Mid-Term Survival and Risk Factors Associated With Myocardial Injury After Fenestrated and/or Branched Endovascular Aortic Aneurysm Repair

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Short title: Myocardial Injury after F/BEVAR

Mid-Term Survival and Risk Factors Associated With Myocardial Injury After Fenestrated and/or Branched Endovascular Aortic Aneurysm Repair

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WHAT THIS PAPER ADDS

This study is the first to show that myocardial injury after non-cardiac surgery (MINS; as defined using a high sensitivity troponin assay) was particularly frequent in patients who underwent fenestrated or branched endovascular aortic repair (F/BEVAR). MINS was associated with worse in

hospital outcomes and a lower two year survival rate. Age, cardiac risk index, duration of surgery, pre-operative estimated glomerular filtration rate, and haemoglobin level were identified as key predictors of MINS after F/BEVAR.

Objective: Myocardial injury after non-cardiac (MINS) surgery is an independent predictor of postoperative mortality in non-cardiac surgery patients and may increase health costs. Few data are available for MINS in vascular surgery patients, in general, and those undergoing fenestrated/branched endovascular aortic repairs (F/BEVAR), in particular. The incidence of MINS after F/BEVAR, the associated risk factors, and prognosis have not been determined. The objective of the present study was to help fill these knowledge gaps.

Methods: A single centre, retrospective study was carried out at a high volume F/BEVAR centre in a university hospital. Adult patients who underwent F/BEVAR between October 2010 and December 2018 were included. A high sensitivity troponin T (HsTnT) assay was performed daily in the first few postoperative days. MINS was defined as a HsTnT level ≥ 14 ng/L ($MINS_{14}$) or ≥ 20 ng/L ($MINS_{20}$). After assessment of the incidence of MINS, survival up to two years was estimated in a Kaplan–Meier analysis and the groups were compared according to MINS status. A secondary aim was to identify predictors of MINS.

Results: Of the 387 included patients, 240 (62.0%) had $MINS_{14}$ and 166 (42.9%) had $MINS_{20}$. In multivariate Cox models, both conditions were significantly associated with poor two year survival (MINS14: adjusted hazard ratio [aHR] 2.15, 95% confidence interval [CI] 1.10 – 4.19; $MINS_{20}$: aHR 2.43, 95% CI 1.36 – 4.34). In a multivariate logistic regression, age, revised cardiac risk index, duration of surgery, pre-operative estimated glomerular filtration rate (eGFR), and haemoglobin level were independent predictors of MINS.

Conclusion: After F/BEVAR surgery, the incidence of MINS was particularly high, regardless of the definition considered ($MINS_{14}$ or $MINS_{20}$). MINS was significantly associated with poor two year survival. The modifiable predictors identified were duration of surgery, eGFR, and haemoglobin level.

Keywords: Endovascular aortic aneurysm repair, High sensitivity troponin, Mid-term survival, MINS, Risk factors

INTRODUCTION

Postoperative myocardial complications are among the leading causes of death after non-cardiac surgery, particularly in high-risk surgical patients.[1–3] Recently, it was shown that myocardial injury after non-cardiac surgery (MINS; i.e., cardiomyocyte injury that does not meet the universal definition of myocardial infarction [MI]) is far more frequent than MI and is associated with a higher mortality rate.[4] The pivotal Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) family of studies has strengthened this body of evidence and, more importantly, has shown that MINS related deaths can occur within a few weeks of the troponin peak, suggesting the presence of a window for intervention.[4–7]

Patients suffering from thoraco-abdominal or pararenal abdominal aortic aneurysms (AAAs) are burdened by arteriosclerosis related comorbidities and are likely to suffer from myocardial complications.[8–10] In this population, the short term postoperative outcome is better for fenestrated and/or branched endovascular aortic repairs (F/BEVAR) than for open surgery, and so F/BEVAR has become the most frequent procedure (in around 80% of eligible patients).[11] However, a risk of myocardial complications, in general, and MINS, in particular, persists and may contribute to a worsening over time in the good short term prognosis for F/BEVAR.[12,13] To the best of the authors' knowledge, MINS has not previously been studied in this specific, growing patient population.

However, there are several definitions of MINS in the literature. In the first VISION study, the threshold was the 99th percentile increase in the level of fourth generation troponin I (≥ 0.03 ng/L).[4] For these high risk vascular surgery patients, debate continues over whether a similar definition must be used for high sensitivity troponin T (HsTnT), with a threshold of ≥ 14 ng/L ($MINS_{14}$) recommended by the assay's manufacturer, or a threshold of ≥ 20 ng/L ($MINS_{20}$) used in the VISION studies.[7]

Hence, the objectives of the present investigation of patients having undergone F/BEVAR were to (1) determine the incidences of $MINS_{14}$ and $MINS_{20}$; (2) analyse the possible associations of MINS with short term outcomes and mid-term survival; and (3) identify independent predictors of MINS.

MATERIALS AND METHODS

This retrospective observational study was performed in the Department of Cardiovascular Anaesthesia and Intensive Care at Lille University Hospital (Lille, France) and was reported in compliance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. The study was approval was by the hospital's institutional review board, which waived the need for informed consent. In line with France's legislation on data protection, all databases were registered with the French National Data Protection Commission (*Commission nationale de l'informatique et des libertés* [Paris, France]; reference: DEC20140415-1148).

Data collection and sources

Demographic, anaesthetic, laboratory, and outcome data were extracted from a data warehouse connected to the corresponding, specific hospital information systems. More precisely, pre-operative and intra-operative data were obtained from our anaesthesia information management system (DIANE; Bow Medical, Amiens, France), which prospectively collects this information. Laboratory data were retrieved from the laboratory results management system (Molis; CompuGroup Medical, Koblenz, Germany), and in hospital outcomes were retrieved from our hospital's reporting and billing system (CORA Production; Maincare Solutions, Canejan, France); the latter included reports drafted by the attending physicians during their clinical practice. Detailed information on the data warehouse's implementation, data validation, and management have been reported elsewhere.[14,15] For the further validation and retrieval of variables not present in the data warehouse, medical records were checked manually and retrospectively. All records were checked for outcome variables and HsTnT values, and 20% of the records were randomly selected for validation of the remaining variables. Mortality data from the data warehouse was compared with a prospective national database of deaths in France (curated by the French National Institute for Statistics and Economic Studies [*Institut national des statistiques et des études économiques*], Paris, France), in order to confirm in hospital deaths and retrieve out of hospital deaths.[16]

Patients

All adults (age ≥ 18 years) who had undergone F/BEVAR for thoraco-abdominal aortic aneurysms and complex AAAs and who had data on at least one troponin assay during the first three postoperative days were included. The study period ran from October 2010 to December 2018 because the HsTnT assay was introduced at the authors' centre in October 2010. The main exclusion

criteria were the presence of end stage chronic kidney disease (CKD; defined according to the Kidney Disease Improving Global Outcome [KDIGO] criteria[17] as a creatinine based estimated glomerular filtration rate [eGFR] < 15 mL/min/m^2, and/or ongoing dialysis) and the lack of outcome data.

Clinical management

Surgical management. Endovascular procedures were performed using fenestrated or branched Zenith endografts (Cook Medical, Bloomington, IN, USA) with a motorised image intensifier (GE-OEC 9900; GE Healthcare, Milwaukee, WI, USA) prior to December 2012, and with a fusion imaging guidance system (Discovery IGS 730; GE Healthcare, Chalfont St Giles, UK) after 10 December 2012. Low osmolar iohexol contrast medium (Omnipaque, 300 mg I/mL; GE Healthcare, Cork, Ireland) or iso-osmolar iodixanol contrast medium (Visipaque, 320 mg I/mL; GE Healthcare, Dublin, Ireland) were used, as appropriate.

Anaesthesia management. Anaesthesia was induced with propofol, etomidate, or ketamine, combined with sufentanil or remifentanil. Neuromuscular blockade was obtained with rocuronium, cisatracurium, or atracurium. For maintenance, total intravenous anaesthesia or sevoflurane was used with bispectral index monitoring (Aspect Bis Monitor XP) between 40 and 60. Mechanical ventilation was performed with an endotracheal tube (internal diameter: 7 – 8.5 mm) and an Aysis Carestation system (General Electric Healthcare, Chicago, IL, USA) or a Zeus Infinity system (Dräger Medical, Lübeck, Germany).

For haemodynamic management, a mean arterial pressure (MAP) > 65 mmHg and an arterial lactate < 2 mmol/L were targeted. However, when the risk of spinal cord ischaemia was high, a MAP of > 80 mmHg, a central venous pressure < 12 mmHg, and a haemoglobin level > 10 g/dL were targeted. In selected patients at high risk of spinal cord ischaemia, cerebrospinal fluid was drained (medullar pressure 10 cmH_2O). If necessary, fluids, red blood cell transfusions, and/or vasopressors were used to achieve these goals.

Definitions and outcomes

Definition of $MINS_{14}$ and $MINS_{20}$. $MINS_{14}$ was defined as a HsTnT level ≥ 14 ng/L (corresponding to the 99th percentile, by analogy with the ≥ 0.03 ng/L threshold for fourth generation troponins), as suggested by Botto *et al*.[4] $MINS_{20}$ was defined as a HsTnT level ≥ 20 ng/L, as suggested by the VISION study group.[7]

Troponin concentrations were measured routinely using electrochemiluminescence immunoassays (ECLIA; Roche Diagnostics, Meylan, France). Measurements were performed on the day of surgery (at the discretion of the attending anaesthesiologist) and then on postoperative day(s) 1 and/or 2. At the discretion of the attending physician and depending on the patient's condition, further measurements could be made at any time during the hospital stay.

Prognostic variables. Variables with short term prognostic value included acute kidney injury (AKI; defined according to the creatinine based KDIGO criteria),[18] postoperative pulmonary complications,[18] length of stay (LOS) in the Intensive Care Unit (ICU) and in hospital, in hospital death, and major adverse cardiovascular events (MACE; a composite of death, stroke, acute MI [according to the third universal definition of myocardial infarction][18,19] and non-fatal cardiac arrest). For all patients, all-cause mortality was assessed from the time of surgery until 1 June 2020.

Statistical analysis

Continuous variables were quoted as the mean ± standard deviation or (for non-normally distributed variables) the median (interquartile range [IQR]). The normality of distribution was assessed graphically and by using the Shapiro–Wilk test. Categorical variables were quoted as the frequency (percentage).

Comparisons of in hospital outcomes according to the presence or absence of $MINS_{14}$ and $MINS_{20}$ were performed using a chi square test or Fisher's exact tests (for binary outcomes) or a competing risk survival analysis (Gray's test) for hospital LOS (by considering hospital discharge alive as the event of interest and death as a competing event). Lastly, two year overall survival was estimated (using the Kaplan–Meier method) and Cox regression models were used to assess the association between $MINS_{14}$ or $MINS_{20}$ and two year overall survival. Multivariable Cox models were used to adjust for the following confounders: age, coronary artery disease, chronic heart failure, CKD, and the type of aortic aneurysm.

Associations between baseline clinical and intra-operative characteristics, on the one hand, and $MINS_{14}$ and $MINS_{20}$, on the other hand, were first investigated in univariate analyses by using the Student's *t* test, the Mann–Whitney *U* test, a chi-square test, or Fisher's exact test, as appropriate.

To identify potential independent predictors of MINS, all baseline characteristics with a *p* value < .10 in univariate analyses were entered in backward stepwise multivariable logistic models with a removal criterion of $p > .10$. Before developing the multivariable models, the log linearity assumption for continuous variables (irrespective of the previous univariate analyses) was examined using restricted cubic spline functions.[20] The absence of co-linearity between candidate predictors was investigated for by calculating the variance inflation factors[21] and applying an alert threshold of 2.5. To accommodate the log-linearity assumption, a log transformation was applied for creatinine. In cases of collinearity, the variable with the lowest Akaike information criterion in the univariable logistic regression model was selected as the candidate; therefore, eGFR (which was collinear with creatinine), time with diastolic arterial pressure < 50 mmHg (which was collinear with time with MAP < 65 mmHg and time with systolic arterial pressue < 80 mmHg), and the revised cardiac risk index (which was collinear with coronary artery disease) were selected. The performance of the selected multivariable models was examined by applying the Hosmer–Lemeshow goodness-of-fit test and the level of discrimination examined by calculating the c statistic.[20] To avoid case deletion in the multivariate analyses (due to missing data for potential predictors), multiple imputation and regression switching was applied (chained equations with m = 20). Imputation was performed with the missing at random assumption, using all baseline characteristics and MINS variables. A predictive mean matching method was applied for continuous variables and a logistic regression model (binomial, ordinal, or multinomial) as applied for categorical variables. Estimates obtained in the various imputed data sets were combined using Rubin's rules.

All tests were two tailed, and the threshold for statistical significance was set to $p < .05$. Data were analysed using SAS software (release 9.4; SAS Institute, Cary, NC, USA).

RESULTS

Study population

Of the 388 patients screened for this study, one was excluded because of a lack of data on hospital outcomes other than death. Hence, 387 patients were included in the final analysis. The study

population's baseline clinical characteristics and intra-operative characteristics are summarised in Table 1.

Incidence of MINS

The overall incidence was 62.0% (n = 240) for $MINS_{14}$ and 42.9% (n = 166) for $MINS_{20}$. MINS occurred more frequently in patients with CKD than in patients free of CKD ($MINS_{14}$: n = 99 [77.3%] *vs* n = 141 [54.7%]; $p < .001$; $MINS_{20}$: n = 80 [62.5%] *vs* n = 86 [33.3%]; $p < .001$). Similarly, MINS was more frequent in patients with AKI than in patients without AKI ($MINS_{14}$: n = 27 [79.4%] *vs* n = 210 [60.3%]; p =.029; $MINS_{20}$: n = 22 [64.7%] *vs* n = 142 [40.8%]; p = .007).

In hospital outcomes in patients with and without MINS

The overall in hospital mortality rate was 2.8% (n = 11). As shown in Table 2, MACE, MI, AKI, and acute lung injury occurred more frequently in patients with $MINS_{14}$ or $MINS_{20}$ than in patients without MINS. Moreover, the hospital LOS was longer in patients who experienced $MINS_{14}$ or $MINS_{20}$.

Association between MINS and mid-term survival

The one year mortality rate was 9.8% (n = 38), and the estimated two year mortality rate was 14.7% (n = 56). The median length of follow up was 1 826 days (IQR 1 084 – 2 453; range 529 – 3 476) from surgery. The two year follow up index was 1.

$MINS_{14}$ (unadjusted hazard ratio [HR] 2.58, 95% confidence interval [CI] 1.49 – 4.47; $p <$ .001) and $MINS_{20}$ (HR 2.38, 95% CI 1.25 – 4.51; p = .025) were significantly associated with poor two year survival (Figs 1 and 2, respectively). In a multivariate analysis, both $MINS_{14}$ (adjusted HR [aHR] ???, 95% CI 1.10 – 4.19; p = .025) and $MINS_{20}$ (aHR 2.43, 95% CI 1.36 – 4.34; p = .003) remained significantly associated with poor two year survival (Figs 1 and 2, respectively).

Predictors of $MINS_{14}$ and $MINS_{20}$

Detailed results of the univariate analyses of $MINS_{14}$ and $MINS_{20}$ predictors are provided in Table 3. Multivariate analyses showed that the following variables were independent predictors of $MINS_{14}$ and $MINS_{20}$: age; duration of surgery; eGFR; and haemoglobin level (Table 4). Furthermore, the revised cardiac risk index was independently associated with $MINS_{20}$ (Table 4). The selected models had good levels of discrimination ($MINS_{14}$: c statistic 0.764, 95% CI 0.760 – 0.768; $MINS_{20}$: c statistic 0.788, 95% CI 0.786 – 0.789) and calibration (median p = .170 [range .079 – .390] for $MINS_{14}$ and p = .530 [range .093 – .780] for $MINS_{20}$ in the Hosmer–Lemeshow goodness of fit test).

In a sensitivity analysis of patients without AKI, all aforementioned predictors (apart from age) were associated with MINS (supplementary Tables 1 and 2). The intra-operative heart rate was also found to be predictive of both $MINS_{14}$ and $MINS_{20}$.

DISCUSSION

The present study's main finding was that $MINS_{14}$ and $MINS_{20}$ are particularly common among patients who have undergone F/BEVAR. These complications were associated with worse in hospital outcomes, including an elevated incidence of MACE, prolonged LOS in the ICU and in hospital (for both $MINS_{14}$ and $MINS_{20}$), and AKI (for $MINS_{20}$ only). It was also found that MINS was associated with poor mid-term survival. The CI was narrower for $MINS_{20}$, which might indicate that this is a more relevant definition of MINS. Lastly, pre-operative predictors (three of which are modifiable) for $MINS_{14}$ and $MINS_{20}$ in this specific patient population were identified.

The incidence of MINS observed in this study was far greater than reported in the literature. The VISION investigators group and Botto *et al*. estimated the incidence of MINS (using a fourth generation troponin assay) to be only 8%.[4] In a subsequent study based on HsTnT by the same research group, the incidence was higher (17.9%).[7] Interestingly, a 2019 prospective study by Ackland *et al*. (using a similar HsTnT assay)[22] found the incidence rate of MINS to be 24.5%. There are several possible explanations for these discrepancies.

Firstly, the troponin assays used to define MINS differ in their performance levels. HsTnT assays have a much better analytical performance than all earlier troponin assays,[23] which results in higher sensitivity and thus a greater incidence of MINS. Secondly, the study populations differed in their level of surgical risk. The two pivotal VISION studies prospectively included more than 15 133 and 21 842 non-cardiac surgery patients, respectively, but the latter were highly heterogenous with regard to type of surgery and level of surgical risk.[4,7] In these two studies, the proportions of vascular

surgery patients were only 3.3% and 8.6%, respectively and the proportion of high risk surgical patients was 34%. Moreover, the fact that vascular surgery was an independent predictor of mortality highlights the particular prognosis associated with these patients.[4]

In the first study of MINS, 14% of the patient population underwent vascular surgery. The researchers included patients having undergone abdominal aortic surgery and used an early Dade Behring third generation troponin I assay with a threshold ≥ 1.5 ng/L to define MINS (including myocardial damage and infarction).[24] In a secondary analysis of vascular surgery patients in the VISION cohort, the incidence of MINS was higher (19.1%) after applying the 99th percentile threshold for a fourth generation troponin T assay (≥ 0.03 ng/L).[5] This emphasises a shift toward a higher incidence with a more recent troponin assay. As mentioned above, the latter study had a high proportion of heterogenous and low risk vascular surgery patients. Szczeklik *et al*. found a higher rate of MINS (25.5%) in a more homogenous population of patients with critical limb ischaemia having undergone endovascular surgery. The researchers defined MINS not only as a HsTnT level ≥ 14 ng/L (as in the prsent study), but also required a relative increase of at least 30%;[25] this may have reduced the crude incidence. Lastly, it could be suggested that the high incidence of MINS observed in the present study was due to the high proportion of patients with CKD (33.2%). However, the incidence of MINS was still high after the exclusion of patients with CKD or AKI.

The prognostic value of MINS has been consistently observed in several follow up studies of non-cardiac surgery patients.[4,6,7,26] Specific studies of heterogeneous populations of vascular surgery patients found similar short and mid-term results.[24,27–29] The present findings showed that MINS is associated with a poor prognosis in patients having undergone F/BEVAR. Importantly, a strong association between MINS and low two year survival was found. The observed difference in the in hospital death rate was not statistically significant, possibly because of the small number of events (*n* = 11). As shown in Figures 1 and 2, the size of the effect of MINS on survival increased over time. The possibility that MINS concerned a specific group of patients with more severe atherosclerotic disease, and who might require more intense treatment regardless of surgery, cannot be ruled out. This treatment strategy should be implemented soon after surgery and, most importantly, should be maintained in the mid-term. Knowledge of the precise cause of death in the study population would have helped us the selection of an appropriate treatment; unfortunately, this information could not be retrieved. In the meantime, postoperative cardiac stress testing (currently limited to pre-operative cardiovascular risk stratification for high risk candidates)[1,3] might be useful for detecting asymptomatic coronary artery disease in patients with MINS. Furthermore, cardiovascular risk factors should be screened for and managed more aggressively. The maintenance of long term

treatment with beta blockers is one of the strongest recommendations for high risk non-cardiac surgery.[1,9] The maintenance of statins before surgery is also recommended because it appears to be associated with a lower incidence of MINS and mortality.[1,9,30] In patients who have experienced MINS, the initiation or intensification of statin treatment should be considered.[31,32]Another relevant point is pre-operative optimisation;[33] the reduction in short term mortality observed in patients with MINS treated with dabigatran (*versus* placebo) in a randomised controlled trial remains to be confirmed in the mid- and long term.[34]

Several pre-operative predictors and one intra-operative predictor of MINS were identified, half of which are potentially modifiable. The duration of surgery could be reduced in high volume centres with experienced operators,[35,36] and through optimised surgical scheduling[37] and technical improvements. With regard to pre-operative haemoglobin level, the results confirm previous findings from several surgical settings. Pre-operative haemoglobin level can be optimised by early aetiological detection and treatment of anaemia. By way of an example, iron supplementation or even erythropoietin treatment can be considered but is not fully supported by the current scientific evidence.[38] Pre-operative transfusion should be avoided because liberal transfusion is known to be associated with worse outcomes after major surgery.[39] Concerning the eGFR, nephrotoxic agents (e.g., contrast media) should be avoided or withdrawn whenever possible. With regard to intra-operative heart rate, pain and volaemia control during the procedure should be monitored more closely.

The present study had several limitations and several strengths. Firstly, the study's retrospective design is an obvious source of bias. Secondly, the study was performed in a single centre (albeit a high volume centre for F/BEVAR), which weakens the external validity of the results. Although only patients with aortic aneurysms were studied, the population was somewhat inhomogeneous because thoraco-abdominal and pararenal aneurysms were present.

The relatively large, specifically defined patient population was a strength of the study. Furthermore, the proportion of missing critical data was low; all variables were obtained from a data warehouse that was prospectively and systematically fed with intra-operative, laboratory, and outcome variables (including available mid-term survival data). However, well powered prospective studies are needed to (1) confirm the observations, (2) determine the most appropriate definition of MINS in patients undergoing F/BEVAR; and (3) identify specific treatments for MINS.

Conclusion

In a large population of patients who have undergone F/BEVAR, MINS (defined using HsTnT) was particularly frequent and was associated with worse in hospital outcomes and poor two year survival. Predictors of MINS were identified, some of which are potentially modifiable: eGFR, duration of surgery, and pre-operative haemoglobin level. The present findings call for pre-operative optimisation of these predictors and for the short and mid-term intensification of treatments following surgery.

CONFLICTS OF INTEREST

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FIGURE LEGENDS

Figure 1. Cumulative Kaplan–Meier estimate of two year overall survival of 387 patients undergoing fenestrated/branched endovascular aortic repair (F/BEVAR), according to the presence or absence of myocardial injury after non-cardiac surgery at high sensitivity troponin T level ≥ 14 ng/L ($MINS_{14}$). Adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using a multivariable Cox regression model that included confounders (age, coronary artery disease, chronic heart failure, chronic kidney disease, and the type of aortic aneurysm).

Figure 2. Cumulative Kaplan–Meier estimate of two year overall survival of 387 patients undergoing fenestrated/branched endovascular aortic repair (F/BEVAR), according to the presence or absence of myocardial injury after non-cardiac surgery at high-sensitivity troponin T level ≥ 20 ng/L ($MINS_{20}$). Adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using multivariable Cox regression model that included confounders (age, coronary artery disease, chronic heart failure, chronic kidney disease, and the type of aortic aneurysm).

Figure 1. Two-year overall survival according to presence or absence of $MINS_{14}$

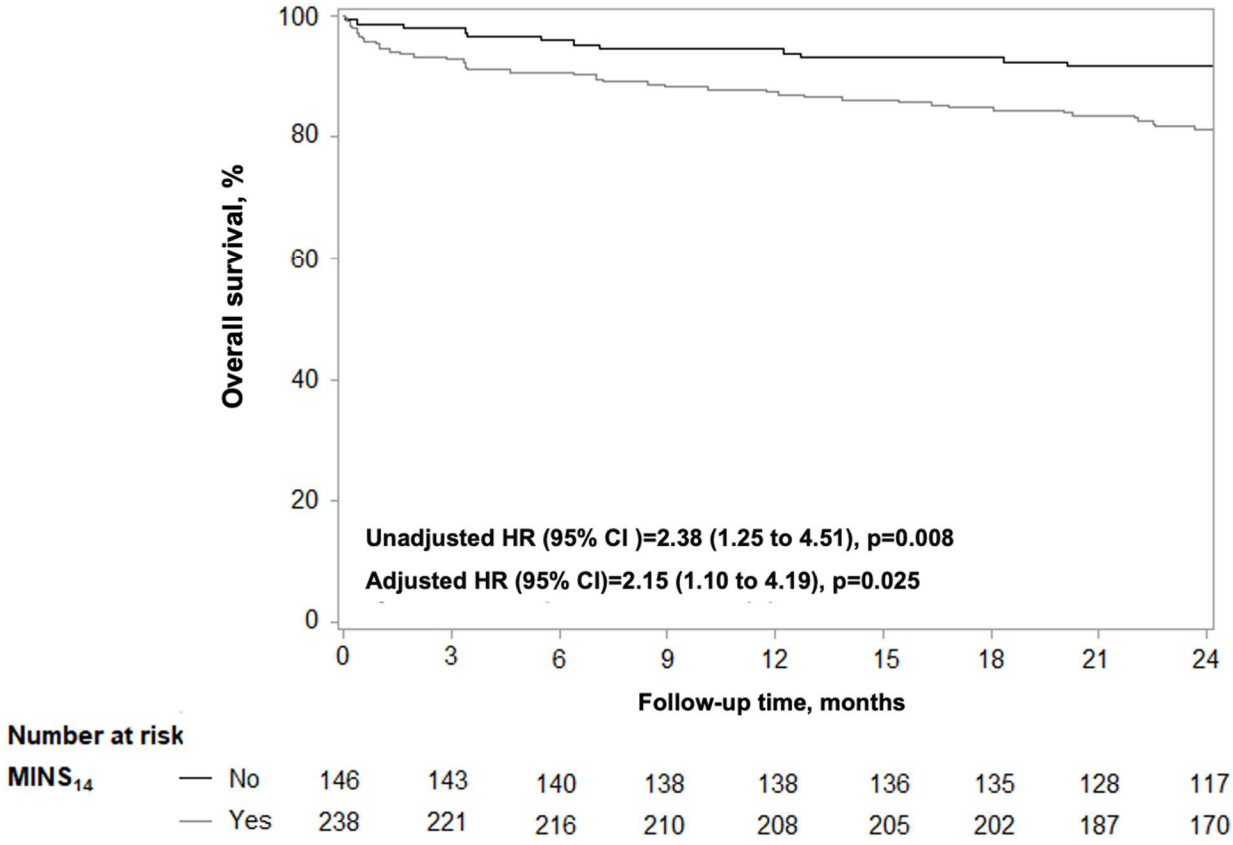

Figure 2. Two-year overall survival according to presence or absence of $MINS_{20}$

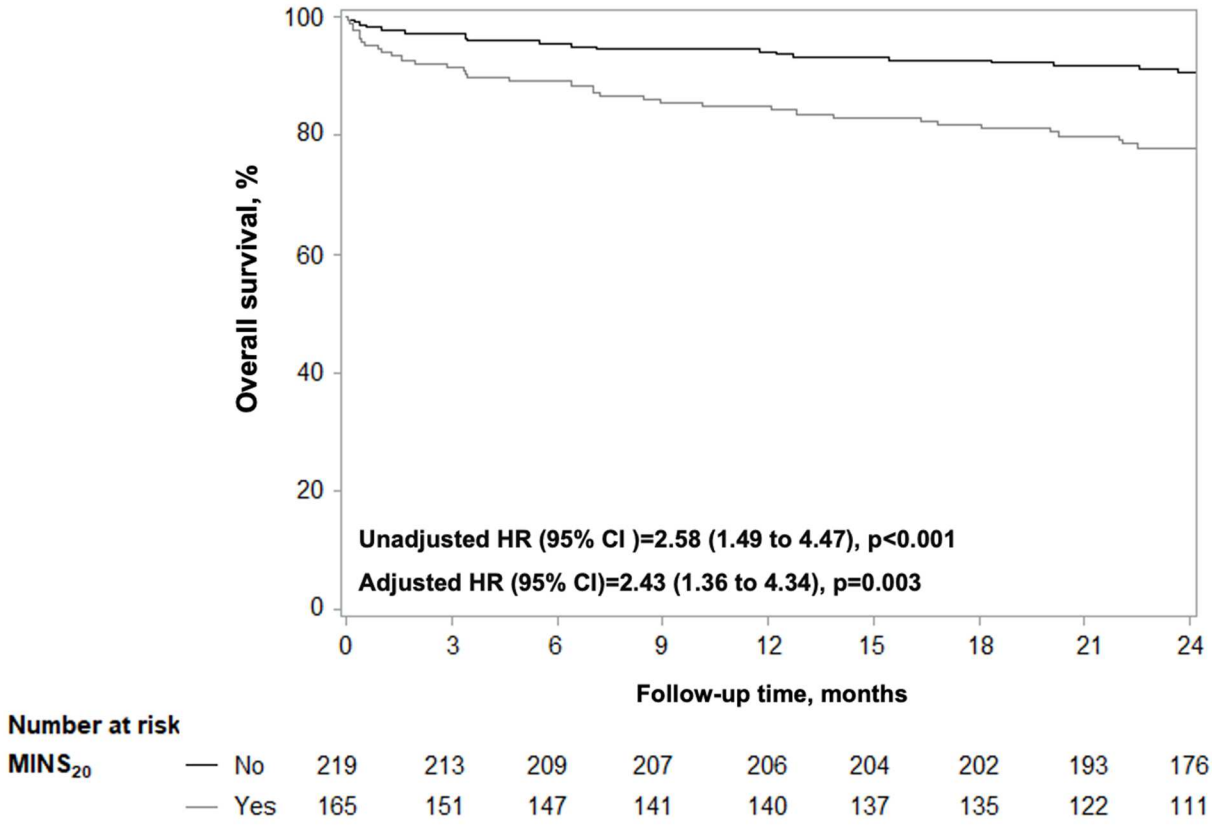

Table 1. Preoperative and intraoperative characteristics of the study population (N=387).

	N	Values
Preoperative variables		
Age – years	387	69 ± 9
Men	387	359 (92.8)
Body mass index – $kg.m^{-2}$	383	27.6 ± 5.2
Atrial fibrillation	386	62 (16.1)
History of stroke	386	12 (3.1)
Coronary artery disease	386	156 (40.4)
Positive cardiac stress testing	373	53 (14.2)
Diabetes	386	70 (18.1)
Hypertension	386	308 (79.8)
Chronic heart failure	386	19 (4.9)
Chronic kidney disease	386	128 (33.2)
COPD	387	347 (89.7)
Revised cardiac risk index		
1	387	131 (33.9)
2		155 (40.1)
3		79 (20.4)
4		20 (5.2)
5		2 (0.5)
6		0 (0.0)
ASA score >2	384	353 (91.9)
Type of aortic aneurysm		
Pararenal/juxtarenal	387	286 (73.9)
TAAA IV		49 (12.7)
TAAA I/II/III		52 (13.4)
Type of surgery		
Isolated multifenestred/branched	387	347 (89.7)
Thoracic extension		40 (10.3)

Number of fenesters/branches	387	4 (3–4)
Creatinine – $mg.L^{-1}$	382	10 (9–12)
eGFR – $mL.min^{-1}$	380	75 ± 28
Haemoglobin – $g.dL^{-1}$	339	14 ± 2
Platelet count – $G.L^{-1}$	354	219 ± 73
Intraoperative variables		
Dobutamine	376	5 (1.3)
Epinephrine	376	0 (0.0)
Norepinephrine	377	62 (16.4)
Ephedrine	377	227 (60.2)
Crystalloids – mL	366	1000 (500–1000)
Gelatins – mL	369	500 (500–500)
Duration of anaesthesia – min	380	263 (225–313)
Duration of surgery – min	335	180 (150–231)
Intraoperative heart rate – m^{-1}	369	62 ± 12
Intraoperative DAP – mmHg	372	60 ± 8
Intraoperative MAP – mmHg	372	78 ± 8
Intraoperative SAP – mmHg	372	116 ± 12
Intraoperative SpO_2 – %	351	98.8 (97.5 – 99.7)
Time with DAP <45 mmHg – min	338	4 (0–19)
Time with DAP <50 mmHg – min	338	21 (5–57)
Time with MAP <55 mmHg – min	338	1.5 (0–10)
Time with MAP <65 mmHg – min	338	22 (6–47)
Time with SAP <80 mmHg – min	338	2 (0–8)
Time with SAP <90 mmHg – min	338	15 (4–29)
peak HsTnT – $ng.L^{-1}$	387	17 (11–28)
Time to peak HsTnT – days	387	1 (1–2)

Values are quoted as the n (%), mean ± standard deviation or median [interquartile range].
Abbreviations: AAA=Aortic abdominal aneurysm; ASA= American Society of Anesthesiologists; TAAA= Thoraco-abdominal aortic aneurysm; HsTNT= High-sensitivity troponin T; COPD= Chronic obstructive pulmonary disease; DAP= diastolic arterial pressure; eGFR= estimated glomerular filtration rate; MAP= mean arterial pressure; SAP= systolic arterial pressure; SpO_2= pulsed oxygen saturation.

Table 2. Association of $MINS_{14}$ and $MINS_{20}$ with in-hospital outcomes.

	No $MINS_{14}$ N=147	$MINS_{14}$ N=240	*P*-value	No $MINS_{20}$ N=221	$MINS_{20}$ N=166	*P*-value
Acute kidney injury	7 (4.8)	27 (11.3)	.029	12 (5.4)	22 (13.3)	.007
Pulmonary complications	3 (2.0)	19 (7.9)	.015	7 (3.2)	15 (9.0)	.014
MACE	6 (4.1)	35 (14.6)	.001	12 (5.4)	29 (17.5)	<.001
Postoperative stroke	1 (0.7)	5 (2.1)	.41	2 (.9)	4 (2.4)	.41
Non-fatal cardiac arrest	2 (1.4)	5 (2.1)	.71	2 (0.9)	5 (3.0)	.14
Acute myocardial infarction	3 (2.0)	24 (10.0)	.003	6 (2.7)	21 (12.7)	.001
Hospital mortality	1 (.7)	10 (4.2)	.058	3 (1.4)	8 (4.8)	.061
Length of hospital stay[1] – days	9 (8–10)	10 (8–14)	<.0011	9 (8–11)	10 (8–16)	<.001

[1] P-value calculated using Gray's test, considering hospital discharge alive as the event of interest and hospital death as a competing event. Values are quoted as n/N. (%), mean ± standard deviation or median [interquartile range].

MINS: myocardial injury after non-cardiac surgery: MACE: major adverse cardiovascular events (a composite of stroke death, myocardial infarction, and cardiac arrest with return to spontaneous circulation). Acute kidney injury was defined according to the creatinine-based Kidney Disease: Improving Global Outcomes definition[18]. ICU, intensive care unit. Pulmonary complication was defined according to the European Perioperative Clinical Outcome (EPCO) definition standards for postoperative complications[18]

Table 3. Preoperative and intraoperative characteristics, according to the presence or absence of MINS

	No $MINS_{14}$ (n=147)	$MINS_{14}$ (n=240)	*P*-value	No $MINS_{20}$ (n=221)	$MINS_{20}$ (n=166)	*P*-value
Preoperative variables						
Age – years	67 ± 9	71 ± 9	<.001	68 ± 8	72 ± 9	<.001
Men	138 (93.9)	221 (92.1)	.51	210 (95.0)	149 (89.8)	.032
Body mass index – $kg.m^{-2}$	27.7 ± 4.8	27.6 ± 5.4	.87	27.8 ± 5.0	27.4 ± 5.4	.52
Atrial fibrillation	19 (13.0)	43 (17.9)	.20	32 (14.5)	30 (18.1)	.26
Coronary artery disease	54 (37.0)	102 (42.5)	.28	77 (35.0)	79 (47.6)	.023
Positive cardiac stress test	23 (16.1)	30 (13.0)	.41	28 (13.0)	25 (15.8)	.59
Diabetes	23 (15.8)	47 (19.6)	.34	33 (15.0)	37 (22.3)	.079
Hypertension	112 (76.7)	196 (81.7)	.24	171 (77.7)	137 (82.5)	.36
Chronic heart failure	3 (2.1)	16 (6.7)	.042	6 (2.7)	13 (7.8)	.041
Chronic kidney disease	29 (19.9)	99 (41.3)	<.001	48 (21.8)	80 (48.2)	<.001
COPD	127 (86.4)	220 (91.7)	.098	195 (88.2)	152 (91.6)	.19
Cardiac risk index						
1	65 (44.2)	66 (27.5)	<.001	98 (44.3)	33 (19.9)	<.001
2	59 (40.1)	96 (40.0)		85 (38.5)	70 (42.2)	
3	16 (10.9)	63 (26.3)		30 (13.6)	49 (29.5)	
4	7 (4.8)	13 (5.4)		8 (3.6)	12 (7.2)	
5	0 (0.0)	2 (0.8)		0 (0.0)	2 (1.2)	
ASA score >2	127 (87.6)	226 (94.6)	.015	196 (89.5)	157 (95.2)	.040
Type of aortic aneurysm						
Pararenal/juxtarenal	109 (74.1)	177 (73.8)	.98	163 (73.8)	123 (74.1)	.88
TAAA IV	18 (12.2)	31 (12.9)		29 (13.1)	20 (12.0)	
TAAA I/II/III	20 (13.6)	32 (13.3)		29 (13.1)	23 (13.9)	
Type of surgery						
Isolated multifenestred/branched	132 (89.8)	215 (89.6)	.95	198 (89.6)	149 (89.8)	.73
Thoracic extension	15 (10.2)	25 (10.4)		23 (10.4)	17 (10.2)	
Number of fenesters/branches	4 (3–4)	4 (3–4)	1.00	4 (3–4)	4 (3–4)	.66
Creatinine – $mg.L^{-1}$	9 (8–10)	11 (9–14)	<.001	9 (8–11)	12 (9–15)	<.001
Creatinine eGFR – $mL.min^{-1}$	88 ± 26	67 ± 25	<.001	84 ± 25	64 ± 27	<.001
Haemoglobin – $g.dL^{-1}$	14.3 ± 1.4	13.5 ± 2.0	<.001	14.2 ± 1.8	13.3 ± 1.9	<.001
Platelet count – $G.L^{-1}$	225 ± 73	216 ± 73	.23	222 ± 71	217 ± 76	.53
Intraoperative variables						

Norepinephrine	15 (10.6)	47 (19.9)	.019	26 (12.1)	36 (22.1)	.011
Ephedrine	81 (57.4)	146 (61.9)	.40	120 (56.1)	107 (65.6)	.064
Crystalloids – L	0.7 (0.5–1)	1 (0.5–1)	.13	0.5 (0.5–1)	1 (0.5–1)	.031
Gelatins – L	0.5 (0.5–0.5)	0.5 (0.5–0.5)	.71	0.5 (0.5–0.5)	0.5 (0.5–0.6)	.48
Duration of anaesthesia – min	254 (214–296)	267 (234–328)	.005	255 (219–293)	284 (238–339)	<.001
Duration of surgery – min	180 (150–216)	189 (155–240)	.024	180 (148–210)	210 (160–255)	<.001
Intraoperative heart rate – min^{-1}	61 ± 10	63 ± 13	.18	62 ± 11	63 ± 13	.14
Intraoperative DAP – mmHg	60 ± 7	60 ± 8	.62	60 ± 7	60 ± 8	.67
Intraoperative MAP – mmHg	78 ± 8	78 ± 8	.86	78 ± 8	78 ± 8	.96
Intraoperative SAP – mmHg	116 ± 12	116 ± 12	.48	116 ± 12	117 ± 12	.51
Intraoperative SpO_2 – %	99 (97–100)	99 (98–100)	.88	99 (98–100)	99 (97–100)	.20
Time with DAP <45 mmHg – min	3 (0–16)	5 (1–19)	.10	4 (0–18)	5 (1–24)	.25
Time with DAP <50 mmHg – min	18 (2–45)	22 (6–64)	.64	20 (3–46)	23 (6–68)	.072
Time with MAP <55 mmHg – min	1 (0–9)	2 (0–10)	.14	1 (0–10)	2 (0–9)	.36
Time with MAP <65 mmHg – min	19 (4–44)	24 (9–54)	.080	19 (5–45)	25 (9–57)	.11
Time with SAP <80 mmHg – min	2 (0–7)	3 (0–9)	.081	2 (0–8)	3 (0–10)	.13
Time with SAP <90 mmHg – min	14 (3–27)	17 (5–31)	.22	14 (3–28)	17 (5–31)	.26

Values are quoted as n/N. (%), mean ± standard deviation or median [interquartile range].

Abbreviations: AAA=Aortic abdominal aneurysm; ASA= American Society of Anesthesiologists; TAAA= Thoraco-abdominal aortic aneurysm; HsTNT= High-sensitivity troponin T; COPD= Chronic obstructive pulmonary disease; DAP= diastolic arterial pressure; eGFR= estimated glomerular filtration rate; MAP= mean arterial pressure; SAP= systolic arterial pressure; SpO2= pulsed oxygen saturation.

Table 4. Multivariate analysis of predictors of $MINS_{14}$ and $MINS_{20}$

	$MINS_{14}$		$MINS_{20}$	
Predictors	**OR [95%CI]**	***P*-value**	**OR [95%CI]**	***P*-value**
Age – year *	1.34 [1.01–1.78]	.046	1.36 [1.01–1.83]	.041
Cardiac risk index †	*Not selected*	-	1.62 [1.23–2.12]	.001
eGFR – $mL.min^{-1}$ ‡	0.44 [0.32–0.59]	<.001	0.49 [0.36–0.67]	<.001
Haemoglobin – $g.dL^{-1}$ ‡	0.66 [0.49–0.89]	.006	0.73 [0.55–0.96]	.021
Duration of surgery – min §	1.30 [1.03–1.63]	.025	1.48 [1.17–1.87]	<.001

$MINS_{14}$ and $MINS_{20}$ are defined as myocardial injury after non–cardiac surgery with the respective thresholds for high-sensitivity troponin: ≥14 ng/L and ≥20 ng/L.

OR, odd ratio; CI, confidence intervals. ORs are quoted *per 10-years increment, † per point increment, ‡ per SD increment, § per 60 minutes increment.

Candidate variables included in multivariable backward-stepwise logistic models were:

- For $MINS_{14}$: age, chronic heart failure, chronic kidney disease, COPD, cardiac risk index (as an ordinal variable), ASA score>2, eGFR, haemoglobin, norepinephrine, duration of anaesthesia, duration of surgery, and time with DAP <50 mmHg.
- For $MINS_{20}$: age, gender, BMI, chronic heart failure, chronic kidney disease, cardiac risk index (as an ordinal variable), diabetes, ASA score >2, creatinine eGFR, haemoglobin, norepinephrine, ephedrine, crystalloids, duration of anaesthesia, duration of surgery, and time with DAP <50 mmHg
- The selected models' discrimination (median c-statistic from 20 imputed datasets =.764 [.760 – .768] for $MINS_{14}$ and .788 [.786 – .789] for $MINS_{20}$) and calibration, as indicated by the Hosmer-Lemeshow goodness-of-fit test (median *P* – value from 20 imputed datasets =.17 [.079 – .39] for $MINS_{14}$ and *P* – value =.53 [.093 – .78] for $MINS_{20}$).