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Screening based on risk factors for abdominal aortic aneurysm in the cardiology clinic

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ABSTRACT

Background: The risk factors for abdominal aortic aneurysm (AAA) are present in many of the patients that attend our cardiology service. The aim of this study was the evaluation of the prospects of examining the abdominal aorta during our consultations and the relationship of AAA with risk factors and ischemic cardiopathy.
Methods: A descriptive transversal observational study was designed including 274 male patients aged ≥60 years, attended consecutively in the cardiology service, in which we studied the abdominal aorta and adjusted a logistic regression model to determine the risk factors associated with AAA.
Results: We were able to visualize and measure the abdominal aorta in 95.4% of cases in a fast and reliable way. The prevalence of AAA was 8.76%. 75% of patients with AAA presented ischemic heart disease. Patients with AAA were characterized by the presence of ischemic cardiopathy (Odds Ratio (OR): 4.27, 95% Confidence Interval (CI): 1.37–13.31, $p = 0.012$), dyslipidemia (OR: 4.99, 95% CI: 1, 07–23.31; $p = 0.041$), arterial hypertension (OR: 4.14, 95% CI: 1.07–15.98, $p = 0.039$), and a longer history of smoking (OR: 1.03; 95% CI: 1002–1.054; $p = 0.037$).
Conclusions: The evaluation of the abdominal aorta during cardiology consultations is feasible with the standard resources. Patients treated in the cardiology service present a high prevalence of AAA. We have adjusted and validated a clinical prediction model based on risk factors that allows the identification, in the cardiology consult, of patients with the highest risk of suffering from AAA.

1. Introduction

The diameter of the abdominal aorta in the diaphragm of adults is typically <2 cm, which decreases down to 1.5 cm before its bifurcation into the iliac arteries. The abdominal aortic aneurysm (AAA) is defined as the dilation of the abdominal aorta to ≥3 cm, being usually found in infrarenal locations. The risk factors related to AAA are age, smoking history, male gender, family history of AAA, and atherosclerosis [1–3]. In some studies, the presence of diabetes has been linked to a lower risk of AAA [4].

The prevalence in males older than 65 years is approximately 5.5%, being very infrequent at ages younger than 60 years [1]. The risk of rupture is directly related to the size and is especially frequent in AAAs with a diameter > 55 mm [5].

AAAs are usually silent until their rupture, presenting at that time a mortality rate of over 60–70%, in contrast to the survival rate of over 95% after programmed surgery, a reason that justifies the importance of their early diagnosis [1].

Although the main Scientific Societies recommend screening in the groups of patients with the highest prevalence according to the data provided by the MASS study [6,7], most developed countries have not yet implemented programs for AAA detection.

Several studies have demonstrated the possibility of examining the abdominal aorta in patients referred to Cardiac Imaging Units for transthoracic echocardiography [8–13].

Given the widespread presence of echocardiography equipment in cardiology clinics, and taking into account the risk profile of the patients treated in our consults, we designed the present study whose main objective was the assessment of the prospects of examining the abdominal aorta in the cardiology service with the means available for our

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usual clinical practice, in addition to assessing the relationship of AAA with ischemic heart disease and the different risk factors.

2. Methods

A descriptive, transversal observational study was designed, in which a total of 274 male patients aged ≥60 years were included, who were consecutively attended in a general clinical cardiology practice. Inclusion in the study required acceptance by the patient, who signed the corresponding informed consent. The lack of participation acceptance was considered a criterion for exclusion in the study.

The recruitment period was 6 months after approval of the study by the corresponding Regional Research Ethics Committee.

A data collection questionnaire was designed with the following variables: age, ischemic cardiopathy (defined by the presence of documented myocardial infarction (AMI) and/or demonstrated significant coronary disease), history of smoking and duration (in years), arterial hypertension (AHT, defined as systolic blood pressure of ≥140 mm Hg or diastolic pressure of ≥90 mm Hg or under antihypertension treatment), dyslipidemia (D, previous treatment or LDL levels > 130 mg/dl and/or triglycerides > 150 mg/dl), diabetes mellitus (DM), chronic renal failure (CRF, defined as a glomerular filtration rate below 60 ml/min), peripheral and/or carotid arterial disease, history of stroke, abdominal perimeter, maximum abdominal aortic diameter (anteroposterior or transverse), presence of aneurysm, location of the aneurysm, and exploration time. The characteristics of the aortic wall and its lumen were also collected, which indicated the presence of atherosclerosis/calcification, mural thrombosis, or dissection. All this data are summarized in Table 1.

The patients were treated following standard clinical practices, including the collection of the clinical history, a physical examination, and an electrocardiogram. In the patients fulfilling the inclusion criteria for the study, we attempted the visualization and measurement of the abdominal aorta with the echocardiography equipment available in the consult, independently of the possibility of performing an echocardiogram at that time.

2.1. Echocardiographic study

The examination was performed by a single cardiologist using a portable ultrasound scanner Philips Cx50 equipped with an S5–1 probe. The measurements were performed at infrarenal level by 2D imaging during systole from outer edge to outer edge, trying to obtain a cross-section perpendicular to the area of greatest dilatation. In the case of detecting AAA at the infrarenal level, we would also proceed to its measurement. For patients with an aortic diameter ≥ 25 mm where we could not visualize the aorta during the consult, an abdominal ultrasound was performed by the Radiodiagnosis Service with a Toshiba Aplio MX instrument equipped with an abdominal probe Convex PVT-375BT.

2.2. Statistical analysis

A consecutive sampling was done until reach 274 patients. This sample size allowed us to reduce the estimated error to 2.70% with an expected prevalence of 5.5% [1] and a 95% confidence level, ensuring the representativeness of the sample (Epidat Software 4.2). On the other hand, this size warranted the minimum number needed to perform logistic regression according to Freeman's classic formula [14]: $n = 10 * (k + 1)$; where k is the number of independent variables.

The continuous variables are presented as means and standard deviations, while the categorical variables are expressed as counts and percentages. To evaluate the univariate statistical significance, a *t*-test for independent samples (continuous variables) or a Chi-square test (categorical variables) was performed. To adjust the multivariate logistic regression model, we randomly selected 2/3 of the sample, that is, 188 patients (derivation sample). The remaining third of the sample (86 patients) was used to validate the model (validation sample). This model has been used to estimate the probability that a patient suffers from AAA. For its construction, we took into account all the variables that presented a *p*-value < 0.10 in the univariate study. We calculated the odds ratio and its 95% confidence interval from the coefficients of the definitive model. To validate it, we performed the Hosmer and Lemeshow (HL) goodness of fit test. We used the Nagelkerke R^2 value to estimate the proportion of variability.

Discrimination and prediction accuracy was assessed by ordinal area under the curve (AUC) of receiver operating characteristics (ROC) curve calculation. AUC ranges from bellow 0.5 are considered non-informative and near 1.0 as perfect prediction models. The Integrated Discrimination Improvement index (IDI) and the Net Reclassification Improvement (NRI) has been calculated as described by Pencina et al. and compared to the R^2, HL, Specificity, sensitivity and AUC measurements [15,16]. A *p*-value of <0.05 was considered significant. The statistical analysis was performed with the SPSS package (Version 25.0, Armonk, NY: IBM Corp).

Table 1
Descriptive parameters of the observed variables.

		Presence of aneurysm		
		No	Yes	p-Value
		n (%)	n (%)	(Chi-Squared)
Ischemic cardiopathy	No	159 (65,43)	6 (25)	**0,000**
	Yes	84 (34,57)	18 (75)	
Smoker	No	109 (44,86)	5 (20,83)	**0,045**
	Yes	18 (7,41)	4 (16,67)	
	Former Smoker	116 (47,74)	15 (62,5)	
AHT	No	86 (35,54)	3 (12,5)	**0,023**
	Yes	156 (64,46)	21 (87,5)	
Dyslipidemia	No	105 (43,21)	3 (12,5)	**0,004**
	Yes	138 (56,79)	21 (87,5)	
DM	No	155 (63,79)	16 (66,67)	0,828
	Yes	88 (36,21)	8 (33,33)	
CRF (GF < 60)	No	201 (82,72)	15 (62,5)	**0,026**
	Yes	42 (17,28)	9 (37,5)	
Peripheral and/or carotid arterial disease	No	225 (92,59)	21 (87,5)	0,416
	Yes	18 (7,41)	3 (12,5)	
Stroke	No	225 (92,59)	20 (83,33)	0,121
	Yes	18 (7,41)	4 (16,67)	
Location of the aneurysm	Infrarenal	0 (0)	22 (95,65)	–
	Suprarenal	0 (0)	0 (0)	
	Infra and suprarenal	0 (0)	1 (4,35)	
Vascular lumen	Normal	184 (78,3)	3 (14,3)	**0,000**
	Calcification and /or thrombo	51 (21,7)	18 (85,7)	
Age	<65 years	27 (11,1)	3 (12,5)	0,241
	E65-75 years	113 (46,5)	7 (29,2)	
	>75 years	103 (42,4)	14 (58,3)	

	No	Yes	p-Value
	Mean ± SD	Mean ± SD	(t-test)
Years smoking	20,16 ± 20,87	32,67 ± 22,72	**0,005**
Abdominal perimeter (cm)	103,27 ± 11,06	104,61 ± 9,82	0,575
Maximum diameter (mm)	19,39 ± 3,25	40,15 ± 13,64	–
Exploration time (s)	88,22 ± 49,94	204,8 ± 117,29	**0,000**
Maximum diameter (radiology service) (mm)	22,89 ± 3,13	40,2 ± 13,34	–
Age (years)	74,36 ± 7,26	77 ± 8,42	0,095

3. Results

The study included a total of 274 patients with a mean age of 74.53 ± 7.38 years. In 262 patients (95.4%), it was possible to measure the maximum diameter of the abdominal aorta during the cardiology consult. For 12 patients where the abdominal aorta could not be measured during the cardiology consult, abdominal ultrasound was performed in the Radiology Service, allowing for the visualization of the abdominal aorta in 5 of them (41.7%), none of which presented AAA. The abdominal perimeter was significantly higher in patients for which we could not measure the abdominal aorta during the cardiology consult (117.17 ± 9.750 vs 103.04 ± 10.739 cm, $p < 0.001$).

In 35 patients presenting an abdominal aortic diameter ≥ 25 mm, an abdominal ultrasound was performed in the Radiology Service. The measurements made in the cardiology consultation and those made in the Radiology Service showed good correlation ($r = 0.974$).

Of the 274 patients included in the study, 24 were identified to present AAA (8.76%), all of them at infrarenal location except one patient who presented both supra and infrarenal involvement. In patients who attended the cardiology consult and had a history of AMI or documented coronary heart disease, the prevalence reached 17.6%. Eighteen patients with AAA (75%) presented also a history of ischemic heart disease. More than half of the detected AAAs were diagnosed during this study (58.3%).

Patients with AAA are older in average than those without aneurysm; however, the difference does not reach statistical significance (77.00 ± 8.42 vs 74.36 ± 7.26, $p = 0.095$). We did not find statistically significant differences in the prevalence of AAA for the different age categories studied (<65, 65–75, and >75 years old). Patients with AAA were or had been smokers for longer than patients without AAA (32.67 ± 22.72 vs 20.16 ± 20.87, $p = 0.005$). We found no relationship between the abdominal perimeter and the presence of AAA ($p = 0.575$). The mean exploration time was very short (88.22 ± 49.94 s) in the group without AAA, which was logically longer in patients presenting aneurysm (204.8 ± 117.29 s).

We found a significant direct association ($p < 0.05$) between AAA and ischemic heart disease, smoking history, AHT, dyslipidemia, and renal failure, where patients with these characteristics presented a higher prevalence of AAA. When analyzing the relationship between AAA and the arterial wall pathology, patients with AAA were found to present greater calcification and/or thrombosis. No statistically significant differences were detected in the prevalence of AAA related to the presence of DM, peripheral or carotid arterial disease, and stroke (Table 1).

Table 2
Probability of the presence of AAA according to the combination of signif. risk factors in the model (p = 0,10).

Significant risk factors	Years smoking 0	10	20	40	60
Not CAD, D, AHT	0,003	0,004	0,005	0,008	0,013
AHT	0,011	0,014	0,019	0,032	0,053
D	0,013	0,017	0,022	0,038	0,063
D + AHT	0,053	0,068	0,087	**0,140**	**0,219**
CAD	0,011	0,015	0,019	0,033	0,055
CAD + AHT	0,045	0,059	0,075	**0,123**	**0,193**
CAD + D	0,054	0,070	0,089	**0,144**	**0,224**
CAD + D + AHT	**0,192**	**0,237**	**0,289**	**0,411**	**0,545**

The final model adjusted with the derivation sample identified four significant independent variables to indicate the presence of AAA: ischemic cardiopathy (IC), years of smoking, dyslipidemia (D), and hypertension (Table 1 Supplemental information). The *p*-value associated with the HL goodness of fit test was 0.391, and the Nagelkerke R^2 value was 0.265. The adjusted model affords an area under the ROC curve of 0.819 (95% CI: 0.73–0.91, $p < 0.001$). A cut-off point of 0.10 provides a sensitivity of 78.9% and specificity of 74.5%. The positive predictive value was set in 15.3% and the negative predictive value in 98.4%. This cut-off point allows us to classify proportions of similar patients in the validation sample, with an area under the ROC curve of 0.882 (95% CI: 0.80–0.97, $p = 0.004$) (Fig. 1). The values of R^2, HL, Specificity, Sensitivity, AUC, IDI and NRI associated to the incorporation of each risk factor to the adjusted model are presented (Table 2 supplemental information).

As can be observed in Fig. 2 and Table 2, these data allow us to identify in detail the influence of different risk factors combinations for the prediction of AAA presence considering several years of smoking.

4. Discussion

4.1. Evaluation of the abdominal aorta

This work demonstrates that the abdominal aorta can be measured in most patients attended at the cardiology service in a quick and reliable way. Abdominal obesity and/or the interposition of intestinal gas

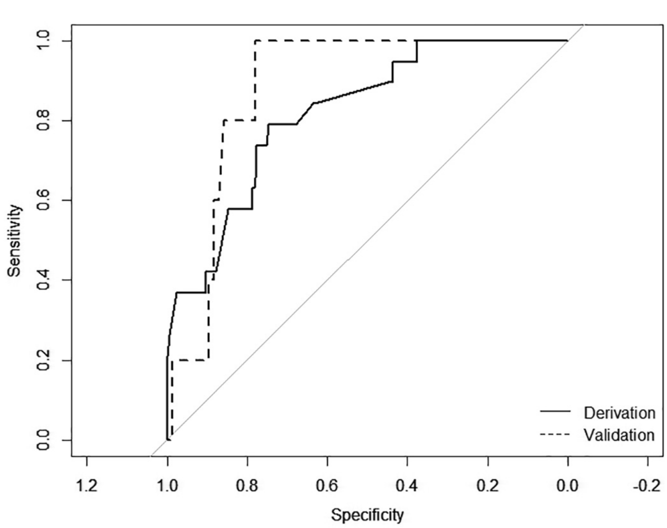

Fig. 1. ROC curves for the derivation and validation samples. The area under the curve in the derivation sample is 0.82 (95% CI: 0.72–0.91), while that for the validation sample is 0.88 (95% CI: 0.80–0.97).

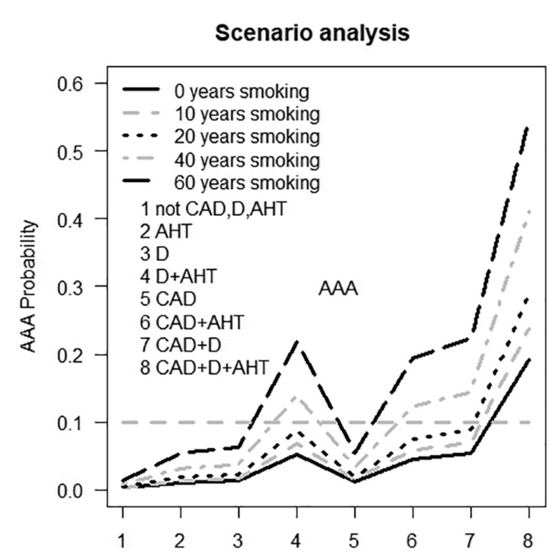

Fig. 2. Probability of the presence of AAA according to the combination of significant risk factors in the model (coronary artery disease, CAD; dyslipidemia, D; arterial hypertension, AHT; and smoking history).

can hamper, in some cases, the visualization of the abdominal aorta. The measurements made in the cardiology consult and in the Radiology Service show good correlation, with an overestimating tendency for the diameters measured in the cardiology consult, especially in patients presenting tortuosity of the abdominal aorta.

4.2. AAA and cardiovascular risk

AAA is considered a multifactorial disease of uncertain pathogenesis and, although atherosclerosis is present in many patients with AAA, they are two clearly differentiated diseases. At the genetic level, mutations related to AAA but not to atherosclerosis have been identified [17]. Risk factors such as DM or obesity that are clearly related to atherosclerosis do not present the same relationship with AAA. Other factors, such as smoking, AHT, or renal failure, have great influence on both atherosclerosis and AAA. The age can be related to the presence of AAA; in many cases, it can even be considered a degenerative disease, being very infrequent in individuals younger than 60 years [1–3].

The smoking habit expressed in number of years of smoking is significantly related to the appearance of AAA. Some authors have described that smoking is a more important risk factor for AAA than atherosclerosis [18]. Our results suggest that smoking is more important in the evolution of AAA in patients with other associated risk factors (Fig. 2).

Patients with ischemic heart disease present high prevalence of AAA and, conversely, the presence of AAA is associated with higher incidence and greater severity of obstructive coronary lesions, assessed according to the number of affected vessels [19–22]. The risk of fatal and non-fatal complications of AAA is much higher in patients with ischemic heart disease than in those without [21,22]. In a prospective study in patients with AAA, the risk of suffering a fatal AMI at 10 years was 38%, compared to a secondary aneurysm mortality of around 2% [23].

Although previous studies have shown that the prevalence of AAA in patients with ischemic cardiopathy is high, the results are not consistent, possibly due to differences in the characteristics and risk factors of the studied populations. A prevalence of 14% of AAA has been reported in populations with ischemic heart disease [19] and of 6.9% [24] and 18.2% [25] in patients who had undergone coronary revascularization surgery. In our study, the prevalence of AAA in patients attending the cardiology service is 8.76%, reaching 17.6% in the group of patients with ischemic heart disease. The chronification of patients with severe ischemic heart disease and a larger number of risk factors contributes, in our opinion, to the high prevalence of AAA in the studied population. In our study, 75% of patients with AAA presented ischemic heart disease and, of these, 50% (9 patients) had a history of long-standing coronary disease (over 10 years). Only 11% (2 patients) presented a coronary disease in the previous 5 years. In the literature reviewed, we did not find studies with a population similar to ours with which to compare the present results.

The relationship of ischemic cardiopathy and AAA is of such magnitude that, based on a retrospective analysis, it has been postulated that by studying male patients with ischemic heart disease, one could detect approximately 43% of all AAAs in the population and avoid 30% of AAA ruptures [26].

4.3. Opportunities for AAA diagnosis

A large number of patients with asymptomatic undiagnosed AAA visit us periodically in cardiology services, are admitted to hospital, and even undergo coronary revascularization procedures without us realizing, in many cases, the presence of this potentially deadly disease. In a series of patients with ruptured AAA, 77% of the patients had received hospital care during the previous 5 years [27].

In this study, we identified 24 patients with AAA; 50% of them (12 patients) had been hospitalized in Cardiology Services in the last 5 years and over 90% of the patients with AAA (22 patients) had attended at some point an external cardiology clinic in the last 5 years.

In 10 cases (41.7%), they had been previously diagnosed with AAA and their diagnosis was made mostly, as is usually the case, by chance when performing imaging techniques for other purposes. Except for the patients whose diagnosis was the result of being included in this study, no AAA was diagnosed by a cardiologist despite the multiple existing (and missed) opportunities for diagnosis.

4.4. AAA screening

The results of the large randomized trials conducted in the 1990s, such as the MASS study, motivated the implementation of AAA screening programs in some countries such as the United States, United Kingdom, and Sweden. In the US, the USPSTF recommends screening in men between 65 and 75 years old who have ever smoked. Their results, after a follow-up of over 10 years, showed significant effects on the total mortality in a marginal way. A 2014 update of the recommendations point to the possibility of selective evaluations to non smoking males with additional AAA risk factors [28]. Screening in women, according to the available evidence, does not seem to provide any benefits [28,29]. A recent analysis of the Swedish screening program in men aged 65 to 74 years found, after six years of follow-up, non-significant reductions in mortality associated with AAA screening, which would probably not compensate for the possible drawbacks of overdiagnosis and overtreatment. By comparing their results to those of the seven-year MASS study, the authors found a benefit of approximately half in relative terms and 7% of benefit in absolute terms [30].

The reduced prevalence of AAA in some countries and greater number of incidentally diagnosed cases by different imaging tests without the need for specific detection programs may be factors that limit the benefits of these programs by compromising their cost/benefit relationship [30]. In our opinion, such fortuitous diagnosis should not replace screening programs since this could accentuate differences in mortality by AAA in populations with different socioeconomic levels.

The implementation of cardiovascular prevention measures has been related to a parallel reduction of the incidence of stroke, myocardial infarction, and AAA [31]. The risk factors present in patients with AAA may lead to greater growth and risk of rupture of the aneurysm, whose treatment is recommended in the absence of concluding randomized studies [32,33].

The outcome of AAA detection programs could be improved through a global vascular approach including the detection and treatment of other cardiovascular diseases as well as their risk factors [34] or through better detection of the population at risk based on risk factors, being this a study area that has already been proposed by different entities.

4.5. Utility of a diagnostic AAA score in the cardiology clinic

The ease of diagnosing AAA by conventional means and the close relationship between risk factors, ischemic heart disease, and AAA renders advisable the inclusion of the evaluation of the infrarenal abdominal aorta in the cardiovascular assessment of many of our patients. The aneurysms detected in patients suffering from ischemic heart disease present higher risk of complications, which is why the expected benefits of such screening in the cardiology clinic in terms of the mortality could be even higher. Most of the aneurysms diagnosed in our study were small (<55 mm), offering the possibility of acting early on the evolution of the disease through cardiovascular prevention measures.

Although in our study, AHT, dyslipidemia, smoking, renal failure, or ischemic heart disease are significantly related to the presence of AAA, none of them alone was sufficient to select patients with higher probability of presenting AAA. Application of the clinical prediction model based on risk factors validated in this study would allow the detection in the cardiology clinic of patients with higher risk of suffering from

AAA by considering four risk factors: ischemic heart disease, years of smoking, dyslipidemia, and AHT.

Based on our results, we can define ischemic heart disease and smoking for >20 years as major risk factors for AAA, while AHT and dyslipidemia are lower risk factors in this score. According to this classification, the infrarenal abdominal aorta should be explored in all male patients older than 60 years who present a major risk factor and two minor risk factors or two major risk factors and one minor risk factor.

Applying these criteria in the studied population, we would have measured the abdominal aorta in 101 of the 274 patients (36.9% of the patients), detecting 20 of the 24 aneurysms of the study (83.3%). One of seven patients (14.3%) with aneurysms classified as requiring surgery, either by presenting a diameter > 55 mm or by already having undergone surgery, would have remained as undiagnosed.

The application of this risk score would avoid many unnecessary explorations and its practicality would be framed within the assessment of the global cardiovascular risk in a scenario that ensures the correct implementation of measures for the control of risk factors and the treatment of any detected diseases.

The increasingly frequent availability of ultrasound equipment in primary care clinics and the ease of measuring the infrarenal aorta after a brief training make attractive the idea of testing the utility of this score in other environments than the cardiology clinic.

Some authors have described AAA as an orphan disease in search of a specialty [35]. Possibly, AAA, more than an orphan disease, is a disease that requires the "shared custody" of several specialties, including Cardiology.

4.6. Study limitations

This study has been carried out in one single center, which could be considered an intrinsic limitation.

The studied population belongs to a rural area with low socioeconomic level, high incidence of ischemic heart disease, and old in age, factors that influence the prevalence of AAA and that may mean that the results of our study cannot be fully extrapolated to other population groups.

Smoking has been considered in terms of years of smoking, although the tobacco load could be reflected more accurately by calculating the number of cigarette packs per year.

The present risk score for AAA requires prospective studies for its validation in clinical use and evaluation of the impact of its application in terms of the benefits regarding the mortality and possible drawbacks such as overdiagnosis and overtreatment.

5. Conclusions

Examination of the infrarenal abdominal aorta during cardiology consultations is possible, in most patients, employing conventional resources. The prevalence of AAA in patients attending the cardiology consult is high, especially in patients suffering from ischemic heart disease. Smoking, expressed in years as a smoker, plays an important role in the evolution of AAA, especially in patients presenting several risk factors. We have adjusted and validated a clinical prediction model based on risk factors that will allow the detection of patients with higher risk of suffering from AAA in the cardiology consult.

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The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.12.059.

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