ORIGINAL ARTICLE

Oral Anticoagulation in Aortic Endovascular Reinterventions

Anticoagulación oral en reintervenciones endovasculares

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ABSTRACT

Background: Endoleak is the main cause for reintervention after endovascular aortic repair. Some patients need prolonged oral anticoagulation, which may increase the incidence of postoperative endoleaks.
Objectives: Our objective was to determine whether postoperative oral anticoagulation has an impact on the incidence of endoleaks.
Methods: This retrospective analysis included all patients with endovascular treatment of abdominal aortic aneurysm at our center between 2009 and 2014. Two groups of patients were determined according to the need for oral anticoagulation. Aortic-related mortality, survival free from reinterventions, any endoleak and non-type II endoleaks, survival free of the composite endpoint of mortality associated with the aorta, reinterventions and endoleaks, and reduction of aneurysmal sac diameter was compared between both groups.
Results: Among 341 treated patients, 33 (9.67%) were anticoagulated. There were no differences between the two groups in terms of aorta-related mortality (2.59% vs. 3.03%, p=ns), reintervention-free survival (84.04% vs. 86.2%; p=ns), any endoleak-free survival (82% vs. 89%, p=0.81) or non-type II endoleak-free survival (88% vs. 88%, p=0.52). Similarly, no significant differences were found when analyzing the composite endpoint-free survival (80% vs. 85%, p=ns). The average reduction of aneurysmal sac diameter was 5.19 mm and 3.51 mm (p=0.2).
Conclusions: No difference was registered in any of the results analyzed. Postoperative oral anticoagulation had no impact on the results of endovascular aortic treatment.

Key words: Aneurysm of the abdominal aorta - Endovascular procedures - Endoleak - Anticoagulation / administration and dosing - Oral administration

RESUMEN

Introducción: La endofuga es la principal causa de reintervención después del tratamiento endovascular de aorta. Algunos pacientes necesitan anticoagulación oral prolongada, lo cual puede aumentar la incidencia de endofugas posoperatorias.
Objetivos: Nuestro objetivo es determinar si la anticoagulación oral posoperatoria tiene impacto en la incidencia de endofugas.
Material y métodos: Este análisis retrospectivo incluyó todos los pacientes con aneurisma de aorta abdominal tratados por vía endovascular entre 2009 y 2014 en nuestro centro. Se determinaron dos grupos de pacientes de acuerdo con la necesidad de anticoagulación oral y se comparó entre ambos grupos la mortalidad relacionada con la aorta; la supervivencia libre de reintervenciones, de cualquier endofuga y de endofugas no tipo II; supervivencia libre de un punto final compuesto por mortalidad relacionada con la aorta, reintervenciones y endofugas, y la reducción del diámetro del saco aneurismático.
Resultados: De 341 pacientes tratados, 33 (9,67%) estaban anticoagulados. No hubo diferencias entre ambos grupos en términos de mortalidad relacionada con la aorta (2,59% vs. 3,03%, p = ns), supervivencia libre de reintervenciones (84,04% vs. 86,2%; p = ns), supervivencia libre de cualquier endofuga (82% vs. 89%; p = 0,81) o supervivencia libre de endofugas no tipo II (88% vs. 88%; p = 0,52). Al analizar la supervivencia libre del punto final compuesto tampoco se encontraron diferencias significativas (80% vs. 85%; p = ns). La reducción promedio del diámetro del saco aneurismático fue de 5,19 mm y 3,51 mm (p = 0,2).
Conclusiones: No se registró diferencia en ninguno de los resultados analizados. La anticoagulación oral posoperatoria no tuvo impacto en los resultados del tratamiento endovascular de aorta.

Palabras clave: Aneurisma de la aorta abdominal - Procedimientos endovasculares - Endofuga - Anticoagulación/administración y dosificación - Administración oral

Abbreviations

AAA Abdominal aortic aneurysm	**EVAR** Endovascular aortic aneurysm repair

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INTRODUCTION

Abdominal aortic aneurysm (AAA) is the fifteenth cause of death in the United States, with a prevalence ranging between 4% (1) and 7.6% (2) that increases with age. About two thirds of patients with AAA have documented coronary heart disease. (3) As life expectancy increases, older patients with more comorbidities require treatment.

Oral anticoagulants are used as prevention of embolic events in various conditions, especially in patients with cardiovascular diseases such as atrial fibrillation, venous thromboembolic disease or mechanical valve prostheses.

Endovascular aortic aneurysm repair (EVAR) has shown a lower perioperative morbidity and mortality than conventional surgery (4-6) and, in recent years, it has become the technique of choice for the treatment of this pathology, especially in patients whose comorbidities represent a high perioperative risk for conventional surgery. (7)

Endoleaks are the main cause for reoperation in patients with endovascular treatment. (8) Theoretically, oral anticoagulation may increase the risk of endoleaks after EVAR or may hinder spontaneous closure; however, the existing literature on this subject is contradictory.

The aim of the present study was to establish whether oral anticoagulation affects the results of endovascular treatment in our population of patients with AAA.

METHODS

A retrospective analysis of our database was conducted including all patients with infrarenal and juxtarenal AAA electively and consecutively treated with EVAR in a single center between 2009 and 2014. The study also included patients with common iliac artery aneurysms in whom, due to anatomical restrictions, it was necessary to use bifurcated devices with extension to the infrarenal aorta. Cases of isolated iliac aneurysms, in which an adequate seal could be obtained at the level of the iliac artery without need to extend to the abdominal aorta, were not included in the analysis. In addition, patients treated for emergencies due to ruptured aneurysms and patients with pararenal or adrenal aneurysms were excluded.

Two groups were established according to the indication of oral anticoagulation in the postoperative period, and the following results were compared: aortic-related mortality, any endoleak-free survival, non-type II endoleak-free survival, related reintervention-free survival, and average reduction of residual aneurysmal sac diameter in absolute terms and as percentage of preoperative diameter. In addition, a composite endpoint of mortality related to the aorta, reinterventions and non-type II endoleaks was determined, and composite endpoint-free survival was compared between both groups.

All procedures were performed in the operating room with a portable angiograph. Patients were treated with general anesthesia or neuroleptoanalgesia in combination with local anesthesia according to the preoperative clinical status and the preference of the treating physicians. According to the endovascular device used, access was made by dissection of the ipsilateral femoral artery and contralateral puncture or bilateral femoral dissection.

The postoperative follow-up protocol consisted of an abdomen and pelvis CT scan with intravenous contrast one month and 6 months after the procedure, and then one per year if the previous ones were normal. In the case of contraindications for the administration of intravenous contrast, the control was performed with contrast-free CT scan and aortoiliac echo-Doppler.

Statistical analysis

Mean and standard deviation or median and interquartile range were reported for the descriptive analysis of continuous variables according to the normality of their distribution, assessed using the D'Agostino test. Categorical variables were reported as percentages. The chi-square test was used to compare categorical variables and Student's t test or the Mann-Whitney test for continuous variables, according to the distribution of each variable. Kaplan-Meier curves were built to analyze survival and compared using the log-rank test. In all cases, statistical significance was established for $p<0.05$.

Ethical considerations

The protocol design of the ARGEN-IAM-ST registry was evaluated and approved by the Bioethics Committee of the Argentine Society of Cardiology, and was subjected to evaluations of the participating center's committees, depending on local regulations and institutional policies.

RESULTS

The analysis included 341 patients consecutively treated between 2009 and 2014 at Instituto Cardiovascular de Buenos Aires. Among them, 33 patients (9.67%) were receiving oral anticoagulants (31 acenocoumarol and 2 dabigatran) and 308 patients (90.3%) were not treated with oral anticoagulants. The demographic characteristics of both groups are summarized in Table 1 and the characteristics of the aortic anatomy are shown in Table 2. Median follow-up was 16 months (3-33), and 33 patients (9.67%) did not register control measurements.

There was no difference in terms of aortic-related mortality between both groups (2.59% in non-anticoagulated vs. 3.03% in anticoagulated patients, $p=0.44$). The causes of death were rupture (n=4) and sepsis secondary to wound infection in a patient who developed a pseudoaneurysm.

There were also no significant differences in terms of any endoleak-free survival (82% vs. 89%, $p=0.81$) (Figure 1), non-type II endoleak-free survival (88% vs. 88%, $p=0.52$), reintervention-free survival (84% vs. 86%, $p=0.79$) (Figure 2), and composite endpoint-free survival (80% vs. 85%, $p=0.99$) (Figure 3).

Of the total endoleaks detected, the majority (32%) was type II and corresponded to 6% of the total number of patients. Twenty-five percent was type IB (4.6% of the total number of patients); 17% were type IA and type IIIA (3.3% of the population) and, finally, 3% were type 3B (0.7% of patients). In the remaining 5%, the type could not be determined, so they were charac-

Table 1. Baseline demographic characteristics of no oral anticoagulation and oral anticoagulation patients

	NO OAC (n = 308)	OAC (n = 33)	p
Age	72.45 +/- 7.74	75.81 +/- 7.91	0.01
Male gender	91%	93%	0.59
Hypertension	81%	79%	0.74
Dyslipidemia	74%	73%	0.83
Smoking	64%	79%	0.07
Diabetes	16%	6%	0.13
COPD	13%	9%	0.52
Serum creatinine	1.15 (0.99-1.44)	1.2 (1.1-1.39)	0.39

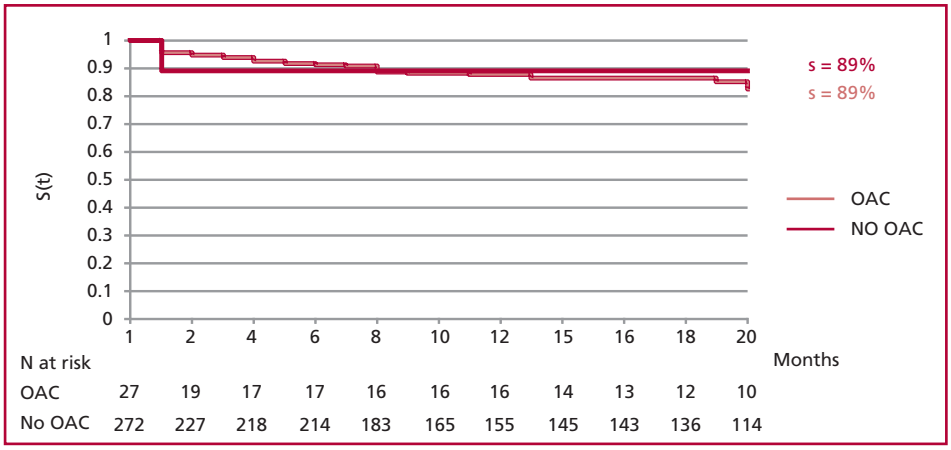
OAC: Oral anticoagulation. COPD: Chronic obstructive pulmonary disease

Table 2. Anatomical characteristics of the aneurysm in no oral anticoagulation and oral anticoagulation patients

	NO OAC (n = 308)	OAC (n = 33)	p
Maximum diameter	57 (52-63)	60 (50-68)	0.73
Neck length	22 (15-31)	28 (15-37)	0.43
Neck diameter	26 (23-29)	25 (22-28)	0.27
Conical neck	15%	6%	0.23
Neck thrombus >50%	5%	4%	0.72
Neck calcification >50%	7%	4%	0.48
Neck angle >60°	14%	24%	0.15

OAC: Oral anticoagulation.

Fig. 1. Kaplan-Meier curve showing any endoleak-free survival in no oral anticoagulation and oral anticoagulation patients.



terized as indeterminate (in 1% of patients).

Among the total number of reinterventions (n=56), more than half (55%) was due to endoleaks and three of these cases required conversion in patients who presented with rupture. Twenty-one percent was due to complications related to the device branches, either by occlusion, stenosis or kinking, 11% was due to wound infections and another 11% to complications related with the accesses, such as pseudoaneurysms or occlusion of femoral arteries. Finally, a definitive vascular access was done in a patient (2%), since permanent dialysis treatment was required after hospitalization in which the index procedure was performed.

The average reduction of the aneurysmal sac diameter did not show any difference between the groups either when analyzed as absolute value (5.19 mm vs. 3.51 mm, p=0.2) or as percentage of the original diameter (8.34% vs. 6.4%, p=0.16).

DISCUSSION

In our analysis, we did not register a significant difference between the two groups in any of the analyzed short- and mid-term results. Both mortality related to the aorta, as reintervention- and endoleak-free survival, and the reduction of the residual aneurysmal sac diameter, were similar in the two groups.

These data are consistent with several previous reports. In a retrospective study of 232 patients, Fairman et al. (9) showed no difference in the incidence of early or late endoleaks in patients anticoagulated

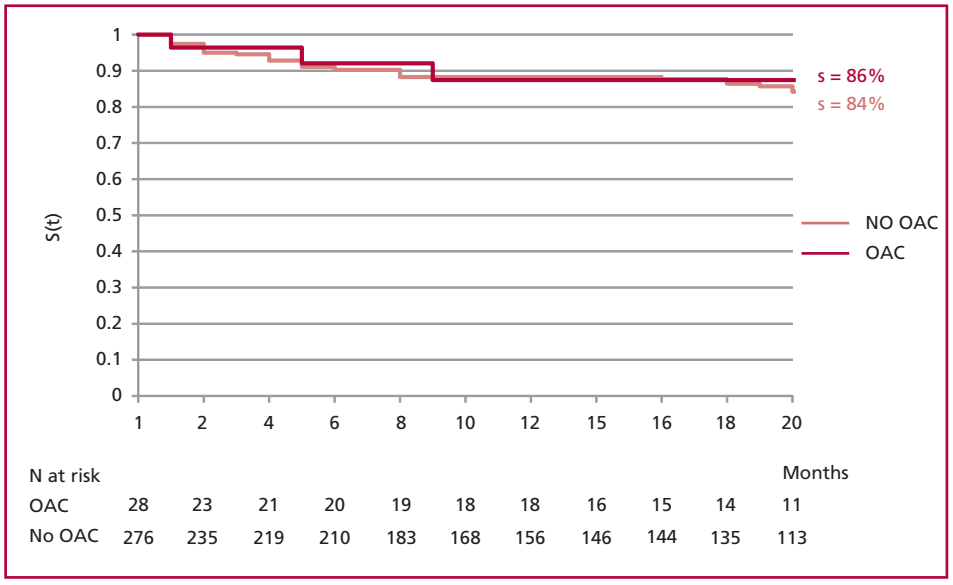


Fig. 2. Kaplan-Meier curve showing reintervention-free survival in no oral anticoagulation and oral anticoagulation patients.

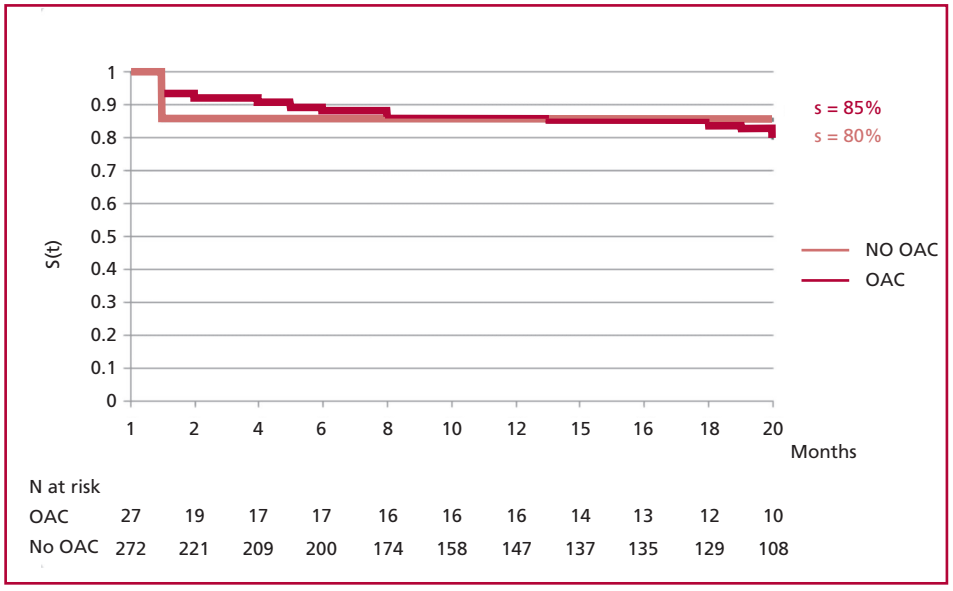


Fig. 3. Kaplan-Meier curve showing aortic mortality-, endoleak- and reintervention-free survival in no oral anticoagulation and oral anticoagulation patients.

with warfarin, although there was a trend towards less reduction of the aneurysmal sac in the group of anticoagulated patients. Similarly, in his retrospective analysis of 182 patients, Biebl et al. (10) found no differences in endoleak-free survival at 1, 2 and 3 years between the groups of anticoagulated and non-anticoagulated patients. They also found no difference in terms of aneurysmal sac remodeling. Moreover, Johnson et al. (11) also found no difference in the incidence of endoleaks between anticoagulated (16.2%) and non-anticoagulated patients (11.5%) in their series of 363 patients with a median follow-up of 29 months.

In contrast, in a retrospective analysis of 127 consecutive patients with a 2-year follow-up, Bobadilla et al. (12) reported a higher incidence of endoleaks, especially type II endoleaks, in anticoagulated patients, as well as 16% increase in the volume of the residual aneurysmal sac compared with 9% reduction in non-anticoagulated patients. Likewise, De Rango et al. (13) reported the results of 1,409 patients with a follow-up of 60 months, which is the largest series and with the longest follow-up, comparing the effects of oral anticoagulation in patients treated with EVAR. In this study, anticoagulated patients had a higher incidence of early endoleak (at 30 days, 28.2% vs. 17.6%) and lower endoleak-free survival at 5 years (57.5% vs. 69.2%). Reintervention- and conversion-free survival was also significantly lower in anticoagulated patients.

In our series, the percentage of anticoagulated patients was 9.67%. Compared with series from the

United States, this proportion is lower (Biebl: 11.5%, Johnson: 18.2%, Fairman: 15%, Bobadilla: 18.9%) and more similar to the Italian series (De Rango: 7.6%). These disparities between series could be an indicator of differences in the strategy of prevention of embolic events used in different countries.

Only two patients in our series were treated with new oral anticoagulants, particularly dabigatran. The majority of patients (29/31) was receiving acenocoumarol. Therefore, an evaluation of their impact on EVAR postoperative results cannot be made. As the use of new anticoagulants increases, a comparative analysis with traditional oral anticoagulants may reveal whether there are differences in their impact on the postoperative period of endovascular aortic treatment.

In addition to the inherent limitations of any single-center retrospective study, we would like to highlight in our analysis the absence of type II endoleaks in the group of anticoagulated patients. This type of endoleak is the most frequent after endovascular treatment of the aorta. The most probable explanation for this particular finding is sample size. The proportion of anticoagulated patients in our series was lower than in most of the other series, while the series of patients reporting a proportion of anticoagulated patients similar to ours included in its analysis almost 4 times more patients than in our study.

CONCLUSIONS

In the present retrospective analysis, we did not demonstrate that treatment with oral anticoagulants affects the results of endovascular aortic treatment in terms of aortic-related mortality, endoleak-free survival, reintervention-free survival, or remodeling of the residual aneurysmal sac.

Conflicts of interest

None declared.

(See authors conflicts of interest forms on the website/ Supplementary material).

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