Safety of Chronic Anticoagulation Therapy After Endovascular Abdominal Aneurysm Repair (EVAR) CME ☆

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WHAT THIS PAPER ADDS

Knowledge of the negative impact (higher risk of loss of stentgraft sealing, reintervention, and conversion) of chronic anticoagulation on early and late outcomes of endovascular aortic repair (EVAR) shown in this study should inform the future decision-making approach for patients with both abdominal aortic aneurysms (AAA) and cardiac disease, who may require prolonged anticoagulation treatment.

Objective: Current data supporting the effect of anticoagulation drug use on aneurysm sealing and the durability of endovascular abdominal aneurysm repair (EVAR) are conflicting. This study assessed the safety of chronic anticoagulation therapy after EVAR.

Methods: Records of 1409 consecutive patients having elective EVAR during 1997—2011 who were prospectively followed were reviewed. Survival, reintervention, conversion, and endoleak rates were analyzed in patients with and without chronic anticoagulants. Cox proportional hazards models were used to estimate the effect of anticoagulation therapy on outcomes.

Results: One-hundred and three (7.3%) patients were on chronic anticoagulation drugs (80 on vitamin K antagonists) at the time of EVAR. An additional 46 patients started on anticoagulants after repair were identified. Patients on chronic anticoagulation therapy at repair (mean age 73.6 years; 91 males) had more frequent cardiac disease (74.8% vs. 44.2%; $p < 00001$), but no other differences in demographic and major baseline comorbidities with respect to the others. At baseline, mean abdominal aortic aneurysm (AAA) diameter was 56.43 mm vs. 54.65 mm ($p = .076$) and aortic neck length 26.54 mm vs. 25.21 mm ($p = .26$) in patients with and without anticoagulants, respectively. At 5 years, freedom from endoleak rates were 55.5% vs. 69.9% ($p < .0001$), and freedom from reintervention/conversion rates were 69.4% vs. 82.4% ($p < .0001$) in patients with (including those with delayed drug use) and without chronic anticoagulants, respectively. Controlling for covariates with the Cox regression method, at a mean follow-up of 64.3 ± 45.2 months after EVAR, use of anticoagulation drugs was independently associated with an increased risk of endoleak (odds ratio, OR 1.6; 95% confidence interval, CI: 1.23—2.07; $p < .0001$) and reintervention or late conversion rates (OR 1.8; 95% CI: 1.31—2.48; $p < .0001$).

Conclusions: The safety of anticoagulation therapy after EVAR is debatable. Chronic anticoagulation drug use risks exposure to a poor long-term outcome. A critical and balanced decision-making approach should be applied to patients with AAA and cardiac disease who may require prolonged anticoagulation treatment.

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Vitamin K antagonists (VKAs) and heparins have been used as an effective therapy to prevent the thromboembolic complications of atrial fibrillation (AF), valvular heart disease (VHD), and venous thromboembolism (VTE). The use of chronic anticoagulation drugs is expected to further increase in the Western world because of the aging population and the introduction of new oral anticoagulants with safer profiles.[1] However, chronic anticoagulant therapy is extremely challenging in clinical practice: the target level of anticoagulation involves a balance between prevention of ischemic events and avoidance of hemorrhagic complications.[2] The risk/benefit ratio should be estimated in each individual patient and is particularly important for elderly patients with AF. Specifically, in old patients with abdominal aortic aneurysms (AAA) and cardiac disease (often requiring

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chronic anticoagulant therapy), endovascular aneurysm repair (EVAR) is usually preferred to open surgery to minimize the operative complications and hemorrhagic risks of open surgery. Therapeutic doses of anticoagulants could theoretically prevent spontaneous aneurysm sac thrombosis and increase the incidence of endoleak and, therefore, of EVAR failure. Nevertheless, the effect of the patient coagulation status on the success of endovascular aneurysm exclusion in the early stages, and particularly in the long term, is a reason for concern. This remains unresolved in the current literature because studies that specifically analyze the effect of chronic anticoagulation on outcomes of EVAR are limited and the results discordant.[3–8]

The aim of this study was to analyze early and late outcomes of EVAR patients on chronic anticoagulation therapy in a large series of patients.

METHODS

From April 1997 to December 2011, all patients with infrarenal AAA who underwent EVAR were prospectively entered into a database. Recorded data included demographics, clinical comorbidities, baseline drug use including anticoagulation methods, aneurysm morphology details, EVAR devices, intraoperative details, and follow-up outcomes. Patients treated as an emergency for AAA rupture and those receiving fenestrated stentgrafts were excluded from the present study that focused on 1409 patients receiving anticoagulant therapy or not. The collected data were reviewed to investigate whether the use of chronic anticoagulation drugs before EVAR affected EVAR outcome. Patients were divided into two groups: those on chronic anticoagulation therapy (VKAs or heparins) and those not, at the time of EVAR. However, the database only included drug data at the time of operation and data were not collected on the use of anticoagulants during follow-up after EVAR. For the purpose of this study, to further investigate the potential effect of chronic anticoagulants on late outcomes of EVAR, patients were contacted by telephone and specifically questioned about the introduction of anticoagulation therapy following EVAR. The overall group of patients with long-standing (on therapy at the time of EVAR) and delayed (started after discharge) anticoagulation treatment was separately assessed.

Patients on anticoagulants and those not, were compared for perioperative variables and outcomes at 60 months. The primary outcomes were survival and the need for reintervention. Secondary outcomes were aneurysm-related survival, need for conversion, and endoleak incidence.

Patients received intraoperative intravenous unfractionated heparin (100 U/kg). EVAR was performed by a dedicated team under general or local anesthesia using different device models depending on the aorto-iliac morphology, stentgraft availability, and operator preferences. There were $n = 610$ (43.3%) Zenith (Cook Inc., Blooomington, IN, USA); $n = 235$ (16.7%) AneuRx (Medtronic Vascular, Santa Rosa, CA, USA); $n = 167$ (11.8%) Talent (Medtronic Vascular, Santa Rosa, CA, USA); $n = 71$ (5.0%) Endurant (Medtronic Vascular, Santa Rosa, CA, USA); $n = 232$ (16.5%) Excluder (Gore & Associates, Inc, Flagstaff, AZ, USA); $n = 35$ (2.5%) Fortron (Johnson & Johnson – Cordis Corporation, Bridgewater, NJ, USA); $n = 53$ (3.8%) Anaconda (Terumo Vascutek, Inchinnan Renfrewshire, UK), and $n = 6$ (0.4%) others.

After EVAR, patients were scheduled for serial follow-up including clinical evaluation and imaging with duplex ultrasound and computed tomography angiography (CTA) scan at 1, 6, and 12 months, and yearly thereafter. Use of CTA was less frequently applied in the most recent years. A vascular dedicated digital workstation (TeraRecon Aquarius Workstation, Terarecon, Foster City, CA, USA) was used for CTA-scan imaging analysis and three-dimensional (3D) reconstructions. Endoleaks and complications were recorded and classified according to Standardized Reporting Practices in Vascular Surgery.[9] Reinterventions were performed at the discretion of the attending surgeon, but, in general, treatment was applied when AAA showed type I/III endoleak or persisting type II endoleak/endotension associated with a diameter increase >5 mm after EVAR or in the presence of major complications (migration, disconnections, limb occlusion, rupture). The type of treatment was individualized to aneurysm anatomy and endoleak source.[10]

Because of the retrospective analysis of prospectively collected data, there was no requirement for local ethical committee approval.

Statistical analysis

Descriptive statistics for categorical variables were presented as relative frequencies (percentages); chi-square test or Fisher exact test, when appropriate, were used to evaluate univariate differences between the chronic anticoagulant (VKAs or heparin) and non-anticoagulant groups. Continuous variables were expressed as mean with standard errors (SE) and ranges. Kaplan–Meier survival estimates were used to determine survival, aneurysm-related survival, and freedom from reintervention, conversion, and endoleak in patients with and without chronic anticoagulation therapy. Log-rank test was used to assess difference between groups.

The odds ratio (OR) and 95% confidence intervals (CIs) for different outcomes were estimated with multivariate analyses using Cox regression models. Backward selection was used to evaluate time-to-event effects of chronic anticoagulation and the development of need for reintervention and endoleak occurrence while controlling for the following confounders: age, gender, diabetes, hypertension, cardiac disease (CAD), peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), aneurysm diameter, intraluminal thrombus, and anticoagulation treatment.

Findings were considered statistically significant if the resulting p value was less than .05. SPSS for Mac/OS version 20.0 (SPSS Inc. Chicago, IL, USA) was used for all statistical analyses.