

# ABO Blood Type Does Not Influence the Risk of Cardiovascular Complications and Mortality after Vascular Surgery

E.J. Bakker <sup>a,b</sup>, T.M. Valentijn <sup>a</sup>, S.E. Hoeks <sup>a</sup>, K.M. van de Luijtgarden <sup>b</sup>, F.W. Leebeek <sup>c</sup>, H.J.M. Verhagen <sup>b\*</sup>, R.J. Stolker <sup>a</sup>

<sup>a</sup> Department of Anesthesiology of the Erasmus Medical Center, Rotterdam, The Netherlands

<sup>b</sup> Department of Vascular Surgery of the Erasmus Medical Center, Rotterdam, The Netherlands

<sup>c</sup> Department of Hematology of the Erasmus Medical Center, Rotterdam, The Netherlands

## WHAT THIS PAPER ADDS

ABO blood type is a major determinant of the risk of atherothrombotic events in the general population. This is the first study to assess the prognostic implications of ABO blood type in vascular surgery patients. ABO blood type did not influence the risk of perioperative cardiovascular complications and long-term mortality in vascular surgery patients.

**Objectives:** Thrombotic complications are common in vascular surgery patients. Non-O blood types are associated with an increased risk of thrombo-embolic diseases. The aim of this study is to assess the prognostic implications of non-O vs. O blood type regarding 30-day cardiovascular events and long-term mortality after vascular surgery.

**Methods:** The population of this retrospective cohort study consisted of 4679 patients undergoing elective major vascular surgery between the years 1990 and 2011. Baseline characteristics, ABO blood type and follow-up were obtained. Multivariable regression analyses, adjusted for age, gender, medical history, medication and smoking were used to evaluate the impact of non-O blood type on 30-day cardiovascular events (cardiovascular death, myocardial infarction and stroke) and long-term mortality.

**Results:** Non-O blood type was present in 2627 (56%) patients. Within 30 days after surgery, 129 (4.9%) non-O and 112 (5.5%) O patients suffered a cardiovascular event ( $P = 0.42$ ). Non-O blood type was not associated with increased mortality during long-term follow-up (adjusted hazard ratio (aHR) 0.96; 95% confidence interval (CI) 0.88–1.04, with a median follow-up of 4 years). Anti-platelet and anticoagulant drugs did not interact with the relationship between ABO blood type and long-term outcome.

**Conclusion:** Non-O blood type is not associated with either 30-day cardiovascular complications or long-term mortality in vascular surgery patients.

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Atherosclerosis is a systemic disease that affects multiple organ systems.<sup>1</sup> Patients with peripheral arterial disease commonly suffer from concomitant coronary artery disease or cerebrovascular disease.<sup>1,2</sup> These patients are therefore at increased risk for both perioperative and long-term cardiovascular events, including stroke and myocardial infarction.<sup>3,4</sup> Arterial thrombosis is responsible for the majority of these, both in the perioperative and the non-surgical setting.<sup>5</sup>

Several studies reported an increased risk of thrombotic events, including myocardial infarction, ischaemic stroke,

peripheral arterial disease and venous thrombo-embolism, in people with non-O blood types in the general population.<sup>6–10</sup>

It is unclear whether or not ABO blood type influences outcome after vascular surgery. We conducted the current study to evaluate the effect of ABO blood type on both perioperative cardiovascular complications and long-term survival after vascular surgery.

## MATERIALS AND METHODS

This retrospective, single-centre study comprised a population of 4679 patients, referred for elective major vascular surgery, including abdominal aortic, carotid artery and lower limb arterial repair. All patients underwent surgery between 1990 and 2011. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the Erasmus Medical Center.

\* Corresponding author. H.J.M. Verhagen, Erasmus Medical Centre, 's Gravendijkwal 230, Room H-810, PO Box 2040, 3000 CA Rotterdam, The Netherlands. Tel.: +31 10 7031810; fax: +31 10 7032890.

E-mail address: [h.verhagen@erasmusmc.nl](mailto:h.verhagen@erasmusmc.nl) (H.J.M. Verhagen).

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The obtained medical history included risk factors according to the Revised Cardiac Risk Index: ischaemic heart disease (history of angina pectoris, myocardial infarction or coronary revascularisation), heart failure (clinical signs according to the New York Heart Association, previous hospitalisation for decompensated heart failure), cerebrovascular disease (history of transient ischaemic attack or ischaemic or haemorrhagic stroke), renal dysfunction (serum creatinin  $>2$  mg/dl) and diabetes mellitus (fasting blood glucose  $\geq 7.0$  mmol  $l^{-1}$  or insulin or oral anti-diabetic drug use). Further, age, sex, smoking status, hypertension (systolic blood pressure  $>140$  mmHg or diastolic  $>90$  mmHg in non-diabetics, systolic blood pressure  $>130$  mmHg or diastolic blood pressure  $>80$  mmHg in diabetics or use of anti-hypertensive medication) and chronic obstructive pulmonary disease were recorded, as well as medication use, with focus on anti-platelet and anticoagulant drugs. Open abdominal aortic repair and open lower limb revascularisation were categorised as high-risk procedures, all other procedures as intermediate risk.

Per hospital protocol, chronic aspirin therapy is routinely continued perioperatively. The decision whether or not to interrupt vitamin K antagonist therapy and whether or not to initiate bridging therapy with heparin or low-molecular-weight heparin (LMWH) was made on a case-to-case basis. Per hospital protocol, thromboprophylaxis is routinely initiated the night prior to surgery using prophylactic doses of LMWH in patients not receiving therapeutic doses of LMWH or oral anticoagulants. LMWH is continued until discharge from the hospital.

Study 'end' points were 30-day cardiovascular events, including cardiovascular mortality, non-fatal myocardial infarction and cerebrovascular events, and 30-day and long-term all-cause mortality. Myocardial infarction was defined as the presence of biochemical evidence of myocardial necrosis (the typical rise and fall of either cardiac Troponin T with at least one measurement  $>0.03$  ng  $ml^{-1}$  or of creatine kinase with an MB fraction of  $>10\%$ ) combined with characteristic symptoms or electrocardiographic signs of ischaemia (new-onset ST-T changes or left bundle branch block or development of pathological Q-waves). Cause of death within 30 days after surgery was obtained from hospital records and was classified as either cardiovascular or non-cardiovascular death. Cardiovascular death was defined as any death with a cerebro-cardiovascular complication as primary or secondary cause, including death following myocardial infarction, cardiac arrhythmias, congestive heart failure, stroke and surgery-related bleeding complications. Sudden unexpected death was also classified as a cardiovascular death.

All data were tabulated according to O and non-O blood type. Categorical variables are described as numbers and percentages. Continuous variables were described as means  $\pm$  standard deviation. Duration of follow-up was described as median with interquartile range (IQR). Categorical data were compared using a chi-squared test. Continuous data were compared using analysis of variance (ANOVA). Cumulative long-term survival was determined using the

Kaplan–Meier method and the log-rank test. Logistic regression analysis was performed to evaluate the effect of non-O blood type on 30-day cardiovascular events. Cox regression analysis was performed to assess the effect of non-O blood type on long-term survival. Subgroup analysis was performed for age ( $>65$  and  $<65$  years), gender, statin use and anti-platelet/anticoagulant medication use. Multivariate regression analyses were adjusted for high-risk type of surgery, gender, age, hypertension, diabetes mellitus, smoking status, renal failure, ischaemic heart disease, hypercholesterolaemia, congestive heart failure, cerebrovascular disease, chronic obstructive pulmonary disease and the use of beta-blockers, statins and anti-platelet and anticoagulant drugs. We reported crude and adjusted odds ratios (ORs) and hazard ratios (HRs) and their 95% confidence intervals (CIs). For all tests, a  $P < 0.05$  (two-sided) was considered significant. All analyses were performed using PASW version 17.0 statistical software (SPSS Inc., Chicago, IL, USA).

## RESULTS

The study population consisted of 4679 consecutive patients who underwent elective vascular surgery. Abdominal aortic repair was performed in 1814 (39%) patients, lower extremity revascularisation in 1834 (39%) patients and carotid surgery in 1027 (22%) patients, respectively. The median follow-up was 4 (IQR 2–8) years. The majority of patients were men (73%) and the mean age was  $66 \pm 12$  years. Non-O blood type was present in 2627 (56%) patients. Of all patients, 52% had no or one risk factor, 31% had two risk factors and 17% had three or more risk factors according to the Revised Cardiac Risk Index. O and non-O groups differed significantly regarding male gender (74% vs. 72%,  $P = 0.04$ ), ischaemic heart disease (34% vs. 37%,  $P = 0.02$ ) and aspirin use (48% vs. 45%,  $P = 0.04$ ). There were no significant differences between O and non-O groups regarding other co-morbidities, medication use, age and surgical characteristics, as demonstrated in Table 1.

During 30-day follow-up 241 (5.2%) patients had a cardiovascular event, including 132 (2.8%) cardiovascular deaths, 66 (1.4%) non-fatal myocardial infarctions and 36 (0.8%) non-fatal strokes, as presented in Table 2. No significant differences between O and non-O blood types were observed regarding stroke (1.0% vs. 0.6%,  $P = 0.09$ ), non-fatal myocardial infarction (1.5% vs. 1.4%,  $P = 0.51$ ), cardiovascular death (2.8% vs. 2.8%,  $P = 1.00$ ) and cardiovascular events (5.5% vs. 4.9%,  $P = 0.42$ ). Within 30 days of surgery, 228 patients died of any cause. No significant difference was observed between O and non-O blood type (4.9% vs. 4.8%,  $P = 0.89$ ). Multivariate analyses demonstrated that non-O blood type was not associated with 30-day cardiovascular events (OR 0.87, 95% CI 0.67–1.13,  $P = 0.32$ ).

During long-term follow-up 1233 (47%) patients with non-O blood type died, compared with 981 (48%) patients with O blood type ( $P = 0.60$ ). Cumulative survival for all patients is shown in Fig. 1 (log rank  $P = 0.88$ ). In a multivariate model, non-O blood type was not associated with

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