

Burden of ischemic heart disease in Spain: incidence, hospital mortality and costs of hospital care

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Author contributions: JD contributed to the investigation by analyzing and interpreting the burden associated to ischemic heart disease in Spain and was a major contribution in the intellectual content revision. AM analyzed the current situation of ischemic heart disease in Spain, interpreted the statistical data and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

Acknowledgements: Not applicable.

Abstract

Background: Ischemic heart disease (IHD) is the leading global cause of death and is assumed to entail a significant social and economic burden globally. This study aimed to evaluate incidence and mortality trends of IHD in Spain and to estimate direct medical costs.

Methods: Admission files corresponding to patients with IHD registered between 2011 and 2019 were obtained from a Spanish hospital discharge database and analyzed in a retrospective study.

Results: Admission data corresponding to 814,740 patients with IHD was analyzed. The majority of patients were males, and about half of the hospitalizations were due to an acute myocardial infarction. Incidence decreased significantly in most age groups over time, while hospital mortality rate remained stable (4.4%). Additionally, mortality rate was significantly higher among females (6.6%). Median admission cost was €5175; the higher costs per admission were found in patients with an acute myocardial infarction and in admissions with an ICU stay. The annual cost of hospital care was €693.8 million.

Conclusions: Despite the decreasing trends described in the general population, hospital mortality rate was constant among hospitalized patients during the study period. The higher hospital mortality rate described among females should be considered in further studies and protocol revisions.

Keywords: direct medical costs; hospital mortality; incidence; ischemic heart disease; Spain.

1. Introduction

Ischemic heart disease (IHD) is the leading global cause of death and the second cause of disability [1]. Coronary artery disease (CAD) is usually the underlying cause, with a variety of clinical presentations that include acute and chronic syndromes, being myocardial infarction is the most common presentation [2]. Numerous risk factors have been identified associated with the development of IHD and CAD, including hypertension, obesity and diabetes mellitus [3].

In terms of epidemiology, estimating the real prevalence of IHD is complex; global data indicates a rise in the prevalence of these conditions, while in developed countries incidence appears to decrease [4,5]. On the other hand, mortality associated to CAD has decreased in the past decade in most high-income countries, including Spain, primarily due to the reduction of major risk factors and improved treatments [6,7]. Overall, ischemic heart disease and coronary artery disease are associated to a significant burden in terms of disability and mortality, as well as significant medical costs [8]. The costs associated to IHD have only been partially evaluated in several regions, with numerous studies focusing on myocardial infarction [9-11]. In this direction, disease cost studies or cost of illness studies have special relevance, aiming to quantify the medical costs of a certain disease or condition in order to emphasize the need for preventive measures, improved treatments or policy changes [12]. The most extensive study to date, developed in Japan, estimated a direct cost of IHD that reached the €4.351 million (589.9 billion yen) in 2014 [13].

The objective of this study was to evaluate incidence and mortality trends of IHD in Spain by reviewing hospital admission data and to estimate the direct medical costs of IHD in the country.

2. Methods

2.1. Study setting

Hospital admission records corresponding to patients with IHD registered in Spanish hospitals between 1 January 2011 and 31 December 2019 were analyzed in a retrospective multicenter study. Data was obtained from a Spanish National discharge database that covers 90% of hospitals in Spain and collects data from all Spanish regions. Healthcare centers are responsible for data collection, codification and confidentiality; data is codified using the International Statistical Classification of Diseases and Related Health Problems, 9th version (ICD-9) prior to 2016 and 10th version (ICD-10) the year 2016 [14,15]. Data is validated internally, and the database undergoes periodic audits; in this process, any errors or unreliable data are excluded.

2.2. Data extraction

The ICD-9 and ICD-10 codes corresponding to IHD were used to claim hospital admission files from the database (410 to 414 and I20 to I25, respectively). The conditions coded were angina pectoris, myocardial infarction, current complications following a myocardial infarction (within the 28-day period), other acute ischemic heart diseases (acute coronary thrombosis, Dressler's syndrome and other forms of acute heart disease) and other chronic ischemic heart disease. Data was anonymized and recoded prior to extraction, in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki, and there was no access to identifying information. In this context, patient consent and ethics committee approval are not required in Spain [16].

2.3. Study variables

The variables obtained from the database were: patients' age, patients' sex, admission date, admission type (programmed or non-scheduled), discharge date, discharge type

(including in-hospital death), primary diagnosis, up to 20 secondary diagnoses registered during the admission, medical procedures registered during the admission and total admission cost. All costs correspond to €2019.

2.4. Data analysis

Patients were classified by sex and into four age groups: $\geq 0 < 45$ years, $\geq 45 < 65$ years, $\geq 65 < 75$ years and ≥ 75 years. Patient characteristics were obtained from the first admission registered per patient, while admission details and costs were analyzed using all admission files. Incidence was calculated as the annual number of patients with IHD within the total population assigned. Hospital mortality rate corresponded to the number of deaths registered in hospital centers within the total number of patients admitted due to IHD. Direct medical costs of hospital care were obtained from the database, where they are assigned based on the standardized average expenses of admissions and medical procedures determined by the Spanish Ministry of Health (this includes all of the costs related to examination, medication, treatment and resources). Normality was tested by means of the Kolmogorov-Smirnov test. For dichotomous variables, frequencies and percentages are presented, and mean or median and interquartile range (IQR) were calculated for continuous variables. The Spearman correlation test was used to analyze possible time trends. Two-tailed non-parametric independent t-test (Mann-Whitney U test) or one-way analysis of variance (Kruskal-Wallis test) were used as appropriate. A $p < 0.05$ was considered statistically significant.

3. Results

A total of 971,193 hospital admission files were analyzed, corresponding to 814,740 individual patients admitted with IHD between 2011 and 2019. The majority of patients were males (71.0%), with a median age of 69 years (Table 1). Males hospitalized for IHD

were significantly younger than females ($p < 0.0001$). Most of the patients were diagnosed with acute myocardial infarction, with a median age of 69 years, and chronic ischemic heart disease, with a median age of 68 years. Patients diagnosed with angina pectoris had a median age of 72 years and those with other acute ischemic heart diseases presented a median age of 74 years. Only 682 patients were included followed for complications of an old myocardial infarction, with a median age of 69 years.

In addition, patients presented a number of comorbid conditions. The conditions found in over 10% of admissions were hypertension, hypercholesterolemia and hyperlipidemia, diabetes mellitus, tobacco use disorder, dysrhythmias, heart failure, hypertensive heart and kidney disease, overweight and obesity, chronic kidney disease and chronic obstructive pulmonary disease (COPD), in addition, female patients presented anemia and thyroid disease.

Half of all hospital admissions (51.2%) were registered via emergency care, 11.3% were admissions per patient initiative, 8.9% via other hospital services and 7.9% via ambulatory services (Table 2). Additionally, 77.5% of the admissions were urgent or non-scheduled vs. 22.0% being programmed admissions. Median length of hospital stay was 5 days, with no differences between males and females (mean: 6.5 days). Patients admitted due to angina pectoris, complications of an old myocardial infarction and chronic ischemic heart disease had a median length of stay of 4 days (mean: 6.2 and 6.0 days, respectively). Mean length of stay decreased significantly over time from 6.9 days in 2011 to 6.2 days in 2019 ($p < 0.0001$). In addition, in 33.5% of admissions a stay in an intensive care unit (ICU) was registered, median length of ICU stay was 2 days (mean: 2.7 days).

The age-adjusted incidence rate of IHD was 28.5 per 10,000 males and 8.21 per 10,000 females over the study period. In patients over 75 years of age the incidence rate was 148.7 per 10,000 males and 70.7 per 10,000 females. Incidence rate decreased significantly in all patient groups over time, except in males aged 65-74 years and females under 45 years (Figure 1a,b).

The mortality rate of IHD measured in hospital centers was 4.4%, reaching the 6.6% in females, and increasing with patients' age (Table 2). Hospital mortality rate was 1.8% in patients with angina pectoris, 7.0% in patients with acute myocardial infarction, 7.9% in patients admitted for complications of old myocardial infarction, 4.8% in patients with other acute ischemic heart diseases and 1.3% in patients with chronic ischemic heart disease. No significant trends were identified in the mortality rate over time (Figure 1c,d).

The most frequent medical procedures registered during the admission were diagnostic procedures (Table 3). Therapeutic procedures comprised the removal of coronary artery obstructions and stent insertion, bypass anastomosis for heart revascularization, the injection of therapeutic substances, primarily anticoagulant, antibiotics, electrolytes, and thrombolytic agents, followed by respiratory therapy and blood transfusions.

Median admission cost was €5175, €5366 for males and €4519 for females (Table 4). Median admission cost was €2703 in patients with angina pectoris, €7185 in patients with acute myocardial infarction, €5303 in patients admitted for complications of old myocardial infarction, €3391 in patients with other acute ischemic heart diseases and €5124 in patients with chronic ischemic heart disease. Admission cost increased significantly with length of stay ($p < 0.0001$) and decreased significantly with patients' age ($p < 0.0001$). The median cost of admissions with ICU stay was €7454. No significant

trends were identified in admission costs over time (Figure 2). The total annual cost of hospital care was €693.8 million, €513.5 million corresponding to male patients.

4. Discussion

IHD represents a significant social and economic burden worldwide. This study evaluates predominantly descriptive data associated to the hospital care of IHD and the associated medical costs. Over 814,740 patients were treated in Spanish hospitals with a form of ischemic heart disease between 2011 and 2019. The majority of the patients were males (71.0%). The youngest patients were those registered with myocardial infarction and complications of an old infarction, and those with a form of chronic ischemic heart disease. The predominance of patients over 75 years of age is consistent with the typical age of onset of IHD [4]. In addition, male patients were significantly younger than females at the hospital level, which has also been observed in global studies [4]. Several well-known risk factors for the development of IHD were identified in the population as secondary diagnoses, including hypertension, hypercholesterolemia, diabetes mellitus and tobacco use disorder. The identification of lifestyle risk factors has been crucial to improve prognosis of patients with IHD, via prevention and treatment measures, while the role of genetic factors is further examined [3].

The nature of hospital attention required by these patients was evaluated via the analysis of hospital admission data. Half of the patients were hospitalized through emergency care admissions, with a median length of stay of 5 days. Length of stay was somewhat shorter in patients with angina pectoris, complications of an old myocardial infarction and chronic ischemic heart disease. Great variations have been reported in hospitalization times among regions, with 6.9 days on average reported in North America, 12.9 days in western Europe or 5.2 days in Argentina in 2016; while a tendency

to reduce hospitalization times has been reported in New Zealand (7.8 to 6.7 days between 2006 and 2016) and in France (6.0 to 5.7 days between 2009 and 2014) [17-19]. Only 33.5% of admissions registered a stay in an intensive care unit, with a median length of ICU stay of 2 days.

The age-adjusted incidence rate of IHD was 28.5 per 10,000 males over the study period, 8.21 per 10,000 females. In accordance with epidemiology data reported for other developed countries, incidence rate was found to decrease over the study period in most patient groups, however, this was not observed in males aged 65-74 years and females under 45 years [20]. In terms of mortality, global data indicates a decrease in the mortality rate of IHD, in correlation with improved treatments and preventive measures [21]. A study analyzing all deaths associated to IHD in Spain, based on data from the National Institute of Statistics, reported a decrease in mortality rates between 1998 and 2018 [22]. This was not observed in this study, considering solely hospital mortality; herein, the hospital mortality rate was 4.4% and remained stable over the study period. the highest mortality rates were registered in patients hospitalized due to an acute myocardial infarction and in those with complications of and old infarction. In this direction, bleeding complications in patients with acute coronary syndromes have been associated with a worsened prognosis, however, hemoglobin content could not be evaluated herein [23]. Sex was also a factor influencing in-hospital mortality, with significant differences found in mortality rates between males and females in patients under 65 years of age and in those over 75 years. The increased IHD case-fatality in women has been previously described, linked to differences in disease presentation and female underrepresentation in clinical trials [24-26].

The analysis of disease management was limited to the data registered in the database during the hospitalization. The data registered corresponded primarily to diagnostic procedures. Nevertheless, costs were obtained independently and were not associated to registered procedures. The median admission cost in this study was €5175, with the highest cost per admission found in patients with acute myocardial infarction (€7185). Interestingly, median admission cost decreased with patients' age, and it was associated to length of stay. In admissions that included an ICU stay, median admission cost raised to €7454. The total annual cost of hospital care was €693.8 million in this study.

IHD entails a significant economic burden for healthcare systems and society, considering its high incidence, mortality and associated disability; however, few data is available quantifying this cost [8]. The mean direct medical cost for CAD per admission goes from the €1122-€1746 reported in 2017 in France to the €10,914 (US\$11,477) reported in China in 2009, while the total economic burden reached the €4.351 million (589.9 billion yen) in 2014 in Japan [13,27,28]. When specified, direct costs were primarily attributed to surgical procedures [27]. Further studies will be required to quantify the total burden of IHD considering indirect and societal costs.

A number of limitations may have influenced the results obtained. The retrospective study design may be associated to limitations including confounding, an inferior level of evidence to that in prospective studies and a possible misclassification bias. Additionally, the population included in the study corresponds to hospitalized patients. Similarly, medical conditions and procedures were limited to those registered in the database by means of the ICD-9 and ICD-10 codes. Furthermore, statistical results should be interpreted with caution and considering the large sample size.

5. Conclusions

The incidence of IHD has decreased over the past decade in Spain in most age groups; however, the decreasing mortality rate observed in the general population was not reflected among hospitalized patients. The persistent differences in disease severity and outcomes between males and females should be considered in the revision of protocols and the design of forthcoming clinical trials.

6. Transparency section

6.1. Ethics approval and consent to participate

Ethics committee approval and consent were not required for this study.

6.2. Data availability statement

Data sharing is restricted due to legal stipulations, yet the data that support the findings of this study is fully available from the Spanish Ministry of Health via the Unit of Health Care Information and Statistics (Spanish Institute of Health Information) for researchers who meet the criteria for access to confidential data at: <https://www.mscbs.gob.es/estadEstudios/sanidadDatos/home.htm>.

6.3. Declaration of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

6.4. Declaration interest

The authors declare that they have no competing interests.

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8. Figures

Figure 1 Incidence of ischemic heart disease in males (a) and females (b) stratified by age; hospital mortality of ischemic heart disease in males (c) and females (d) stratified by age.

Figure 2 Median hospital medical costs of ischemic heart disease in (a) males and (b) females stratified by age.

9. Tables

Table 1 Characteristics of patients diagnosed with ischemic heart disease.

	Total	Males	Females	P-value
Admissions, N	971,193	690,407	280,739	-
Patients, N	814,740	578,329	236,370	-
Median age, years (IQR)	69 (20)	67 (19)	75 (18)	<0.0001
- ≥ 0 < 45 years, N	29,640	24,613	5026	<0.0001
- ≥ 45 < 65 years, N	283,469	231,582	51,866	<0.0001
- ≥ 65 < 75 years, N	210,858	154,789	56,065	<0.0001
- ≥ 75 years, N	290,772	167,345	123,413	<0.0001
Primary diagnosis, N	-	-	-	-
- <i>Angina pectoris</i>	91,980	55,415	36,562	<0.0001
- <i>Acute myocardial infarction</i>	475,170	337,337	137,800	0.0454
- <i>Complications of old myocardial infarction</i>	682	483	199	0.9094
- <i>Other acute ischemic heart diseases</i>	83,916	52,963	30,952	<0.0001
- <i>Other chronic ischemic heart disease</i>	319,445	244,209	75,226	<0.0001
Comorbidities, %	-	-	-	-
- <i>Hypertension</i>	51.0	49.2	55.6	<0.0001
- <i>Hypercholesterolemia and hyperlipidemia</i>	48.9	49.1	48.6	<0.0001
- <i>Diabetes mellitus</i>	37.0	35.2	41.3	<0.0001
- <i>Tobacco use disorder</i>	20.4	24.3	10.7	<0.0001
- <i>Cardiac dysrhythmias</i>	18.7	17.6	21.4	<0.0001
- <i>Heart failure</i>	15.2	13.3	20.0	<0.0001
- <i>Hypertensive heart and chronic kidney disease</i>	13.6	12.2	17.2	<0.0001
- <i>Overweight and obesity</i>	13.3	12.2	16.0	<0.0001
- <i>Chronic kidney disease</i>	11.4	10.9	12.7	<0.0001
- <i>COPD</i>	10.8	11.8	8.2	<0.0001
- <i>Anemia</i>	7.1	5.6	10.8	<0.0001
- <i>Thyroid disease</i>	5.4	2.8	11.8	<0.0001

IQR: Interquartile range; COPD: Chronic obstructive pulmonary disease. P-value: males vs.

females.

Table 2 Nature of hospital admissions registered in patients with ischemic heart disease.

	Total	Males	Females	P-value
Admissions, N	971,193	690,407	280,739	-
- <i>Via emergency care, %</i>	51.2	49.7	55.2	<0.0001
- <i>Per patient initiative, %</i>	11.3	11.6	10.7	<0.0001
- <i>Via other hospital services, %</i>	8.9	9.4	7.7	<0.0001
- <i>Via ambulatory services, %</i>	7.9	8.3	6.8	<0.0001
Urgent admissions, %	77.5	75.9	81.5	<0.0001
Median length of stay, days (IQR)	5 (6)	5 (6)	5 (5)	<0.0001
ICU admissions, %	33.5	35.4	28.8	<0.0001
Median ICU stay, days (IQR)	2 (2)	2 (2)	2 (2)	>0.9999
Hospital mortality, %	4.4	3.6	6.6	<0.0001
- <i>≥ 0 < 45 years, %</i>	1.1	1.0	1.6	0.0001
- <i>≥ 45 < 65 years, %</i>	1.5	1.4	1.6	0.0001
- <i>≥ 65 < 75 years, %</i>	2.8	2.8	2.8	0.9359
- <i>≥ 75 years, %</i>	8.8	7.6	10.5	<0.0001

IQR: Interquartile range; ICU: Intensive care unit. P-value: males vs. females.

Table 3 Medical procedures registered during the hospital admission in patients with ischemic heart disease.

	Total	Males	Females	P-value
Admissions, N	971,193	690,407	280,739	-
- <i>Arteriography, angiocardiography using contrast material</i>	62.2	64.5	56.6	<0.0001
- <i>Diagnostic ultrasound</i>	51.4	51.2	52.1	<0.0001
- <i>Diagnostic procedures on heart and pericardium</i>	49.8	53.9	39.7	<0.0001
- <i>Cardiac stress tests, pacemaker and defibrillator checks, other cardiac measurements</i>	42.3	42.3	42.5	0.0566
- <i>Removal of coronary artery obstruction and insertion of stent(s)</i>	32.2	35.0	25.2	<0.0001
- <i>Injection of therapeutic substances</i>	26.4	25.7	28.1	<0.0001
- <i>X-ray</i>	26.3	25.0	29.6	<0.0001
- <i>Bypass anastomosis for heart revascularization</i>	9.1	10.7	5.1	<0.0001
- <i>Respiratory therapy</i>	6.4	6.1	7.3	<0.0001
- <i>Transfusion of blood and blood components</i>	6.0	5.6	6.7	<0.0001

P-value: males vs. females.

Table 4 Summary of hospital medical costs of ischemic heart disease.

	Total	Males	Females	P-value
Admissions, N	971,193	690,407	280,739	-
Mean admission cost, € (SD)	6429 (5881)	6694 (6147)	5779 (5112)	<0.0001
Median admission cost, € (IQR)	5175 (3925)	5366 (4207)	4519 (3396)	<0.0001
- ≥ 0 < 45 years, %	6226	6492	5045	<0.0001
- ≥ 45 < 65 years, %	5516	6041	5081	<0.0001
- ≥ 65 < 75 years, %	5248	5366	4948	<0.0001
- ≥ 75 years, %	4626	4867	4509	<0.0001
Median cost admission ≤ 5 days, €	4948 (3465)	5082 (3804)	4363 (3486)	<0.0001
Median cost admission > 5 days, €	5379 (4826)	6226 (5192)	5045 (4151)	<0.0001
Median cost ICU admission, €	7454 (4735)	7454 (4735)	7267 (4735)	<0.0001

SD: Standard deviation; IQR: Interquartile range; ICU: Intensive care unit. P-value: males vs.

females.