

Special article

# Spanish Cardiac Catheterization and Coronary Intervention Registry. 28th Official Report of the Spanish Society of Cardiology Working Group on Cardiac Catheterization and Interventional Cardiology (1990–2018)



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ABSTRACT

**Introduction and objectives:** The Working Group on Cardiac Catheterization and Interventional Cardiology presents its annual report on the activity data for 2018.

**Methods:** Data were voluntarily provided by participating centers. The information was introduced online and was analyzed by the Steering Committee of the Working Group on Cardiac Catheterization and Interventional Cardiology.

**Results:** In 2018, data were reported by 109 hospitals, 83 of these centers are public. A total of 157 632 diagnostic procedures (140 670 coronary angiograms) were performed. This year, the number of percutaneous coronary interventions increased to 72 520 (2.2% increase). There was also an increase in the complexity of coronary interventions: 10.6% in chronic total occlusions and 4.2% in unprotected left main treatment. A total of 21 261 interventional procedures were performed in the acute myocardial infarction setting, of which 91% were primary angioplasties (9.6% higher than in 2017). A total of 108398 stents were implanted, of which 93.8% were drug-eluting stents (3.5% increase). Radial approach was used in 89.4% of interventional procedures. The number of transcatheter aortic valve implantations continued to increase (25.3% increase, n = 3537), as well as the number of percutaneous mitral valve repair procedures (21.4% increase, n = 328), left atrial appendage closures (10.6% increase, n = 644) and patent foramen ovale closures (81% increase, n = 514).

**Conclusions:** An increase in diagnostic and therapeutic procedures was reported in 2018, particularly in primary percutaneous coronary interventions. The use of the radial approach and complex procedures also increased. The number of structural procedures rose significantly, following the trend seen in recent years.

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## Registro Español de Hemodinámica y Cardiología Intervencionista. XXVIII Informe Oficial de la Sección de Hemodinámica y Cardiología Intervencionista de la Sociedad Española de Cardiología (1990–2018)

RESUMEN

**Introducción y objetivos:** La Sección de Hemodinámica y Cardiología Intervencionista presenta su informe anual con los datos del registro de actividad correspondiente a 2018.

**Métodos:** Los centros españoles con laboratorio de hemodinámica proporcionan sus datos voluntariamente. La información se introduce *online* y la analiza la Junta Directiva de la Sección de Hemodinámica y Cardiología Intervencionista.

**Resultados:** Han participado en el registro nacional 109 centros, de los cuales 83 son públicos. Se realizaron 157.632 estudios diagnósticos, entre ellos 140.670 coronariografías, un 1,6% más que en 2017. Los procedimientos intervencionistas coronarios aumentaron en un 2,2% (n = 72.520), y se registró un incremento en la complejidad del intervencionismo: del 10,6% en el tratamiento de oclusiones crónicas y del 4,2% en tronco no protegido. Se realizaron en total 21.261 procedimientos en infarto agudo de miocardio, de los cuales un 91% fueron angioplastias primarias (el 9,6% más que en el año previo). El acceso radial alcanzó el 89,4% de los procedimientos intervencionistas. En intervencionismo estructural, destaca un incremento en el implante percutáneo de válvula aórtica del 25,3% (n = 3.537), en las

Palabras clave:

Registro

Cateterismo cardiaco

Intervencionismo coronario

Intervencionismo estructural

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reparaciones percutáneas de la válvula mitral del 21,4% (n = 328), en los cierres de la orejuela izquierda del 10,6% (n = 644) y en los cierres del foramen oval permeable del 81% (n = 514).

**Conclusiones:** En 2018 se ha registrado un incremento en los procedimientos diagnósticos y terapéuticos en intervencionismo coronario, especialmente en angioplastia primaria. Destaca el alto porcentaje de abordaje radial y el incremento en intervencionismo complejo. El intervencionismo estructural continúa con el crecimiento exponencial registrado en años anteriores.

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## Abbreviations

AMI: acute myocardial infarction

PCI: percutaneous coronary intervention

TAVI: transcatheter aortic valve implantation

## INTRODUCTION

One of the fundamental tasks of the Steering Committee of the Working Group on Cardiac Catheterization and Interventional Cardiology is the collection of activity data from Spanish catheterization laboratories to prepare the annual registry. This work, which has been carried out uninterrupted since 1990,<sup>1–27</sup> allows a general view of the changes over time in interventional cardiology and helps to detect opportunities for improvement.

To reflect the growth and diversification of interventional activity in recent years, new variables corresponding to recently emerged techniques and procedures have gradually been introduced into the registry while those that have become outdated have been simplified or modified. Data are voluntarily contributed via an online database to facilitate participation. Data cleaning is performed by members of both the steering committee and the working group, given that the preliminary results are presented at the annual meeting of the working group, which took place in 2019 on May 9th and 10th in Ibiza, Spain.

The value of our annual activity record lies in its ability to reveal the degree of implementation of percutaneous techniques in Spain and to relate it to the international setting, as well as to evaluate and compare the development of interventional cardiology in the different autonomous communities. Even with the limitations of a voluntary registry,<sup>28</sup> the free availability of the data promotes understanding of the actual distribution of resources and the trends in the use of diagnostic and therapeutic procedures. Therefore, these data serve as a reference to guide interventions to improve health care in multiple ways, such as in research, prevention, treatment, and resource distribution. Moreover, the combined effort of the interventional cardiology field to record its activity exemplifies, besides its transparency, its commitment to continuously improving a health care system that is defined by its equity and universality.

This article represents the 28th report on interventional activity in Spain and collects activity from both public and private centers corresponding to 2018.

## METHODS

In the present registry, data were collected on the diagnostic and cardiac interventional activity of most Spanish hospitals in 2018. Data collection was voluntary and was not audited. Anomalous data or data that deviated from the trend observed in a hospital in recent years were referred back to the responsible

researcher from the center for reassessment. Data were collected via a standard electronic questionnaire that could be accessed, completed, and consulted through the website of the Working Group on Cardiac Catheterization and Interventional Cardiology.<sup>29</sup> The data were analyzed by the Tride company (Madrid), in conjunction with a member of the committee. The data were compared with those obtained in previous years by the working group's steering committee. The results are published in this article, but a preliminary draft was presented as a slideshow at the working group's annual meeting.

As in previous years, the population-based calculations for both Spain and each autonomous community were based on the population estimates of the Spanish National Institute of Statistics up until July 1st, 2018, as published online.<sup>30</sup> The Spanish population was estimated to have increased to 46 722 980 inhabitants. As in recent years, the number of procedures per million population for the country as a whole was calculated using the total population.

## RESULTS

### Infrastructure and Resources

A total of 109 hospitals performing interventional activity in adults participated in this registry; most of these centers (n = 83) were public (appendix 1). This number effectively represents the activity carried out in Spain, with most of the volume performed in centers with public funding. There were 239 catheterization laboratories: 144 (60.2%) were exclusively for cardiac catheterization, 62 (25.9%) were shared rooms, and 33 (13.8%) were hybrid rooms.

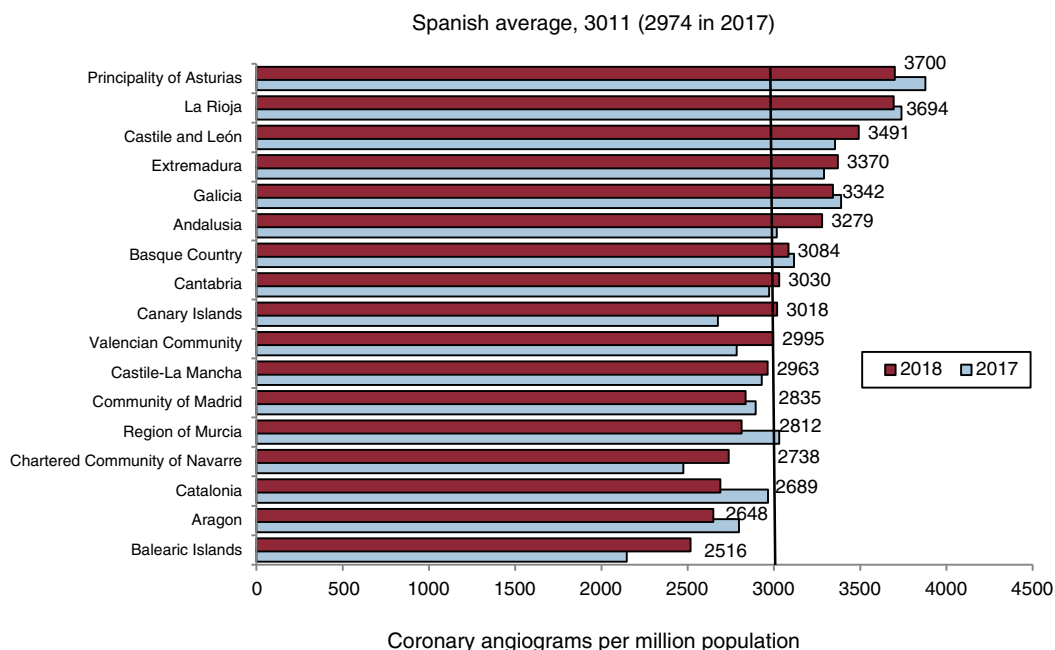
In terms of staff, the 109 centers had 463 active interventional cardiologists in 2018 (411 of them accredited). Of the total number of interventional cardiologists recorded, 99 (21.4%) were women, a figure that progressively increases each year (and is 12.5% more than in 2017). The number of residents in training increased to 90 in 2018 (12% higher than in 2017). Of nursing staff, there were 701 registered nurses and 81 radiology technicians.

### Diagnostic Procedures

In 2018, 157 632 diagnostic studies were performed, representing a 2.1% increase vs 2017. Of these procedures, 140 670 (89.2%) were coronary angiograms (1.6% more than in 2017). There was another increase in the radial approach, used in 87.4% of all diagnoses in 2017 (a 1.7% increase vs 2017).

The average number of diagnostic studies was 3374 procedures per million population in Spain; in terms of coronary angiography, the Spanish average was 3011 per million, slightly higher than that registered in 2017 (2974). The distribution by autonomous community of coronary angiograms per million population is shown in figure 1.

In line with the tendency of previous years, there was another progressive increase in intracoronary diagnostic techniques. In



**Figure 1.** Coronary angiograms per million population. Spanish average and total by autonomous community in 2017 and 2018. Source: Spanish National Institute of Statistics.<sup>30</sup>

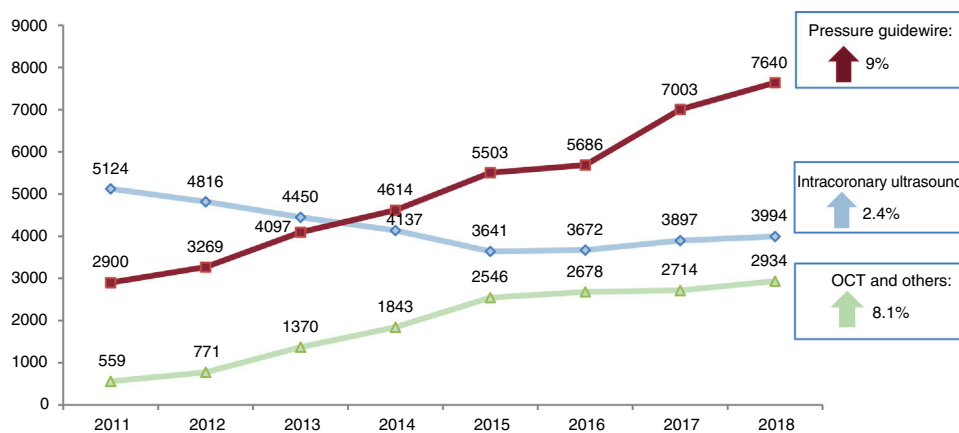
total, 7640 functional study procedures were performed with the pressure guidewire (9% more than in 2017). The gradual decrease in intracoronary ultrasound in favor of optical coherence tomography in recent years stopped in 2016 and 2017 and even reversed in 2018, with a 2.4% increase. However, the use of optical coherence tomography, whose application had stagnated, also underwent significant growth in 2018 vs 2017 (8.1%; 2934 cases vs 2714 in 2017). The changes in intracoronary diagnostic techniques in recent years are shown in figure 2.

### Percutaneous Coronary Interventions

The number of percutaneous interventions (PCIs) recorded in 2018 was 72 520, which is 2.2% higher than the 70 928 PCIs

in 2017. The changes in PCIs over time are shown in figure 3. There were 1551 PCIs per million population (vs 1524 in 2017 and 1478 in 2016). As in recent years, the PCI/coronary angiography ratio remained at around 0.5.

The reported data reveal a clear tendency for an increase in the number of interventional procedures considered complex. There was further growth in procedures performed on the left main vessel, reaching a total of 3815 (4.2% more than in 2017), which comprised PCI of the unprotected left main coronary artery in 75%. In addition, 2594 lesions were considered by operators to be chronic total occlusions (10.6% more than in 2017), as well as 7768 bifurcation lesions (17% more than in 2017). Finally, the number of restenosis interventions fell to 2695 (vs 2812 in 2017). The progressive decrease in recent years in this procedure parallels the greater penetration of the drug-eluting stent.



**Figure 2.** Changes in the numbers of the different intracoronary diagnostic techniques. OCT, optical coherence tomography.

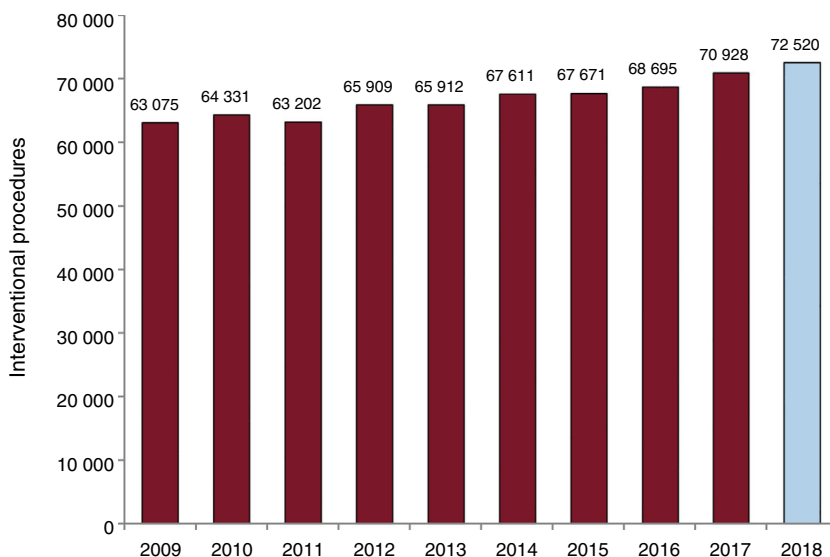


Figure 3. Changes in the number of percutaneous coronary interventions between 2009 and 2018.

As with diagnostic activity, the radial approach predominated in PCIs and was used in 89.4% of interventional procedures (88.4% in 2016). The changes over time since its introduction are shown in figure 4, from an equal standing with the femoral approach in 2010 to its current dominance.

The distribution by autonomous community of the 1551 PCIs per million population in Spain is shown in figure 5. Regarding the distribution per hospital, 23 centers performed more than 1000 PCIs in 2018 (2 less than in 2017) and 51 between 500 and 1000 (2 more than in 2017). In 2018, 72% of the centers reported the immediate outcome variables: a successful outcome without complications was reported for 96.6%; 1% reported severe complications (death, acute myocardial infarction [AMI], or the need for urgent cardiac surgery); and only 0.4% reported intraprocedural death.

### Stents

Implanted stents numbered 108 398 in 2018, which was a slight increase vs 2017 (105 529 stents). The stent/procedure ratio was 1.6, similar to that of previous years. The percentage of drug-eluting stents continued to increase, reaching 93.8% (101 713) vs 90.3% (95 253) in 2017. When the use of drug-eluting stents was analyzed by autonomous community (figure 6), a generalized increase was observed. Notably, these stents comprised 98% of all stents implanted in more than half of communities. The number of procedures with bioabsorbable devices was still very low (488 cases, 0.5% of implanted stents), as well as the number of procedures performed with dedicated bifurcation stents (179 cases, 0.2% of the total) or with self-expanding stents (33 cases, 0.03%). There was a significant increase in the use of polymer-free stents, which

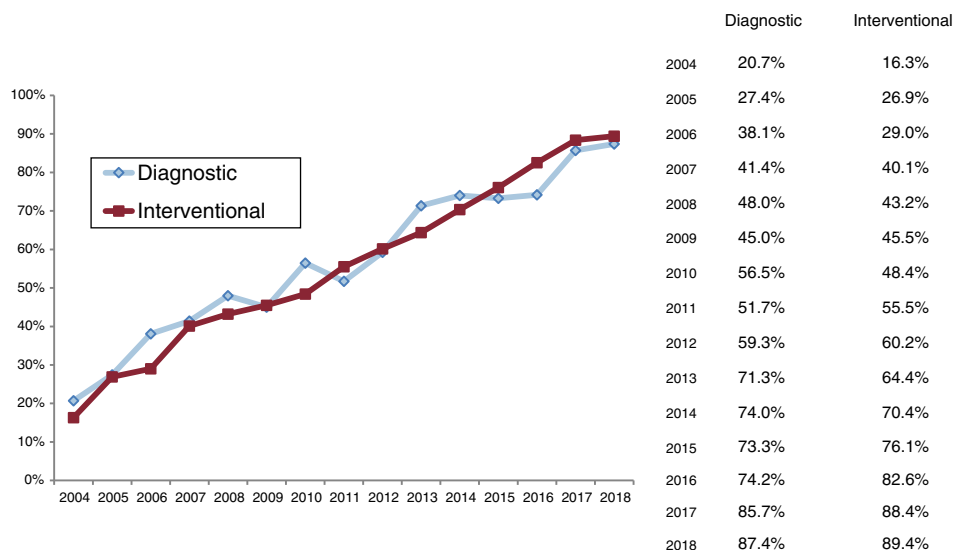
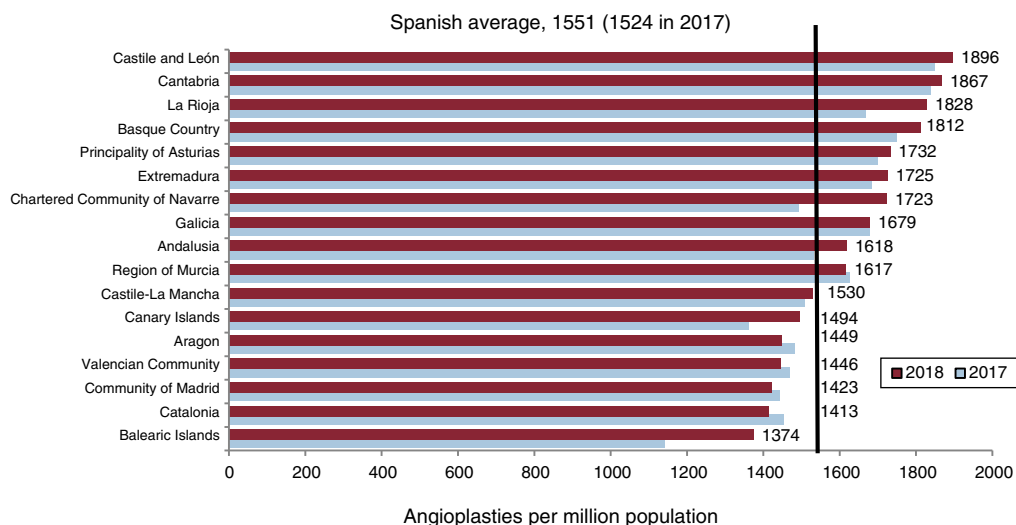


Figure 4. Changes in the number of diagnostic and interventional procedures involving the radial approach since 2004.



**Figure 5.** Percutaneous coronary interventions per million population, Spanish average and total by autonomous community in 2017 and 2018. Source: Spanish National Institute of Statistics.<sup>30</sup>

represented 5.3% of all implanted stents in 2018 (5792 cases) vs 3.6% in 2017 (3711 cases).

**Other Devices and Procedures Used in Percutaneous Coronary Intervention**

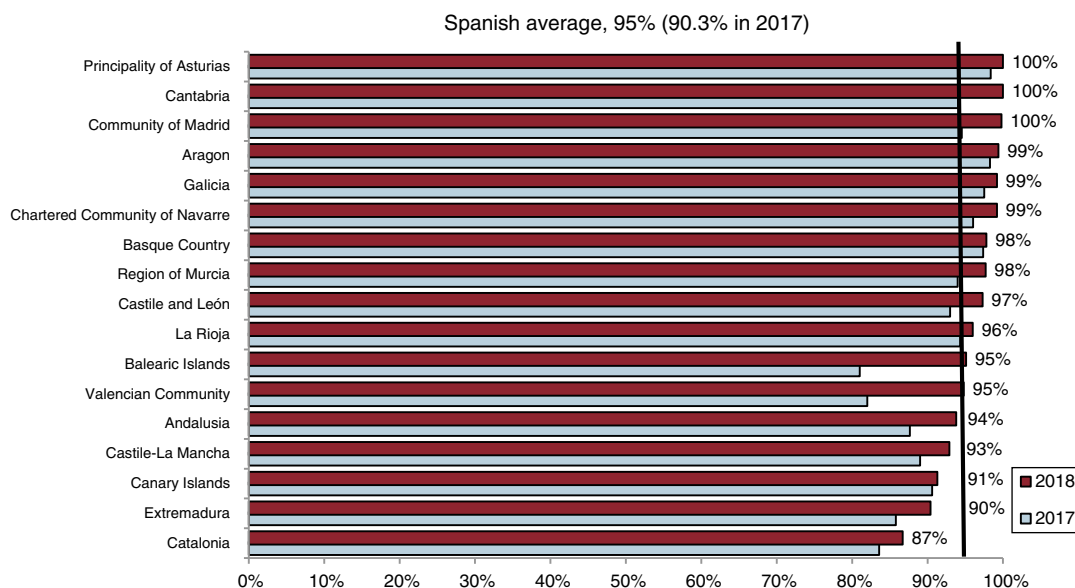
Parallel to the increased complexity of interventional procedures, there was a marked increase in the use of plaque modification devices. On the one hand, the use of rotational atherectomy devices reached a peak of the last 10 years with 1517 reported cases (1324 in 2017 and 1171 in 2016), while laser atherectomy devices experienced a marked increase vs 2017 (88 cases in 2018 vs 58 vs 2017). On the other hand, there was also an increased use of special balloons, such as cutting balloons (from 2096 in 2017 to 2925 in 2018), scoring balloons (from

1931 in 2017 to 2044 in 2018), and drug-coated balloons (from 2664 in 2017 to 2727 in 2018). Notably, due to their recent introduction, 47 procedures were performed with intracoronary lithotripsy balloons.

In 2018, there was a repeat in the tendency observed in 2017 for a significant increase in the implantation of short-term circulatory assist devices during complex interventions. The use was reported of 109 extracorporeal membrane oxygenators (vs 68 in 2017) and of 149 Impella devices (vs 106 in 2017).

**Percutaneous Coronary Interventions in Acute Myocardial Infarction**

The number of PCIs in AMI stabilized in 2018, with similar numbers to those recorded the previous year (21 261 interventions



**Figure 6.** Use of drug-eluting stents by autonomous community.

in AMI vs 21 395 in 2017). The most notable finding in this section is the marked increase in primary angioplasties, a 9.6% increase vs 2017 (19 490 vs 17 785), representing 91.6% of all PCIs in AMI. Regarding the pharmacoinvasive strategy, 680 rescue PCIs were recorded after fibrinolysis administration (3.1% of the total number of AMI procedures), as well as 1089 delayed or elective PCIs (5.1% of the total number of AMI procedures).

Primary PCI accounted for 26.8% of all angioplasties. The average number of primary PCIs per million population in Spain was 417 (vs 382 in 2017 and 356 in 2016). There was a largely generalized increase in the primary angioplasty rate by autonomous community (figure 7), although the growth was especially marked in Andalusia, the Balearic Islands, the Canary Islands, Aragon, and Castile and León. However, there may be a bias because some hospitals may not have introduced their data; thus, these figures should be taken with caution. The number of centers performing more than 300 primary PCIs per center was maintained (21 in 2018 and 2017), as well as the number of centers performing between 200 and 300 (21 in 2018 vs 22 in 2017). However, there was an increase in those that performed between 100 and 200 primary PCIs (31 in 2018 vs 27 in 2017).

In terms of the technical aspects of AMI treatment, the radial approach, in line with the above-mentioned results, was the approach of choice and was used in 87% of PCIs in AMI. The same situation was seen with the use of drug-eluting stents in the setting of infarction, which reached 98% (92% in 2017). Finally, the number of procedures using thrombus extractor devices slightly decreased, from 32% in 2017 (6907) to 29% in 2018 (6205).

### Percutaneous Coronary Intervention in Adult Congenital Heart Disease

The most noteworthy finding in this section is the considerable increase in the number of permeable foramen ovale closures, which doubled in 2018 (from 284 cases in 2017 to 514 in 2018). There were 2 cases of device embolization and 3 implantation failures without complications. The number of atrial septal defect closures was stable vs 2017 (294 cases in 2017 and 2018), with

3 cases of device embolization. There were 22 patent ductus arteriosus closures (25 in 2017) and 12 ventricular septal defect closures (11 in 2017), 3 congenital and 9 acquired. Percutaneous pulmonary valve implantations were performed in 35 cases (32 in 2019), with a success rate of 97%.

### Percutaneous Coronary Intervention in Structural Heart Disease

In 2018, 528 valvuloplasties were recorded in adults, 51% on the aortic valve, 42% on the mitral valve, and 7% on the pulmonary valve. The number of isolated aortic valvuloplasties continued to increase, with 268 procedures in 2018 (252 in 2017); success was achieved in 261 patients (98.8%). Breaking with the tendency of recent years, there were also more mitral valvuloplasties: 225 were reported in 2018 (202 in 2017). The technique was successful in 216 patients (96%) and 6 complications were reported (3 severe mitral regurgitations and 3 cardiac tamponades).

Once again, transcatheter aortic valve implantation (TAVI) was the interventional procedure showing the greatest increase in use in structural heart disease. Overall, 3537 implantations were registered in 2018 vs 2821 in 2017 (a 25.3% increase), representing an average of 76 procedures per million population (vs 61 in 2017). If this growth is assessed by autonomous community (figure 8), there was a substantial increase for most of them vs 2017, with Cantabria, Galicia, Principality of Asturias, Community of Madrid, Castile and León, and the Basque Country above the average. TAVIs were implanted in 1894 patients older than 80 years of age (53.5%) and, regarding the indication, half of the patients had surgical contraindication or high surgical risk (49.5% vs 61% in 2017); the risk was intermediate in 17% of patients and not specified in the remainder. In terms of the type of prosthesis used, the expandable balloon valve was used in 1441 cases (40.7%), whereas the self-expanding valve was used in 1623 cases (45.8%); in 473 procedures, the type of valve used was not specified. In percutaneous procedures, femoral access predominated and was used in 2722 cases. For the first time in Spain, the transsubclavian/axillary approach was used (16 cases), as well as the transcaval

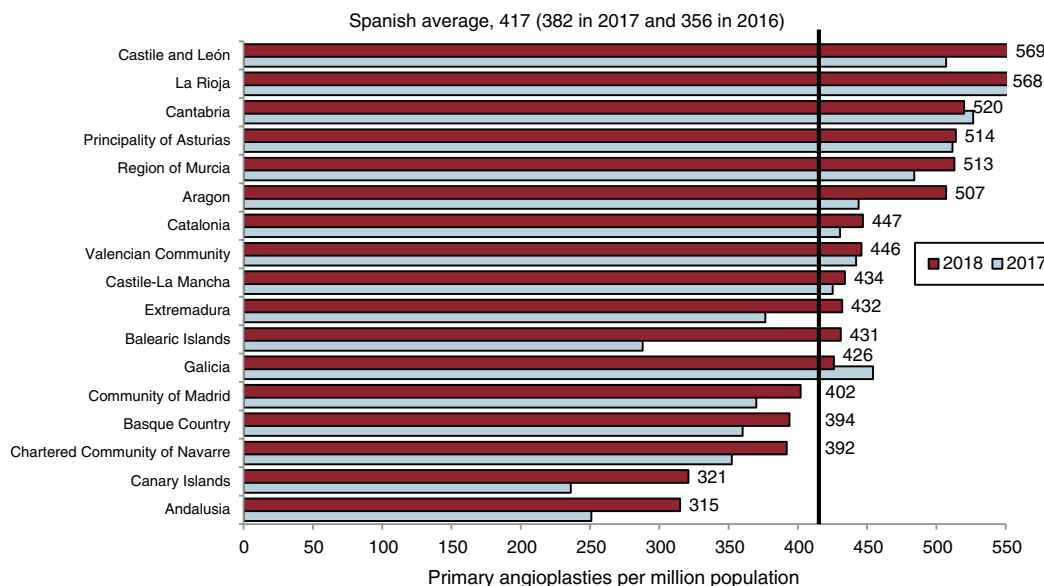
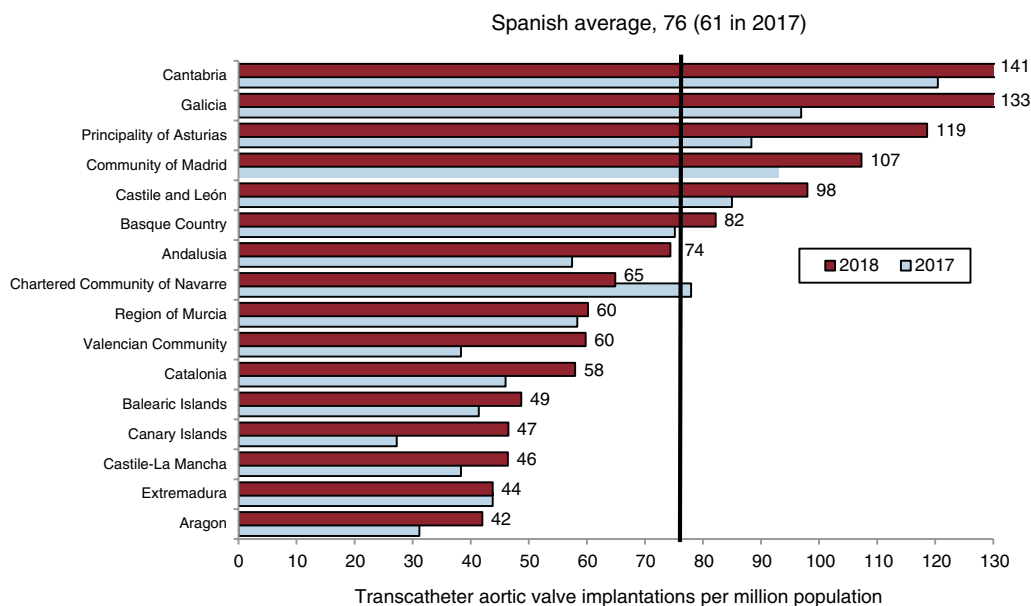


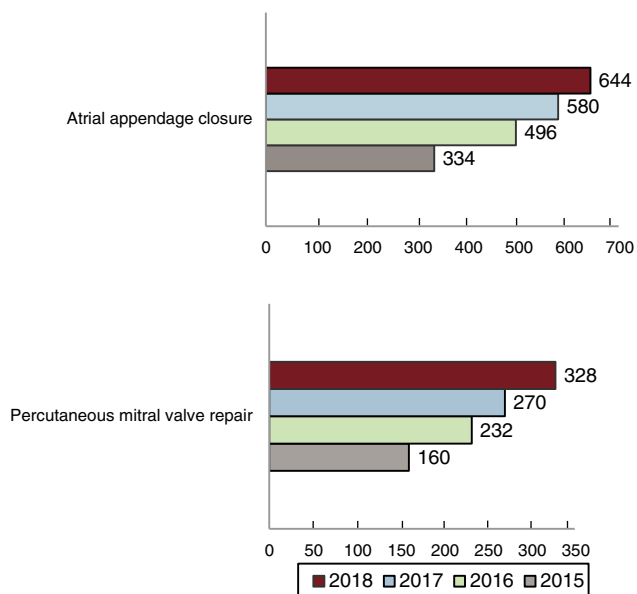
Figure 7. Primary angioplasties per million population, Spanish average and total by autonomous community in 2017 and 2018.



**Figure 8.** Transcatheter aortic valve implantation per million population. Spanish average and total by autonomous community in 2017 and 2018. No data are available for La Rioja.

(2 cases); surgical access was used in 360 patients, 50% transfemoral, and the transapical approach fell from 2.5% of cases in 2017 to 1.8% in 2018. Regarding in-hospital outcomes, 143 major intraprocedural complications (4%) were reported. Conversion to surgery was required for 0.4% (14 cases, 13 of them urgent). In-hospital death was reported in 65 patients (1.7%). A total of 346 patients (9.8%) required definitive pacemaker implantation.

In 2018, 644 left atrial appendage closure procedures were performed, representing a 10.6% increase vs 2017 (582 cases)



**Figure 9.** Changes from 2015 to 2018 in atrial appendage closure and percutaneous mitral valve repair procedures.

(figure 9). Closures were performed with a disc-and-lobe device in 399 patients (58.8% of the total) and with a 1-piece device in 205 (31.8% of the total); in the remaining cases, the type of closure was not specified. There were 12 cases of procedural complications, defined as tamponade, embolism, or death, representing 1.8% of the total.

Another notable finding was the significant growth in 2018 in percutaneous valvular repair with the MitraClip device (figure 9). The registry recorded 328 cases of mitral repair (270 in 2017, a 21.4% increase), with a total of 469 clips (1.4 clips per procedure, the same as in 2017). In addition, functional mitral regurgitations comprised 65.8% while 19.1% were degenerative and 15.1% mixed. In terms of outcomes, the mitral regurgitation was reduced to < grade 2 in 306 patients (94%; 9 without residual mitral regurgitation, 192 with grade 1 residual mitral regurgitation, and 105 with grade 2); insufficient improvement was achieved in the remaining 6%. Complications developed in 9 patients. Another notable finding from analysis of the registry data was the introduction to Spain of percutaneous techniques for treating the tricuspid valve; in 2017, the MitraClip device was used for the compassionate treatment of tricuspid regurgitation in 4 patients. Its use increased in 2018: 18 patients were treated with this technique, without complications. In addition, the first 2 prostheses were percutaneously implanted in 2018 using a bicaval technique, as well as the first Navigate tricuspid prosthesis.

Finally, there were 38 cases of endovascular aortic repair and 29 cases of renal denervation (24 in 2017). Each year sees the inclusion of new variables to reflect all of the techniques that have been introduced. Thus, it is notable that 11 procedures were performed with a coronary sinus reducer device in 2018 (1 in 2017) and 10 with the V-wave device (3 in 2017).

**DISCUSSION**

The activity recorded in 2018 clearly reflects the changes over time in interventional cardiology in Spain and allows us to

envisage the future path for this field. PCI activity continues to show slow but steady growth and a clear qualitative leap, whose strongest indicators are the increase in all intracoronary diagnostic techniques, the high percentage of radial access, and the greater use of plaque modification devices in complex patients. In structural heart interventions, the overall number of techniques performed has increased in recent years, with significant growth in the number of TAVI, percutaneous mitral valve repair, patent foramen ovale closure, and atrial appendage closure procedures.

Regarding diagnostic activity, it is worth noting the higher number of procedures guided by intracoronary diagnostic techniques. In line with the recommendations of the recent European clinical practice guidelines on myocardial revascularization,<sup>31</sup> which prioritize the use of intracoronary ultrasound for the diagnosis and treatment of left main coronary artery disease, an increase has been observed for the third consecutive year of the use of intracoronary ultrasound, parallel to the increase in percutaneous treatment of the left main trunk. In addition, and also in line with the new recommendations of the above-mentioned guidelines, which upgrade the indication for the use of optical coherence tomography for stent implant optimization (from IIb C to IIa B), this technique experienced significant growth in 2018 (8.1%) after plateauing in recent years. Particularly relevant is the continuous increase in the use of the pressure guidewire (9% vs 2017), supported by the excellent results obtained both in chronic patients and in those with AMI.<sup>32</sup> In addition, the development of nonhyperemic indices, which facilitate and expedite the procedure,<sup>33</sup> has helped to popularize this technique.

Despite the unstoppable growth of interventional activity in structural heart disease, the activity in PCI, far from being reduced, increased by 2.2% vs 2017. In 2018, PCI activity reached a rate of 1524 PCIs per million population, although this figure is still far from the recently published European average (2300 PCIs per million).<sup>34</sup> Analysis of the collected data highlighted the considerable increase in complex PCIs. On the one hand, there was a higher number of PCIs in the unprotected left main trunk and bifurcations and, particularly, a significant increase (10.3% vs 2017) in the management of chronic occlusions. The latter is supported by the publication of several studies with positive results, most notably the EuroCTO<sup>35</sup> European trial, which demonstrated the superiority of revascularization of chronic occlusions vs optimal medical therapy in improving quality of life. On the other hand, the indicators of an increase in the complexity of the procedures being performed are the large increase in the use of rotational and laser atherectomy, the greater use of cutting balloons, and the introduction of intracoronary lithotripsy<sup>36</sup> and plaque modification systems for severely calcified lesions. Finally, it is important to note that, although we face more and more complex procedures, the use of the radial approach continues to increase in PCIs. Thus, 89.4% of PCIs in 2018 were performed via radial access, with the levels placing Spain at the forefront in this field.

One of the figures to highlight regarding PCIs in AMI is the significant increase in the number of primary angioplasties (9.6% more than in 2017), particularly in autonomous communities such as Andalusia, the Balearic Islands, and the Canary Islands, which have strengthened their health care network protocols for AMI. This is one of the best quality indicators of interventional activity in our country,<sup>37</sup> which exceeded 400 primary PCIs per million

population (417) for the first time and brings the Spanish average closer to the 455 primary PCIs per million population reported as the European average.<sup>34</sup>

Regarding the treatment of congenital heart diseases in adults, the number of permeable foramen ovale closures doubled. Undoubtedly, the indication for this technique has been expanded by the recent publication of several studies showing its efficacy vs medical therapy in the reduction of recurrent stroke in patients with a history of cryptogenic stroke.<sup>38</sup>

The growth in interventional activity in structural heart disease has been unstoppable in recent years and the annual activity record has allowed documentation of the temporal changes in these techniques in Spain. In 2018, the number of TAVIs increased again, from 61 implantations per million population in 2017 to 71. This figure places us above the recently published European average,<sup>39</sup> although we are still at a distance from countries such as France and Germany. The incontestable evidence in favor of this technique and the extension of its indication to low-risk patients<sup>40,41</sup> favor its continued growth and augurs well for its accelerated growth in the future. Another of the main protagonists in 2018 was percutaneous mitral valve repair, which increased by 20.4% vs 2017. This technique has mostly been applied to patients with functional mitral regurgitation and high surgical risk, with a high success rate. These data are consistent with those recently published in the COAPT study,<sup>42</sup> which showed reduced rehospitalization and mortality with this technique vs optimal medical therapy in patients with functional mitral regurgitation after adequate clinical and echocardiographic selection.

## CONCLUSIONS

The 2018 Spanish Cardiac Catheterization and Coronary Intervention Registry has revealed a slow but steady increase in the number of diagnostic and therapeutic coronary procedures, as well as a significant qualitative leap in the use of intracoronary diagnostic techniques and plaque modification devices in complex patients. The elevated use of the radial approach and the progressive increase in primary PCI as a treatment for AMI are clear indicators of the quality of Spanish interventional activity. In structural heart interventions, the overall number of techniques implemented in recent years has increased, with a significant growth in the number of TAVI, percutaneous mitral valve repair, patent foramen ovale closure, and atrial appendage closure procedures.

## ACKNOWLEDGMENTS

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## CONFLICTS OF INTEREST

None.



**APPENDIX 1. HOSPITALS PARTICIPATING IN THE REGISTRY**

Community	Public hospitals	Private hospitals
Andalusia	Complejo Hospitalario Torrecárdenas	Hospital Vithas Virgen del Mar
	Hospital Universitario Puerto Real	
	Hospital Universitario Jerez de la Frontera	
	Hospital Universitario Puerta del Mar	
	Hospital Universitario Reina Sofía	
	Hospital Universitario Virgen de las Nieves	
	Hospital Universitario Juan Ramón Jiménez	
	Complejo Hospitalario de Jaén	
	Hospital Regional Universitario de Málaga Carlos Haya	
	Hospital Clínico Universitario Virgen de la Victoria	
	Hospital Universitario San Cecilio	
	Hospital Costa del Sol	
	Hospital Universitario Virgen del Rocío	
	Hospital Universitario de Valme	
Aragon	Hospital Clínico Universitario Lozano Blesa	
	Hospital Universitario Miguel Servet	
Principality of Asturias	Hospital Universitario Central de Asturias	Centro Médico de Asturias
	Hospital Universitario de Cabueñes	
Cantabria	Hospital Universitario Marqués de Valdecilla	
Castile and León	Hospital Clínico Universitario de Salamanca	Hospital Recoletas Campo Grande
	Hospital Universitario de Burgos	
	Hospital Clínico Universitario de Valladolid	
Castile-La Mancha	Hospital Universitario de León	
	Complejo Hospitalario Universitario de Albacete	
	Hospital General Universitario de Ciudad Real	
	Hospital Universitario de Guadalajara	
Catalonia	Complejo Hospitalario de Toledo	Hospital General de Cataluña
	Hospital Universitario Mútua de Terrassa	
	Hospital del Mar	
	Hospital Universitario Vall d'Hebron	
	Corporació Sanitària Parc Taulí	
	Hospital Universitari Germans Trias i Pujol	
	Hospital Universitari de Bellvitge	
	Hospital de la Santa Creu i Sant Pau	
	Hospital Universitari Clínic i Provincial	
	Hospital Universitario Dr. Josep Trueta	
Hospital Universitario Arnau de Vilanova		
Valencian Community	Hospital Universitario Joan XXIII	Hospital Clínica Benidorm
	Hospital Universitario San Juan de Alicante	
	Hospital General Universitario de Elche	
	Hospital General Universitario de Alicante	
	Hospital General Universitario de Castellón	
	Hospital General Universitario de Valencia	
	Hospital Universitario Vinalopó-Torreveja	
	Hospital Universitario La Fe	
	Hospital Clínico Universitario de Valencia	
	Hospital de Manises	
Hospital Universitario Dr. Peset		
Extremadura	Hospital Universitario de la Ribera	Hospital Vithas Perpetuo Socorro Internacional
	Complejo Hospitalario Universitario de Badajoz	
	Hospital de Mérida	
	Complejo Hospitalario de Cáceres	

**APPENDIX 1. HOSPITALS PARTICIPATING IN THE REGISTRY** (Continued)

Community	Public hospitals	Private hospitals
Galicia	Complejo Hospitalario Universitario de Santiago	Hospital San Rafael
	Complejo Hospitalario Universitario de A Coruña	
	Hospital Universitario Lucus Augusti	
	Complejo Hospitalario Universitario de Vigo-Álvaro Cunqueiro	
Balearic Islands	Hospital Universitario Son Espases	Hospital Juaneda Miramar
		Clínica Rotger
		Clínica Quirónsalud Palmaplanas
		Policlínica Nuestra Señora del Rosario
Canary Islands	Hospital Universitario Insular de Gran Canaria	Hospital Rambla Sur
	Hospital Universitario Dr. Negrín	
	Hospital Universitario Nuestra Señora de Candelaria	
	Hospital Universitario de Canarias	
Community of Madrid	Hospital General Universitario Gregorio Marañón	Hospital Universitario Sanitas La Zarzuela
	Hospital Universitario Ramón y Cajal	Hospital Vithas Nuestra Señora de América
	Hospital de La Princesa	Hospital La Milagrosa
	Hospital Central de la Defensa Gómez Ulla	Hospital Universitario Sanitas La Moraleja
	Hospital Universitario 12 de Octubre	Hospital Universitario HM Montepríncipe
	Fundación Jiménez Díaz/Hospital General de Villalba	Hospital Ruber Internacional
	Hospital Universitario Puerta de Hierro	Hospital Nuestra Señora del Rosario
	Hospital Universitario de Torrejón	
	Hospital Universitario Fundación Alcorcón	
	Hospital Clínico San Carlos	
	Hospital Universitario La Paz	
Region of Murcia	Hospital Universitario Virgen de la Arrixaca	Hospital Quirónsalud Murcia
	Hospital General Universitario Santa Lucía	Hospital HLA La Vega
Chartered Community of Navarre	Complejo Hospitalario de Navarra	Clínica Universidad de Navarra/Madrid
Basque Country	Hospital Universitario Araba-Txagorritxu	
	Hospital de Galdakao-Usansolo	
	Hospital Universitario de Cruces	
	Hospital de Basurto	
	Policlínica Gipuzkoa-Hospital Universitario Donostia	
La Rioja	Complejo de Salud San Millán-Hospital San Pedro	

The data from the Jiménez Díaz Foundation and the General Hospital of Villalba are grouped, as well as those of the University Clinic of Navarra and its headquarters in Madrid.

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