CLINICAL STUDY

Influence of Statin Therapy on Aneurysm Sac Regression after Endovascular Aortic Repair

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ABSTRACT

Purpose: To determine whether statin therapy is associated with abdominal aortic aneurysm (AAA) sac regression after endovascular aneurysm repair (EVAR).

Materials and Methods: A total of 109 patients treated with EVAR were retrospectively analyzed (no-statin group, n = 45; statin group, n = 64). The primary endpoint was the incidence of AAA sac regression. To investigate independent predictors of AAA sac regression, regression analysis was performed. The mean age was 74 years (range, 55–90 y), and 87.2% of patients were men.

Results: The no-statin group had higher rates of AAA sac regression than the statin group at 1 year (no-statin group, 66.7%; statin group, 45.3%; $P = .028$). The incidence of AAA sac regression increased over time in the statin group, and no statistical difference was seen between the two groups at 2 years (no-statin group, 66.7%; statin group, 57.8%; $P = .350$). The difference between the changes in maximum AAA diameter was significant between groups at 1 year (no-statin group vs statin group, −4.9 mm ± 5.9; $P = .041$), but the difference did not reach statistical significance at 2 years (no-statin group, −10.0 mm ± 10.1; statin group, −8.0 mm ± 9.6; $P = .306$). Statin therapy was not associated with AAA sac regression on univariate (odds ratio [OR], 0.685; 95% confidence interval [CI], 0.310–1.516; $P = .351$) and multivariate analyses (OR, 0.617; 95% CI, 0.215–1.772; $P = .369$).

Conclusions: Statin therapy had no effect on AAA sac regression at 2 years. There is insufficient evidence to recommend statin therapy for AAA sac regression.

ABBREVIATIONS

AAA = abdominal aortic aneurysm, CAD = coronary artery disease, CI = confidence interval, EVAR = endovascular aneurysm repair, MMP = matrix metalloproteinase, OR = odds ratio

The goal of endovascular aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA) is to prevent aneurysm-related death from rupture by excluding the aneurysm from the circulation. A decrease or stability in the size of the AAA sac on follow-up imaging is considered a treatment success (1). However, it has been found that aneurysm size regression occurs in only 60% of patients who undergo EVAR, and that the aneurysm diameter does not change or increases in the remaining 40% (2). Consequently, pharmacotherapies to enhance AAA sac regression after EVAR have received attention (3). Studies have shown an association between pharmacotherapies and down-regulation of matrix metalloproteinase (MMP) production in the aortic wall, where attenuation of MMP activity in aneurysmal aortic tissue is one of the primary mechanisms for a reduction in AAA expansion rate (4). Commonly prescribed antihypertensive medications such as angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, and β-blockers downregulate MMP production in vitro, specifically MMP-2 and MMP-9, and have been linked with reduced AAA growth rates in vivo (5,6). Several studies showed that statin agents reduced MMP concentrations in the AAA wall, including some results demonstrating an association between statin agent use and

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reduced AAA growth in small AAAs (7,8). However, there have been few data published on the effect of statin use on AAA sac regression after EVAR (9,10). If statins can demonstrate the ability to limit AAA sac expansion and enhance AAA sac regression after EVAR, it would have a major impact on overall management of AAA after EVAR. The present study investigated whether statin therapy is beneficial to AAA sac regression in patients undergoing EVAR.

MATERIALS AND METHODS

Study Population and Inclusion and Exclusion Criteria

The study protocol was developed in accordance with the Declaration of Helsinki and was approved by the institutional review board. All consecutive patients admitted to a single institution between January 2005 and December 2013 who underwent elective EVAR for infrarenal AAAs were evaluated. Patients were suitable for inclusion if they had undergone initial successful EVAR for infrarenal AAAs with follow-up of at least 2 years. Because the type of stent graft may affect the degree of AAA sac regression after EVAR, we included only patients treated with the EXCLUDER device (W. L. Gore & Associates, Flagstaff, Arizona), which was the most commonly used stent graft at our institution during the relevant time period (11). Patients treated for thoracic aortic aneurysms, thoracoabdominal aortic aneurysms, juxtarenal AAAs with short proximal necks ($\leq$ 15 mm), symptomatic or ruptured aneurysms, infectious aneurysms, anastomotic pseudoaneurysms, or isolated iliac aneurysms were excluded from the study. To limit confounding factors, patients were included only if they met the criteria of treatment success, defined as the absence of the following: (*i*) type I and III endoleaks on initial posttreatment angiography and follow-up computed tomographic (CT) angiography, (*ii*) type II endoleak on follow-up CT angiography, (*iii*) rupture or surgical conversion, and (*iv*) stent-graft migration or failure (12). Any patient with an endoleak or endotension on follow-up imaging was excluded. Cases involving stent-graft use on an off-label basis or not in compliance with instructions for use were excluded, including "chimney"/"snorkel" technique, "sandwich" techniques, hybrid EVAR with debranching procedures, or any procedure to eliminate periprocedural endoleak such as the use of a proximal aortic cuff, Palmaz stent (Cordis, Bridgewater, New Jersey), EndoAnchor system (Medtronic, Minneapolis, Minnesota), and/or sac embolization. Finally, patients with unavailable, incomplete, or missing case notes or who underwent imaging and clinical follow-up at another institution were excluded.

The medical records of 344 patients who underwent EVAR with the EXCLUDER device between January 2005 and December 2013 were identified. After careful review of the exclusion criteria, 109 patients were included in the analysis (Fig 1). Of these, 64 received statin therapy (58.7%) and 45 did not (41.3%). A total of 56 patients (87.5%) were receiving statin therapy before EVAR. Baseline characteristics of patients in relation to statin group are given in Table 1. The mean age was 74 years (range, 55–90 y), and 87.2% of the patients were men. The statin group had more coronary artery disease (CAD; no-statin group, 35.6%; statin group, 62.5%; $P = .006$) and hyperlipidemia (no-statin group, 26.7%; statin group, 100%; $P < .001$) than the no-statin group. Medical therapy at follow-up included a β-blocker in 51 patients (46.8%), angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in 44 (40.4%), and a calcium channel blocker in 31 (28.4%). The statin group was more likely to be prescribed a β-blocker than the no-statin group (no-statin group, 31.3%; statin group, 57.8%; $P = .006$; Table 1). Anatomic parameters are presented in Table 2. The average baseline AAA maximum diameter was 57.3 mm ± 8.7. Eighty patients (73.4%) had a maximum AAA diameter < 60 mm (classified as medium size), and 29 (26.6%) had a maximum AAA diameter ≥ 60 mm (classified as large size). The average AAA proximal neck diameter was 22.5 mm ± 2.8, with a mean length of 25.6 mm ± 10.6 and a mean angle of 23.2° ± 13.1. Overall, the differences between diameters, lengths, and angle profiles of AAAs between the two groups were not statistically significant.

Index Procedure and Follow-up

EVAR was considered when the maximum AAA diameter was at least 50 mm and/or when an increase in the maximum diameter of at least 5 mm was observed over a period of 6 months (12). CT angiographic follow-up visits were scheduled at 1 month, 6 months, and 12 months after EVAR and yearly thereafter to monitor AAA sac behavior.

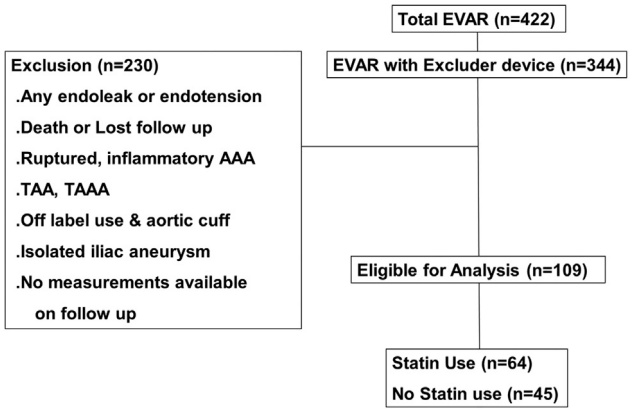

Figure 1. Flowchart showing patient selection. TAAA = thoracoabdominal aortic aneurysm.