REC: CardioClinics

www.reccardioclinics.org

Original article

Characterizing the "iceberg peak" in valvular heart disease: Outcomes and costs of in-hospital procedures in Spain

Mercedes Álvarez-Bartolomé[a,*], *Ignacio Cruz-González*[b,c,d], *Ana Pardo-Sanz*[c,e], *José Luis Zamorano*[c,e], *Paloma González*[f], *Óscar Martínez-Pérez*[g], *Jesús Cuervo*[g], *Manuel Carnero-Alcázar*[h]

[a] *Dirección Médica, Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[b] *Sección de Hemodinámica e Intervencionismo Estructural, Servicio de Cardiología, Complejo Asistencial Universitario de Salamanca (CAUSA), Salamanca, Spain*
[c] *Centro de Investigación Biomédica en Red Enfermedades Cardiovasculares (CIBERCV), Spain*
[d] *Instituto de Investigación Biomédica de Salamanca (IBSAL), Salamanca, Spain*
[e] *Departamento de Cardiología, Hospital Universitario Ramón y Cajal, Madrid, Spain*
[f] *Edwards Lifesciences, Madrid, Spain*
[g] *Axentiva Solutions, Barcelona, Spain*
[h] *Servicio de Cirugía Cardiaca de Adultos, Hospital Clínico San Carlos, Madrid, Spain*

ARTICLE INFO

Article history:
Received 29 January 2024
Accepted 23 February 2024
Available online 21 March 2024

Keywords:
Valvular heart diseases
Health care cost
Hospitalization
Spain
Burden of disease

ABSTRACT

Introduction and objectives: The aim was to describe the burden of disease of valvular heart disease (VHD) in-hospital interventions in Spain.
Methods: The analysis involved all cases between 2016 and 2019 in the Spanish Ministry of Health database under the International Classification of Diseases 10th Revision. Procedure rates by region and year ($\times 10^6$), patient risk profile (comorbidities), health outcomes (death), length of stay (LoS), and costs were examined.
Results: A total of 57 878 procedures were analyzed, representing a national rate from 292 in 2016 to 321 in 2019 ($\times 10^6$ inhabitants). Comorbidities measured by the age-adjusted Charlson Comorbidity Index ranged between 3.47 and 3.77 and increased over the period. The in-hospital complications have remained constant over the years with some exceptions. Death rate ($\times 10^6$ inhabitants) was 18.0, and the in-hospital mortality per year range was statistically constant and between 5.23% and 6.20%. The unadjusted LoS ranged from 14.68 to 15.34 days (standard deviations [SD], 16.03 and 15.79) including 2.68 to 3.27 days (SD, 6.57–7.82) in the intensive care unit. VHD procedures costs amounted to €1403.13 million in the period, representing an annual cost of €350.8 million. These costs decreased by 3.17% over the period. Per-procedure mean cost also decreased from €24 801.81 (SD, €10 231.91) to €24 015.50 (SD, €9825.39).

Abbreviations: a-CCIage, adjusted Charlson Comorbidity Index; DRG, diagnosis related group; LoS, length of stay; VHD, valvular heart disease.

* *Corresponding author.*
E-mail address: mmalvarezb@telefonica.net (M. Álvarez-Bartolomé).

https://doi.org/10.1016/j.rccl.2024.02.006

Conclusions: VHD entails a large and increasing volume of procedures in Spain. While a decline in the per-procedure mean cost was noted, the overall annual cost increased. This underscores the substantial burden on the national health system, even when considering solely in-hospital procedures.

El «pico del iceberg» en la enfermedad valvular: resultados y costes de procedimientos hospitalarios en España

Palabras clave:
Enfermedades de las válvulas cardiacas
Costes sanitarios
Hospitalización
España
Carga de enfermedad

RESUMEN

Introducción y objetivos: El propósito fue describir la carga de las intervenciones hospitalarias en la enfermedad valvular cardiaca (EVC) en España.

Métodos: El análisis incluyó los registros de la base de datos bajo la Clasificación Internacional de Enfermedades, 10.ª Revisión del Ministerio de Sanidad de España entre 2016-2019. Se examinaron tasas de procedimientos por región y año, perfil de riesgo (comorbilidades), resultados (defunciones), duración de la estancia y costes.

Resultados: Se analizaron 57.878 procedimientos, representando una tasa nacional de 292 en 2016 a 321 en 2019 ($\times 10^6$ habitantes). El índice de comorbilidad de Charlson ajustado por edad estuvo entre 3,47-3,77 y aumentó durante el periodo descrito. Las complicaciones hospitalarias fueron constantes durante los años, con excepciones. La tasa de mortalidad ($\times 10^6$ hab.) fue de 18,0 y la mortalidad hospitalaria por año se mantuvo estadísticamente constante entre 5,23-6,20%. La estancia hospitalaria sin ajustar fue de 14,68-15,34 días (desviación estándar [DE]: 16,03-15,79), incluyendo 2,68-3,27 días (DE: 6,57-7,82) en la unidad de cuidados intensivos. El coste fue 1.403,13 millones de euros en el periodo, lo que representa un coste anual de 350,8 millones de euros. Estos disminuyeron un 3,17% durante el periodo. El coste medio por procedimiento disminuyó de 24.801,81 euros (DE: 10.231,91 euros) a 24.015,50 euros (DE: 9.825,39 euros).

Conclusiones: La EVC implica un volumen importante y creciente de procedimientos en España. Aunque el coste por procedimiento parece que disminuyó, el coste anual total ha aumentado. Esto representa una carga sustancial al sistema de salud nacional, incluso considerando únicamente intervenciones hospitalarias.

Introduction

Valvular heart disease (VHD) is a clinical umbrella term referring to any structural cardiovascular condition provoked by a malfunction of any of the four valves of the heart. This abnormal functioning can be caused by congenital defects, damage related to infections, inflammatory processes, and multiple or individual modifiable risk factors besides ageing.[1,2] Although the initial stages of the disease usually remain asymptomatic, when mild to moderate alterations occur, VHD eventually leads to significant impairment in patients' well-being due to dyspnoea, fatigue, arrhythmia, and palpitations related to heart failure. In addition, VHD is associated with a higher risk of morbi-mortality in comparison to matched populations without VHD, particularly, if suboptimal treatment is provided.[3,4]

Recent research conducted in Europe outlined a VHD incidence rate of 16.3 cases per 10 000 person-years, being mitral regurgitation the most common condition (8.2%; 95% confidence interval [95%CI], 8.0–8.4), followed by aortic stenosis (7.2%; 95%CI, 7.0–7.3) and aortic regurgitation (5.0%; 95%CI, 4.9–5.2).[5] This epidemiological burden has been also highlighted in the US using an indirect approach based on the International Classification of Diseases 9th Revision (ICD-9) and 10th Revision (ICD-10).[6,7] It is clear that educational programmes, prevention strategies, technological advances in diagnosis along with innovations widening the opportunity to treat VHD patients,[8] are crucial for reducing the clinical impact of VHD. However, considering the increasing life expectancy and the progressive ageing of our societies,[9] VHD imposes a challenge to national healthcare services that have been recently affected by the severe acute respiratory syndrome coronavirus-2 pandemic.[10]

Previous research in Spain has shed light on aortic stenosis incidence and its management with a special focus on transcatheter aortic valve replacement or surgical valve replacement, showing an increase in the annual number

of procedures in our country during the last years, while observing positive outcomes such as reduced in-hospital mortality.[11,12] However, despite their clinical importance, little attention has been paid to mitral regurgitation and tricuspid regurgitation to date. Consequently, we designed this research to characterize the magnitude of the burden of disease associated with VHD (in relation to aortic, mitral, and tricuspid valves procedures) and to gain knowledge about patient characteristics, and how VHD is being managed at the National Health Service and the results being obtained. To this end, public data available from the Hospital Discharge Records in the Registry of specialized healthcare activity-minimum data set (RAE-CMBD), regulated by the Royal Decree 69/2015 of February 6 (BOE-A-2015-1235), is a useful source to recognize the casuistry related to heart valve pathology in terms of its diagnosis, the procedures performed, and the results obtained. This is the case because of the mandatory nature of the administrative registry, which is integrated into the Health Information System of the National Health Service and is required for all health centres that maintain an inpatient regimen. In addition to its high standardization, there are multiple examples of the use of this data source for the detailed analysis of the reality of healthcare in our country.[11–14] This reinforces its use as a valid resource for research despite the limitations of its retrospective nature. Some of these inherent limitations in the database stem from the existence of centres and autonomous communities (AC) which, despite the mandatory character, have not provided the data to the RAE-CMBD during the years 2016–2017, or which have made non-systematic provisions.

In this publication, we describe the procedures performed at the public hospitals (including private hospitals publicly funded, as known as subsidized centres) in our country between 2016 and 2019 for aortic, mitral, and tricuspid valve disease and the outcomes observed in terms of mortality. Additionally, patients' length of stay (LoS) is outlined as a core driver for hospital burden and costs.

Methods

The analysis has been carried out following the reference methodological guidelines SAMPL (Statistical Analyses and Methods in the Published Literature)[15] and STROBE (Strengthening the Reporting of Observational Studies in Epidemiology).[16]

Following a formal request, the Ministry of Health of Spain authorizes the use of RAE-CMBD data for research. No authorization from the Ethics Committee is required since the administrative database is completely anonymized, and no patient medical records are reviewed. This anonymization and data processing carried out by the Ministry itself is covered in Royal Decree 69/2015, of February 6, regulating the Registry of Specialized Healthcare Activity, and complies with the requirements of Organic Law 3/2018, of December 5, on the Protection of Personal Data and Guarantee of Digital Rights, which incorporates the General Data Protection Regulation of the European Union.

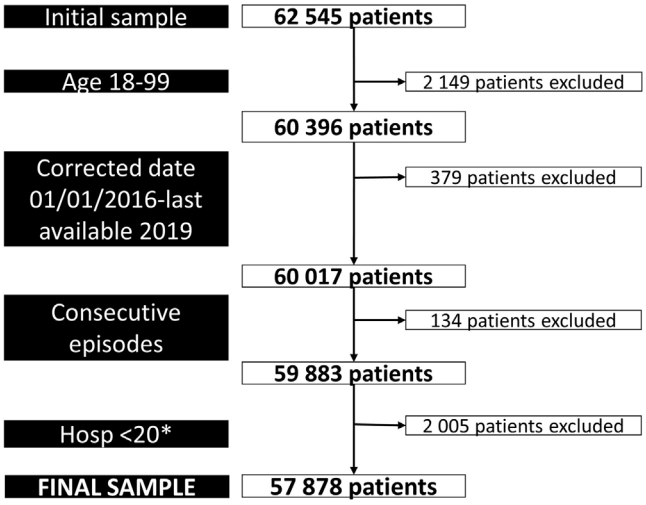

Fig. 1 – Flowchart of the sample selection process. *Exclusion of hospitals with less than 20 interventions per year and events transferred to other hospitals without data from the second admission. Hosp, hospital.

Source for the analysis

Standardized public data was extracted from RAE-CMBD for the last available years at the time of the study (2016–2019). All available cases aged 18–99 years, in which a heart valve procedure had been carried out during a hospital stay in a public and subsidized centre were included in the analysis ($n = 57\,878$). In accordance with the study's objective, all accessible records were incorporated to ensure a comprehensive assessment of the implications of VHD management within the healthcare system, extending beyond the influence of patients' clinical characteristics on such management. This global VHD scope includes percutaneous and surgical procedures for aortic, mitral, and tricuspid valves, both isolated and concomitant. Procedures, whether concomitant with other coronary or aortic procedures or not, have also been included, without exclusion of cases involving endocarditis or post-myocardial infarction rupture of the mitral valve.

Procedures were grouped for in-depth analysis following the clinical criteria for the management of VHD. This group classification was made using the ICD-10 procedure codes (see "Methods" in the supplementary data). Regarding data management, in the situation of several records associated with the same case (variable "recoded CIP SNS"), the consecutive episodes were consolidated (see "Methods" in the supplementary data). Finally, all hospitals with less than 20 procedures per year were excluded to avoid incorporating into the sample centres that may potentially compromise certain aspects of the management of VHD analysis. In the specific case of La Rioja, all procedures from the autonomous community were excluded since only six procedures were conducted in that region. Fig. 1 shows the flow chart with the entire sample selection process and the loss of observations in each step. In all these final sample, days of stay, stays in the intensive care unit (ICU), exitus, and complications of all the episodes have been computed jointly.

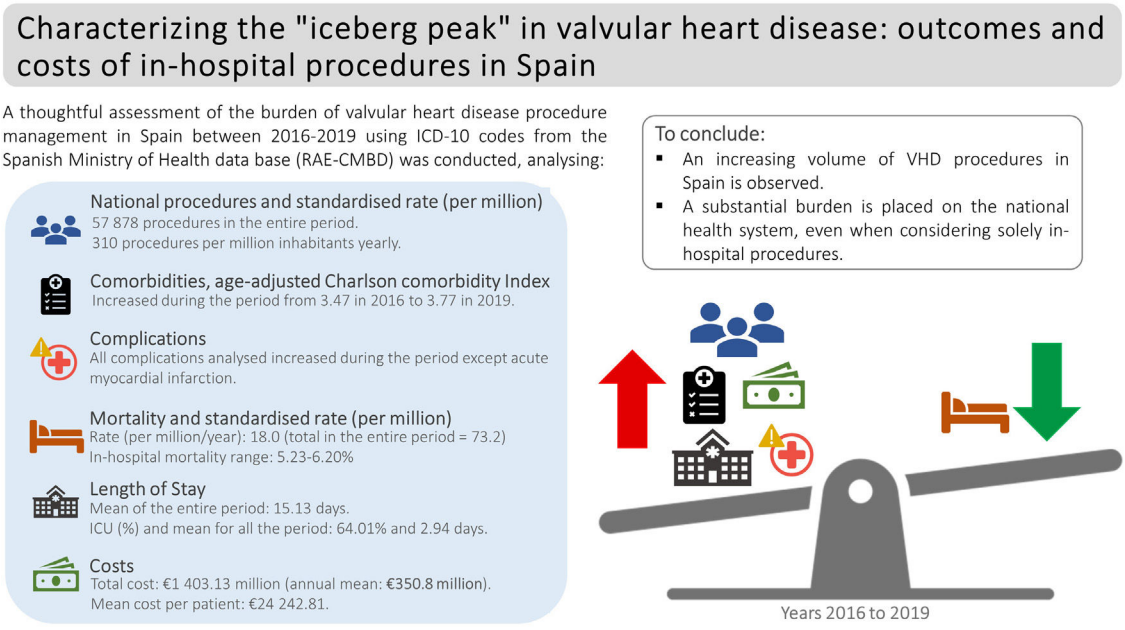

Fig. 2 – Central illustration: compilation of findings and results. ICD-10, International Classification of Diseases 10th Revision; ICU, intensive care unit; VHD, valvular heart disease; RAE-CMBD, Registro de Atención Especializada – Conjunto Mínimo Básico de Datos.

Statistical approach

First, a descriptive analysis of the study variables was conducted to quantify the procedures performed based on age, comorbidities, and complications (see Table 1 of the supplementary data for ICD-10 codification), among others. This analysis included the total number of VHDs procedures in Spain carried out by AC and year.

Second, crude, and standardized rates ($\times 10^6$ inhabitants) of each AC and year were calculated, considering the seasonal population (person-year) and sex, according to the information available at *Instituto Nacional de Estadística*. Additionally, the ratio of procedure rates (95%CI, log-normal) was calculated using the standardized national rate as a reference. Subsequently, mortality in absolute frequency and adjusted rates were also assessed.

Third, comorbidities were analyzed by computing the Charlson Comorbidity Index adjusted for age (a-CCI)[17,18] through an algorithm defined for ICD-10 codes and based on respective patient on admission information available.[19,20]

Additionally, a descriptive analysis was carried out to focus on the burden of the disease corresponding to LoS, both in the ward and the ICU, and the associated costs. LoS corresponded to the period between patient admission and patient discharge or death and, a separate analysis of the sample of the patients who died during their stay and the patients who did not was carried out separately.

For the estimation of mean annual costs related to the procedures, all the available costs were updated based to 2019 costs. The costs included in the RAE-CMBD database depend on the combination of diagnosis related group (DRG) and severity level as described by the Unit of Health Care Information and Statistics of the Ministry of Health.[21] Therefore, the homogenization has been carried out by assigning the cost by DRG and severity level of 2019. Moreover, before making this assignment, we verified the existence of changes in the coding versions of the DRGs to ensure the highest possible precision. In the case of a significant change, and only if there was not a clear correspondence in 2019 coding, an update of the costs based on the Consumer Price Index was applied to avoid any overestimation of the costs by the duplication of DRGs. In addition, the three more common DRGs from each year were added with their respective costs to have a more precise detail of this important burden of disease factor. Regarding the statistical analysis, *t*-tests or ANOVA tests were applied to contrast differences between independent samples of continuous variables in the case of parametric distribution. Mann–Whitney *U* –Wilcoxon or Kruskal–Wallis was applied if the variables followed a non-parametric distribution, according to the Anderson–Darling Normality Test. Likewise, Fisher's exact test was applied in the contrasts between independent samples of categorical variables, and the Chi-squared test was applied in cases where Fisher's exact test was not applicable. Statistical contrasts were two-tailed (bilateral) and were considered significant when the *P*-value was <.05. The statistical management of the data was carried out with R software (version 4.1.2).

Results

Management of valvular heart disease: total number of procedures and use rates

The total number of procedures increased during the period of the study, being 2019 the year with the highest number ($n = 15\,364$) of procedures (Fig. 2).

Table 1 – Descriptive summary of annual valvular heart disease procedures.

Variable	Year				P-value
	2016	2017	2018	2019	
VHD procedures					
n	13 374	14 697	14 443	15 364	
Age	69.57 (12.43)	69.95 (12.53)	70.10 (12.71)	70.35 (12.66)	<.001
Sex, male (%)	7409 (55.40)	8209 (55.85)	8021 (55.54)	8679 (56.49)	.238
a-CCI	3.47 (1.79)	3.59 (1.87)	3.71 (1.93)	3.77 (1.95)	<.001
Mitral (%)	2464 (18.42)	2686 (18.28)	2578 (17.85)	2805 (18.26)	.630
Tricuspid (%)	155 (1.16)	180 (1.22)	233 (1.61)	245 (1.59)	<.001
Transc (%)	1714 (12.82)	2342 (15.94)	3052 (21.13)	3850 (25.06)	<.001
AVR (%)	6533 (48.85)	6784 (46.16)	5988 (41.46)	5831 (37.95)	<.001
MitTri (%)	675 (5.05)	631 (4.29)	730 (5.05)	740 (4.82)	.007
AorMit (%)	887 (6.63)	1010 (6.87)	862 (5.97)	822 (5.35)	<.001
AorMitTri (%)	268 (2.00)	255 (1.74)	265 (1.83)	281 (1.83)	.412

a-CCI, age-adjusted Charlson Index; AorMit, aortic and mitral; AorMitTri, aortic, mitral, and tricuspid; AVR, aortic valve replacement (surgical and transcatheter); MitTri, mitral and tricuspid; Transc, transcatheter excluding isolated valvuloplasties; VHD, valvular heart disease.
All groups contemplate transcatheter and surgical procedures except for the transcatheter group. The transcatheter group includes isolated procedures on the mitral, tricuspid, or aortic valves.
Data are expressed as no. (%).

The AC with the greatest number of procedures was the Community of Madrid (Table 2 of the supplementary data) with *n* = 10 192 (17.61%), followed by Catalonia and Andalusia with *n* = 9336 and *n* = 9324 (16.13% and 16.11%), respectively. In contrast, Castile-La Mancha registered the lower number of procedures (1.21% of the total).

The national utilization rate for the study period was 1252×10^6 inhabitants. The Community of Madrid had the highest use rate (1665×10^6 inhabitants) followed by Principality of Asturias and Galicia (1616 and 1582×10^6 inhabitants, respectively).

Regarding the utilization rates per year, 2016 had the lowest rate (292×10^6 inhabitants) while 2019 had the highest (321×10^6 inhabitants).

It is also notable that transcatheter procedures increased over the years, rising significantly (*P*-value <.001) from 1714 in 2016 to 3850 in 2019.

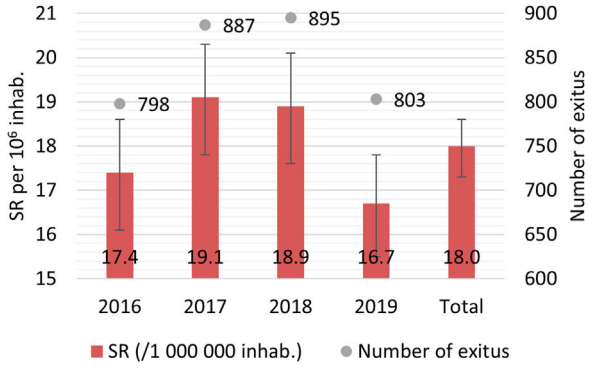

Fig. 3 – Standardized in-hospital mortality rate per year for heart valvular disease. Inhab: inhabitants; SR: standardized rate.

Comorbidities, Charlson Comorbidity Index

Comorbidities registered at the time of admission, measured through the a-CCI, were between 3.47 and 3.77. The complexity of cases increased during the study period (*P*-value <.001, Table 1). Mean age of patients hovering at about 70 years, which showed an upward trend throughout the analyzed timeframe (*P*-value <.001). The a-CCI has also shown an increase within each age group. Specifically, there has been a 4.93% increase in a-CCI for individuals under 60, 6.98% for patients aged 61–70, 5.42% for patients aged 71–80, and 6.50% for individuals over 80 years old. Furthermore, male sex represented over 55% of the patient population each year.

Complications

In broad terms, complications analyzed during the hospital stay (Table 2) exhibited an upward trend over the course of the study period, except for acute myocardial infarction (AMI), which showed no significant change (*P* = .621). Among the various complications, those associated with prosthesis displayed the greatest increase (85.05%) between the years 2016 and 2019 (*P*-value <.001).

Rates of in-hospital mortality

The mean national in-hospital mortality rate was 5.85%. This rate exhibited a temporal evolution, decreasing from 5.97% in the initial year to 5.23% in the last year (Fig. 3). A similar pattern can be observed in the standardized rates $\times 10^6$ inhabitants. Specifically, the rate stood at 17.4 in 2016, increasing to approximately 19 in 2017 and 2018, and subsequently decreasing to 16.7.

Length of stay: ward and intensive care unit

The annual mean LoS was 15.13 days and decreased (*P* < .001) over the years (Table 3). The mean hospital LoS until discharge for patients who did not die was 14.58 with 2.45 days in the ICU (Table 4). LoS for patients who died during the stay was

Table 2 – Annual valvular heart disease procedures complications summary.

Variable	Year				P-value
	2016	2017	2018	2019	
VHD procedures					
AF (%)	1214 (9.08)	1373 (9.34)	1517 (10.50)	1476 (9.61)	<.001
AMI (%)	80 (0.60)	88 (0.60)	85 (0.59)	77 (0.50)	.621
Prot (%)	107 (0.80)	124 (0.84)	158 (1.09)	198 (1.29)	<.001
IS (%) G45*[a]	19 (0.14)	32 (0.22)	29 (0.20)	31 (0.20)	.001
IS (%), others[b]	135 (1.01)	151 (1.03)	197 (1.36)	229 (1.49)	
ARF (%)	167 (1.25)	183 (1.25)	221 (1.53)	240 (1.56)	.024
PPm (%)	954 (7.13)	1157 (7.87)	984 (6.81)	1425 (9.27)	<.001
IntubTrac (%)	138 (1.03)	204 (1.39)	206 (1.43)	185 (1.20)	.011

AF, atrial fibrillation; AMI, acute myocardial infarction; ARF, acute renal failure requiring renal replacement therapy; IntubTrac, prolonged intubation requiring tracheotomy; IS, ischaemic stroke; PPm, permanent pacemaker implantation; Prot, prosthesis complications; VHD, valvular heart disease.

[a] G45*: transient cerebral ischaemic attacks and related syndromes.

[b] Others: intraoperative cerebrovascular infarction (I97.81*), postprocedural cerebrovascular infarction (I97.82*), cerebral infarction due to thrombosis of cerebral arteries (I63.3*), cerebral infarction due to embolism of cerebral arteries (I63.4*), and cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries (I63.5*).

Note: The symbol * refers to any alphanumeric character that follows the one exposed, thus meaning any possible termination of the code. Data are expressed as no. (%).

Table 3 – Annual valvular heart disease in-hospital mortality, length of stay, and costs summary.

Variable	Year				P-value
	2016	2017	2018	2019	
VHD procedures					
n	13 374	14 697	14 443	15 364	
Exitus (%)	798 (5.97)	887 (6.04)	895 (6.20)	803 (5.23)	.002
LoS (mean, median [p25–p75])	15.31, 10.00 [8.00–17.00]	15.34, 10.00 [8.00–17.00]	15.23, 10.00 [7.00–17.00]	14.68, 10.00 [7.00–16.00]	<.001
ICU stay (%)	8059 (60.32)	9204 (62.69)	9688 (67.12)	10 092 (65.86)	<.001
LoS ICU (mean, median [p25–p75])	2.68, 1.00 [0.00–3.00]	2.79, 1.00 [0.00–3.00]	3.27, 1.00 [0.00–3.00]	2.99, 1.00 [0.00–3.00]	<.001
Cost per-patient APR (mean, median [p25–p75])	24 801.81, 23 185.94 [20 908.72–24 599.22]	24 100.01, 22 095.06 [19 900.69–28 270.40]	24 112.31, 21 761.87 [21 761.87–24 599.75]	24 015.50, 23 045.74 [22 105.18–23 423.62]	<.001
Most frequent DRG per-patient cost (DRG: (*n*), mean)	163: (9248) 25 889.80 175: (1920), 16 225.30 162: (1032) 34 432.33	163: (9641) 24 868.91 175: (2526) 17 175.51 162: (1098) 33 340.51	163: (6731) 23 642.34 160: (3076) 26 498.92 175: (2870) 18 490.52	163: (6569) 23 964.77 175: (3572) 19 028.05 160: (3272) 27 228.76	–

APR, all patient refined; DRG, diagnosis related groups; ICU, intensive care unit; LoS, length of stay; VHD, valvular heart disease.

Table 4 – Length of stay summary according to health outcome in valvular heart disease procedures.

	Stratification variables	
	Non exitus	Exitus
LoS (days)	14.58	23.93
ICU admissions (%)	59.91%	4.09%
ICU LoS (days)	2.45	10.68
	Non-ICU	ICU
LoS (days)	13.35	16.16
ICU LoS (days)	–	4.69

ICU, intensive care unit; LoS, length of stay.

23.93 days; this high figure was also observed for the ICU stay, averaging nearly 11 days. The percentage of deceased patients that were admitted to this unit was 6.39%. Regarding the mean length of hospitalization, when examining it separately based on ICU admission, those who had been admitted to the ICU experienced a longer duration, specifically a difference of nearly 3 days. Nevertheless, the mean duration of ICU stays for patients who have been admitted to this unit is 4.7 days.

Analysis of ICU LoS showed an increase ($P < .001$, Table 3) of nearly 0.5 days, reaching up to 3 days on mean. Moreover, patients who needed a stay on this unit have increased during the studied period ($P < .001$).

Mean annual costs

Total costs related to VHD procedures summed up to €1403.13 million in the total period, which represents a total annual cost of €350.8 million and an annual cost per procedure of €24 198.92 (SD, €11 685.17). These costs decreased (*P*-value <.001) throughout the studied period by 3.17% (Table 3). However, the total annual cost increased over the period, rising from €331 699 449 to €368 974 098 million. The most frequent

DRG was 163 (procedures on heart valves without AMI or complex diagnosis) throughout the 4-year period, with a mean cost ranging from €23 642.34 to €25 889.80.

Discussion

This article provides detailed representative description of the in-hospital procedures for the management of VHD in Spain, responding to the need for information of the different agents involved in the national healthcare system to monitor the quality of healthcare provisions. While conventional approaches typically scrutinize outcomes within valvular and etiological subgroups, this publication directs its attention to the complete findings, aiming to better understand the magnitude of the VHD in term of procedures. Overall, this research showed a growing trend of the number of VHD procedures between 2016 and 2019, with a 14.9% increase during this period. This substantial increase aligns with UK VHD diagnoses projections based on the OxVALVE population cohort study[3] and the cumulative number of mitral and aortic procedures recently reported by Tung et al.[5] This tendency, which has been highlighted by previous research with data up to 2018,[12] might be partly explained by the expansion of transcatheter approaches for aortic valve replacement with widened candidate populations.[1] Also, newer transcatheter developments for mitral and tricuspid valves might explain this progression to a lesser extent.[8,22–24] However, since our cohort included cases up to 2019, this factor should be further explored in the near future, once these innovations have been fully incorporated into the healthcare system and hospitals have recovered their activity since the pandemic situation. In any case, this growth in VHD procedures can be justified considering recent epidemiological research and the ageing of our population.

With respect to the complexity of cases treated, a-CCI worsened during the study period, in agreement with the severity observed in recent research.[11,12] Given that the mean age has also increased over the study period, one might think that this increase in a-CCI could be attributed to the older profile of the patients. However, upon observing a rise in case complexity within each age group, a direct relationship cannot be conclusively established. Despite the complex risk profile of patients, VHD procedures appear reasonably safe with low rates of major complications (AMI, atrial fibrillation, cerebrovascular complications, and others) in all groups analyzed over the years. However, it should be noted that the permanent pacemaker implant rate increased in 2019 with respect to previous years (up to 9.27% permanent pacemaker implants in 2019). It is also possible that the low incidence of postoperative atrial fibrillation was due to the undercoding of this complication. Although these rates are consistent with recent research, further monitoring to understand this specific finding should be carried out in future research. Furthermore, an adjusted national rate of 73.2 in-hospital deaths per million inhabitants was observed. It should be noted that patients with endocarditis were not excluded. Excluding patients with endocarditis has the effect of reducing the mortality in the analyzed sample. Specifically, when endocarditis is excluded the in-hospital mortality rate was observed to decrease significantly (*P*-value <.001) from 5.85% to 5.25%. This reduction can be attributed to the higher mortality rate of 23.72% observed in patients with endocarditis. However, according to evidence from recent observational data with median follow-up post-surgery of up to 54 months,[25] this rate of endocarditis would probably rise after discharge. Furthermore, patients who underwent procedures for ischaemic heart disease or procedures involving the ascending or descending thoracic aorta were not excluded. All these factors would contribute to a significant reduction (*P*-value <.001) in overall mortality to 4.99% during the entire studied period.

Regarding hospitalizations, the LoS was 15 days on mean and 64% of patients required admission to ICU. The frequency of ICU admissions exhibited an upward trend throughout the analyzed period. Furthermore, these admitted patients presented a significantly longer mean LoS, extended by approximately 3 days. Additionally, a noticeable increase of nearly 0.5 days in the mean duration of ICU stays has been observed over the years examined. Taking these findings into account, and despite a mild decrease in the LoS (−4.11%), the utilization of resources remains significant. A detailed analysis by valve affectation etiologies and procedures would provide detailed information about these trends.

Finally, the mean cost per patient dropped from €24 801 in 2016 to €24 015 in 2019. This finding was surprising considering that the costs increased in the study period by 11.23%. This is most probably explained by the progressive increase in the annual proportion of transcatheter interventions conducted. Another factor to consider in the impact on costs is the proportion of patients with specific DRGs. Given that mean costs in this database are contingent upon the quantity of cases categorized under each DRG, this information holds significance in comprehending the composition of the mean cost itself. However, conducting a comprehensive analysis of these factors is imperative to reliably attribute causality to the observed changes in costs. Nonetheless, the feasibility of conducting such an exhaustive analysis is called into question due to the inherent composition of the database.

Limitations

First, although we used the national census of VHD procedures from a standardized, validated, and compulsory source representing the national hospital activity (for public and subsidized centres), data may be affected by some inherent error. This is due to the possibility of coding failures or omissions in the information registered which may have diminished the precision of the results. To mitigate the potential problems arising from coding errors, certain measures were implemented. Specifically, the consolidation of consecutive episodes that has been described in detail in both the "Methods" section and supplementary material. These procedures aim to minimize any adverse effects stemming from the codification process, such as procedures being codified also in

the support hospital or the hospital where the patient recovers from the procedure. These data procedures provided by the RAE-CMBD do not include the practice of private centres. These cases may account for 10%–30% of the total depending on the AC. Likewise, it must also be considered that the AC for which information is available is the one in which the procedure is performed and does not have to coincide with the residence. This can affect the overestimation and underestimation of procedures depending on the region. Furthermore, it is worth noting that comorbidities have not been directly extracted from the medical records but rather from the specific diagnoses present on admission for each stay. Therefore, if any of these diagnoses were not coded, the calculated a-CCI would result in a lower value than the real one.

Second, our analysis is based on VHD procedures performed between 2016 and 2019 and the in-hospital outcomes registered. Therefore, we were limited in other important aspects of interest related to VHD burden, such as postoperative complications during follow up after discharge, resources employed during diagnosis, hospitalizations not requiring a procedure, or ambulatory follow up.

Third, the number of undiagnosed cases in comparable populations should not be forgotten, our figures outline one part of the real burden of the disease. In relation to this limited scope, another constraint lies in the fact that only the hospital admission in which the procedure was performed could be analyzed and there was no possibility of obtaining the long-term results, which would have provided information of great value when evaluating the full scope and cost of healthcare.

Fourth, in our research, outcomes of the most recent innovations (i.e., transcatheter edge-to-edge repairs approaches included in recent clinical guidelines), are not reflected and further analyses are warranted to monitor their outcomes. Finally, some aspects should be considered when interpreting the results and this analysis. It is known that the significance of the *P*-values is influenced by increasing the sample size considerably, therefore this could have caused distortions in the inference.[26–28]

Conclusions

This article provides a comprehensive overview of VHD procedures in Spain, highlighting the significant increase (14.9%) in procedures from 2016 to 2019. This growth aligns with UK VHD projections and may be linked to transcatheter advancements. Besides, the study reflects the rising complexity of cases and an increased rate of permanent pacemaker implants in 2019. Although a causal effect cannot be determined by this study, there is an increase in hospitalizations, especially related to ICU admissions, which leads to greater utilization of resources and costs. Fortunately, in-hospital mortality rates decreased. Finally, it is important to know that this study provides useful information from the hospital perspective, but the outlined burden of disease only captures the resources corresponding to the procedures, so the global burden of disease needs complementary studies to provide a complete analysis.

What is known about the subject?

- VHD encompasses structural cardiovascular conditions and is associated with higher morbidity and mortality rates without optimal treatment. It often progresses asymptomatically but can lead to symptoms like dyspnoea, fatigue, arrhythmia, and palpitations.
- Incidence rates for specific valve conditions, such as mitral regurgitation and aortic stenosis, have been documented in Europe. In Spain previous research has examined aortic valve procedures and reduced in-hospital mortality was found, but mitral and tricuspid regurgitation have received limited attention.

Does it contribute anything new?

- This study provides a comprehensive overview of procedures for all conditions in VHD management in Spain, addressing the need for quality healthcare information.
- This study reveals a significant increase in VHD procedures in Spain from 2016 to 2019, aligning with UK VHD projections. Despite worsening case complexity, VHD procedures remained reasonably safe, with lower in-hospital mortality rates, while hospitalizations trended upward, particularly in the intensive care unit.

Funding

This study received financial support from Edwards Lifesciences. The company was involved in shaping the research scope and methodology. The analysis and interpretation of the results were conducted independently.

Ethical considerations

Following a formal request, the Ministry of Health of Spain authorized the use of RAE-CMBD data for research. No authorization from the Ethics Committee was required since the administrative database is completely anonymized, and no patient medical records are reviewed. This anonymization and data processing carried out by the Ministry itself is covered in Royal Decree 69/2015, of February 6, regulating the Registry of Specialized Healthcare Activity, and complies with the requirements of Organic Law 3/2018, of December 5, on the Protection of Personal Data and Guarantee of Digital Rights, which incorporates the General Data Protection Regulation of the European Union. Furthermore, this work has considered the potential variables of sex and gender in accordance with the SAGER guidelines. STROBE guidelines were followed.

Statement on the use of artificial intelligence

No artificial intelligence tool was used to prepare this article.

Authors' contributions

All authors were involved in the initial design of the study. Analyses were performed by O. Martínez-Pérez, J. Cuervo, M. Carnero-Alcázar, and M. Álvarez-Bartolomé. All authors aided in interpreting the results and have made a significant contribution to the final manuscript.

Conflicts of interest

P. González is employed by Edwards Lifesciences. O. Martínez-Pérez and J. Cuervo are members of Axentiva Solutions, which received consultancy fees from Edwards Lifesciences. I. Cruz-González and M. Carnero-Alcázar received consultancy fees from Medtronic, Edwards Lifesciences, and Abbott Laboratories. M. Álvarez-Bartolomé, A. Pardo-Sanz and J.L. Zamorano received consultancy fees from Edwards Lifesciences. M. Carnero-Alcázar received consultancy fees from Atricure and is the is the Secretary-General of SECCE. I. Cruz-González received consultancy fees from Boston Scientific and Biosensors. J.L. Zamorano received consultancy fees from Bayer, Pfizer, Daiichi, and Novartis.

Acknowledgements

We extend our gratitude to the Unit of Health Care Information and Statistics at the Spanish Ministry of Health for their invaluable assistance in providing high-quality data for this study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.rccl.2024.02.006.

REFERENCES

1. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2022;43:561–632.
2. Institute of Medicine (US) Committee on Social Security Cardiovascular Disability Criteria. *Cardiovascular Disability, Updating the Social Security Listings*. US: National Academies Press; 2010. Available from: https://pubmed.ncbi.nlm.nih.gov/24983036/ [accessed 10.01.23].
3. D'Arcy JL, Coffey S, Loudon MA, et al. Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study. *Eur Heart J*. 2016;37:3515–3522.
4. Doi K, Ogawa H, Ishigami K, et al. Impact of valvular heart disease on mortality, thromboembolic and cardiac events in Japanese patients with atrial fibrillation – the Fushimi AF registry. *Circ J*. 2020;84:714–722.
5. Tung M, Nah G, Tang J, Marcus G, Delling FN. Valvular disease burden in the modern era of percutaneous and surgical interventions: the UK Biobank. *Open Heart*. 2022;9:e002039.
6. Mallow PJ, Chen J, Moore M, Gunnarsson C, Rizzo JA. Incremental direct healthcare expenditures of valvular heart disease in the USA. *J Comp Eff Res*. 2019;8:879–887.
7. Moore M, Chen J, Mallow PJ, Rizzo JA. The direct health-care burden of valvular heart disease: evidence from US national survey data. *Clinicoecon Outcomes Res*. 2016;8:613–627.
8. Lugo D, Ramirez ALP, Presti SLo, Nappi F, Mihos CG. Structural heart disease: the year in valvular and complex coronary intervention trials. *J Thorac Dis*. 2020;12:2910–2918.
9. United Nations Department of Economic and Social Affairs Population Division. *World Population Ageing 2019 (ST/ESA/SER.A/444)*; 2020. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Report.pdf [accessed 12.01.23].
10. Statistics WH. *Monitoring Health for the SDGs, Sustainable Development Goals*. World Health Statistics: Monitoring Health for the SDGs, Sustainable Development Goals; 2022. Available from: https://www.who.int/publications/i/item/9789240074323 [accessed 18.10.22].
11. Carnero-Alcázar M, Maroto-Castellanos LC, Hernández-Vaquero D, et al. Isolated aortic valve replacement in Spain: national trends in risks, valve types, and mortality from 1998 to 2017. *Rev Esp Cardiol*. 2021;74:700–707.
12. Carnero-Alcázar M, Rodríguez-Caulo E, Hernández-Vaquero D, et al. Variablity of mechanical or tissue valve implantation in patients undergoing surgical aortic valve replacement in Spain: national retrospective analysis from 2007 to 2018. *J Clin Med*. 2021;10:3209.
13. Goicolea Ruigómez FJ, Elola FJ, Durante-López A, Fernández Pérez C, Bernal JL, Macaya C. Coronary artery bypass grafting in Spain. Influence of procedural volume on outcomes. *Rev Esp Cardiol*. 2020;73:488–494.
14. Íñiguez Romo A, Bertomeu Martínez V, Rodríguez Padial L, et al. The RECALCAR Project. Healthcare in the Cardiology Units of the Spanish National Health System, 2011 to 2014. *Rev Esp Cardiol*. 2017;70:567–575.
15. Lang TA, Altman DG. Basic statistical reporting for articles published in Biomedical journals: the "Statistical Analyses and Methods in the Published Literature" or The SAMPL Guidelines. *Int J Nurs Stud*. 2015;52:5–9.
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61:344–349.
17. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol*. 1994;47:1245–1251.
18. Charlson ME, Charlson RE, Peterson JC, Marinopoulos SS, Briggs WM, Hollenberg JP. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. *J Clin Epidemiol*. 2008;61:1234–1240.
19. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43:1130–1139.
20. Quan H, Li B, Couris CM, et al. Updating and validating the Charlson Comorbidity Index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol*. 2011;173:676–682.

21. Subdirección General de Información Sanitaria. *Norma Estatal RAE-CMBD 2019 – Nota Informativa*; 2021. Available from: https://www.sanidad.gob.es/estadEstudios/estadisticas/cmbdAnteriores.htm [accessed 21.04.22].
22. Alperi A, Almendárez M, Álvarez R, et al. Transcatheter tricuspid valve interventions: current status and future perspectives. *Front Cardiovasc Med*. 2022;9:994502.
23. Nettersheim FS, Baldus S. ESC/EACTS guidelines 2021 on the management of valvular heart diseases: what are the most important innovations? *Herz*. 2022;47:19–30.
24. Ponzoni M, Fiocco A, Caraffa R, et al. Institutional re-evolution of mitral valve procedures. *J Geriatr Cardiol*. 2022;19:551–554.
25. Cahill TJ, Raby J, Jewell PD, et al. Risk of infective endocarditis after surgical and transcatheter aortic valve replacement. *Heart*. 2022;108:639–647.
26. Betensky RA. The p-value requires context, not a threshold. *Am Stat*. 2019;73(suppl 1):115–117.
27. Wasserstein RL, Lazar NA. The ASA's statement on p-values: context, process, and purpose. *Am Stat*. 2016;70:129–133.
28. Wasserstein RL, Schirm AL, Lazar NA. Moving to a world beyond "p < 0.05". *Am Stat*. 2019;73(suppl 1):1–19.