of the descending aorta after the left subclavian artery, with discrete post-stenosis dilatation of the descending aorta (11 mm), tortuosity and dilatation of the right and left internal mammary arteries, and also of the intercostal arteries (Figure 2 A-C). At 11 days of age, the Department of Cardiothoracic Surgery performed extended coarctectomy and end-to-end anastomosis, without complications.
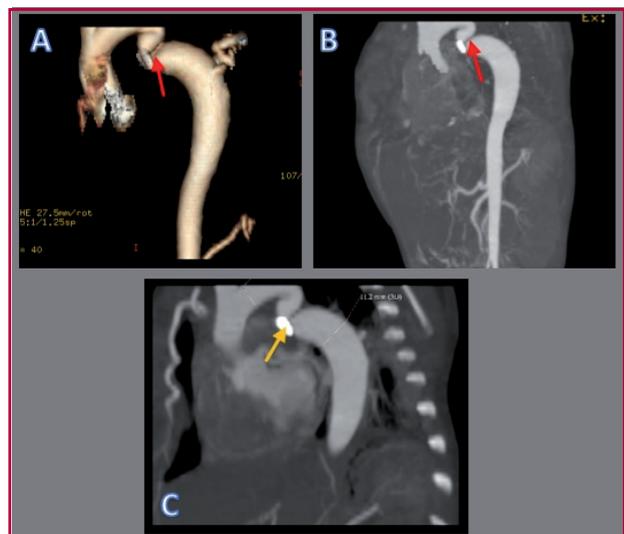
Extubation was achieved 48 hours after the co-

arctectomy, with adequate tolerance. Enteral feeding was initiated once the patient was hemodynamically stable, with good weight gain and favorable course, being discharged after 43 days of hospitalization with home O2 therapy, ASA, and enalapril. At 3 months of age, control echocardiography showed normal, competent aorta; no stenosis was observed in the juxtaductal region, and the left ventricle and pulmonary pressure were normal.

In conclusion, this is a case where CoA is diagnosed after surgical closure of PDA, which could not be visualized in the first controls due to the large size of the ductus, causing sudden decompensation of the neonate with several criteria (critical CoA, coarctation gradient >20 mmHg, and radiological evidence of significant collateral circulation) (3)

Fig. 1. A. Pressure gradient of 61 mmHg at the coarctation site (severe) and "diastolic runoff". **B.** Aortic arch (blue) and coarctation segment (red) can be observed. **C.** Coarctation at the juxtaductal region (*red arrow*).

Fig. 1. A & B. Chest CT angiography showing the aortic coarctation site (*red arrows*). C. Titanium clip adjacent to the coarctation site (*yellow arrow*).

for urgent intervention according to the American Heart Association and the American College of Cardiology. Coarctectomy with end-to-end anastomosis has excellent results, and the incidence of late re-interventions is low; however, recoarctation should be considered as a potential long-term complication. (4) Proper management of systemic hypertension is an important aspect to improve survival rate. (5) In our patient, the ACEI was stopped at 3 months of age, with controls of blood pressure within the percentiles for his age. The estimated 10-year survival after repair is >90%, and mortality rate is <1% – which is influenced by age, type of surgery, and associated comorbidities. (6) A detailed physical examination together with fetal echocardiography should be performed, as this will allow early detection and timely corrective management of CoA, thus reducing cardiovascular complications in childhood and adulthood.

Conflicts of interest
None declared.

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Gonococcal Endocarditis: A Rare Complication of an Emerging Disease

Gonorrhea is a sexually transmitted infection (STI) caused by Neisseria gonorrhoeae, a fastidious growing Gram-negative diplococcus. It is manifested with urethritis or cervicitis, and its incidence is estimated at 600,000 cases annually in the USA. (1) Disseminated infection occurs in 1–3 % of all gonococcal infections, and it may manifest as polyarthritis, tenosynovitis, septic arthritis, and endocarditis. Endocarditis develops in 1–2 % of these disseminated infections. In 1933, the first case of gonococcal heart valve disease was reported, and between 1939 and 2014, only 70 cases were reported in the literature worldwide. (2)

We present the case of a 32-year-old male patient, immunocompetent host, heterosexual, with risky sexual behaviors, without previous heart valve disease or other relevant history. The patient presented with a self-limited episode of urethral secretion, and after three weeks, asymmetrical, additive polyarthralgias of large and small joints involving his hands. It was interpreted as acute nonspecific tenosynovitis and was therefore treated with corticoids and NSAIDs. After about two weeks, the patient progressed to persistent fever syndrome, subungual splinter lesions, and subconjunctival petechiae associated with systolic murmur in a mitral focus of 3/6 intensity. No edema or other signs of heart failure were present. In view of suspected infective endocarditis, empirical treatment with ampicillin, gentamicin, and ceftriaxone (CTX) was initiated after collecting three blood cultures (BC) by automated method.

Lab test results were the following: WBC 16,220/mm3; ESR 130 mm/1º h; CRP 15 mg/dL and urine sediment revealed microhematuria.

Transthoracic echocardiography (TTE): Heterogeneous tumor on the atrial side of the mitral valve major leaflet with a broad implantation base over the leaflet and high motility towards both the atrium and the ventricle at end diastole. Diameters were 27 mm x 17 mm. It caused moderate mitral regurgitation, considering the antegrade velocity and the jet that contacts with the atrial posterior wall by color Doppler. Systolic function was preserved.

Transesophageal echocardiography (TEE): Tricuspid aortic valve. In the anterior leaflet of the mitral valve, an attached image was visualized with a wide base of implantation and heterogeneous echogenicity of 2.67 cm x 1.47 cm maximum diameter, which prolapsed towards the left ventricle at end diastole. A smaller image, 0.56 cm x 0.77 cm, was also observed in the posterior leaflet. Both findings were consistent with vegetations. Doppler showed two jets of mitral regurgitation (Figure 1).

Three blood culture samples were collected in Bactec Aerobic/F bottles. Seventeen hours later, 3/3 were positive. A Gram stain revealed gram-negative diplococci. Neisseria gonorrhoeae was identified in

culture by manual methods and confirmed by molecular biology (conventional PCR). The patient continued on intravenous treatment with CTX (IV) 2 g/day. No signs of heart failure were observed, but given the size of the vegetation, valve replacement with mechanical prosthesis was performed. No bacterial development was obtained either in control BC or in culture of referred surgical material (vegetation); however, the germ was confirmed by PCR technique in valve tissue, and the coexistence of Chlamydia trachomatis was ruled out. The patient completed a six-week course on antibiotics with good clinical progress, and did not present mechanical post-surgical complications. Oral anticoagulation was started due to the mechanical valve replacement.

According to what has been published so far, disseminated infection only occurs in 1–3 % of all gonococcal infections, with scarce genital symptoms and more frequent in women. (2) In contrast, endocarditis is more common in males. The coexistence of Chlamydia trachomatis in disseminated forms of the disease is described. According to the literature, the main characteristics of this entity are a median time of 4 weeks from the onset of symptoms to the diagnosis. It affects young male adults, with native and healthy heart valve involvement, mainly the aortic and mitral valves in order of frequency, and is manifested with heart failure of acute evolution. Its onset may be preceded by osteoarticular manifestations (arthritis, myositis). In our case, the patient presented with osteoarticular manifestations consistent with the data in the literature, but differently from other reports, had also symptoms of urethritis a few weeks before the onset. Clinical manifestations of infective endocarditis (IE) do not differ from those caused by common germs, and include fever, heart murmur, tachycardia, embolic phenomena and splenomegaly. Anemia, leukocytosis and increased concentration of reactants in the acute phase can be identified in lab tests. Echocardiography (TTE and TEE) shows large-sized vegetation associated with valve thickening and dysfunction. Blood cultures are positive in more than 90% of cases, unlike other disseminated forms of gonococcal infection in which it varies between 10% and 30%. Development of disseminated forms occurs in susceptible hosts, including: complement deficiencies, systemic lupus erythematosus (SLE), and HIV infection, among others. Some characteristics of the strains are associated with disseminated forms: absence of surface II protein, which confers resistance to destruction by natural killer cells, and expression of the IA protein, which provides serum resistance and easy membrane crossing. Our patient was treated with glucocorticoids and it could have contributed to the development of this complication. Among the differential diagnoses, infective endocarditis should be considered with other more frequent etiologies and autoimmune rheumatologic diseases such as systemic lupus eythromatosus (SLE) and rheumatoid arthritis (RA), among others.

In the preantibiotic era, gonococcal endocarditis caused 11-26% of the total infective endocarditis, and was associated with high mortality rate. (3) Even with the advent of antibiotics, the mortality rate remains high, close to 20%. Nowadays, it is a rare complication, but it should be considered in light of the emergency of sexually transmitted infections. (4) We should consider gonococcal endocarditis as a diagnostic possibility in young adult patients presenting with osteoarticular manifestations and stigmas suggestive of infective endocarditis. It often presents with few genitourinary symptoms and greater osteoarticular repercussion. (5) A high index of suspicion is essential due to the fatal prognosis without proper treatment. In addition, coexistence of Chlamydia trachomatis should also be taken into account. Regarding the antibiotic therapy, CTX continues to be the drug of choice according to the sensitivity profiles in Argentina.
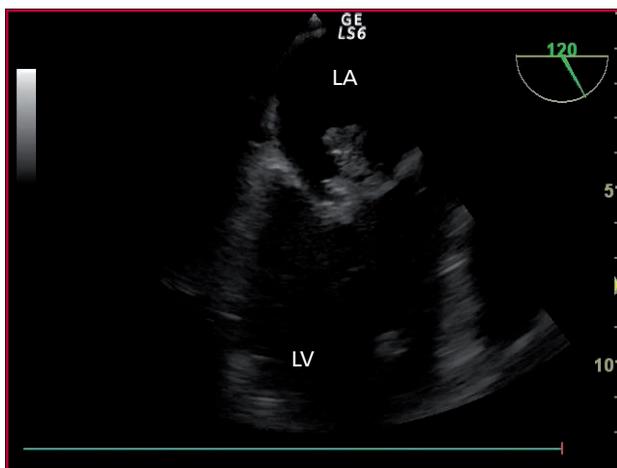

Fig. 1. TEE image showing vegetation. LA: Left atrium. LV: Left ventricle.

Conflicts of interest
None declared.
    (See authors' conflicts of interest forms on the website/ Supplementary material).

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