

Outcome After Surgery for Acute Aortic Dissection: Influence of Preoperative Antiplatelet Therapy on Prognosis

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Objectives: Outcome in patients with acute coronary syndrome (ACS) is improved with dual antiplatelet therapy (DAPT). Patients with acute aortic dissection type A (AAD) often present with similar symptoms and may therefore be prescribed DAPT before diagnosis. The aim of this study was to evaluate the use of antiplatelet therapy (APT) prior to AAD surgery and patient outcome, including indications according to the European Society of Cardiology's (ESC) recent guidelines.

Design: A retrospective, observational study.

Setting: A tertiary University Hospital, Rigshospitalet, Heart Centre, Copenhagen, Denmark.

Participants: The study included 171 patients operated for AAD during 2010 to 2014.

Interventions: The independent relationship of preoperative APT was explored on 30-day mortality, intraoperative bleeding and perioperative transfusion requirements. Furthermore, the indications for APT were obtained.

Measurements and Main Results: Patients receiving APT ($n = 73$) did not have an increased 30-day mortality (29% v 20%, $p = 0.18$). However, APT increased intraoperative bleeding by 45% ($p < 0.001$) and increased perioperative

transfusion of red blood cells by 71%, fresh frozen plasma by 52%, and platelets by 56% ($p = 0.002$). Among patients receiving APT preoperatively, 26 patients received acetylsalicylic acid (ASA) alone and 46 patients received DAPT. Bleeding was significantly more pronounced in patients receiving DAPT (5.6 ± 4.1 L), compared to ASA alone (3.6 ± 3.1 L) and no APT (3.3 ± 4.8 L) ($p < 0.001$). However, there was no significant difference in mortality between groups. DAPT, including ticagrelor, increased intraoperative bleeding by 62% compared to DAPT with clopidogrel ($p = 0.004$). Among patients receiving DAPT, only 30% of the patients fulfilled ESC criteria for ACS treatment.

Conclusions: The use of APT was associated with increased intraoperative bleeding and transfusion requirement; however, it was not associated with a statistically significant increased mortality. Only a minority of patients fulfilled ESC criteria for ACS treatment with DAPT.

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KEY WORDS: aortic dissection, acute coronary syndromes, outcome, aortic surgery, antiplatelet therapy, bleeding

ANTIPLATELET THERAPY (APT) is a cornerstone in the treatment of acute coronary syndrome (ACS).¹ Early initiation of APT is recommended to reduce mortality and the risk of adverse cardiac events.¹⁻³ Administration of APT prior to cardiac surgery, however, is associated with increased mortality and bleeding complications,⁴⁻⁸ especially if the patient requires emergency surgery.⁹

The clinical presentation of ACS is most commonly chest pain, with or without shortness of breath and malaise.¹ Similar symptoms are often present in patients with acute aortic dissection type A (AAD). These similarities frequently result in preoperative treatment with APT.^{10,11} The study by Hansson et al observed that administration of dual antiplatelet therapy (DAPT) prior to AAD surgery was associated with an increased 30-day mortality and the occurrence of perioperative bleeding complications. Furthermore, the same study found that a substantial proportion of patients did not fulfill the indications for ACS treatment with APT.¹¹ Since the study was published in 2011, ticagrelor has been incorporated in the European Society of Cardiology's (ESC) guidelines, currently recommending DAPT with aspirin and ticagrelor as first-line treatment in ACS.¹ Ticagrelor was found to be superior to clopidogrel in preventing recurrent ischemic events in ACS patients, but also may increase bleeding complications in this setting.^{1,12-15} If treatment with ticagrelor prior to surgery for AAD is associated with increased bleeding has not been investigated previously.

In this retrospective observational study, the authors wanted to evaluate the use of APT prior to AAD surgery and to see if APT influenced patient outcome after surgery. The authors' primary endpoint was 30-day mortality and secondary endpoints were intraoperative bleeding and postoperative

transfusion requirements, in terms of red blood cells, fresh frozen plasma, and platelet pools. Furthermore, the authors wanted to evaluate if the shift to ticagrelor according to the updated ESC guidelines influenced the patient's bleeding risk. Finally, the authors wanted to investigate the indications for ACS treatment with APT in patients operated on for AAD.

METHODS

Patients

The study was conducted as a retrospective single-center observational study. Patients who underwent emergency surgery for AAD, from January 1, 2010 to December 31, 2014 at Rigshospitalet, Copenhagen, Denmark, were included. Patients were identified through the hospital surgical database and national registry. Of 193 patients with AAD, 22 patients were excluded because they were either included in a randomized clinical trial including a coagulation-modifying intervention, diagnosed with chronic aortic dissection, or due to other

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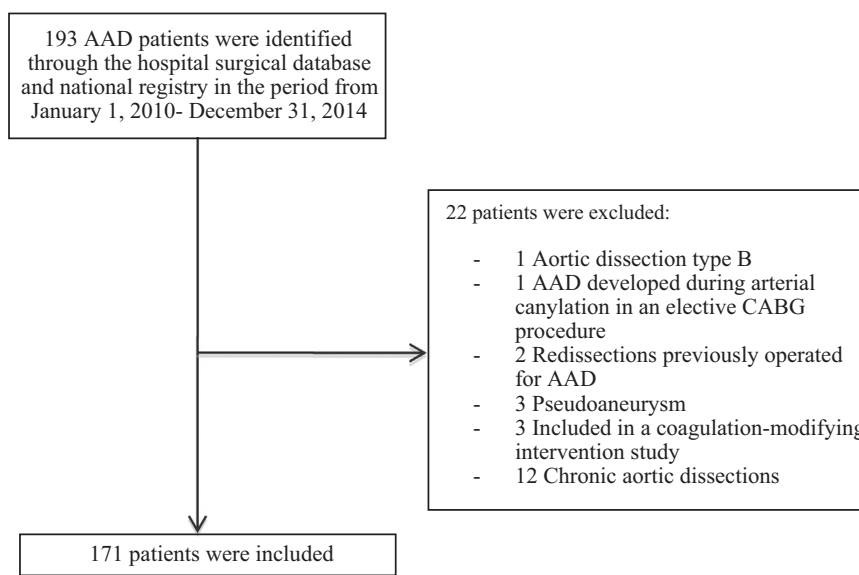


Fig 1. Inclusion or exclusion of patients.

reasons excluding surgery for AAD (Fig. 1). Data were collected from patient records, intensive care unit patient data management system, anesthesia, and perfusion records. The collection and processing of data were approved by the Danish Data and Protection Agency (j. no: 2012-58-0004). One patient was lost to follow-up as the patient was a foreign citizen and referred back to the home hospital within 30 days after surgery.

The University hospital, Rigshospitalet, is 1 of 4 specialized cardiothoracic centers in Denmark with a referral area including eastern Denmark, Greenland, and the Faroe Islands. Among the 171 patients included in the study, 24% were women ($n = 41$) and the mean patient age was 62 ± 11 years.

Intraoperative Management

All surgeries were performed through a median sternotomy with patients on cardiopulmonary bypass (CPB). The arterial cannulation was done via the subclavian or the femoral artery and the venous return was obtained from the right atrium or the femoral vein. From a total of 171 patients included in the study, 137 patients (80%) had surgery with selective cerebral perfusion with a mean duration of 25 minutes. Furthermore, 101 patients (59%) had surgery using circulatory arrest with a mean duration of 6 minutes. The mean minimal temperature among patient surgeries with and without circulatory arrest was 21°C ($\pm 3^{\circ}\text{C}$) and 23°C ($\pm 4^{\circ}\text{C}$), respectively. A supracoronary graft was inserted in 132 patients (77%), while the remaining received a composite graft. Coronary artery bypass grafting (CABG) was performed in 41 patients (24%). Cell saver was used intraoperatively in all cases and all patients received tranexamic acid. During massive bleeding, transfusion of blood products was given as packages of 5:5:2 of red blood cells, fresh frozen plasmas, and pooled platelets, respectively. When hemostasis was improved, the remaining blood products were guided by thromboelastography and multiplate analyses at the discretion of the treating physician. Transfusion of red blood cells was given according to the National Guidelines at a hemoglobin level of 80 g/L or at higher levels if there was

suspicion of organ ischemia.¹⁶ Data regarding the intraoperative bleeding were obtained from the anesthesia journals. Sources included suction, CPB pump prime volume, and cell saver volume.

Definitions

Aortic dissections were defined as acute if treated within 14 days after diagnosis was established. Patients were grouped according to treatment with or without any kind of APT prior to surgery. In patients receiving APT, a subgroup analysis was performed for those receiving DAPT preoperatively. APT included acetylsalicylic acid (ASA), clopidogrel, ticagrelor, or prasugrel. DAPT was defined as treatment with ASA and 1 additional antiplatelet agent. Indication for APT was defined according to guidelines of the ESC as occurrence of chest discomfort, new-onset ST-segment changes on electrocardiography (ECG), and/or elevated biomarkers defined as cardiac troponin or creatine kinase.¹

Impaired ejection fraction was defined as an ejection fraction below 50%. Mean ejection fraction was calculated in patients with impaired left ventricular function. Transfusion requirements were measured during surgery and for 24 hours postoperatively. Cardiac tamponade was defined as a pericardial hemorrhage with systemic effect on circulation. Reoperation for bleeding complications was recorded if occurring within 24 hours postoperatively.

Statistics

Data were examined for normal distribution using the Shapiro–Wilk test. Comparisons of 2 groups were performed with Student's t-test if data were normally distributed, and if not a Mann-Whitney U-test was used. All variables were unpaired. Categorical variables were compared with χ^2 -test. For simplicity, all data are presented as mean and standard deviation. Statistical significance was assumed with p values < 0.05 . Statistical analyses were performed using SPSS Statistics version 22.

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