Mejora en el manejo de la sospecha del síndrome aórtico agudo en urgencias mediante un algoritmo clínico y el estudio de factores predictivos

Lumbreras-Fernández, B.; Vicente Bártulos, A.; Fernandez-Felix, B. M.; Corres González, J.; Zamora, J.; Muriel, A.

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IMPROVEMENT IN THE MANAGEMENT OF SUSPECTED ACUTE AORTIC SYNDROME IN THE EMERGENCY ROOM THROUGH A CLINICAL ALGORITHM AND STUDY OF PREDICTIVE FACTORS

ABSTRACT

Background and objective: Acute aortic syndrome (AAS) is uncommon and difficult to diagnose, with great variability in clinical presentation. To develop a computerized algorithm, or clinical decision support system (CDSS), for managing and requesting imaging in the emergency department, specifically computerized tomography of the aorta (CTA), when there is suspicion of AAS, and to determine the effect of implementing this system. To determine the factors associated with a positive radiological diagnosis that improve the predictive capacity of CTA findings.

Materials and methods: After developing and implementing an evidence-based algorithm, we studied suspected cases of AAS. Chi-squared test was used to analyze the association between the variables included in the algorithm and radiological diagnosis, with three categories: no relevant findings, positive for AAS, and alternative diagnoses.

Results: 130 requests were identified; 19 (14.6%) had AAS and 34 (26.2%) had a different acute pathology. Of the 19 with AAS, 15 had been stratified as high risk and 4 as intermediate risk. The probability of AAS was 3.4 times higher in patients with known aortic aneurysm (p = 0.021, 95% CI 1.2–9.6) and 5.1 times higher in patients with a new aortic regurgitation murmur (p = 0.019, 95% CI 1.3–20.1). The probability of having an alternative severe acute pathology was 3.2 times higher in patients with hypotension or shock (p = 0.02, 95% CI 1.2–8.5).

Conclusion: The use of a CDSS in the emergency department can help optimize AAS diagnosis. The presence of a known aortic aneurysm and new-onset aortic

regurgitation were shown to significantly increase the probability of AAS. Further studies are needed to establish a clinical prediction rule.

RESUMEN

Antecedentes y objetivos: el síndrome aórtico agudo (SAA) es poco común y de difícil diagnóstico, con una gran variabilidad en la presentación clínica. Desarrollar un algoritmo computarizado, o sistema de apoyo a la decisión clínica (SADC), para el manejo y solicitud de imágenes en el servicio de urgencias, específicamente de tomografía computarizada aórtica (TCA) en caso de sospecha de SAA, y determinar el efecto de la implementación de este sistema. Determinar los factores asociados a un diagnóstico radiológico positivo para SAA que mejoren la capacidad predictiva de los hallazgos de la TCA.

Materiales y métodos: tras desarrollar e implementar un algoritmo basado en la evidencia, estudiamos los casos sospechosos de SAA. Se utilizó la prueba de Chi-cuadrado para analizar la asociación entre las variables incluidas en el algoritmo y el diagnóstico radiológico, con tres categorías: sin hallazgos relevantes, positivo para SAA y diagnósticos alternativos.

Resultados: se identificaron 130 casos; 19 (14,6%) con SAA y 34 (26,2%) con una patología aguda diferente. De los 19 casos con SAA, 15 se habían estratificado como alto riesgo y 4 como riesgo intermedio. La probabilidad de SAA fue 3,4 veces mayor en pacientes con aneurisma aórtico conocido (p = 0,021, IC 95% 1,2-9,6) y 5,1 veces mayor en pacientes con un nuevo soplo de insuficiencia aórtica (p = 0,019, IC 95% 1,3-20,1). La probabilidad de tener una patología aguda grave alternativa fue 3,2 veces mayor en pacientes con hipotensión o shock (p = 0,02, IC 95% 1,2-8,5).

Conclusión: el uso de un SADC en el servicio de urgencias puede ayudar a optimizar el diagnóstico de SAA. La presencia de un aneurisma aórtico conocido y la regurgitación aórtica de nueva aparición demostraron aumentar significativamente la probabilidad de SAA. Se necesitan más estudios para establecer una regla de predicción clínica.

KEY WORDS: acute aortic syndrome, chest pain, thoracic pain, algorithm, aortic CT angiography, clinical decision support system (CDSS).

INTRODUCTION

Acute aortic syndrome (AAS) has an estimated incidence of 2-3.5/100,000 population/year (1).The classical presentation is of sudden onset of intense chest, abdominal, or back pain, although there is great variety in clinical presentation (2) and mimickers (3).Due to its rapid progression and high mortality (1) (4) (5) algorithms or clinical decision support systems (CDSS) are essential.

Prior to the use of algorithms, AAS was misdiagnosed in more than 30% of cases (6,7). In 2010, the American College of Cardiology Foundation/American Heart Association (ACCF/AHA), along with other North American scientific societies and colleges published an algorithm for its diagnosis and management using a scoring system based on the presence of defined risk factors: the Aortic Dissection Detection Risk Score (ADD-RS)(1). In 2014 the European Society of Cardiology (ESC) (4) and the American College of Radiology (ACR) (5) published guidelines for the diagnosis and treatment of aortic disease and appropriate use of tests.

The main objectives of this study were:

1. To develop a CDSS to improve the appropriateness of computed tomography of the aorta (CTA) when AAS is suspected in the emergency department and to determine the effect of its implementation.

2. To identify the risk factors (past medical history, presentation, examination findings) associated with a positive diagnosis of AAS on CTA and that could help in developing a clinical prediction rule.

MATERIALS AND METHODS

This study forms part of the multicenter project *MAPAC-imagen* (***M**ejora de la **A**decuación de la **P**ráctica **A**sistencial y **C**línica*, meaning *Improvement of Appropriateness of Health Care and Clinical Practice*) funded by the ISCIII (Instituto de Salud Carlos III) as part of their *Acción Estratégica en Salud* (*Strategic Health Action*) between 2013 and 2016.

The project was approved by the hospital ethics committee.

The study was conducted in the following phases:

PHASE 1: Development of the algorithm for radiological management in cases of suspected AAS

1.1 Literature review

The databases Best Practice, Dynamed, UptoDate, Ovid, MEDLINE and EMBASE were consulted, as well as repositories of clinical practice guidelines, ACR guidelines (ACR appropriateness criteria), guidelines from the ACCF/AHA and the ESC, to identify relevant documents on the diagnostic management and risk factors for AAS (figure 1). A specific search was made by a documentalist looking for clinical prediction rules and validity.

1.2 Development of the algorithm, consensus and implementation

The documents identified in the search were screened, and those considered most relevant as a source of evidence were selected to create the decision support algorithm on the use of CTA for diagnosis of AAS. With the selected literature we created a narrative synthesis, to design an algorithm that took into account the risk factors analyzed in these studies. It was performed by a panel of experts (six emergency physicians with 10-25 years of experience; 12 radiologists with 7-20 years of

experience, eight methodologists with 5-18 years of experience) using the Delphi panel technique.

The final algorithm (figure 2) was integrated in the electronic medical record system of our hospital, to generate a pop-up window with questions prompting selection of risk factors when CTA was requested in patients with suspicion of AAS. It stratified the degree of suspicion of AAS, and the system would then indicate whether or not CTA would be appropriate. For imaging findings, the criteria of the ACCF / AHA guidelines (1) have been considered. In appropriate cases, a triphasic CT was performed (unenhanced and postcontrast in arterial and venous phase).

PHASE 2: Analysis of the outcomes of implementation

Design

- **Impact of implementation of the algorithm:**

This was a prospective study based on before-and-after observations (6 months pre-implementation and 6 months post-implementation of the CDSS), in which all requests for CTA for suspected AAS were collected. We evaluated the number of requests for CTA for suspected AAS and the diagnostic yield of these (normal study, findings of AAS, or other unrelated findings).

- **Exploration of risk factors associated with radiological findings:**

All cases of suspected AAS in the 27 successive months after implementation of the algorithm (from March 2016 to June 2018) were studied. We evaluated the association between the factors included in the CDSS and the radiological findings on CTA.

Statistical analysis

Univariate multinomial regression models were used to evaluate the association between the risk factors included in the algorithm and the radiological findings, with three categories: normal study or irrelevant/nonpathological findings, study diagnostic of AAS, or study with findings of other acute pathologies different from AAS. No multivariate models were used due to the low frequency of positive findings.

P-values <0.05 were considered indicative of statistical significance.

For statistical analysis the program STATA v.15.1 (StataCorp LLC, 4905 Lakeway Drive, College Station, Texas, USA) was used.

RESULTS

1. Literature review

The screening and selection process is shown in Figure 3.

The included studies were clinical practice guidelines (1) (4), imaging appropriateness guidelines (5),(6),(7), systematic reviews (8) (9) (10) (11) (12) and meta-analyses (13) and other studies that evaluated risk factors for AAS (14) (15). No clinical prediction rules were identified.

2. Development and application of the algorithm

Based on the algorithm proposed by the ACCF/AHA (1) we created a modified decision support algorithm (figure 2) by consensus of the panel of experts (through a subsequent telematic survey).

It was designed for use in patients with clinical suspicion of AAS, identifying risk factors and takes into account the presence, or not, of risk factors from the past medical history, clinical presentation, and examination findings.

3. Analysis of the outcomes of implementation

In the 6-month-periods analyzed, before and after implementation of the CDSS, a similar number of patients were attended the emergency department (69081 and 72915, respectively, p=0.067). The total number of CTs requested was also similar (5081 and 5563, respectively, p=0.083). After implementation of the CDSS, the number of CTA requested for suspicion of AAS doubled (10 vs 21 requests). In the pre-implementation period, all the tests were negative for AAS; in the post-implantation period, there was one case (5%). Acute pathologies mimicking AAS increased (5 cases, 24% vs no cases registered before).

In the 27-month-post-implementation follow-up period, 130 CTA requests for suspected AAS were recorded; 19 of these (14.6%) were diagnostic of AAS and 34 (26.2%) of other acute pathology. In total, 53 patients (40.8%) benefitted from undergoing urgent CTA because of significant pathological findings.

The most frequent variables classified as risk factors were high-risk pain characteristics (63.2%), past history of aortic aneurysm (AA) (52.6%), known valve disease (36.8%), murmur of aortic regurgitation (26.3%) and hypotension or shock (26.3%) (table 1).

Table 1. Absolute and relative frequencies of each of the positive risk factors recorded on CTA requests according to radiological diagnosis.

	NO RELEVANT FINDINGS	AAS	ALTERNATIVE DIAGNOSIS
	n=77	n=19	n=34
MARFAN SYNDROME	0 (0.0%)	0 (0.0%)	3 (8.8%)
CONNECTIVE TISSUE DISEASE	2 (2.6%)	1 (5.3%)	3 (8.8%)
FAMILY HISTORY OF AORTIC DISEASE	5 (6.5%)	1 (5.3%)	4 (11.8%)
KNOWN VALVE DISEASE	26 (33.8%)	7 (36.8%)	5 (14.7%)
RECENT AORTIC MANIPULATION	6 (7.8%)	4 (21.1%)	3 (8.8%)
AORTIC ANEURYSM	19 (24.7%)	10 (52.6%)	6 (17.6%)
HIGH-RISK PAIN	48 (62.3%)	12 (63.2%)	23 (67.6%)
PERFUSION DEFICIT	13 (16.9%)	4 (21.1%)	11 (32.4%)
MURMUR OF AORTIC REGURGITATION	5 (6.5%)	5 (26.3%)	5 (14.7%)
HYPOTENSION OR SHOCK	10 (13.0%)	5 (26.3%)	11 (32.4%)

Regarding risk stratification, 10 patients (7.7%) were in the low-risk group, 48 (36.9%) were in the intermediate-risk group and 72 (55.4%) were in the high-risk group.

Table 2 shows the number of CTA that were positive for AAS, and for other serious acute pathologies, grouped according to pretest probability.

The alternative radiological diagnoses in the patients with acute pathology other than AAS were cardiac disease (11 patients, 32.4%), abdominal disease (8 patients, 23.5%), pulmonary thromboembolism (PTE) (3 patients, 8.8%), pulmonary disease non-PTE (7 patients, 20.6%), aortic prosthesis complication (3 patients, 8.8%) and bone fracture (2 patients, 5.9%).

RISK CATEGORY	NO RELEVANT FINDINGS	AAS	ALTERNATIVE DIAGNOSIS	TOTAL
LOW	7 (70%)	0 (0%)	3 (30%)	10
INTERMEDIATE	27 (56.3%)	4 (8.3%)	17 (35.4%)	48
HIGH	43 (59.7%)	15 (20.8%)	14 (19.4%)	72
TOTAL	77 (59.2%)	19 (14.6%)	34 (26.2%)	130

Table 2. Association between risk groups by pretest probability of AAS; absolute and relative frequencies of findings on CTA grouped into no relevant findings, positive findings for AAS and findings associated with other acute processes

The univariate analysis of the association of the different radiological diagnoses with each of the factors included in the decision support algorithm is shown in table 3. The probability of AAS was 3.4 times higher in patients with known AA (p = 0.021; 95% CI 1.2–9.6) and 5.1 times higher in patients with a new murmur suggestive of aortic regurgitation (p = 0.019; 95% CI 1.3–20.1). The probability of having an alternative acute severe pathology was 3.2 times higher in patients with hypotension or shock (p = 0.02, 95% CI 1.2–8.5). This variable did not show an increased risk of AAS that reached statistical significance.

Chest X-ray was performed in 54 patients and provided an alternative diagnosis in 20 of them (37%). When analyzed with Chi-squared test, the probability of having an alternative acute severe pathology was twice as high in patients with abnormalities on chest X-ray including mediastinal widening and aortic and/or cardiac contour anomalies (p = 0.022).

	Univariate multinomial logistic regression	
	AAS RRR (95% CI)	**ALTERNATIVE DIAGNOSIS RRR (95% CI)**
MARFAN SYNDROME	Not estimable	Not estimable
CONNECTIVE TISSUE DISEASE	2.08 (0.18–24.26)	3.63 (0.58–22.79)
FAMILY HISTORY OF AORTIC DISEASE	0.80 (0.09–7.28)	1.92 (0.48–7.65)
KNOWN VALVE DISEASE	1.14 (0.40–3.25)	0.34 (0.12–0.98)
RECENT AORTIC MANIPULATION	3.16 (0.79–12.57)	1.15 (0.27–4.88)
AORTIC ANEURYSM	3.39 (1.20–9.59)	0.65 (0.24–1.82)
HIGH-RISK PAIN	1.04 (0.37–2.93)	1.26 (0.54–2.97)
PERFUSION DEFICIT	1.31 (0.37–4.60)	2.35 (0.93–5.99)
MURMUR OF AORTIC REGURGITATION	5.14 (1.31–20.15)	2.48 (0.67–9.22)
HYPOTENSION OR SHOCK	2.39 (0.71–8.09)	3.20 (1.20–8.53)

Table 3. Univariate multinomial logistic regression analysis of the association of the risk factors from the decision support algorithm with findings of AAS or other unrelated findings. (CI = confidence interval; RRR = relative risk ratio).

DISCUSSION

Implementation of the CDSS has improved the indication of CTA in suspected AAS, finding more pathologies than in the preimplantation period and, therefore, improving the management of these patients as 14.6% were positive for AAS and 26.2% for other acute pathology (40.8% in total).

The high prevalence of cardiac disease mimicking AAS justifies our recommendation to rule this out with an ECG before applying the algorithm. To perform a chest X-ray in patients with intermediate or low risk provides an alternative diagnosis in 37% of these patients. We added D-dimer measurement in patients who are low or intermediate risk, based on the results of a recent meta-analyses (16).

In the validation study of ADD-RS applied to the 2011 International Registry of Acute Aortic Dissection (IRAD) database (17), the results by risk group were similar to ours.

However, in our study, all AAS were included in the categories of intermediate and high risk.

The main risk factor for AAS in our series was high-risk pain, the same as in the IRAD database published in 2018 (18). We also found a similar prevalence of hypotension and hypoperfusion. We obtained discordant results for history of AA (24.7% vs 52.6%) and aortic regurgitation murmur (40% vs 26.3%). We also found discrepancies compared with the ADD-RS validation study (17) for known aortic valve disease (11.9% vs 36.8%) and recent aortic manipulation (2.8% vs 21.1%).

Recently, alternative scoring systems have been published, such as the 2020 Canadian guidelines (19), and the AORTAs score (20), in which history of AA was associated with a significantly higher probability of AAS. Both algorithms gave greater value to hypotension or shock, while in our series this variable was associated with alternative diagnoses. The great variability in presentation of AAS makes it necessary a sensitive algorithm to avoid underdiagnosis without performing unnecessary investigations in patients with low pretest probability.

Limitations:

The differences from other studies based on IRAD must be interpreted with caution, as our study, unlike IRAD, included the whole AAS spectrum taking into account complicated aneurysms and prostheses.

This is a small sample, a fact that explains the wide CI of the RRR of the risk factors studied. Increasing the sample size could reveal a higher and / or significant RRR for risk factors that have not shown statistical significance.

Since the reference test was not carried out for those classified as low risk, the specificity cannot be calculated, nor can it be known how many AAS were not diagnosed for this reason.

The marked increase in CT requests after the implementation of the algorithm could be due to an observational bias and/or a consequence of learning through the algorithm itself about the clinical diagnosis of the AAS and its differential diagnoses.
This CDSS was implemented in a tertiary hospital, so we cannot extrapolate the results to other non-tertiary hospitals. We did not assess the satisfaction of the professionals using the algorithm or the potential difficulties of putting the system into practice.
The study period was very short due to issues with the electronic medical record system at our hospital. The number of observations are insufficient to develop a clinical prediction rule. A prospective validation study of the score with more patients is needed.

As a conclusion, the use of a sensitive algorithm in the emergency department can be useful to optimize the diagnosis of AAS. The implementation at our hospital of this evidence-based pathway for requesting CTA in patients with suspected AAS achieved an improvement in AAS management. The presence of a known aortic aneurysm and new-onset aortic regurgitation were shown to significantly increase the probability of AAS. The existence of hypotension or shock increased the risk of alternative severe acute disease. Further studies are needed to establish a clinical prediction rule.

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Conflicts of interest: none

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