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Clinico-epidemiological characterization with a surgical approach of infective endocarditis in the central region of Cuba

Alain Allende González, MD; Gustavo de J. Bermúdez Yera, MD, MSc; Roger Mirabal Rodríguez, MD, MSc; Yolepsis F. Quintero Fleites, MD; Yoandy López de la Cruz, MD, MSc; and Ernesto Chaljub Bravo, MD

Department of Cardiovascular Surgery, *Hospital Provincial Cardiocentro Ernesto Che Guevara*, y *Universidad de Ciencias Médicas* (University of Medical Sciences) *de Villa Clara*. Santa Clara, Villa Clara, Cuba.

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Abbreviation
IE: infective endocarditis

ABSTRACT

Introduction: Infective endocarditis has not decreased its incidence and mortality in the last 30 years.

Objective: To characterize patients operated on due to diagnosis of active infective endocarditis.

Methods: A retrospective, descriptive study was carried out, which included 109 patients with a diagnosis of this disease, who underwent surgery at Cardiocentro Ernesto Che Guevara (Cuba), from July 2010 to June 2018. The information was obtained from the medical records and the surgical report.

Results: Prosthetic valve infective endocarditis was diagnosed in 15 patients (13.8%), but the most frequent was the one related to intracardiac device colonization (51.4%), reason why the most used surgical procedure was the change of the electrical stimulation system. The main surgical indication was the uncontrolled infection in 63 cases (57.8%), followed by heart failure (38 patients; 34.9%) and in 67 cases (61.5%), the blood cultures were negative. The native valve replacement for a mechanical prosthetic valve was performed in 28 patients (25.7%), of which 15 (13.8%) were in mitral position. The replacement of a mechanical prosthetic valve for another with the same characteristics was carried out in 14 (12.8%) cases, 8 (7.3%) of them were mitral. Overall mortality was of 17.4%, more evident in those with left-side prosthetic valve endocarditis (7/15).

Conclusions: Male gender and age over 60 years old predominated, as well as the presence of vegetations on intracardiac devices, and negative blood cultures. The prosthetic valve endocarditis was significantly associated with mortality.

Keywords: Infective endocarditis, Cardiac surgery, Intracardiac device, Heart valves, Mortality

Caracterización clínico-epidemiológica con enfoque quirúrgico de la endocarditis infecciosa en la región central de Cuba

RESUMEN

Introducción: La endocarditis infecciosa no ha disminuido su incidencia y mortalidad en los últimos 30 años.

Objetivo: Caracterizar los pacientes operados por diagnóstico de endocarditis infecciosa activa.

Método: Se realizó un estudio descriptivo retrospectivo que incluyó a 109 pacientes con diagnóstico de esta enfermedad y fueron intervenidos quirúrgicamente en

✉ *A Allende González*
Cardiocentro Ernesto Che Guevara. Calle Cuba 610, e/ Barcelona y Capitán Velasco. Santa Clara, CP 50200. Villa Clara, Cuba.
E-mail address:
alainag@infomed.sld.cu

Authors' contribution
AAG and GJBY: Idea and design of the research; obtaining, analyzing and interpreting the data, as well as writing the manuscript.
RMR and YFQF: Raw data collection and helped to draft the manuscript.
YLC and ECB: Conception of the research, analyzing and interpreting the data.
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el Cardiocentro Ernesto Che Guevara (Cuba) desde julio de 2010 hasta junio de 2018. La información se obtuvo de las historias clínicas y el informe operatorio.
Resultados: La endocarditis infecciosa sobre válvula protésica fue diagnosticada en 15 pacientes (13,8%), pero la más frecuente fue la relacionada con la colonización de dispositivos intracardíacos (51,4%), razón por la que el procedimiento quirúrgico más utilizado fue el cambio de sistema de estimulación. La principal indicación quirúrgica fue la infección incontrolada en 63 casos (57,8%), seguida por la insuficiencia cardíaca (38 pacientes; 34,9%) y en 67 casos (61,5%) los hemocultivos resultaron negativos. La sustitución de la válvula nativa por una prótesis mecánica se realizó en 28 pacientes (25,7%), de los cuáles 15 (13,8%) fueron en posición mitral. El recambio de una prótesis mecánica por otra de igual características se llevó a cabo en 14 (12,8%) casos, 8 (7,3%) de ellos mitrales. La mortalidad global fue de 17,4%, más evidente en aquellos con endocarditis sobre válvula protésica izquierda (7/15).
Conclusiones: Predominaron el sexo masculino y la edad mayor de 60 años, así como la presencia de vegetaciones sobre dispositivos intracardíacos y los hemocultivos negativos. La endocarditis sobre válvula protésica se asoció significativamente con la mortalidad.
Palabras clave: Endocarditis infecciosa, Cirugía cardíaca, Dispositivo intracardíaco, Válvulas cardíacas, Mortalidad

INTRODUCTION

Infective endocarditis (IE) is a rare disease in the general population[1]. Its incidence and mortality have not decreased in the last 30 years, and it is not a uniform disease, but it is present in a variety of forms that vary according to the initial clinical manifestation, the underlying heart disease (which usually exists), the involved microorganism, the presence or absence of complications and the characteristics of the patient. The IE is a changing disease, with variations in its microbiological profile, a higher incidence of healthcare related cases, in elderly patients and in patients with cardiac devices or prostheses[1]. In contrast, cases related to rheumatic disease are now less frequent in industrialized countries[1-2].

Infective endocarditis is part of two major current health problems[2]: infectious diseases and cardiovascular diseases. Its mortality is high, between 15 and 38% of treated cases, although in some less developed and less well-resourced countries it is as high as 50%; and, of course, it is close to 100% in untreated cases[3-5]. The hospital mortality rate in patients with IE ranges from 9.6 to 26%, but it considerably differs from one patient to another.

The Cardiocentro Ernesto Che Guevara, a tertiary care center and a reference institution in the central region of Cuba for the diagnosis and treatment of cardiovascular diseases, with recognized national and international prestige, is propitious for the compilation of descriptive data of patients with this disease, in order to continue developing an area of research in this field and to establish new measures and interventions that might contribute to prevention, diagnosis and treatment of this disease in the future; all of which justifies the development of this work, with the aim of characterizing some clinico-epidemiological and surgical variables, including mortality, in patients operated on for active IE.

METHOD

A retrospective descriptive study was carried out in all patients (109) diagnosed with active infective endocarditis, who underwent surgery, as part of their treatment, at Cardiocentro Ernesto Che Guevara from Santa Clara, Cuba, from July 2010 to June 2018.

Demographic and clinico-bacteriological variables were analyzed, and the related risk factors, classification of the disease, the surgical technique used, the most frequent complications in these patients, and mortality were established.

Information was collected from individual medical records and the surgical report. The obtained data were statistically processed using the SPSS 17.0 program and are presented in tables and graphics.

The information was summarized according to

the type of variables, for the qualitative ones, numbers and percentages were used, and for the quantitative ones, minimum, maximum, mean and standard deviation values were used. In order to determine associations between the qualitative variables, the significance associated with Fisher's exact test was used, and for quantitative variables, the Mann-Whitney U test. The associations between the analyzed variables were considered significant according to the obtained p-value, which was considered significant when $p<0.05$. The odds ratio (OR) and its 95% confidence interval were calculated as risk measures.

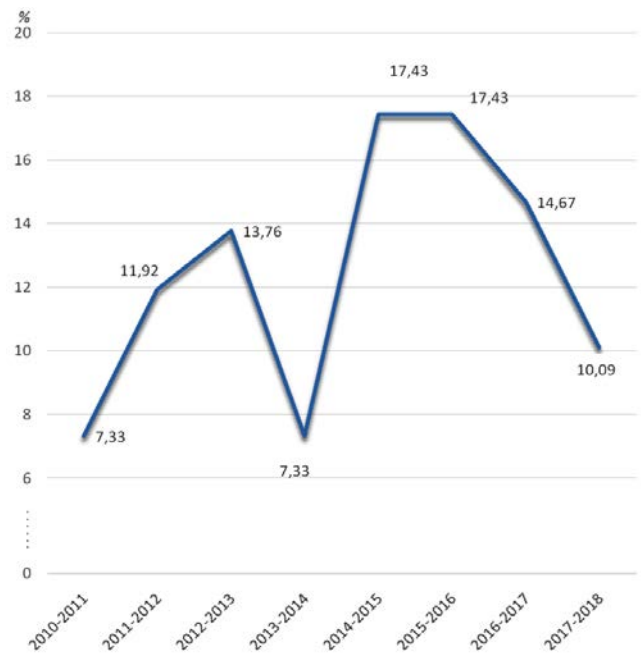

Figure 1. Chronological behavior of infective endocarditis with indication of surgical treatment at Cardiocentro Ernesto Che Guevara (July 2010 - June 2018).

RESULTS

When analyzing the behavior of the IE along the studied time interval (**Figure 1**), its increasing trend is highlighted, although more data should be collected to ensure that this trend is maintained.

From the 109 patients who made up the sample, 85 were men (77.9%) and 45 (41.3%) belonged to the group of 60 years and older) (**Table 1**). The average age was 55.5 and 52.9 years old for men and women, respectively, and no significant differences were found.

Table 1. Difference in age groups according to sex.

Age groups (years)	Sex				Total (n=109)	
	Female (n=24)		Male (n=85)			
	Nº	%	Nº	%	Nº	%
Under 30	3	12.5	6	7.1	9	8.3
30 - 44	5	20.8	15	17.6	20	18.3
45 - 59	7	29.2	28	32.9	35	32.1
60 and over	9	37.5	36	42.4	**45**	**41.3**

Fever and new or changing heart murmurs were the main symptoms and signs found

The location of the vegetations shows that in most patients (51.4%) they settled on intracardiac devices (**Table 2**), and prosthetic valve IE (15 patients; 13.8%) was subdivided into early (6/15) and late (9/15). In 26.6% of cases, endocardial colonization occurred on native valves.

Table 2. Distribution of patients according to the location of the infective endocarditis.

Classification	Nº	%
Left-sided native valve	29	26.6
Left-sided prosthetic valve (6 early and 9 late)	15	13.8
Right	9	8.2
Related to intracardiac devices	56	**51.4**

Regarding microbiology (non tabulated data), only 42 patients (38.5%) showed positive blood cultures; in the remaining 61.5%, the blood samples obtained at Cardiocentro Ernesto Che Guevara were negative. There were patients to whom more than one germ was isolated on different occasions, and the most commonly found microorganism was staphylococcus (16.5%), with a predominance of co-

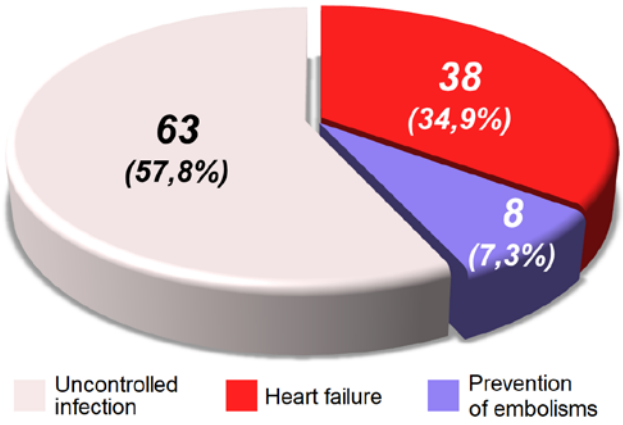

Figure 2. Main surgical indication.

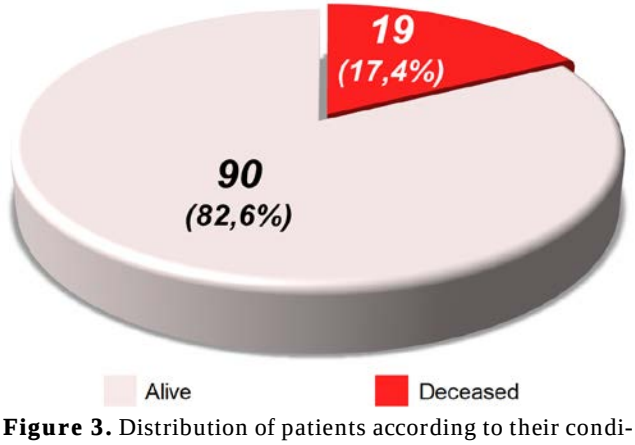

Figure 3. Distribution of patients according to their condition at the time of discharge.

agulase-negative, followed by the group of streptococcus and pseudomonas, which grew in continuous culture in six patients (9.84%) and, in a smaller percentage, acinetobacter and stenotrophomona maltophilia. From the 15 patients with prosthetic valve IE, only 5 had positive blood cultures; all of them with early endocarditis.

The main surgical indication was uncontrolled infection in 63 cases (57.8%), followed by heart failure, which led to surgery in 38 patients (34.9%), and prevention of embolisms due to large vegetations (**Figure 2**).

In **table 3** is shown the distribution of patients according to the used surgical technique. The most used procedure was the change of system on devices for programmed electrical stimulation (44.9%); extraction of the endocardial system and placement of another, usually epicardial, was performed. The valve repair technique was only performed in right-sided infective endocarditis (13.8%): 13 tricuspid and 2 pulmonary valvuloplasties, including a reconstruction with autologous pericardium. Native valve replacement by mechanical prosthesis (25.7%) was necessary in 15 cases of mitral valve replacement (13.8%), 8 (7.3%) aortic and 2 tricuspid (1.8%), the rest were double valve (mitroaortic) replacements. Prosthesis replacements were also performed (12.8%), biological prosthesis implantation (4.6%) and other associated procedures (11.0%).

The most frequent post-operative complications were acute respiratory failure, low cardiac output and some other disorders of cardiac rhythm and conduction.

There were 19 deaths in total (**Figure 3**), representing 17.4% of the total sample; but it is important to point out that mortality from prosthetic valve endocarditis –all of them left-sided– was of 46.7% (7/15) which, at the same time, represented the 36.8% (7/19) of the total number of deaths (**Table 4**), and it was the only type of endocarditis, according to its location, which was significantly associated with mortality, with a risk of death of approximately six times higher (OR 5.97, CI 2.88-66.07, p=0.001) than those who do not have IE on a left-sided prosthetic valve (mitral or aortic).

DISCUSSION

Our results regarding sex and age of the studied patients coincide with those of the other authors[6-9], which corresponds with the epidemiological changes that have taken place in the disease in recent decades. Ramírez *et al*[10], in an article about the results of surgical treatment of infective endocarditis at the *Instituto de Cardiología y Cirugía Cardiovascular* in Havana, showed male predominance of 70.5% and the age group with the highest incidence was 60 years and older (23.4%). Perdomo Garcia *et al*[11], in a study from 1988-2008 at the *Cardiocentro* of Santiago de Cuba, reported a predominance of men (62.5%) and the 15-45 year old age group; while Al Abri *et al*[12], in a study carried out at a tertiary level hospital in Oman, found 69% of male patients with infective endocarditis, and Eusse *et al*[13], in Colombia, found that 68.5% of their patients were men, with a mean

Table 3. Distribution of patients according to the used surgical technique (n=109).

Surgical Technique	Nº	%
Valve repair	**15**	**13.8**
Replacement of native valve by mechanical prosthesis		
- Mitral	15	**13.8**
- Aortic	8	7.3
- Mitroaortic	3	2.8
- Tricuspid	2	1.8
Prosthetic valve replacement with new mechanical prosthesis		
- Mitral prosthesis	8	7.3
- Aortic prosthesis	4	3.7
- Mitroaortic prosthesis	2	1.8
Replacement of native valve for biological prosthesis		
- In tricuspid position	4	3.7
- In aortic and tricuspid position	1	0.9
Other associated procedures		
- Excision of a mass from a pulmonary artery branch	1	0.9
- Ring expansion with pericardial patch	1	0.9
- Primary closure of ventricular septal defect	1	0.9
- Ventricular septal defect closure with pericardial patch	2	1.8
- Ventricular septal defect closure + right lower lung lobectomy	1	0.9
- Primary closure of patent foramen ovale	1	0.9
- Coronary artery bypass grafting	3	2.8
- Repair of the non-coronary sinus of Valsalva aneurysm	1	0.9
- Repair of the left sinus of Valsalva aneurysm	1	0.9
Change of stimulation system	49	**44.9**

Table 4. Relationship between the condition at the moment of discharge and the classification of the infective endocarditis, according to its location.

Endocarditis location	Condition at the moment of discharge		Total (109)	OR CI (95%)	p (exact)
	Alive (n=90)	Deceased (n=19)			
Left-sided native valve	26 (28.9)	3 (15.8)	29 (26.6)	0.31 (0.06-1.42)	0.182
Left-sided prothesic valve	8 (8.9)	**7 (36.8)**	15 (13.8)	**5.97 (2.88-66.07)**	**0.001**
Right	9 (10.0)	0 (0.0)	9 (8.2)	-	0.330
Associated to mechanical intracardiac devices	47 (52.2)	9 (47.4)	56 (51.4)	0.86 (0.22-3.31)	1.000

Data show n(%). CI, confidence interval; OR, odds ratio

age of 57.5 years old and only 14.8% of the total corresponded to patients over 60 years old, contrary to what was reported in the literature for populations from developed countries such as the United States and Europe, where more than 50% of IE occurs in this age group.

Francischetto *et al*[8], in Sao Paulo, found a higher incidence of IE in left-sided native valves, while Watt *et al*[14], in Thailand, do not even mention endocarditis on the pacemaker electrode, which is very frequent in other media, including ours. A proportion greater than 43% was found by Castillo *et al*[15], whereas Al Abri *et al*[12] have reported up to 82.7% of endocarditis on native valves. The incidence of endocarditis on prosthetic valves in our study was in an international range, with an incidence of 10-30%, in France 16% and in a European study 26%, all quoted in the 2015 guidelines of the European Society of Cardiology for the treatment of IE[16]. On the other hand, in Oman, this incidence was 15.6%[12], very similar to that one found in the series of the national cooperative study from Chile (14.5%)[17].

Other studies[9,13] have shown greater involvement of the mitral valve apparatus, and some of the aortic one (in Thailand)[14]; probably related to the higher incidence of rheumatic heart diseases as befits countries with limited resources. Eusse *et al*[13] found disturbance of the mitral valve apparatus in 44.5% of cases and 7.5% of 2-valve involvement; while for Ramirez *et al*[10] the mitral one was affected in 21.4% and the aortic one in 16.1% of their patients. However, in a study of 165 patients with native valve infective endocarditis in Germany, who were referred for surgical treatment, the most affected valve was found to be the aortic one (50.3%), followed by the mitral one (20%), the tricuspid one (10.6%) and the pulmonary one (1.2%)[18].

The latest European guidelines[16] expose up to 31% of cases with negative blood cultures, and other studies report figures between 10-30%[13] and 19%[12]. Even in countries where classic disease patterns persist, such as Tunisia, up to 50% of blood cultures without growth are found[1]; but all these data differ from our results where a high percentage of negative blood cultures were obtained (61.5%), which is mainly attributed to the fact that the hospital where this research was carried out is a tertiary care center and patients who were transferred from other hospitals had already been using antibiotics for some weeks, which is a recognized cause of infective endocarditis with negative blood culture. In addition, the automated blood culture analysis system or the molecular, serological and immunological techniques that would help determine the causal germ are not available. Moreover, the positivity of the microbiological study does coincide with the current trend, with a predominance of the staphylococcus group isolation, but in lower proportions than those found in other studies, as is the case of Colombia[13], where this bacterium was responsible for 40.7% of the positive blood cultures.

In the national cooperative study from Chile[17], heart failure as a surgical indication was present in 63.6% of patients, and persistent infection in 30.7%; which coincides with our results. In the same article[17], there are mentioned the intracardiac complications (rupture of any structure, perforation and abscesses) in 73.1%. For Ramirez *et al*[10], the non-treatable cardiac failure (44.5%) and the infection resistant to the treatment (40.4%) were the main surgical indications. This behavior corresponds with most of the information that appears in literature; however, it differs from that one found by Saito *et al*[9]; in Peru, in a 13-years study, where out of 27 patients operated on —several due to more than one cause— the main indications for surgical treatment were the risk of embolism (74.07%), refractory heart failure (70.37%) and uncontrolled infection (51.85%).

Regarding the location of vegetations and surgical technique, the results of Ramirez *et al*[10] at the *Instituto de Cardiología y Cirugía Cardiovascular* from Havana, Cuba, are similar to ours: mitral valve replacement (25.1%), aortic valve replacement (18.1%), mitroaortic valve replacement (4.0%), tricuspid valve replacement (1.1%), and extraction of right ventricular electrodes and vegetectomy (36.5%).

Our results, regarding overall mortality (17.4%), were also in the range of those found by other authors[3-5,7,9,16,19,20]. In centers with extensive experience in valve surgery, mortality in prosthetic valve endocarditis is reported to be between 22-46%, which may increase in relationship to subgroups of patients with increased risk, and in Cuba, perioperative mortality was found to be 16.5% and mortality in early prosthetic endocarditis 57.1%[10]. However, there are reports of low overall hospital mortality rates, such as that one of a study in Germany (10.9%), where age over 70 years old and diabetes mellitus are described as important predictors[18].

CONCLUSIONS

Male patients and those over 60 years old predomi-

nated. The presence of vegetations on intracardiac devices and the predominance of negative blood cultures were the most found characteristics. The main surgical indications were refractory heart failure and uncontrolled infection, and the most used surgical procedure was the change of system of devices for programmed electrical stimulation. Mortality from prosthetic valve endocarditis was high and, at the same time, it was the only variable that was significantly associated with mortality.

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