Association between preoperative pulse pressure and perioperative myocardial injury: an international observational cohort study of patients undergoing non-cardiac surgery

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Abstract

Background

The management of elevated blood pressure before non-cardiac surgery remains controversial. Pulse pressure is a stronger predictor of cardiovascular morbidity in the general population than systolic blood pressure alone. We hypothesised that preoperative pulse pressure was associated with perioperative myocardial injury.

Methods

Secondary analysis of the Vascular Events in Non-cardiac Surgery Patients Cohort Evaluation (VISION) international cohort study. Participants were aged ≥45 years undergoing non-cardiac surgery at 12 hospitals in eight countries. The primary outcome was myocardial injury, defined using serum troponin concentration, within 30 days after surgery. The sample was stratified into quintiles by preoperative pulse pressure. Multivariable logistic regression analysis explored associations between pulse pressure and myocardial injury. We accounted for potential confounding by systolic blood pressure and other co-morbidities known to be associated with postoperative cardiovascular complications.

Results

1191/15,057 (7.9%) patients sustained myocardial injury, which was more frequent amongst patients in the highest two preoperative pulse pressure quintiles (63-75 mmHg, risk ratio [RR] 1.14 [1.01-1.28] p=0.03; >75mmHg, RR 1.15 [1.03-1.29] p=0.02). After adjustment for systolic blood pressure, preoperative pulse pressure remained the dominant predictor of myocardial injury (63-75 mmHg, RR 1.20 [1.05-1.37]; p<0.01; >75mmHg, RR 1.25 [1.06-1.48]; p<0.01). Systolic blood pressure >160mmHg was not associated with myocardial injury in the absence of pulse pressure >62mmHg (RR 0.67 [0.30-1.44]; p=0.31).

Conclusions

Preoperative pulse pressure >62 mmHg was associated with myocardial injury, independent of systolic blood pressure. Pulse pressure may be a useful biomarker to guide strategies to reduce perioperative myocardial injury.

Introduction

One in ten patients sustain asymptomatic myocardial injury after non-cardiac surgery, which is strongly associated with mortality.[1-4] In the general population, elevated pulse pressure - the difference between systolic and diastolic blood pressure - predicts myocardial infarction and congestive cardiac failure, independent of high systolic and diastolic blood pressures (including 'white coat' hypertension). However, the risk of perioperative cardiovascular complications associated with elevated preoperative arterial pressure or pulse pressure is unclear.[5-7]

Patients presenting for surgery with high blood pressure pose a daily challenge for perioperative practitioners. Internationally, the prevalence of poorly controlled blood pressure in patients with hypertension is high, while a significant proportion of the general population have undiagnosed hypertension.[8] Surgical procedures are frequently cancelled due to high preoperative systolic blood pressure on the day of surgery.[9-11] This reflects widespread uncertainty about whether or not isolated elevated blood pressure readings increase the risk of perioperative cardiovascular complications. Clinical guidelines suggest that surgery can be undertaken safely if the preoperative blood pressure is below 160/110 mmHg.[9, 12] However, this guidance, which varies internationally,[13] is derived from a very limited evidence base constructed from small studies using subjective clinical outcome measures, rather than prognostic biomarkers for morbidity (e.g. high sensitivity troponin) and mortality.[5, 14]

Elevated pulse pressure is associated with an excess risk of multiple adverse cardiovascular outcomes in the general population, independently of hypertension.[15-18] Pulse pressure reflects left ventricular stroke volume, cardiac contractility and arterial wall compliance, key factors that influence cardiovascular performance in the perioperative setting.[19, 20] Preoperative pulse pressure may therefore refine risk assessment for perioperative cardiovascular complications in patients undergoing non-cardiac surgery. We hypothesised that pulse pressure is associated with an increased risk of myocardial injury within 30 days of non-cardiac surgery, independent of preoperative systolic arterial pressure.

Methods

We undertook a planned secondary analysis of the Vascular Events in Non-cardiac Surgery Patients Cohort Evaluation (VISION) study. The methods of this prospective international observational cohort study have been previously described in detail elsewhere.[2, 21] The study was approved by institutional review boards or ethics committees at each site, and was registered with clincaltrials.gov (NCT00512109). It was conducted in accordance with the principles of the declaration of Helsinki and institutional guidelines. Participants were approached for written informed consent before surgery. When this was not possible, for example before emergency surgery, written consent was sought within 24 hours after surgery. Eight sites used a deferred consent process for patients with no next of kin and who were unable to provide consent before surgery.

Participants

Participants were aged 45 years or older and underwent non-cardiac surgery using general or regional anaesthesia, and with at least an expected overnight hospital stay. Participants were excluded if they refused consent or if they had previously enrolled in the study.

Data Collection

Researchers collected a detailed and standardised dataset from patients and their medical records, before and during the 30 days after surgery; the full details have been published previously.[2] A past history of hypertension was defined by a previous physician diagnosis. Full definitions of the variables included in this analysis are documented in the supplementary file. Clinical staff measured arterial blood pressure in millimetres of mercury (mmHg) as part of routine patient care according to local practice. Specific details of the equipment used to measure blood pressure are not available. Preoperative arterial blood pressure was defined as the systolic and diastolic arterial pressure measurements before and closest to the induction of anaesthesia. Preoperative arterial pulse pressure was defined as the arithmetic difference between preoperative systolic and diastolic arterial pressures.

Blood samples were taken between six and twelve hours after the end of surgery, and on postoperative days one, two and three. If participants developed an ischaemic symptom during the 30 days after surgery, investigators were encouraged to take additional blood samples.[1] Serum troponin T (TnT) concentration was measured using a Roche 4th generation assay (Elecsys™). If TnT was raised above 0.04ng/mL, the standard laboratory threshold at the start of the study, an electrocardiogram was performed.

Outcome measure

Myocardial injury, defined as any TnT measurement ≥0.03ng/mL judged due to an ischaemic aetiology, within 30 days of surgery was the primary outcome measure. This definition is used by the ESA-ESICM taskforce for perioperative clinical outcomes.[22] For each TnT measurement ≥0.03ng/mL, one of 15 independent adjudicators reviewed the clinical information, including the medical record, electrocardiograms and echocardiograms, and decided if there was evidence of a non-ischaemic cause of the TnT elevation (e.g. pulmonary embolus, sepsis, renal failure etc.). Participants with TnT ≤0.04ng/mL did not undergo electrocardiograms and were not assessed for clinical symptoms to rule out myocardial ischaemia.

Statistical analysis

We planned the statistical analysis before taking custody of the data. We used SPSS version 22 (IBM, New York, USA) and STATA version 14 (StataCorp LP, Texas, USA) to analyse the data. We ordered the sample according to integer values of preoperative pulse pressure and divided it into five approximately equal groups (quintiles) using cut-points closest to each 20th percentile. We presented baseline characteristics of the cohort stratified by pulse pressure quintiles. Binary data were expressed as percentages, normally distributed continuous data as mean with standard deviation (SD) and non-normally distributed continuous data as median with interquartile range (IQR).

We used multivariable logistic regression analysis to test for association between pulse pressure and myocardial injury. We considered pulse pressure quintiles as an ordered categorical variable. To avoid isolating any single pulse pressure quintile as the reference group, we used deviation contrasts to compare each pulse pressure category to the unweighted average effect across the whole sample.[23, 24] The models were corrected for potentially confounding variables that were associated with myocardial injury or cardiac complications in previous perioperative studies: coronary artery disease, atrial fibrillation, heart failure, peripheral vascular disease, diabetes, age (45-64, 65-75, >75 years), previous stroke or transient ischaemic attack (TIA), chronic obstructive pulmonary disease, estimated glomerular filtration rate (eGFR), neurosurgery, urgent/emergency surgery and major surgery (full definitions are in the supplementary file).[1, 2, 25, 26] eGFR was considered as a categorical variable (<30, 30-44, 45-60, >60 ml/min), to be consistent with previous research in the field.[2] The selection of covariates was based on prior evidence of association with the dependent variable or similar clinical outcomes, rather than using univariable analysis or p-value based approaches.[27, 28] Covariates were treated as categorical variables. Odds ratios were converted to risk ratios using Grant's equation.[29] Missing data were handled by list-wise deletion. Sensitivity analyses, including adjustment for systolic blood pressure, are described in the supplementary file.

Results

Study personnel recruited 16,079 patients into the study between 6th August 2007 and 11th January 2011. After excluding participants that were missing data for preoperative pulse pressure or myocardial injury, 15,057 remained (figure 1 and table 1). The mean age of participants was 65 (+/- 11.8) years, 7,289 (48.4%) were male and the majority (85.9%) underwent elective surgery. The frequency of co-morbidities progressively increased across pulse pressure quintiles 1 to 5 (<45 mmHg, 46-53 mmHg, 54-62 mmHg, 63-75 mmHg and >75 mmHg; table 1). Advanced age, diabetes mellitus, pre-existing hypertension, previous stroke or TIA, peripheral vascular disease, and eGFR <30ml/min were significantly more common in pulse pressure quintiles 4 and 5 compared to other quintiles of pulse pressure (supplementary table 1).

Myocardial injury was more frequent among participants in the two highest pulse pressure quintiles (>62 mmHg) compared to other quintiles. Participants who were missing predefined covariates were excluded from the multivariable logistic regression analyses (figure 1). Preoperative pulse pressure >62 mmHg was associated with myocardial injury amongst patients in quintile 4 (63-75 mmHg, RR 1.14 [1.01-1.28]; p=0.03), and quintile 5 (>75 mmHg, RR 1.15 [1.03-1.29]; p=0.02) independent of confounding factors (table 2). Pulse pressure of 46-53 mmHg was associated with reduced incidence of myocardial injury (RR 0.83 [0.72-0.96]; p=0.02).

Sensitivity analyses

When we repeated the primary multivariable analysis adjusted for preoperative systolic blood pressure divided into quintiles and considered as an ordered categorical variable, pulse pressure 63-75 mmHg and >75 mmHg remained associated with myocardial injury (RRs 1.20 [1.05-1.37]; p<0.01 and 1.25 [1.06-1.48]; p<0.01 respectively). However, preoperative systolic blood pressure was not associated with myocardial injury (table 3). When we repeated the primary multivariable analysis adjusting for preoperative systolic blood pressure as a continuous variable, elevated pulse pressure remained associated with myocardial injury, but systolic blood pressure was not associated with myocardial injury (supplementary table 2). Multivariable fractional polynomial regression analysis confirmed that the probability of myocardial injury increased with increasing pulse pressure in a linear fashion (figure 2; supplementary table 3). When we stratified the cohort by pulse pressure >62 mmHg and systolic blood pressure >160 mmHg, pulse pressure >62 mmHg was independently associated with myocardial injury, irrespective of systolic blood pressure (supplementary table 4). Multivariable logistic regression analysis showed that systolic blood pressures >139 mmHg were independently associated with pulse pressure >62 mmHg (supplementary table 5). Results of additional sensitivity analyses are presented in the supplementary file.

Discussion

The principal finding of this analysis of ~14,000 patients was that elevated preoperative pulse pressure (>62 mmHg) occurred in two out of every five patients and is associated with myocardial injury, defined as TnT ≥0.03ng/mL judged due to an ischaemic aetiology within 30 days after non-cardiac surgery. This association persists after adjusting for preoperative systolic blood pressure. Patients with elevated preoperative systolic blood pressure (>160 mmHg) were only at increased risk of myocardial injury if the preoperative pulse pressure was >62 mmHg.

A preoperative diagnosis of arterial hypertension has been reported to have a small but significant influence on cardiac outcomes following non-cardiac surgery,[30-32] However, these heterogeneous studies did not use a robust, independently prognostic biomarker for myocardial injury (troponin) as the primary endpoint or undertake prospective data collection in a large selection of patients. Consequently, the impact of high blood pressure immediately before surgery has remained unclear.[33-35] Our data provide the novel observation that preoperative pulse pressure is a more important marker for the development of myocardial injury, compared to systolic blood pressure. Whilst the degree of association between elevated pulse pressure and myocardial injury was modest, due to the high volume of surgical treatment (~8 million in the UK per year), this could still have a clinically significant impact on patient outcome.[4] At the population level, small increases in risk from multiple independent factors are widely considered to be central to the development of non-communicable disease. Our research focuses on identifying simple exposures that could be modified to prevent or treat perioperative disease.

Several large, international non-operative registry studies have reported that higher pulse pressure confers increased risk of multiple adverse cardiovascular events independent of systolic blood pressure and 'white coat' hypertension.[15-18] Pulse pressure tends to increase with age as a result of increasing systolic and falling diastolic blood pressures. In the Framingham study, increasing age was associated with a shift from diastolic to systolic, and then pulse pressure, as the best predictor of cardiovascular risk.[36] Our study is the first to identify a relationship between pulse pressure and perioperative myocardial injury, an association that is independent of age. Furthermore, the prospective cardiovascular Münster (PROCAM) study reported that normotensive older men with higher pulse pressure were at increased coronary risk, mirroring the excess risk of myocardial injury in elderly men we found in this analysis.[18] The underlying mechanisms linking pulse pressure to myocardial injury remain unclear, but four separate mechanisms may promote cardiovascular morbidity in this particular population. Firstly, elevated systolic blood pressure increases end-systolic myocardial stress and promotes left ventricular hypertrophy, which is an independent predictor of cardiovascular death.[37, 38] Secondly, lower diastolic blood pressure impairs coronary perfusion, which may promote myocardial ischaemia.[18, 38] Thirdly, higher pulse pressure is associated with smaller aortic lumen area, leading to ventricular-aortic decoupling characterised by a cardiac output that is too great to be accommodated by the aortic lumen area.[39, 40] Dramatic changes in pulse pressure typically seen during the perioperative period may exacerbate mismatched ventricular-aortic coupling, leading to ventricular overload and impaired cardiac output despite preserved systolic function. Impaired cardiac output in the perioperative period is associated with increased organ dysfunction and poorer clinical outcomes.[19, 20] Fourthly, elevated pulse pressure may be caused by increased aortic stiffness, which is an independent determinant of sympathetic baroreflex sensitivity in elderly men and women.[41] Impaired baroreflex sensitivity is independently associated with excess cardiovascular and infectious morbidity after major surgery.[42]

This is the largest prospective cohort study to investigate the influence of blood pressure immediately prior to surgery on clinical outcomes after non-cardiac surgery. The sample included patients undergoing a variety of non-cardiac surgical procedures at multiple international centres, so our results are relevant to the majority of patients having non-cardiac surgery. The large sample size allowed us to control for a large number of confounding variables, including systolic blood pressure. However, we acknowledge that there may be residual, un-measured confounding. The primary outcome measure, myocardial injury, is an objective biochemical endpoint that lacks the subjectivity associated with clinical outcome measures used in previous studies.[14, 43]

Our analysis also has several weaknesses. Preoperative arterial blood pressure was measured by local clinical staff before the induction of anaesthesia. Although blood pressure was measured using the oscilliometric technique, measurement apparatus, timing and location of measurement varied between centres. Since this was a pragmatic study, we do not believe this adversely affected the results or interpretation. We acknowledge that non-invasive blood pressure measurement is less reliable that intra-arterial measurement. It is possible that pre-medication could influence preoperative arterial blood pressure, although the practice of premedication is uncommon in participating centres (particularly since recent practice-changing evidence shows that preoperative sedation fails to improve outcomes).[44] Omission of usual anti-hypertensive therapy preoperatively, typically ACE inhibitors and angiotensin-II receptor blockers, may also have contributed to the high blood pressure readings in patients with established hypertension. However, we did not have access to these data. In any case, our data still suggest that the association between myocardial injury and high blood pressure preoperatively is primarily linked by pathophysiological mechanisms underlying hypertension *per se*, rather than high blood pressure alone driving postoperative morbidity. We corrected the analysis for urgency of surgery, which is a further potential confounding variable, due to expected lower preoperative blood pressures as a result of sepsis or blood loss. We did not measure preoperative troponin, so the incidence of pre-existing myocardial injury is unknown, although we would only expect this to occur in a small proportion of cases.[45] We reported myocardial infarction and mortality to aid comparisons within the perioperative literature (supplementary data). However, we recognise that these are clinically derived outcomes and are subject to observer bias. We attempted to limit this by using standard definitions and excluding these outcomes from the primary analysis. Detailed sub-analyses of patients with heart failure may further refine our findings; lower pulse pressure is independently associated with mortality in patients with reduced ejection fraction heart failure, in contrast to an inconsistent relationship between pulse pressure and clinical outcome observed in patients with preserved ejection fraction heart failure.[46, 47] The preserved association between higher pulse pressure and heart failure in our study likely reflects the nonlinear relationship reported for patients with reduced ejection fraction heart failure,[48] where mortality risk increases at higher pulse pressure (≥50 mmHg). Similarly, mortality risk in patients with preserved ejection fraction heart failure increases with higher pulse pressure,[48] mirroring our findings in the larger, non-heart failure population. In the absence of routine preoperative echocardiography in our cohort, we are unable to comment on whether undiagnosed aortic regurgitation was a potential confounding factor. However, since the population prevalence of aortic regurgitation is less than 2%, this would be unlikely to explain the observed association.[49] The relationships between pulse pressure, preserved/reduced ejection fraction heart failure and postoperative outcomes, including long-term survival, requires further exploration.

Conclusion

These data help address a daily clinical dilemma for anaesthetists and surgeons, as they care for millions of patients worldwide each year, by establishing whether preoperative pulse pressure refines the interpretation of elevated blood pressure evident on the day of surgery. For urgent surgery (e.g. for malignancy) where limited time is available to reduce blood pressure, our data show that patients with higher pulse pressure are at higher risk of myocardial injury and may benefit from closer perioperative monitoring. In particular, special attention to haemodynamic instability,[51, 52] and surveillance for myocardial injury appear to be particularly warranted in this higher-risk group.[1] Conversely, our results should reassure clinicians that in this cohort, patients with high preoperative blood pressure but normal pulse pressure (irrespective of prior normotensive/hypertensive status) were not associated with excess risk of myocardial injury after non-cardiac surgery. These data suggest that a reappraisal of managing elevated blood pressure on the day of surgery is warranted, particularly since abnormal pulse pressure may be a modifiable risk factor. Further research is needed to determine whether targeting elevated preoperative pulse pressure reduces the risk of perioperative myocardial injury.

Author contributions

TEFA, GLA, RP, PD, RR and AA designed the analysis plan. TEFA performed the data analysis with input from RP and GLA. The manuscript was drafted by TEFA, RP and GLA, and revised following critical review by all authors.

Declaration of competing interests

RP holds research grants, and has given lectures and/or performed consultancy work for Nestle Health Sciences, BBraun, Medtronic, GlaxoSmithKline and Edwards Lifesciences, and is a member of the Associate editorial board of the British Journal of Anaesthesia; PD has received other funding from Roche Diagnostics and Abbott Diagnostics for investigator initiated studies; GLA is a member of the editorial advisory board for Intensive Care Medicine Experimental and has undertaken consultancy work for GlaxoSmithKline; there are no other relationships or activities that could appear to have influenced the submitted work.

Transparency declaration

GLA and PD act as guarantors of the data. GLA/PD affirm that this manuscript is an honest, accurate, and transparent account of this secondary analysis being reported; that no important aspects of the analysis have been omitted; and that any discrepancies from the study as planned have been explained.

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Figure Legends

Figure 1. Patient flow diagram showing cases included in the primary analysis.

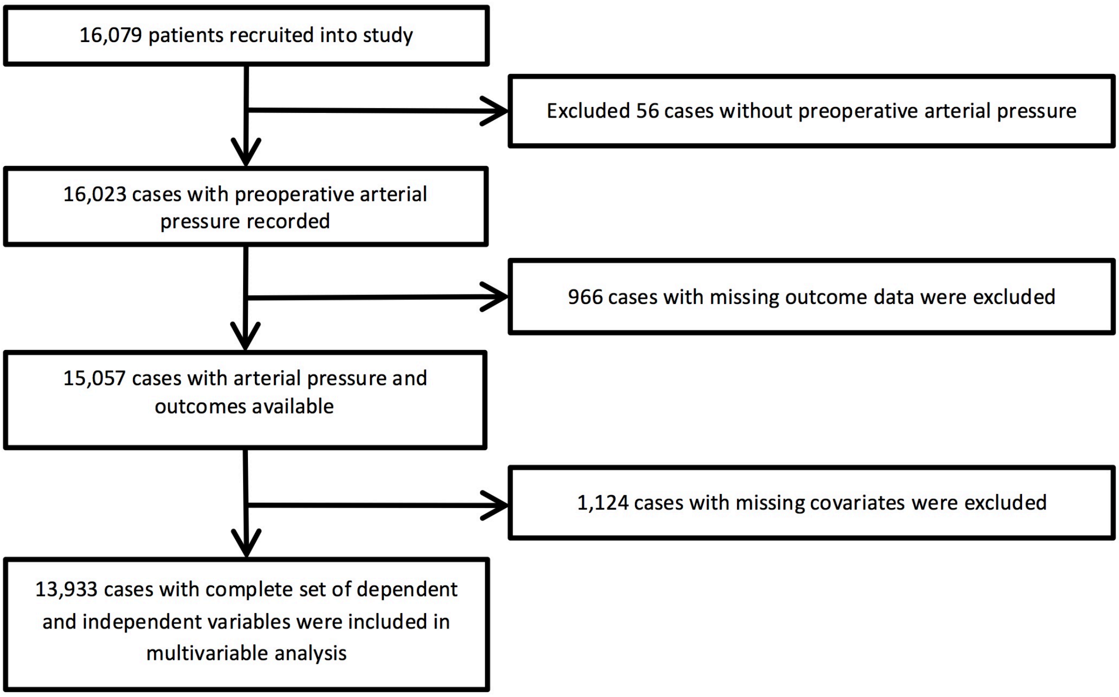

Figure 2. Function plot of the one-term multivariable fractional polynomial logistic regression model. The x-axis shows preoperative pulse pressure in mmHg and the y-axis is the partial predictor + residual.

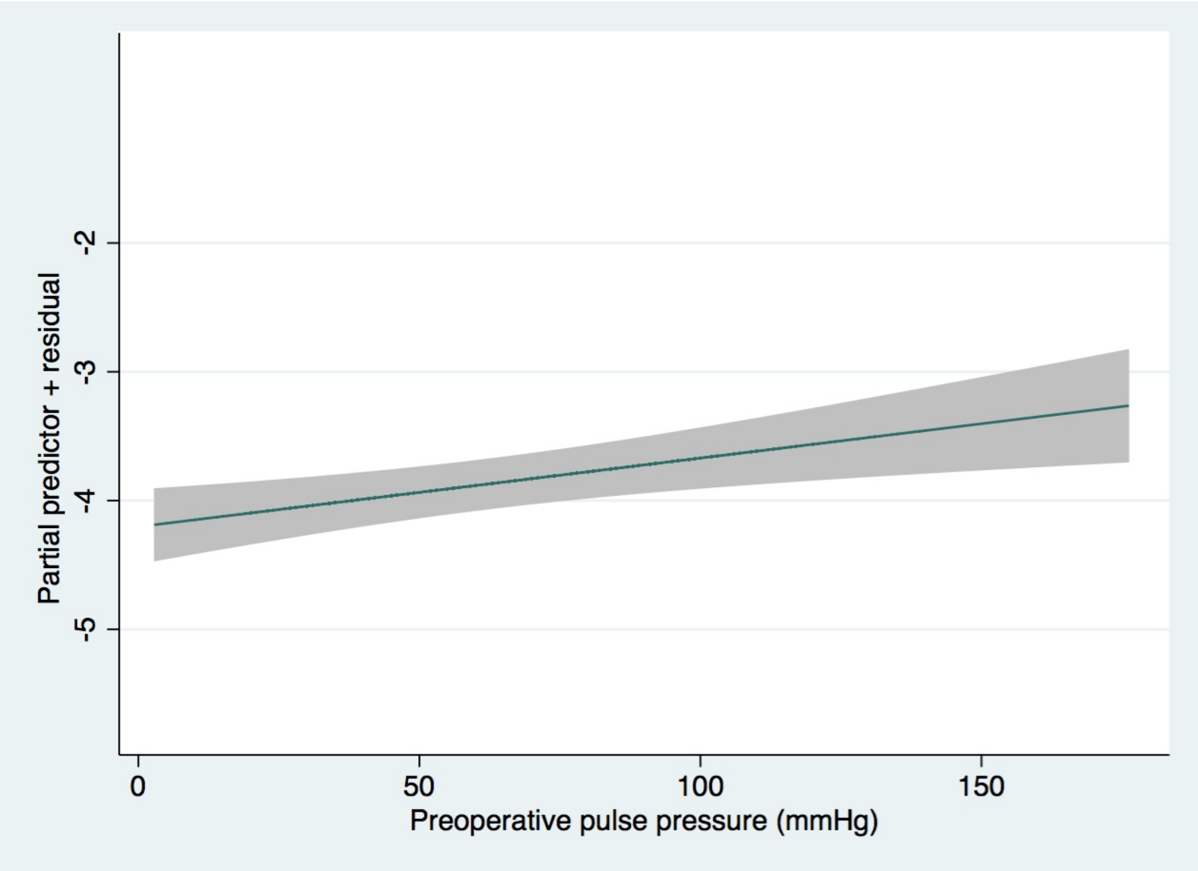

Table 1. Patient characteristics. Descriptive data stratified by preoperative pulse pressure quintiles, presented as frequencies with percentages (%) or means with standard deviations (SD). Age is rounded to nearest whole number. Preoperative pulse pressure in millimeters of mercury (mmHg). Estimated glomerular filtration rate (eGFR).

Preoperative pulse pressure (mmHg)	Whole	≤45	46-53	54-62	63-75	>75
Number of cases (n)	15057	3448	2657	2949	2980	3023
Mean age (SD)	65 (11.8)	60 (10.7)	62 (11.0)	65 (11.4)	68 (11.3)	72 (10.9)
Sex						
Male (%)	7289 (48.4)	1799 (52.2)	1363 (51.3)	1426 (48.4)	1421 (47.7)	1280 (42.3)
Mean preoperative pulse pressure (SD)	60.5 (19.0)	38.3 (5.8)	49.7 (2.1)	58.2 (2.5)	68.7 (3.6)	89.5 (12.4)
Comorbid disorder (%)						
Atrial fibrillation	499 (3.3)	107 (3.1)	73 (2.7)	102 (3.5)	103 (3.5)	114 (3.8)
Diabetes	2934 (19.5)	447 (13.0)	418 (15.7)	595 (20.2)	634 (21.3)	840 (27.8)
Hypertension	7670 (50.9)	1252 (36.3)	1160 (43.7)	1494 (50.7)	1713 (57.5)	2051 (67.8)
Congestive cardiac failure	697 (4.6)	119 (3.5)	110 (4.1)	119 (4.0)	163 (5.5)	186 (6.2)
Coronary artery disease	1820 (12.1)	332 (9.6)	270 (10.2)	339 (11.5)	383 (12.9)	496 (16.4)
Peripheral vascular disease	799 (5.3)	119 (3.5)	111 (4.2)	130 (4.4)	169 (5.7)	270 (8.9)
Previous stroke or transient ischaemic attack	1067 (7.1)	129 (3.7)	122 (4.6)	198 (6.7)	257 (8.6)	361 (11.9)
Chronic obstructive pulmonary disease	1268 (8.4)	254 (7.4)	196 (7.4)	234 (7.9)	297 (10.0)	287 (9.5)
Active cancer	1917 (12.7)	451 (13.1)	364 (13.7)	379 (12.9)	385 (12.9)	338 (11.2)
Preoperative eGFR (%)						
<30 ml/min	514 (3.7)	88 (2.9)	61 (2.5)	73 (2.7)	116 (4.1)	176 (6.1)
30-44 ml/min	751 (5.4)	114 (3.7)	91 (3.7)	126 (4.6)	156 (5.6)	264 (9.1)
45-60 ml/min	1490 (10.7)	230 (7.5)	207 (8.5)	266 (9.8)	341 (12.2)	446 (15.4)
>60 ml/min	11185 (80.2)	2648 (86.0)	2085 (85.3)	2261 (82.9)	2184 (78.1)	2007 (69.4)
Surgical procedure category (%)						
Elective	12935 (85.9)	2981 (86.5)	2313 (87.1)	2544 (86.3)	2556 (85.8)	2541 (84.1)
Urgent	430 (2.9)	86 (2.5)	80 (3.0)	96 (3.3)	77 (2.6)	91 (3.0)
Emergency	1692 (11.2)	381 (11.0)	264 (9.9)	309 (10.5)	347 (11.6)	391 (12.9)
Major surgery (%)	9096 (60.4)	1959 (56.8)	1540 (58.0)	1727 (58.6)	1910 (64.1)	1960 (64.8)
Outcome measures (%)						
Myocardial Injury	1191 (7.9)	198 (5.7)	141 (5.3)	201 (6.8)	279 (9.4)	372 (12.3)

Table 2. Multivariable logistic regression model to predict myocardial injury after non-cardiac surgery. Dependent variable is myocardial injury within 30 days of surgery. Preoperative pulse pressure was divided into quintiles and treated as a categorical variable. Results given as odds ratios with 95% confidence intervals. Estimated glomerular filtration rate (eGFR).

Covariates	odds ratio	p-value
Age (years)		
45-64 (reference)	-	-
65-75	1.02 (0.84-1.22)	0.87
>75	1.88 (1.57-2.25)	<0.01
Male sex	1.39 (1.21-1.59)	<0.01
History of atrial fibrillation	1.67 (1.28-2.17)	<0.01
History of diabetes	1.38 (1.18-1.60)	<0.01
History of hypertension	1.28 (1.09-1.50)	<0.01
History of heart failure	1.59 (1.27-2.00)	<0.01
History of coronary artery disease	1.45 (1.22-1.71)	<0.01
History of peripheral vascular disease	2.13 (1.74-2.61)	<0.01
History of stroke or transient ischaemic attack	1.43 (1.18-1.74)	<0.01
Preoperative eGFR (ml/min)		
<30	10.78 (8.73-13.32)	<0.01
30-44	2.55 (2.06-3.17)	<0.01
45-60	1.67 (1.38-2.03)	<0.01
>60 (reference)	-	-
History of chronic obstructive pulmonary disease	1.21 (0.99-1.48)	0.06
Neurosurgery	1.10 (0.84-1.45)	0.48
Urgent or emergency surgery	1.97 (1.67-2.32)	<0.01
Major surgery	1.68 (1.44-1.96)	<0.01
Pulse pressure quintiles (mmHg)		
≤45	0.91 (0.78-1.05)	0.20
46-53	0.82 (0.70-0.96)	0.02
54-62	1.00 (0.87-1.15)	0.96
63-75	1.15 (1.01-1.31)	0.03
>75	1.16 (1.03-1.32)	0.02

Table 3. Multivariable logistic regression model to predict myocardial injury after non-cardiac surgery. Dependent variable is myocardial injury within 30 days of surgery. Preoperative pulse pressure was divided into quintiles and treated as a categorical variable. Preoperative systolic blood pressure was divided into quintiles and included as a covariate. Results given as odds ratios with 95% confidence intervals. Estimated glomerular filtration rate (eGFR).

Covariates	odds ratio	p-value
Age (years)		
45-64 (reference)	-	-
65-75	1.01 (0.84-1.22)	0.93
>75	1.86 (1.55-2.23)	<0.01
Male sex	1.40 (1.22-1.60)	<0.01
History of atrial fibrillation	1.67 (1.29-2.17)	<0.01
History of diabetes	1.37 (1.18-1.60)	<0.01
History of hypertension	1.29 (1.10-1.51)	<0.01
History of heart failure	1.58 (1.25-1.98)	<0.01
History of coronary artery disease	1.44 (1.21-1.70)	<0.01
History of peripheral vascular disease	2.13 (1.74-2.60)	<0.01
History of stroke or transient ischaemic attack	1.44 (1.18-1.75)	<0.01
Preoperative eGFR (ml/min)		
<30	10.70 (8.66-13.22)	<0.01
30-44	2.56 (2.06-3.17)	<0.01
45-60	1.67 (1.38-2.03)	<0.01
>60 (reference)	-	-
History of chronic obstructive pulmonary disease	1.20 (0.98-1.47)	0.08
Neurosurgery	1.11 (0.84-1.46)	0.47
Urgent or emergency surgery	1.97 (1.67-2.32)	<0.01
Major surgery	1.68 (1.44-1.97)	<0.01
Systolic blood pressure quintiles (mmHg)		
<120	1.07 (0.91-1.24)	0.43
120-131	1.19 (0.97-1.44)	0.09
132-143	0.95 (0.83-1.10)	0.52
144-159	0.93 (0.80-1.07)	0.29
≥160	0.90 (0.75-1.07)	0.24
Pulse pressure quintiles (mmHg)		
≤45	0.81 (0.67-0.98)	0.03
46-53	0.78 (0.66-0.93)	<0.01
54-62	1.01 (0.87-1.17)	0.91
63-75	1.22 (1.06-1.41)	<0.01
>75	1.28 (1.07-1.54)	<0.01