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A Retrospective Cohort Study of SARS-COV2 Infection in Hypertenses Patients in a Primary Care Center.

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Abstract:	Background Our Primary Care Center registered the first case of COVID-19 in Madrid. Since then we have registered 1,470 cases of COVID-19. The aim of this study was to investigate the association of ACEi or ARB use with severity and survival in 318 patients with COVID-19 infection and hypertension in this outpatient setting. Methods Observational, single-center, cohort study. Computerized database of outpatient setting and hospital records. Follow-up through personal assistance, daily telephone control and databases. The data were processed in the STATA satatistical software version 16.0. Findings There were 318 patients with arterial hypertension (median age, 77), 167 patients were older than 75 (52·51%). ACEi or ARB were taking by 183 patients (57·53%). There were 133 (41·82%) hosted in nursing home. Comparing ACEi vs. ARB vs. other treatments, we find no differences between severe vs. non-severe illness or survival. The multivariable analysis showed more severity and non-survival correlation in patients with previous stroke (p 0·0064), smoking habits (p 0·0382), older than 75 years old (p<0.0001) and patients in nursing home (p 0·0009). Interpretation The findings of this report in a primary care setting have not identified a difference in the clinical course among COVID-19 infected people with hypertension, treated with ACE inhibitors vs. ARB vs. others, although having a previous stroke, smoking, being older than 75 years, or living in a nursing home had a worse prognosis. Funding : None.

Covering letter

Dear Sir,
We are writing to you regarding this study:

Hernández-Castilla E, Vallejo-Serrano L, Sáenz-Ausejo M, Pax-Sánchez B, Ramrath K, Fernández-Bravo JM.

A Retrospective Cohort of SARS-COV2 Infection in Hypertenses Patients in a Primary Care Center.

We believe it may be of interest to the scientific community, since COVID-19 is an emerging and highly relevant disease that has affected the world's population causing great human losses and significant social and economic implications.
With 225,216 cases up until today, May 9th, 2020, Spain is the European country with the largest number of known cases of COVID-19.
Little has been written about the role of primary care in this field. Our Primary Care Center registered the first case of COVID-19 in Madrid on February 26th, 2020. Since then, we have registered 1,470 cases of COVID-19.
There is a worldwide controversy about whether COVID-19 positive patients with high blood pressure could be affected in the course of their disease due to drug treatment with renin-angiotensin-aldosterone system inhibitors. For the moment, this doubt has not yet been verified in our environment.
We have conducted a retrospective cohort study to shed more light on this issue since we identified lack of studies in the extrahospitalary environment.
The Lancet Infectious Diseases has quickly provided a specific place for the dissemination of scientific literature in this field, so we think it is the ideal place to publish our results.
We ask that you consider our scientific article for publication. Any input from your peer-reviewers will be very welcome.

Sincerely, the authors.

A Retrospective Cohort of SARS-COV2 Infection in Hypertenses Patients in a Primary Care Center.

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Introduction

With 225,216 cases, Spain is the country in Europe with the highest number of recorded cases of COVID-19 virus and ranks second in the world. Also has the highest number of confirmed cases in terms of rate per 100,000 inhabitants in the world[1].
Our Primary Care Center registered the first case of COVID-19 in Madrid on February 26th, 2020, a young man returning from Milan. Since then, out of the population of 40,000 that corresponds to our Primary Care Center, 1,470 cases of COVID-19 have been registered.
We have experienced the worldwide controversy over whether COVID-19 positive patients with high blood pressure could be affected in the progression of their disease due to drug treatment with renin-angiotensin-aldosterone system inhibitors, angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) [2].
Doubts had arisen because some studies have suggested that ACEi and ARB may increase the regulation of angiotensin-converting enzyme 2 (ACE2) expression, thus increasing the availability of target molecules for SARS-CoV-2. Concerns remain because, although the functional role of ACE2 in the lung appears to be minimal under normal conditions, increased expression may be relevant in certain clinical states (hypertension, heart failure, coronary disease, renal failure)[3].
This controversy has been partially answered by what has been observed in the case of the Chinese population but it does not seem to have been tested in primary care yet[4]. We have conducted a retrospective cohort study to shed more light on the issue.
In this study, we set as main objective to investigate the association between ACEi or ARB and severity of illness and mortality in patients with hypertension in an outpatient setting for COVID-19 infection.

Methods

Study design and participants

In this single-center retrospective, observational study of the 1,470 patients infected with COVID-19 at the Pozuelo-Estación Primary Care Center, Pozuelo de Alarcón. Madrid, Spain, from February 26th to May 9th, 2020, we include a total of 318 hypertensive patients infected with COVID-19, whose cases have been followed by their family doctors. The study complies with international data protection regulations, as well as current Spanish legislation (BOE 294 de 6/12/2018).

Data collection

We used patient data records managed by the primary care software provider APMadrid from the SERMAS, linked to Selene and Horus software used by the hospitals in the area. These databases were searched for the hospitalization history of COVID-19 patients, including severity and survival. The software ConsultaWeb was used for data retrieval.
We locate all individuals over 14 years of age, of both sexes in our population of COVID-19 infected cases, who have been diagnosed and received care in our center, as well as identifying those diagnosed with Arterial Hypertension, Heart Failure and/or Ischemic Cardiopathy, in active treatment with ACEi, ARB and other antihypertensive treatments (beta-blockers, calcium channel blockers and others).
Data were collected on age, sex, nursing homes, co-existing conditions: coronary artery disease, congestive heart failure, diabetes mellitus, chronic obstructive pulmonary disease, chronic kidney disease, cerebrovascular disease, smoking, obesity, severity of COVID-19 infection, survival, antihypertensive drugs and prior treatment with anticoagulants/antiplatelets. A by default routine was stablished to archive electronic medical data onto a local server, from which we retrieved these data.
The follow-up of our patients included in the study has been done through personal assistance, daily telephone control, and hospital database.

Definitions

Patients were considered infected by COVID-19 if they met the diagnostic criteria published by the Spanish Ministry of Health[5].

A patient was considered a case of severe COVID-19 infection if he or she meets one of the following criteria: respiratory frequency of 30/min or greater, blood oxygen saturation levels of 93% or less, lung infiltrates more than 50%, septic shock, pulmonary thromboembolism, Intensive Care Unit stay, and/or multiple organ dysfunction or failure. Mild-moderate COVID-19 infection is considered to be that which has not presented any of the above criteria. Hypertension was defined as a history of diastolic blood pressure of 90 mmHg or greater or a systolic blood pressure of 140mmHg or greater or history of antihypertensive medication use. A patient's ACEI or ARB use was defined as use of these drugs at the time of infection.

Statistical analysis

The description of continuous quantitative variables used median and interquartile range, and qualitative variables are described by absolute frequencies and relative frequencies, expressed as a percentage. Non-parametric Mann-Whitney U tests, Chi-square test or Fisher's exact test, were used. The multivariate study on mortality and all possible factors was performed by means of binary logistic regression. The results of the model are presented in the form of Odds Ratio with the 95% confidence interval. The data were processed in the STATA statistical software version 16.0. Those with an error probability of less than 5% ($p<0.05$) were considered statistically significant differences.

Results

Our Primary Care Center attended 29,739 patients over 14 years old. As of May 9th there were 1,470 patients diagnoses with COVID-19 infection. Within this group we finally select 335 patients with arterial hypertension (n=318) and/or coronary artery disease and/or congestive heart failure under ACEi or ARB treatment.

The median age was 77 years old (IQR 61-89), 218 (68·55%) older than 65 years old, 167 (52·51%) older than 75, and 191 (60·06%) were female.

Most of the patients had chronic diseases, including 13 patients with cerebrovascular diseases (7·10%), 29 patients with congestive heart failure (9·12%) and 60 patients (18·87%) were smokers (current or former). Of those diagnosed with arterial hypertension, 94 patients (29·55%) were under ACEi treatment, 89 patients (27·98%) under ARB treatment, 67 patients (21·06%) under other treatments and 82 patients with high blood pressure, but not yet hypertension, (25·78%) with not antihypertensive medication. Out of 335 patients, 64 (20·13%) were under antiplatelet treatment and 31 (9·75%) under anticoagulant treatment. Finally, there were 133 (41·82%) hosted in nursing home (Table 1).

Data on COVID-19 infections are divided into two categories, 246 (77·35%) patients with mild-moderate infection (non-severe) and 72 (22·64%) with severe infection, 43 died (59·72%). Comparing the different severity levels we observed statistically significant differences related with severity and survival in patients who had previous chronic renal failure (p 0·011), ischemic heart disease (p 0·024), Chronic Obstructive Pulmonary Disease (COPD) (p 0·005) and previous stroke (p 0·002). We also observed statistically significant differences in the number of patients hosted in nursing homes compared with those who were not ($p <0·001$).

Comparing ACEi with ARB and other treatments, we find no differences between patients with severe vs non severe illness in use of ACEi (25·00% vs 31·71%; p 0·65) or ARB (23·62% vs 29·27%; p 0·47) or other treatments. We also did not find differences between survivors and non-survivors in the use of ACEi (30·18% vs 30·23%; p 0·90) or ARB (28·37% vs 25·58%; p 0·90) or other treatments (Table 2).

Due to the comorbidities effects on hypertension, our study focuses on the hypertension patients under ACEi/ARB treatment with comorbidities including ischemic coronary disease, diabetes, COPD, chronic heart failure, renal insufficiency, previous stroke, obesity and smoking habits (current or former). None of the associated comorbidities in our study, when compared to treatment with ACEi/ARB/others, presents statistically significant differences (Table 3).

Finally we performed a multivariable analysis, which concludes on a strong fatality and severity correlation among patients with previous stroke (p 0·0064), former or current smoking habits (p 0·0382), patients older than 75 years old ($p<0.0001$) and patients hosted in a nursing home (p 0·0009) (Table 4).

Discussion

In this COVID-19 study, patients with hypertension, heart failure and/or ischemic coronary disease, treated with ACEi versus ARB or other antihypertensive medications, showed no significant difference in the progression of infection from mild to severe cases or between survivors and non-survivors. The effect of these antihypertensive drugs on infection progression was neutral. This confirms the reports already published in the hospitalized population, and reinforces the position of scientific societies recommending not to change medication for hypertensive patients unless it is necessary due to the evolution of hypertension itself but not due to COVID-19[6].

An important finding of the present report is the worst progression of the infection and the increasing number of deaths of persons over 75 years of age and especially of older persons living in nursing homes. The characteristic of a semi-closed place, the reduced mobility and fragile state of these patients, their close contact with caregivers and physiotherapists, the ease of transmission of the virus in such a scenario and the tendency seen in this infection to an inflammatory state with thrombosis, probably sets the stage for "the perfect storm" and could explain the lethality of these places. Here again, the effect of ACEi or ARBs has not been a determining factor in the progression of the disease.

It has been published that the levels of expression of ACE2 on the cell surface and circulating soluble ACE2 may be different, with soluble being a protective factor against the virus. Since the amount of soluble ACE2 in elderly and diabetic subjects is lower, it is possible that this decrease has an impact on the infectivity of SARS-COV-2, and therefore elderly/diabetic subjects are more vulnerable than younger individuals to COVID-19. In the case of diabetics, unlike other studies, we have not seen worse progression of infection or survival[7]. It should be a priority to clarify the causes of this worse evolution in the elderly because, considering that a second and even a third pandemic wave is expected, we should be prepared to protect these populations even more.

In our study we found a clear relationship between being a current or former smoker and a worse prognosis. We have found in the scientific literature a recent study investigating differences in the expression of the ACE2 gene, which would mean more options for the virus to enter the cell and infect it. This ACE2 expression was studied to identify possible variables among patients that would lead to a higher susceptibility to COVID-19. Most, including race (Asian vs. Caucasian), age (>60 vs. <60), and gender did not correlate with significant disparities in ACE2 gene expression. However, significantly higher expression of the ACE2 gene was found in the lungs of former smokers compared to nonsmokers, suggesting that smoking may be a risk factor for susceptibility to COVID-19[8].

We recorded a significant increase in the severity of disease progression in patients who had had a previous stroke. A stroke can alert to a previous circulatory problem or a clotting problem. Since this virus has demonstrated a strong ability to produce inflammatory states and microthrombosis, it is not surprising that patients with previous strokes may have more easily developed microthrombosis and worse prognosis. It therefore seems prudent to take enhanced measures in patients with a history of stroke during the COVID-19 pandemic [9,10].

We have also analyzed patients with hypertension of COVID-19 who previously took antiplatelet or anticoagulant medications looking for a different progression of the disease. This infection has been characterized by increased inflammatory parameters and produces thrombosis, so a previous treatment with these two classes of drugs could have been beneficial. We have not found a clear relationship between the consumption of these drugs and better progression and decreased risk of death. One recent study published a clearly better prognosis in hospitalized patients or in intensive units, although not specify anything about outpatient setting[11].

This point will be widely discussed in the near future because there are recent publications that advocate the benefit of prophylaxis with anticoagulants, when indicated, in anticipation of new pandemic waves in the coming months.

The strength of this report is that it includes patients from the same local area followed by their current family doctors in a primary care setting.

Limitations

The limitation of this study is that the sample studied was not large enough to significantly answer some questions about whether pre-treatment with antiplatelets or anticoagulants are a protective factor. Adding patients from more health centers will facilitate more participants and should help clarify this issue.

Conclusions

The findings of this report in a primary care setting have not identified a difference in the clinical course among COVID-19 infected people with hypertension, treated with ACE inhibitors vs. ARB vs. others, although having a previous stroke, smoking, being older than 75 years, or living in a nursing home had a worse prognosis. Considering that a second and even a third pandemic wave is expected, we should be prepared to protect these populations even more.

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Tables

	Patients with arterial hypertension under treatment					
	ACEi	**ARB**	**p-value**	**Non-ACEi/ARB**	**p-value**	**Total**
	n=94	**n=89**		**n=135**		**n=318**
Age Median (IQR)	75 (62-88)	78 (64-88)	0·50	76 (60-90)	0·87	77 (61-89)
Age			0·45		0·24	
14-65	30 (31·89%)	23 (25·84%)		47 (34·81%)		100 (31·44%)
66-75	17 (18·09%)	15 (16·85%)		19 (14·07%)		51 (16·04%)
76-85	21 (22·34%)	22 (24·72%)		20 (14·81%)		63 (19·81%)
>86	26 (27·66%)	29 (32·58%)		49 (36·30%)		104 (32·70%)
Sex			0·097		0·91	
Male	44 (46·81%)	30 (33·71%)		53 (39·26%)		127 (39·94%)
Female	50 (53·19%)	59 (66·29%)		82 (60·74%)		191 (60·06%)
COPD	3 (3·19%)	7 (7·87%)	0·20	10 (7·41%)	0·49	20 (6·29%)
Renal insuficiency	10 (10·64%)	9 (10·11%)	1·00	12 (8·89%)	0·71	31 (9·75%)
Stroke	6 (6·38%)	7 (7·87%)	0·78	8 (5·93%)	0·82	21 (6·60%)
ICD	9 (9·57%)	8 (8·99%)	1·00	9 (6·67%)	0·54	26 (8·18%)
Heart failure	5 (5·32%)	13 (14·61%)	**0·046**	11 (8·15%)	0·70	29 (9·12%)
Diabetes	28 (29·79%)	24 (26·97%)	0·74	32 (23·70%)	0·37	84 (26·42%)
Obesity	27 (28·72%)	29 (32·58%)	0·39	34 (25·19%)	0·35	90 (28·30%)
Smoking	21 (22·34%)	16 (17·98%)	0·57	23 (17·04%)	0·45	60 (18·87%)
APT	19 (20·21%)	19 (21·35%)	0·86	26 (19·26%)	0·78	64 (20·13%)
AC	5 (5·32%)	13 (14·61%)	**0·046**	13 (9·63%)	1·00	31 (9·75%)
Nursing Home	39 (41·49%)	33 (37·08%)	0·55	61 (45·19%)	0·30	133 (41·82%)

AC: Anticoagulation; APT: Antiplatelet Therapy; COPD: Chronic Obstructive Pulmonary Disease; ICD: Ischemic Coronary Disease; IQR: Interquartile Range·

Table 1: Characteristics of the ACEi and ARB groups compared with the non ACEi/ARB group in patients with Arterial Hypertension.

		Severity			Survival		
	Total	**Severe**	**Mild-moderate**	**p-value**	**yes**	**no**	**p-value**
	n=318	**n=72**	**n=246**		**n=275**	**n=43**	
Age Median (IQR)	77·00	85·00	72·00	**<0·001**	72·00	87·00	**<0·001**
	(61·00-89·00)	(77·00-91·00)	(59·00-88·00)		(60·00-88·00)	(82·00-92·00)	
Age							
14-65	100 (31·44%)	2 (2·78%)	100 (38·84%)	**<0·001**	100 (38·36%)	0 (0·00%)	**<0·001**
66-75	51 (16·04%)	11 (15·28%)	40 (16·26%)	**<0·001**	47 (17·09%)	4 (9·30%)	**<0·001**
76-85	63 (19·81%)	26 (36·11%)	37 (15·04%)	**<0·001**	48 (17·45%)	15 (34·88%)	**<0·001**
>86	104 (32·70%)	33 (45·83%)	71 (28·86%)	**<0·001**	80 (29·09%)	24 (55·81%)	**<0·001**
Sex				0·27			0·40
Male	127 (39·94%)	33 (45·83%)	94 (38·21%)		107 (38·91%)	20 (46·51%)	
Female	191 (60·06%)	39 (54·17%)	152 (61·79%)		168 (61·09%)	23 (53·49%)	
COPD	20 (6·29%)	10 (13·89%)	10 (4·07%)	**0·005**	15 (5·45%)	5 (11·63%)	0·17
Renal Insuffiency	31 (9·75%)	13 (18·06%)	18 (7·32%)	**0·011**	24 (8·73%)	7 (16·28%)	0·16
Stroke	21 (6·60%)	11 (15·28%)	10 (4·07%)	**0·002**	11 (4·00%)	10 (23·26%)	**<0·001**
ICD	26 (8·18%)	11 (15·28%)	15 (6·10%)	**0·024**	20 (7·27%)	6 (13·95%)	0·14
Heart Failure	29 (9·12%)	8 (11·11%)	21 (8·54%)	0·49	24 (8·73%)	5 (11·63%)	0·57
Diabetes	84 (26·42%)	24 (33·33%)	60 (24·39%)	0·13	69 (25·09%)	15 (34·88%)	0·19
Obesity	90 (28·30%)	18 (25·00%)	72 (29·27%)	0·75	82 (29·82%)	8 (18·60%)	0·67
Smoking	60 (18·87%)	17 (23·61%)	43 (17·48%)	0·098	49 (17·82%)	11 (25·58%)	**0·053**
APT	64 (20·13%)	16 (22·22%)	48 (19·51%)	0·62	54 (19·64%)	10 (23·26%)	0·55
AC	31 (9·75%)	10 (13·89%)	21 (8·54%)	0·18	25 (9·09%)	6 (13·95%)	0·40
Nursing home	133 (41·82%)	46 (63·89%)	87 (35·37%)	**<0·001**	98 (35·64%)	35 (81·40%)	**<0·001**
Treatment	245 (77·04%)	55 (76·39%)	190 (77·24%)	0·87	212 (77·09%)	33 (76·74%)	1·00
ACEi	96 (30·18%)	18 (25·00%)	78 (31·71%)	0·65	83 (30·18%)	13 (30·23%)	0·90
ARB	89 (27·99%)	17 (23·62%)	72 (29·27%)	0·47	78 (28·37%)	11 (25·58%)	0·91
BB´S	65 (20·44%)	16 (22·22%)	49 (19·92%)	0·43	55 (20·00%)	10 (23·26%)	0·65
CCB	55 (17·30%)	15 (20·83%)	40 (16·26%)	0·38	51 (18·55%)	4 (9·30%)	0·19
HCT /α-blockers	74 (23·27%)	25 (34·72%)	49 (19·92%)	**0·011**	60 (21·82%)	14 (32·56%)	0·12

AC: Anticoagulation; ACEi: Angiotensin Converting Enzyme Inhibitors (and combinations with other antihypertensives); APT: Antiplatelet Therapy; ARB Angiotensin Receptor Blocker (and combinations with other antihypertensives); BB`S: Beta Blockers; CCB: Calcium Channel Blockers; COPD: Chronic Obstructive Pulmonary Disease; HCT: Hydrochlorothiazide; ICD: Ischemic Coronary Disease; IQR: Interquartile Range.

Table 2: Characteristics, severity, treatment and coexisting conditions of patients with hypertension and COVID-19 infection.

	Patients with Arterial Hypertension				
	Total	**ACEi**	**ARB**	**Non-ACEi/ARB**	**p-value**
TOTAL	**n=318**	**n=94**	**n=89**	**n=135**	0·24
Non-survivor	43 (13·52%)	12 (12·77%)	11 (12·36%)	20 (14·81%)	
Severe	29 (9·12%)	5 (5·32%)	6 (6·74%)	18 (13·33%)	
Non severe	246 (77·36%)	77 (81·91%)	72 (80·90%)	97 (71·85%)	
ICD	n=26	n=9	n=8	n=9	0·89
Non-survivor	6 (23·08%)	3 (33·33%)	2 (25·00%)	1 (11·11%)	
Severe	5 (19·23%)	1 (11·11%)	2 (25·00%)	2 (22·22%)	
Non severe	15 (57·69%)	5 (55·56%)	4 (50·00%)	6 (66·67%)	
Diabetes	n=84	n=28	n=24	n=32	0·94
Non-survivor	15 (17·86%)	6 (21·43%)	4 (16·67%)	5 (15·63%)	
Severe	9 (10·71%)	2 (7·14%)	3 (12·50%)	4 (12·50%)	
Non severe	60 (71·43%)	20 (71·43%)	17 (70·83%)	23 (71·88%)	
COPD	n=20	n=3	n=7	n=10	0·70
Non-survivor	5 (25·00%)	1 (33·33%)	2 (28·57%)	2 (20·00%)	
Severe	5 (25·00%)	0 (0·00%)	1 (14·29%)	4 (40·00%)	
Non severe	10 (50·00%)	2 (66·67%)	4 (57·14%)	4 (40·00%)	
Heart Failure	n=29	n=5	n=13	n=11	0·54
Non-survivor	5 (17·24%)	1 (20·00%)	1 (7·69%)	3 (27·27%)	
Severe	3 (10·34%)	0 (0·00%)	1 (7·69%)	2 (18·18%)	
Non severe	21 (72·41%)	4 (80·00%)	11 (84·62%)	6 (54·55%)	
Renal Insuffiency	n=31	n=10	n=9	n=12	0·37
Non-survivor	7 (22·58%)	3 (30·00%)	1 (11·11%)	3 (25·00%)	
Severe	6 (19·35%)	0 (0·00%)	3 (33·33%)	3 (25·00%)	
Non severe	18 (58·06%)	7 (70·00%)	5 (55·56%)	6 (50·00%)	
AC	n=31	n=5	n=13	n=13	0·66
Non-survivor	6 (19·35%)	2 (40·00%)	2 (15·38%)	2 (15·38%)	
Severe	4 (12·90%)	1 (20·00%)	2 (15·38%)	1 (7·69%)	
Non severe	21 (67·74%)	2 (40·00%)	9 (69·23%)	10 (76·92%)	
APT	n=64	n=19	n=19	n=26	0·33
Non-survivor	10 (15·63%)	1 (5·26%)	5 (26·32%)	4 (15·38%)	
Severe	6 (9·38%)	1 (5·26%)	1 (5·26%)	4 (15·38%)	
Non severe	48 (75·00%)	17 (89·47%)	13 (68·42%)	18 (69·23%)	
Obesity	n=90	n=27	n=29	n=34	0·72
Non-survivor	8 (8·89%)	1 (3·70%)	4 (13·79%)	3 (8·82%)	
Severe	10 (11·11%)	3 (11·11%)	4 (13·79%)	3 (8·82%)	
Non severe	72 (80·00%)	23 (85·19%)	21 (72·41%)	28 (82·35%)	
Smoking	n=60	n=21	n=16	n=23	0·15
Non-survivor	11 (18·33%)	3 (14·29%)	5 (31·25%)	3 (13·04%)	
Severe	6 (10·00%)	1 (4·76%)	0 (0·00%)	5 (21·74%)	
Non severe	43 (71·67%)	17 (80·95%)	11 (68·75%)	15 (65·22%)	
Nursing Homes	n=185	n=55	n=56	n=74	0·73
Non-survivor	8 (4·32%)	2 (3·64%)	3 (5·36%)	3 (4·05%)	
Severe	18 (9·73%)	4 (7·27%)	4 (7·14%)	10 (13·51%)	
Non severe	159 (85·95%)	49 (89·09%)	49 (87·50%)	61 (82·43%)	
Stroke	n=21	n=6	n=7	n=8	1·00
Non-survivor	10 (47·62%)	3 (50·00%)	4 (57·14%)	3 (37·50%)	
Severe	1 (4·76%)	0 (0·00%)	0 (0·00%)	1 (12·50%)	
Non severe	10 (47·62%)	3 (50·00%)	3 (42·86%)	4 (50·00%)	

AC: Anticoagulation; ACEi: Angiotensin Converting Enzyme Inhibitors (and combinations with other antihypertensives); APT: Antiplatelet Therapy; ARB Angiotensin Receptor Blocker (and combinations with other antihypertensives); COPD: Chronic Obstructive Pulmonary Disease; ICD: Ischemic Coronary Disease.

Table 3: Patients with arterial hypertension under treatment with ACEi, ARB, non-ACEi or ARB and comorbidity and severity.

	Main significatives findings	
	OR (IC95%)	p-value
Previous stroke	5·021 (1·571-16·052)	**0·0064**
Smoker (current or former)	2·697 (1·056-6·891)	**0·0382**
Hosted in nursing home	5·239 (1·964-13·973)	**0·0009**

Table 4: Main significatives findings (multivariate analysis).