

## Patients with cardiac disease: Changes observed through last decade in out-patient clinics

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vascular disease (CVD) and assessing changes through last decade.

**METHODS:** Comparison of patients with established CVD from two similar cross-sectional registries performed in 1999 ( $n = 6194$ ) and 2009 ( $n = 4639$ ). The types of CVD were coronary heart disease (CHD), heart failure (HF) and atrial fibrillation (AF). Patients were collected from outpatient clinics. Investigators were 80% cardiologist and 20% primary care practitioners. Clinical antecedents, major diagnosis, blood test results and medical treatments were collected from all patients.

**RESULTS:** An increase in all risk factors, except for smoking, was observed; a 54.4% relative increase in BP control was noted. CHD was the most prevalent CVD but HF and AF increased significantly, 41.5% and 33.7%, respectively. A significant reduction in serum lipid levels was observed. The use of statins increased by 141.1% as did all cardiovascular treatments. Moreover, the use of angiotensin-renin system inhibitors in patients with HF, beta-blockers in CHD patients or oral anticoagulants in AF patients increased by 83.0%, 80.3% and 156.0%, respectively ( $P < 0.01$ ).

**CONCLUSION:** The prevalence of all cardiovascular risk factors has increased in patients with CVD through last decade. HF and AF have experienced the largest increases.

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**Key words:** Cardiovascular disease; Trends; Heart failure; Coronary heart disease; Atrial fibrillation

**Core tip:** Reduction in acute phase of cardiovascular disease (CVD) has lead to a progressive increase in patients with chronic CVD that are considered high-risk patients and mostly attended in outpatient clinics.

### Abstract

**AIM:** To describe current profile of patients with cardio-

The prevalence of all cardiovascular risk factors has increased in patients with CVD through last decade. Heart failure and atrial fibrillation have experienced the largest increases.

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## INTRODUCTION

Cardiovascular disease (CVD) remains as the leading cause of mortality in the world despite the progressive decrease in last decades and this has been largely due to risk factors control and improvements of acute phases management<sup>[1-4]</sup>. This positive results has lead to a large increase in the prevalence of patients with chronic CVD in the population<sup>[5,6]</sup> that are high-risk patients and benefit from the highest risk factors control<sup>[2]</sup> as well as treatment implementation<sup>[6,7]</sup>. Moreover, the progressive ageing of the population and patients has contributed to increase the complexity of patients, with higher comorbidities and polivascular disease that have higher risk of future cardiovascular events<sup>[8,9]</sup>.

Coronary heart disease (CHD) and heart failure (HF) represent more than half of the mortality attributed to CVD what highlights they relevancy in public health<sup>[1]</sup>. Several registries have depicted the changing profile of patients with CHD<sup>[4,10-12]</sup> or other types of CVD<sup>[3,8,13]</sup> but there scarce evidence concerning the changing prevalence of CVD in outpatient clinics. With the objective of describing current profile of patients with CVD and assessing changes through last decade we compared two clinical registries performed in Spain in 1999 and 2009.

## MATERIALS AND METHODS

### Study design

The CARDIOTENS 2009 registry is a cross-sectional, multicentre and nationwide study of patients with risk factors or cardiovascular disease<sup>[14]</sup>, with similar methodology of CARDIOTENS registry performed in 1999<sup>[15]</sup>; both studies were promoted the Working Group of Hypertension of the Spanish Society of Cardiology and endorsed by the Agencia de Investigación de la Soceidad Española de Cardiología (Research Agency of the Spanish Society of Cardiology). From the 32051 subjects include in the 1999 registry 6194 (19.3%) had established CVD and were compared to the 4639 (18.2% of the 25856) patients with established CVD collected in 2009.

As defined in the 1999 registry established CVD was defined as: (1) CHD if antecedents of angina, myocardial

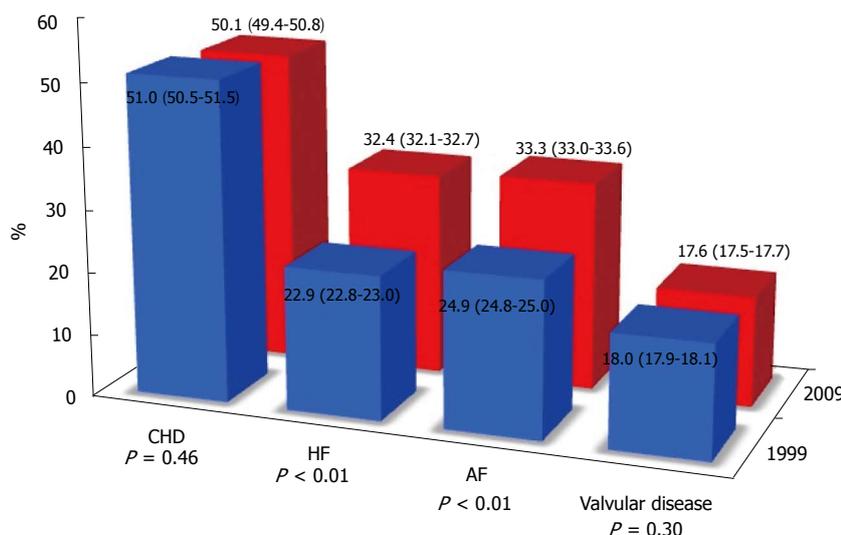
infarction, coronary revascularization or positive stress test were present; (2) HF if patients had at least one hospitalization with such as main diagnosis at discharge medical report as well as those with typical signs and symptoms of HF that had a compatible imagine diagnosis (X-ray or echocardiogram); and (3) atrial fibrillation (AF) if the diagnosis was present in a medical report or any electrocardiographic registry. A brief analysis of guideline-recommended treatments was performed based on the use of beta-blockers in patients with CHD, angiotensin converter-enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) in patients with HF, and oral anticoagulants in AF patients.

Investigators were randomly selected from primary care (88%) and cardiology outpatient clinics (12%). During the first week of November 2009 investigators included all consecutive patients that they attended; if patients had no risk factors or cardiovascular disease, only age. In patients with any risk factor or established cardiovascular disease a more extended protocol was performed in which all risk factors, clinical antecedents, treatments, physical examination and Inclusion criteria were: age  $\geq$  18 years, capability to access to full medical antecedents related to cardiovascular risk factors or events and allowance to participate by signing the informed consent. Exclusion criteria were addiction or consumption of illegal substances (cocaine, cannabis or other) or denial of the informed the consent. The study protocol and informed consent was approved by the ethics committee of the Hospital Universitario de San Juan (Alicante, Spain) and the Agencia of Investigación of the Spanish Society of Cardiology.

A specific collection data report in paper was designed for the study; a modification had to be added once printed and approved by the ethic committee due to an error in the codification of diuretics treatment. Electrocardiogram and biochemical determinations had to be obtained in within the last 6 mo. Blood pressure was measured after ten minutes of resting in the inclusion visit and two determinations were collected. Heart rate had to be measured during the physical examination.

### Variables definition

Hypertension was defined according to the 2007 European Society of Hypertension-European Society of Cardiology guidelines if 2 determinations of blood pressure were  $\geq$  140/90 mmHg or specific treatments with previous diagnosis were present<sup>[16]</sup>. Dyslipidemia was collected if any antecedent of such diagnosis or values of total cholesterol  $>$  220 mg/dL or low-density lipoproteins  $>$  160 mg/dL had been registered previously. The diagnosis of diabetes mellitus was accepted if it had been previously diagnosis in a medical report, specific drug-treatment or 2 consecutive glucose determinations were  $>$  126 mg/dL. Obesity was considered for those with body mass index  $>$  30 kg/m<sup>2</sup> and abdominal obesity if waist circumference was  $>$  102 cm in men or  $>$  88 cm in women. Chronic obstructive pulmonary disease was registered



**Figure 1** Trends in cardiovascular disease prevalence between 1999 and 2009 in both CARDIO-TENS registries. AF: Atrial fibrillation; CHD: Coronary heart disease; HF: Heart failure. Data presented as percentage (99%CI).

if specific treatments were present or previous diagnosis was present. Glomerular filtration rate was assessed by the Modification of Diet in Renal Disease equation:  $(186 \times \text{creatinine}^{-1.154} \times \text{age}^{-0.203}) (\times 0.742 \text{ in women})$ .

### Statistical analysis

Data management was made with statistical package SPSS 15.0 (SPSS Inc, Chicago, IL, United States) and 10.0/SE (Stata Corp, College Station, Tex). All variables had normal distribution so are presented as mean (standard deviation), except triglycerides that are presented as median (interquartile range); mean comparisons were made with ANOVA test and non-parametric  $\chi^2$ . Percentages were compared by *t*-Student and non-parametric Kolmogorov-Smirnov test were used for comparison of means and medians respectively. Comparisons of percentages between the 2 registries were performed by *t*-Student contrast using the analysis of variance of the estimated percentages of each registry. Statistical significance was accepted for  $P < 0.05$ .

## RESULTS

As presented in Table 1, patients of the 2009 registry had higher mean age, as well as higher prevalence of all risk factors except for current-smoking; the most significant raise was noted in patients aged  $> 70$  or  $> 80$  years. A significant reduction in mean systolic and diastolic BP was observed that lead to a 54.4% relative increase in blood pressure control. CHD was the most prevalent from of established CVD and its prevalence remained similar in both registries, as well as valvular heart disease that were the least prevalent CVD; a significant increase in the prevalence of HF (41.5% relative increase) and AF (33.7% relative increase) was observed (Figure 1).

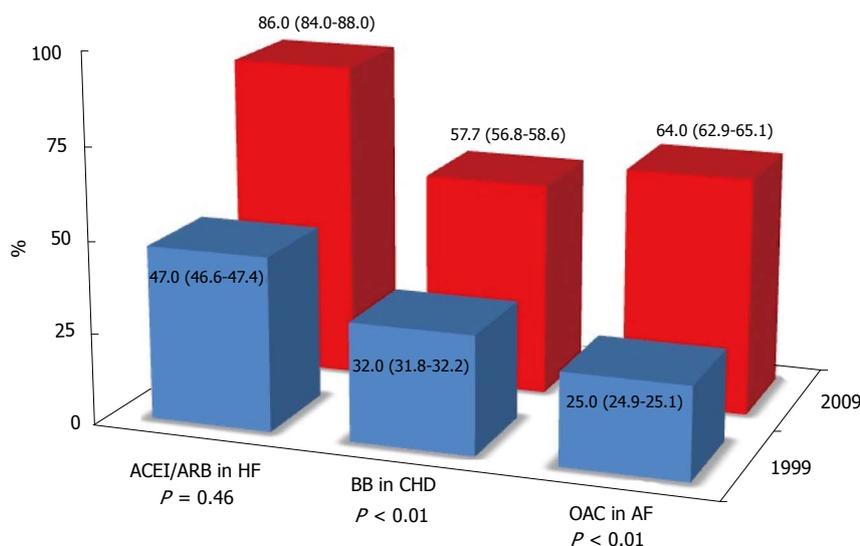
We also observed a significant reduction in serum lipid levels although the prevalence of dyslipidemia increased between both registries (Table 2); in concordance,

a large relative increase in the use of statins, as well as all cardiovascular treatments was observed between both registries, except nitrates (Table 3). Moreover, the use of guideline-recommended treatments, such as ACEI or ARB in patients with HF, beta-blockers in the setting of CHD or oral anticoagulants in patients with AF, increased 83.0%, 80.3% and 156.0% (Figure 2).

## DISCUSSION

The comparison of two large clinical registries performed with similar design and methodology allowed the description of risk factors and CVD prevalence evolution through last decade in Spain. Hypertension was the most prevalent risk factor in 1999 and was present in almost all patients with CVD 10 year later. Moreover, a relevant relative improvement in blood pressure control and guidelines-recommended treatments was observed, despite a slight reduction in mean systolic and diastolic blood pressure values. The prevalence of risk factors, mean age and medical treatments of patients included in 2009 was similar to contemporary registries<sup>[17-22]</sup> what reflects that this population might be representative of clinical relative.

Our results highlight that hypertension is present almost all patients with established CVD and is prevalence experienced a relative increase of 32% through last decade. This overwhelming rise can be explained by several facts; first, blood pressure is usually reported to be one the risk factors with poorest control what leads to a high prevalence of hypertension in patients with incident CVD<sup>[19,23]</sup>; second, the antecedent of hypertension does not impair the prognosis in the acute setting of CVD what leads to a increasing percentage of patients with hypertension and established CVD<sup>[24,25]</sup>; third, subjects with hypertension have benefit from a significantly higher decrease in cardiovascular mortality through last decades<sup>[21]</sup>; and fourth, population has experienced a relevant



**Figure 2** Changes in use of guideline-recommended treatments in each compelling indication between 1999 and 2009 in both CARDIOTENS registries. ACEI: Angiotensin-converter enzyme inhibitors; AF: Atrial fibrillation; ARB: Angiotensin-receptor blockers; CHD: Coronary heart disease; HF: Heart failure; OAC: Oral anticoagulation. Data presented as percentage (99%CI).

**Table 1** Comparative characteristics of the patients included in each registry

|                            | 1999              | 2009              | P vaule |
|----------------------------|-------------------|-------------------|---------|
| Number                     | 6194              | 4639              |         |
| Age (yr)                   | 66.7 ± 10.8       | 70.6 ± 11.3       | < 0.01  |
| Age >70 yr                 | 45.1% (44.7-45.5) | 56.9% (56.0-57.8) | < 0.01  |
| Age > 80 yr                | 13.0% (12.9-13.1) | 18.6% (18.5-18.7) | < 0.01  |
| Males                      | 54% (53.4-54.6)   | 57.2% (56.3-58.1) | < 0.01  |
| BMI > 30 mg/m <sup>2</sup> | 30% (29.8-30.2)   | 31.9% (31.6-32.2) | 0.02    |
| Hypertension               | 65% (64.1-65.9)   | 85.8% (83.8-87.8) | < 0.01  |
| Diabetes                   | 21% (20.9-21.1)   | 38.2% (37.8-38.6) | < 0.01  |
| Dyslipidemia               | 40% (39.7-40.3)   | 59.2% (58.2-60.2) | < 0.01  |
| Current smokers            | 20% (19.9-20.1)   | 12.1% (12.0-12.2) | < 0.01  |
| Left ventricle hypertrophy | 24.0% (23.9-24.1) | 30.9% (30.6-31.2) | < 0.01  |
| Systolic BP (mmHg)         | 138.2 ± 15.2      | 136.6 ± 16.0      | < 0.01  |
| Diastolic BP (mmHg)        | 79.1 ± 10.9       | 78.6 ± 11.5       | < 0.01  |
| BP < 140/90 mmHg           | 36.0% (35.7-36.3) | 55.6% (54.8-56.4) | < 0.01  |

Data collected from CARDIOTENS registries, Spain. Data are presented as mean ± SD or percentage (99%CI). BMI: Body mass index; BP: Blood pressure.

**Table 2** Lipid profile of patients included in each registry

|                           | 1999  | 2009         | P vaule |
|---------------------------|-------|--------------|---------|
| Total cholesterol (mg/dL) | 218.3 | 196.3 (45.8) | < 0.01  |
| HDL (mg/dL)               | 49.5  | 50.2 (15.3)  | < 0.01  |
| LDL (mg/dL)               | 145.1 | 117.0 (37.5) | < 0.01  |
| Triglycerides (mg/dL)     | 142.6 | 145.1 (70.5) | 0.02    |

Data collected from CARDIOTENS registries, Spain. HDL: High-density lipoproteins; LDL: low-density lipoproteins.

increase in clinical features in the population that are closely related to high-blood pressure, as advanced age<sup>[16]</sup>, obesity<sup>[26]</sup> or diabetes<sup>[27]</sup> predispose to a increasing pattern in hypertension prevalence. Our registry included stable patients with CVD and strongly supports these four key-points and provides not only a reasonable profile of

**Table 3** Medical treatments in each registry

|                     | 1999              | 2009              | P vaule |
|---------------------|-------------------|-------------------|---------|
| Antiplatelets       | 42.0% (41.6-42.4) | 76.8% (75.2-78.4) | < 0.01  |
| Diuretics           | 32.0% (31.8-32.2) | 4.4% (4.39-4.41)  | < 0.01  |
| ACEI                | 30.2% (30.0-30.4) | 43.6% (43.1-44.1) | < 0.01  |
| Statins             | 27.0% (26.9-27.1) | 65.1% (63.9-66.3) | < 0.01  |
| CCB                 | 27.8% (27.6-28.0) | 36.7% (36.3-37.1) | < 0.01  |
| Nitrates            | 25.0% (24.9-25.1) | 26.3% (26.1-26.5) | 0.06    |
| Beta-blockers       | 22.2% (22.1-22.3) | 44.6% (44.1-45.1) | < 0.01  |
| Oral anticoagulants | 17.5% (17.4-17.6) | 27.0% (26.8-27.2) | < 0.01  |
| ARB                 | 11.1% (11.0-11.1) | 38.6% (38.2-39.0) | < 0.01  |
| Insulin             | 5.1% (5.09-5.10)  | 13.7% (13.6-13.8) | < 0.01  |
| Oral antidiabetics  | 10.0% (9.9-10.1)  | 43.7% (43.2-44.2) | < 0.01  |

Data collected from CARDIOTENS registries, Spain. Data presented as percentages (99%CI). ACEI: Angiotensin converter-enzyme inhibitors; ARB: Angiotensin receptor blockers; CCB: Calcium channel blockers.

patients with hypertension and CVD but, also, a clinical perspective of its evolution through last decade.

CHD remained as the most prevalent forms of established CVD but experienced no relative change through last decade; nevertheless, the presence of HF and AF increased largely; the study protocol on the 1999 registry did not other forms of CVD, such as stroke or peripheral arterial disease, and we could not obtain data of these two relevant clinical entities<sup>[1]</sup>. HF and AF have been clearly related to age and hypertension and have been reported to rise in the overall population steeply through last decades<sup>[1,28]</sup>. Blood pressure control has been outlined as major target for prevention of HF<sup>[29]</sup> and AF<sup>[30]</sup> especially by the use of ACEI or ARB<sup>[31]</sup> and target organ damage prevention. In contrast, mean age increased in the comparison between both registries and the prevalence of octogenarians reached almost 20%. The evidence of BP control and the optimal objective in elderly patients has been less studied<sup>[16]</sup>; only the Hypertension in the Very Elderly Trial<sup>[32]</sup> study was specifically designed to assess the benefit of BP control and target BP was < 150/80 mmHg. The study demonstrated both

significant improvement in cardiovascular events and mortality in patients actively treated with a diuretic and an ACEI. These results added to net benefit of ACEI or ARB in patients with established CVD might explain the large increase in the use of these treatments observed in our results.

Our results show at least two positive messages: the increase in blood pressure control and the improvement in medical treatments. All guideline-recommended treatments experienced significant increases, being the use of statins, ACEI and ARB the most prominent. The use of statins has spread to majority of patients with established CVD, especially in the patients with CHD<sup>[17,18,23]</sup> and its use in patients with HF is much lower because its clinical benefit in absence of underlying CHD is not clear. Nonetheless, our results highlighted a very relevant increase in the use of ACEI or ARB in patients with HF that agrees with previous reports of other registries<sup>[22,28]</sup>. The use of beta-blockers in patients with CHD also increased but only reached 57%, a very similar percentage of registries that included chronic and stable patients<sup>[6,17,18]</sup>. The increase in the oral anticoagulants in patients with AF was remarkable and treatment rate in our registry was similar to the last report of the European Heart Survey<sup>[33]</sup>.

Our study has several limitations that deserve consideration, mainly derived from its design; for being a cross-sectional study it can only describe clinical associations and causal effects. Moreover, it only included consecutive patients that were attended in outpatient clinics and, therefore, our results are not representative of overall population. The study protocol did not include stroke or peripheral disease as established CVD and, therefore, we can not provide actualized data on these two relevant diseases. Finally, there was an error in the typing of diuretics and, therefore, data collection concerning this medication was not accurate.

In conclusion, the prevalence of all cardiovascular risk factors has increased in patients with established CVD, except smoking. Hypertension is most prevalent risk factors in these patients and a significant improvement in BP control has been achieved although it is still far from optimal goals. A relevant improvement in guideline-recommended treatments could be demonstrated, as well as major cardiovascular treatments, being the use of statins the most remarkable. We describe a positive trend in blood pressure control and guidelines-recommended treatments but there are still opportunities for further improvement.

## COMMENTS

### Background

Reduction in acute phase of cardiovascular disease (CVD) has led to a progressive increase in patients with chronic CVD that are considered high-risk patients and mostly attended in outpatient clinics.

### Research frontiers

Risk factors control and medical treatment has been usually reported as lower in high-risk patients. Many registries have reported relevant increases in blood pressure or cholesterol control, although the changing pattern in clinical profile

and risk factors control of patients with established cardiovascular disease has been far less studied.

### Innovations and breakthroughs

The prevalence of heart failure and atrial fibrillation has increased significantly through the last decade, meanwhile coronary heart disease remained as the most prevalent. Similarly, authors have noted an increase in mean age, especially in the percentage of elderly patients, and all risk factors but smoking. Risk factors control has increases as well as guidelines-recommended medical treatments.

### Applications

Out patients clinics should be prepared, focused and organized to attend more patients with heart failure or atrial fibrillation that have very specific considerations, such as weight-gain, symptoms control, medication use, anticoagulants complications.

### Terminology

Coronary heart disease: patients with the antecedent of myocardial infarction, angina, acute coronary syndromes or any kind of coronary revascularization.

### Peer review

This is a good descriptive study in which authors analyze changes in clinical profile and medical treatments of patients with cardiovascular disease. The results are interesting and highlight the increasing trend in the prevalence of heart failure and atrial fibrillation, two clinical entities that deserve very specific considerations in out-patient clinics.

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