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Arterial pulse pressure and postoperative morbidity in high-risk surgical patients

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Abstract

Background: Systemic arterial pulse pressure (systolic minus diastolic pressure) ≤53 mm Hg in patients with cardiac failure is correlated with reduced stroke volume and is independently associated with accelerated morbidity and mortality. Given that deconditioned surgical and heart failure patients share similar cardiopulmonary physiology, we examined whether lower pulse pressure is associated with excess morbidity after major surgery.

Methods: This was a prospective observational cohort study of patients deemed by their preoperative assessors to be at higher risk of postoperative morbidity. Preoperative pulse pressure was calculated before cardiopulmonary exercise testing. The primary outcome was any morbidity (PostOperative Morbidity Survey) occurring within 5 days of surgery, stratified by pulse pressure threshold ≤53 mm Hg. The relationship between pulse pressure, postoperative morbidity, and oxygen pulse (a robust surrogate for left ventricular stroke volume) was examined using logistic regression analysis (accounting for age, sex, BMI, cardiometabolic co-morbidity, and operation type).

Results: The primary outcome occurred in 578/660 (87.6%) patients, but postoperative morbidity was more common in 243/ 660 patients with preoperative pulse pressure ≤53 mm Hg{odds ratio (OR): 2.24 [95% confidence interval (CI): 1.29–3.38]; P<0.001). Pulse pressure ≤53 mm Hg [OR:1.23 (95% CI: 1.03–1.46); *P*=0.02] and type of surgery were independently associated with all-cause postoperative morbidity (multivariate analysis). Oxygen pulse <90% of population-predicted normal values was associated with pulse pressure ≤ 53 mm Hg [OR: 1.93 (95% CI: 1.32–2.84); *P*=0.007].

Conclusions: In deconditioned surgical patients, lower preoperative systemic arterial pulse pressure is associated with excess morbidity. These data are strikingly similar to meta-analyses identifying low pulse pressure as an independent risk factor for adverse outcomes in cardiac failure. Low preoperative pulse pressure is a readily available measure, indicating that detailed physiological assessment may be warranted.

Clinical trial registration: ISRCT registry, ISRCTN88456378.

Key words: blood pressure; cardiovascular; morbidity

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Editor's key points

- Pulse pressure <53 mm Hg is associated with adverse outcomes among patients with cardiac failure.
- Deconditioned surgical patients might be physiologically similar to those with heart failure.
- The authors analysed correlations between systemic arterial pulse pressure and postoperative outcome in high-risk patients.
- Among deconditioned patients, pulse pressure <53 mm Hg was an independent risk factor for all-cause postoperative mortality.

Arterial pulse pressure, calculated by subtracting diastolic from systolic arterial pressure, reflects the complex haemodynamic interplay between stroke volume, heart rate, aortic compliance, and peripheral vascular tone. In the general medical population, elevated pulse pressure is strongly associated with increased cardiovascular risk for coronary heart disease,[1–3] cardiac failure,[4–8] atrial fibrillation,[9] and all-cause cardiovascular mortality.[1,10–13] This long-established relationship is independent of normotensive or hypertensive status.[6]

In marked contrast, lower pulse pressure in patients with cardiac failure is associated with reduced cardiac index,[14] increased concentrations of natriuretic peptide,[15] and accelerated morbidity, mortality, or both.[8,9,16,17] Notably, in patients with heart failure originating from a non-ischaemic aetiology, pulse pressure appears to be correlated closely with stroke volume.[18] The MAGGIC (Meta-Analysis Global Group in Chronic Heart Failure) meta-analysis identified pulse pressure ≤53mm Hg as a robust independent predictor of mortality in 27 046 patients from 22 separate studies or trials in cardiac failure.[16] Deconditioned surgical patients share similar cardiovascular and autonomic features with cardiac failure patients, including reduced cardiopulmonary reserve.[19] Low preoperative pulse pressure may therefore also be associated with increased risk of postoperative morbidity in higher-risk surgical patients.

In this prospective multicentre cohort study, we hypothesized that the pulse pressure threshold identified in cardiac failure patients (≤53 mm Hg) was associated in a similar manner with postoperative morbidity in higher-risk surgical patients referred for cardiopulmonary exercise testing as part of their routine preoperative assessment. By focusing on low pulse pressure in this analysis, we provide new data highlighting the striking physiological similarities between patients with overt cardiac failure and deconditioned surgical patients.

Methods

We conducted a secondary analysis of a prospective, multicentre observational cohort study of high-risk patients undergoing cardiopulmonary exercise testing before major non-cardiac surgery. The study was approved by the NRES Committee London (Camden & Islington; MREC:12/L0/0453) and registered with Controlled Trials (ISRCTN88456378). Patients gave written, informed consent before undergoing cardiopulmonary exercise testing. The statistical analysis plan was approved before the secondary analysis began. Patients were referred to the local cardiopulmonary exercise testing service by the surgeon, anaesthetist, or both as part of their routine preoperative assessment if they fulfilled the following two criteria: (i) they required major surgery estimated to last >2 h; and (ii) they were deemed to be at higher risk of postoperative morbidity or mortality by their referring clinician, on the basis of their preoperative co-morbidity, the magnitude of the surgical insult, or both. We also calculated Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM) scores for morbidity to confirm this clinically estimated higher risk. Patients were excluded if they refused consent or if there were contraindications to cardiopulmonary exercise testing. Patient age, sex, operative time, established measures of preoperative risk (including diabetes mellitus, cardiac disease, and cerebrovascular disease), and haemoglobin were recorded before surgery.

Cardiopulmonary exercise testing

Patients underwent cardiopulmonary exercise testing on an electronic cycle ergometer using an incremental ramp protocol to maximal tolerance, having continued their normal cardiovascular medications up to and including the day of the test. Equipment was calibrated before each test using standard reference gases. Arterial blood pressure was measured (sitting) at rest before exercise. Continuous 12-lead ECG and breath-by-breath gas exchange analysis were performed throughout testing. All patients were instructed to continue cycling until symptom-limited fatigue occurred. Pulse pressure was calculated retrospectively from routine measurements of arterial systolic and diastolic pressure. Anaerobic threshold was determined by two independent assessors blinded to pulse pressure and according to published guidelines using the modified V-slope method and confirmed by ventilatory equivalents for carbon dioxide ($\dot{V}_E/\dot{V}_{CO_2}$) and oxygen ($\dot{V}_E/\dot{V}_{CO_2}$).[20,21] Arterial pressure was not blinded to staff, but pulse pressure was calculated offline and not recorded at the time of the test.

Perioperative management

Patients were cared for by the normal attending clinicians, blinded to preoperative arterial pressure measurement. All hospitals used enhanced recovery programmes as part of standard care for the types of surgery involved in this study. Surgery and anaesthesia were conducted by consultant staff. Inhalation anaesthesia, fluid therapy, standardized antiemetic regimens, analgesia (regional neuraxial anaesthesia or patient-controlled analgesia), and physiotherapy care were delivered according to usual standard of care. Acute pain services were available for consultation. Postoperative management was conducted according to local clinical guidelines. Surgical antibiotic use at the time of the operation at all centres was undertaken according to local microbiology policies (i.e. preoperative and two subsequent doses). Thus, antibiotic use 48h after surgery was seen as a deviation from normal postoperative care (i.e. suggestive of infectious morbidity).

Transthoracic echocardiography

Given that transthoracic echocardiography was not part of the study protocol, only data from patients at University College London Hospitals referred for transthoracic echocardiography (Vivid E9 or GE Vivid I; GE Healthcare, Little Chalfont, UK) as part of their preoperative assessment were assessed. Echocardiography was undertaken by technicians blinded to the patients' participation in this study.