Non-invasive cardiac stress testing before elective major non-cardiac surgery: population based cohort study

Duminda N Wijeysundera, lecturer,1,2,3 W Scott Beattie, R Fraser Elliot chair in cardiac anaesthesia,2 Peter C Austin, senior scientist,1,3,4 Janet E Hux, senior scientist,1,3,5 Andreas Laupacis, scientist1,3,6,7

ABSTRACT

Objective To determine the association of non-invasive cardiac stress testing before elective intermediate to high risk non-cardiac surgery with survival and hospital stay. Design Population based retrospective cohort study. Setting Acute care hospitals in Ontario, Canada, between 1 April 1994 and 31 March 2004. Participants Patients aged 40 years or older who underwent specific elective intermediate to high risk non-cardiac surgical procedures. Interventions Non-invasive cardiac stress testing performed within six months before surgery. Main outcome measures Postoperative one year survival and length of stay in hospital. Results Of the 271 082 patients in the entire cohort, 23 991 (8.9%) underwent stress testing. After propensity score methods were used to reduce important differences between patients who did or did not undergo preoperative stress testing and assemble a matched cohort (n=46 120), testing was associated with improved one year survival (hazard ratio (HR) 0.92, 95% CI 0.86 to 0.99; P=0.03) and reduced mean hospital stay (difference −0.43; P<0.001). In an analysis of subgroups defined by Revised Cardiac Risk Index (RCRI) score methods were used to reduce important differences between patients who did or did not undergo preoperative stress testing and assemble a matched cohort (n=46 120), testing was associated with improved one year survival (hazard ratio (HR) 0.92, 95% CI 0.86 to 0.99; P=0.03) and reduced mean hospital stay (difference −0.43; P=0.001). In an analysis of subgroups defined by Revised Cardiac Risk Index (RCRI) class, testing was associated with harm in low risk patients (RCRI 0 points: HR 1.35, 95% CI 1.05 to 1.74), but with benefit in patients who were at intermediate risk (RCRI 1-2 points: 0.92, 95% CI 0.85 to 0.99) or high risk (RCRI 3-6 points: 0.80, 95% CI 0.67 to 0.97). Conclusions Preoperative non-invasive cardiac stress testing is associated with improved one year survival and length of hospital stay in patients undergoing elective intermediate to high risk non-cardiac surgery. These benefits principally apply to patients with risk factors for perioperative cardiac complications.

INTRODUCTION

Every year, approximately 900 000 adults worldwide experience major cardiac complications after surgery,1 which are associated with increased mortality2 and hospital stay.3 Preoperative non-invasive cardiac stress testing may help prevent these complications. This strategy detects underlying ischaemic heart disease and identifies individuals who might benefit from preoperative interventions, aggressive intraoperative haemodynamic management, closer postoperative surveillance, or avoiding surgery. Additionally, the results of stress testing can guide the use of perioperative β blockade, which has greatest benefit in patients with inducible ischaemia.4 Given these benefits, the American College of Cardiology and American Heart Association guidelines recommend preoperative non-invasive stress testing,5 but only in individuals with clinical risk factors for cardiac complications.

Conversely, some authors have discouraged the use of preoperative stress testing5,6 because it may delay surgery and has not been shown to improve postoperative outcomes. Instead, they advocate routine perioperative β blockade.6,8 This recommendation was supported by the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo II (DECREASE II) randomised trial, which evaluated routine stress testing in intermediate risk patients receiving perioperative β blockade.9 The study found no significant effect of preoperative stress testing on cardiac complications. None the less, the estimated effect had a wide 95% confidence interval (odds ratio 0.28 to 2.91) that did not exclude either substantial benefit or harm. Additionally, the Perioperative Ischemic Evaluation (POISE) trial has raised concerns about the safety of perioperative β blockade.9

Given the potential benefits of preoperative stress testing but the lack of proved impact on outcomes, we undertook a population based cohort study of non-invasive cardiac stress testing in Ontario, Canada. Our objective was to determine whether stress testing before major elective non-cardiac surgery was associated with improved one year survival and reduced hospital stay.

METHODS

We used linked population based administrative healthcare databases in Ontario, Canada, to undertake a retrospective cohort study. The databases used were the Canadian Institute for Health Information (CIHI) discharge abstract database, which describes all hospital admissions; the Ontario Health Insurance Plan (OHIP) database, which describes physician billing for inpatient and outpatient services; the Registered Persons Database (RPDB), which describes
Using previously described methods, we retrospectively identified all Ontario residents aged 40 years or older who underwent one of the following specific types of elective surgery during fiscal years 1994 to 2003 (1 April 1994 to 31 March 2004): abdominal aortic aneurysm repair; carotid endarterectomy; peripheral vascular bypass; total hip replacement; total knee replacement; large bowel surgery; liver resection; Whipple procedure; pneumonectomy; pulmonary lobectomy; gastrectomy; oesophagectomy; nephrectomy; or cystectomy. These procedures were selected because they are intermediate to high risk for perioperative cardiac complications, applicable to either sex, and described in research studies that used the CIHI database. Procedure codes in the CIHI database have excellent accuracy.

The principal exposure was preoperative non-invasive stress testing, as defined by a physician billing for an outpatient stress test within 180 days before surgery. These tests included graded exercise treadmill testing, nuclear perfusion imaging (exercise or dipyridamole myocardial perfusion imaging using sestamibi or thallium as a radiotracer, with or without single photon emission computed tomography), and stress (exercise or dobutamine) echocardiography. We used OHIP fee codes and methods adapted from previous research. The 180 day window was chosen so that instances where stress testing led to preoperative coronary revascularisation could be included—it accounted for a 90 day period between stress testing and revascularisation and another 90 day window between revascularisation and surgery.

The outcomes of interest were mortality (one year after surgery) and hospital stay. Mortality was determined using the CIHI database (in hospital deaths) and the RPDB (out of hospital deaths). We used the CIHI database to measure hospital stay.

Demographic information was obtained from the RPDB. We used validated administrative data algorithms to identify cases of diabetes and hypertension. The OHIP database was used to identify any patient who required dialysis before the index surgery. We used previously described methods to identify in the CIHI database the following other comorbidities from hospital admissions within two years preceding surgery on the basis of International Classification of Diseases codes (9th revision, clinical modification; or 10th revision): ischaemic heart disease; congestive heart failure; cerebrovascular disease; pulmonary disease; chronic renal insufficiency; malignancy; liver disease; and dementia. When identifying comorbidities, only information from acute care hospital admissions before the index surgery was used to determine the presence of ischaemic heart disease, congestive heart failure, cerebrovascular disease, pulmonary disease, renal insufficiency, and liver disease. Our primary aim was to ensure that postoperative complications were not misclassified as pre-existing comorbid diseases. This approach also ensured that the relevant comorbidity information was almost certainly derived from data available before the preoperative cardiac stress test.

The OHIP database and the CPDB were used to identify outpatient consultations (anaesthesiology, internal medicine, and cardiology) within 60 days before surgery, echocardiography within 180 days before surgery, epidural anaesthesia or analgesia (hereafter referred to as anaesthesia), and intraoperative invasive monitoring. Procedure codes in the OHIP database are very accurate. We imputed patients’ incomes on the basis of their neighbourhood median income in the 2001 Canadian census.

To understand how non-invasive stress testing might influence outcomes, we used the OHIP database to identify related processes of care before surgery—namely echocardiography, coronary angiography, percutaneous coronary intervention, and coronary artery bypass graft surgery—as well as processes of care after surgery—namely admission to a monitored bed (critical care unit or step-down unit) and mechanical ventilation. Additionally, the ODB database was used to identify outpatient prescriptions for β blockers or statins within 100 days before surgery. We defined new users of these medications as those who had prescriptions within 100 days before surgery but no prescriptions during the period from 180 days to one year before surgery.

Analyses

A two tailed P value of less than 0.05 was used to define statistical significance, and all estimates were calculated with 95% confidence intervals. Bivariate tests were initially used to compare the characteristics of patients who did or did not undergo preoperative stress testing (t test, Mann-Whitney U test, χ² test, Fisher’s exact test).

We used propensity score methods to adjust for systematic differences in measured baseline characteristics between the two groups of patients in the study. A non-parsimonious multivariable logistic regression model was developed to estimate a propensity score for preoperative stress testing. Clinical significance guided the initial choice of covariates: age; sex; year of surgery; surgery; income; hospital type (teaching, low volume non-teaching, moderate volume non-teaching, or high volume non-teaching); comorbid disease; specialist consultations (anaesthesiology, general internal
Subgroup analyses were performed on the basis of ischaemic heart disease, surgical procedure (vascular, orthopaedic, intraperitoneal, or intrathoracic), and Revised Cardiac Risk Index (RCRI) class (0 points, 1-2 points, or 3 or more points). The RCRI is composed of six equally weighted clinical risk factors: ischaemic heart disease; congestive heart failure; cerebrovascular disease; diabetes; renal insufficiency; and high risk surgery (intra-abdominal, intrathoracic, or suprainguinal vascular procedures). For the subgroup analyses, we repeated the same propensity score matching process while simultaneously forcing an exact match on the subgroup characteristics. One year survival was then compared within the subgroup specific matched pairs. We used an interaction term in the Cox model to test for any subgroup effects. An additional subgroup analysis was performed among patients older than 66 years to describe preoperative β blocker and statin use. We used this particular subgroup because data on outpatient prescriptions are available only for individuals aged above 65 years in Ontario.

We conducted several sensitivity analyses to test the robustness of our results. Firstly, we assessed the influence of an alternative matching method on our results. The original propensity score was modified to include an estimate of unmeasured disease burden: the number of acute care hospital admissions within two years before surgery. Secondly, we used the CIHI database to determine the association of preoperative testing with an outcome where no differences would be expected, namely surgical site infections. Previous research suggests that administrative data can identify surgical site infections with reasonable accuracy. The purpose of this “tracer” analysis was to assess for unmeasured residual confounding. Given that surgical site infections are associated with increased patient risk but should be unaffected by stress testing, we hypothesised that testing would not be associated with increased rates of these complications.

**RESULTS**

The study cohort consisted of 271 082 patients, of whom 23 991 (8.9%) underwent non-invasive stress testing within 180 days before surgery (tables 1 and 2). Some patients underwent more than one test; hence, a total of 25 877 stress tests were performed. The median time between testing and surgery was 48 days (interquartile range 16 to 101 days). A total of 7795 (30%) of these tests were ordered by cardiologists, 7234 (28%) by internists, 6281 (24%) by family physicians, 3594 (14%) by surgeons, 477 (1.8%) by anaesthesiologists, and 496 (1.9%) by other specialists. Of the patients who underwent preoperative testing, 914 (3.8%) underwent coronary angiography, 149 (0.6%) underwent percutaneous coronary intervention, and 134 (0.6%) underwent coronary artery bypass graft surgery between the dates of stress testing and surgery.

Patients who underwent preoperative testing and those who did not differ with regard to all measured characteristics (tables 1 and 2). Patients who underwent...
Table 2 | Perioperative characteristics of entire cohort. Values are expressed as number (percentage) unless otherwise indicated

| Hospital type               | Stress testing (n=23 991) | No testing (n=247 091) | P value |
|-----------------------------|---------------------------|------------------------|---------|
| Procedure                   |                           |                        |         |
| Abdominal aortic aneurysm repair | 2651 (11.0)              | 5280 (2.1)             |         |
| Carotid endarterectomy      | 2001 (8.3)                | 10 044 (4.1)           |         |
| Peripheral vascular bypass  | 2579 (10.7)               | 13 467 (5.5)           |         |
| Total hip replacement       | 4020 (16.8)               | 60 671 (24.6)          | <0.001  |
| Total knee replacement       | 5694 (23.7)               | 80 771 (32.7)          |         |
| Large bowel surgery         | 3363 (14.0)               | 50 497 (20.4)          |         |
| Liver resection             | 273 (1.1)                 | 1661 (0.7)             |         |
| Whipple procedure           | 76 (0.3)                  | 1030 (0.4)             |         |
| Pneumonecctomy or lobectomy | 1560 (6.5)                | 8709 (3.5)             |         |
| Gastrectomy or oesophagectomy | 623 (2.6)             | 5004 (2.0)             |         |
| Nephrectomy                 | 957 (4.0)                 | 7900 (3.2)             |         |
| Cystectomy                  | 194 (0.8)                 | 2057 (0.8)             |         |
| Intraoperative care         |                           |                        |         |
| Epidural anaesthesia        | 7433 (31.0)               | 49 593 (20.1)          | <0.001  |
| Arterial line               | 11 160 (46.5)             | 70 148 (28.3)          | <0.001  |
| Central venous line         | 3288 (13.7)               | 18 883 (7.6)           | <0.001  |
| Pulmonary artery catheter   | 2270 (9.5)                | 6743 (2.7)             | <0.001  |

Testing were typically men who had surgery at a high volume or moderate volume non-teaching hospital and had an increased burden of comorbid disease. They were also more likely to be evaluated by a specialist before surgery, undergo preoperative cardiac procedures, and require intraoperative care such as epidural anaesthesia or intraoperative invasive monitoring.

Of the patients who underwent stress testing, 23 060 (96%) were successfully matched to a similar patient who did not. The covariate balance between the two arms was improved considerably by propensity score matching (tables 3 and 4): the mean standardised difference between the two groups decreased from 14.9% (range 0.3 to 90.9) to 0.48% (0.02 to 1.5). Of the matched patients who underwent testing, 914 (4.0%) underwent coronary angiography, 136 (0.6%) underwent percutaneous coronary intervention, and 119 (0.5%) underwent coronary artery bypass graft surgery between the dates of stress testing and surgery.

Within the matched cohort, one year survival was higher among patients who had undergone preoperative testing than in those who had not [hazard ratio (HR) 0.92, 95% CI 0.86 to 0.99; P=0.03; fig 1]. This corresponded to a number needed to treat (NNT) of 80 to prevent mortality at one year of 221 (95% CI 111 to 16 067). In hospital mortality and hospital stay were also reduced among patients who underwent stress testing (relative risk (RR) 0.85, 95% CI 0.73 to 0.98; P=0.03 and 8.72 days v 8.96 days, difference −0.24 days, 95% CI −0.07 to −0.43; P<0.001, respectively; table 5).

Patients who had undergone stress testing were more likely to be admitted to a monitored bed after surgery than were those who had not undergone testing (RR 1.09, 95% CI 1.06 to 1.12; P<0.001; table 5). Conversely, rates of postoperative mechanical ventilation were similar in the two groups (RR 1.02, 95% CI 0.98 to 1.08; P=0.25).

In sensitivity analyses, the association of stress testing with improved one year survival was unaffected when the number of previous acute care hospital admissions within two years before the index surgery was added to the original propensity score (HR 0.92, 95% CI 0.86 to 0.99; P=0.02). Additionally, we found no statistically significant association between stress testing and surgical site infections (RR 1.00, 95% CI 0.94 to 1.07; P=0.89; table 5).

The subgroup of individuals older than 66 years consisted of 15 475 patients who underwent stress testing and 15 475 who did not. In this subgroup, 5626 (36%) of those who underwent preoperative stress testing and 3998 (26%) of those who did not were receiving β blockers (RR 1.41, 95% CI 1.36 to 1.45; P<0.001). Additionally, 1895 (12%) patients who had undergone testing were new β blocker users, compared with 827 (5.3%) who had not undergone testing (RR 2.23, 95% CI 2.12 to 2.48; P<0.001). More patients in the stress testing group were receiving statins (5000 (32%)) than were those who had not been tested (3679 (24%)); RR 1.31 to 1.41; P<0.001. A total of 974 (6.3%) patients who had undergone testing were new statin users, compared with 539 (3.5%) of patients who had not (RR 1.81, 95% CI 1.63 to 2.00; P<0.001).

The association of stress testing with mortality was unchanged when the analyses were repeated in subgroups defined by procedure type (P=0.28 for interaction; fig 2). Conversely, the effects of testing on mortality varied with RCRI class (P=0.005) and, to a degree, ischaemic heart disease (P=0.08). Preoperative stress testing was associated with harm in low risk patients (RCRI 0 points: HR 1.35, 95% CI 1.05 to 1.74; however, it was associated with improved survival in intermediate risk patients (RCRI 1-2 points: HR 0.92, 95% CI 0.85 to 0.99) and high risk patients (RCRI 3-6 points: HR 0.80, 95% CI 0.67 to 0.97; fig 2). These differences corresponded to a number needed to treat to prevent mortality at one year of 156 for intermediate risk patients (95% CI 79 to 6127) and 38 for high risk patients (95% CI 21 to 315). Conversely, the number needed to harm in low risk patients was 179 (95% CI 97 to 1090). The relative rates of intervention use (that is, preoperative medications and cardiac procedures) were higher in low risk patients who underwent stress testing than in intermediate or high risk patients who were tested (web table A). The characteristics of the subgroups defined by RCRI class are presented in web table B.

**DISCUSSION**

In this population based retrospective cohort study, non-invasive cardiac stress testing before elective intermediate to high risk non-cardiac surgery was associated with improved one year survival and reduced hospital stay. These benefits largely applied to patients
who were at high risk for cardiac complications on the basis of three or more clinical risk factors. In contrast, stress testing was associated with only minor benefits for intermediate risk patients (1-2 risk factors) and with harm in low risk individuals.

Our results suggest that preoperative stress testing should be reserved for patients with clinical risk factors for cardiac complications. In high risk patients with three or more clinical risk factors, the use of preoperative stress testing was supported by an associated moderate improvement in one year survival and favourable number needed to treat. Conversely, in intermediate risk patients with one or two clinical risk factors, testing was associated with a small, albeit statistically significant, benefit. Given the small magnitude of this effect and the associated relatively large number needed to treat, routine preoperative stress testing is not justified in intermediate risk patients. Our results do, however, support the safety and potential benefits of selective testing in intermediate risk patients. Future research should therefore determine whether stress testing provides additional prognostic information in specific subgroups of intermediate risk patients; for example, in subgroups defined by risk factors that were not captured by administrative data (such as poor functional status) or were suggested by our subgroup analyses (such as previous history of ischaemic heart disease). Our study does not support the use of preoperative stress testing in low risk patients; furthermore, the results suggest that such testing is associated with harm.

Our results are largely consistent with the position of the American College of Cardiology and American Heart Association guidelines, which emphasise stress testing specifically in individuals who are undergoing intermediate to high risk surgery and have one or more clinical risk factors (for example, ischaemic heart disease, congestive heart failure, cerebrovascular disease, diabetes, or renal insufficiency). These guidelines also suggest, however, that testing be restricted to individuals who concurrently have poor or unknown functional capacity. As described above, our data sources did not capture information on exercise tolerance; consequently, further research is needed to determine whether the prognostic significance of preoperative stress testing in intermediate to high risk surgical patients varies with their functional capacity.

Table 3 | Preoperative characteristics of the propensity matched pairs. Values are expressed as number (percentage) unless otherwise indicated

|                      | Stress testing (n=23 060) | No stress testing (n=23 060) | Absolute standardised difference |
|----------------------|--------------------------|-----------------------------|---------------------------------|
| **Demographics**     |                          |                             |                                 |
| Female sex           | 13 572 (58.9)            | 13 623 (59.1)               | 24.6%                           |
| Age (years; mean (SD)) | 69.2 (9.2)              | 69.2 (9.2)                  | 7.6%                            |
| **Socioeconomic status** |                       |                             |                                 |
| Annual income (Canadian dollars; mean (SD)) | 24 837 (5104) | 24 810 (5155) | 3.0% |
| **Comorbid disease** |                          |                             |                                 |
| Ischaemic heart disease | 5272 (22.9)            | 5343 (23.2)                 | 41.1%                           |
| Congestive heart failure | 1011 (4.4)             | 1018 (4.4)                  | 10.2%                           |
| Cerebrovascular disease | 1638 (7.1)             | 1661 (7.2)                  | 12.6%                           |
| Hypertension         | 14 355 (62.3)           | 14 381 (62.4)               | 18.4%                           |
| Diabetes             | 5655 (24.5)             | 5572 (24.2)                 | 17.1%                           |
| Pulmonary disease     | 1528 (6.6)              | 1562 (6.8)                  | 6.7%                            |
| Dialysis or renal disease | 463 (2.0)              | 458 (2.0)                   | 6.6%                            |
| Malignancy           | 2185 (9.5)              | 2210 (9.6)                  | 2.4%                            |
| **Specialist consultation** |                      |                             |                                 |
| Anaesthesiology      | 12 299 (53.3)           | 12 279 (53.2)               | 34.4%                           |
| General internal medicine | 5670 (24.6)           | 5804 (25.2)                 | 1.8%                            |
| Cardiology           | 5084 (22.0)             | 4941 (21.4)                 | 53.0%                           |
| **Preoperative cardiac procedure**† |             |                             |                                 |
| Echocardiogram       | 9948 (43.1)             | 9909 (43.0)                 | 90.9%                           |

*Within 60 days before surgery.
†Within 180 days before surgery.

Fig 1 | Survival curves for postoperative all cause mortality in patients who did (n=23 060) or did not (n=23 060) undergo preoperative stress testing (matched by propensity score) over one year after surgery.
The beneficial effects of stress testing on mortality risk in intermediate to high risk patients are likely to be the result of a reduction in perioperative cardiac complications. Prevention of such complications would be expected to improve both length of hospital stay\(^3\) and one year survival.\(^2\) By comparison, testing was not associated with any difference in the risk of surgical site infections.

Several plausible mechanisms might, in combination, explain a reduction in cardiac complications among individuals who underwent stress testing. Firstly, the results of preoperative stress testing can help guide perioperative drug therapy with β blockers or statins. β blockade across a broad spectrum of surgical patients may cause harm,\(^9\) but it has been associated with strong benefits in patients with multiple clinical risk factors,\(^39\) especially in those with inducible ischaemia.\(^4\) Thus, preoperative stress testing may help identify subgroups of patients that would benefit from β blocker therapy. Similarly, evidence of ischaemic heart disease on preoperative testing may indicate that a patient requires statin therapy, which is also associated with improved postoperative outcomes.\(^40\)

Secondly, clinicians could use preoperative testing to determine which patients warrant closer postoperative surveillance. This hypothesis is supported by the higher rate of postoperative admission to monitored beds among patients who had undergone stress testing before surgery. Thirdly, stress testing can identify patients with high risk ischaemic heart disease who meet usual indications for revascularisation\(^7\) or who would benefit from avoiding surgery. Finally, clinicians might use the results of preoperative testing to determine which patients require more aggressive clinical care, such as stringent haemodynamic management.

In contrast to these benefits for intermediate to high risk patients, we found that stress testing was associated with harm in low risk patients. The increased mortality observed might be explained by the use of unnecessary, and potentially deleterious, interventions such as β blockade.\(^93\) It is noteworthy that the frequency of new β blocker use in low risk patients was 2.8 times higher in those who were tested than in those who were not (web table A).

### Comparison with other studies
Our study warrants comparison with the DECREASE II trial,\(^8\) in which 770 patients with one or two clinical risk factors were randomly allocated to either stress testing or no testing before major vascular surgery. Although the rates of cardiac death or myocardial infarction at 30 days after surgery did not significantly differ between the two strategies, the few outcome events (\(n=16\)) and wide 95% confidence interval (odds ratio 0.28 to 2.91) suggest that the trial was underpowered to detect a plausible treatment effect. Indeed, this confidence interval is still consistent with our finding of a small benefit for intermediate risk patients.

| Hospital type               | Stress testing (\(n=23\,060\)) | No stress testing (\(n=23\,060\)) | Absolute standardised difference |
|-----------------------------|---------------------------------|-----------------------------------|----------------------------------|
| Teaching                    | 7642 (33.2)                     | 7645 (33.2)                       | 4.2% \(\Delta<0.1\%\)           |
| High volume non-teaching    | 5618 (24.4)                     | 5639 (24.5)                       | 9.4% \(\Delta 0.2\%\)           |
| Moderate volume non-teaching| 5432 (23.6)                     | 5336 (23.1)                       | 4.6% \(\Delta 0.9\%\)           |
| Low volume non-teaching     | 4363 (18.9)                     | 4440 (19.3)                       | 9.6% \(\Delta 0.8\%\)           |

### Procedure

- Abdominal aortic aneurysm repair: 2247 (9.7) vs 2262 (9.8), \(36.5\%\) vs \(35.5\%\), \(\Delta 0.2\%\)
- Carotid endarterectomy: 1954 (8.5) vs 1914 (8.3), \(17.8\%\) vs \(17.5\%\), \(\Delta 0.3\%\)
- Peripheral vascular bypass: 2384 (10.3) vs 2393 (10.4), \(19.5\%\) vs \(19.4\%\), \(\Delta 0.1\%\)
- Total hip replacement: 4011 (17.4) vs 4043 (17.5), \(19.4\%\) vs \(19.5\%\), \(\Delta 0.1\%\)
- Total knee replacement: 5632 (24.4) vs 5682 (24.6), \(20.0\%\) vs \(20.1\%\), \(\Delta 0.1\%\)
- Large bowel surgery: 3276 (14.2) vs 3282 (14.3), \(17.1\%\) vs \(17.2\%\), \(\Delta 0.1\%\)
- Liver resection: 272 (1.2) vs 294 (1.3), \(4.9\%\) vs \(5.0\%\), \(\Delta 0.1\%\)
- Whipple procedure: 68 (0.3) vs 57 (0.2), \(1.7\%\) vs \(1.6\%\), \(\Delta 0.1\%\)
- Pneumonectomy or lobectomy: 1460 (6.3) vs 1431 (6.2), \(13.7\%\) vs \(13.5\%\), \(\Delta 0.2\%\)
- Gastrectomy or oesophagectomy: 609 (2.6) vs 589 (2.6), \(3.8\%\) vs \(3.7\%\), \(\Delta 0.1\%\)
- Nephrectomy: 917 (4.0) vs 975 (4.2), \(4.3\%\) vs \(4.4\%\), \(\Delta 0.1\%\)
- Cystectomy: 180 (0.8) vs 188 (0.8), \(0.3\%\) vs \(0.4\%\), \(\Delta 0.1\%\)

### Intraoperative care

- Epidural anaesthesia: 6895 (29.9) vs 6842 (29.7), \(25.2\%\) vs \(25.1\%\), \(\Delta 0.1\%\)
- Arterial line: 10 497 (45.5) vs 10 577 (45.9), \(38.1\%\) vs \(38.3\%\), \(\Delta 0.2\%\)
- Central venous line: 3000 (13.0) vs 3009 (13.0), \(19.7\%\) vs \(19.7\%\), \(\Delta 0.0\%\)
- Pulmonary artery catheter: 2037 (8.8) vs 2070 (9.0), \(28.4\%\) vs \(28.2\%\), \(\Delta 0.2\%\)
Analyses. The dashed vertical line represents the overall treatment effect (hazard ratio 0.92).

### Table 5 | Processes of care and outcomes in the propensity matched pairs. Values are expressed as number (percentage) unless otherwise indicated

| Preoperative cardiac procedure* | Stress testing (n=23 060) | No stress testing (n=23 060) | Difference (95% CI) |
|---------------------------------|---------------------------|-----------------------------|---------------------|
| Coronary angiogram              | 1139 (4.9)                | 549 (2.4)                   | RR 2.08 (1.88 to 2.92) |
| Percutaneous coronary intervention | 288 (1.2)            | 132 (0.6)                   | RR 2.18 (1.78 to 2.68) |
| Aorto-coronary bypass surgery   | 267 (1.2)                 | 213 (0.9)                   | RR 1.25 (1.05 to 1.50) |

**Postoperative care†**
- Admission to a monitored bed: 6175 (26.8) vs. 5682 (24.6), RR 1.09 (1.06 to 1.12)
- Mechanical ventilation: 2672 (11.6) vs. 2596 (11.3), RR 1.02 (0.98 to 1.08)
- Surgical site infection: 1815 (7.9) vs. 1807 (7.8), RR 1.00 (0.94 to 1.07)

**Outcomes**
- One year mortality: 1622 (7.0) vs. 1738 (7.5), HR 0.92 (0.86 to 0.99)
- In-hospital postoperative death: 310 (1.3) vs. 366 (1.6), RR 0.85 (0.73 to 0.98)
- Intra-abdominal or intrathoracic surgery: 1139 (4.9) vs. 549 (2.4), RR 2.08 (1.88 to 2.92)
- Orthopaedic surgery: 288 (1.2) vs. 132 (0.6), RR 2.18 (1.78 to 2.68)
- Aorto-coronary bypass surgery: 267 (1.2) vs. 213 (0.9), RR 1.25 (1.05 to 1.50)

Abbreviations: HR, hazard ratio; RR, relative risk.

*Within 180 days before surgery.
†Within 5 days after surgery.

Surveillance, thereby diminishing the influence of testing on clinical care. Stress testing altered subsequent management only in that patients with extensive ischaemia were considered for preoperative revascularisation, which has not been shown to improve outcomes.41 42

**Strengths and limitations of study**

Our study has several strengths. Previous studies evaluated the diagnostic accuracy of preoperative stress testing, whereas our study focused on the clinically relevant question of whether it influences outcomes. Additionally, the large sample size enabled us to detect small treatment effects that would have been deemed non-significant in smaller studies. The population based sample used describes the effects of preoperative stress testing in “real world” clinical care, as opposed to in a protocol driven randomised trial. Thus, our findings can be generalised to other healthcare systems reasonably similar to that in Ontario, Canada. Finally, our study included only patients scheduled for elective intermediate to high risk surgery. Urgent or emergency procedures are unlikely to be delayed to facilitate preoperative stress testing, whereas patients undergoing low risk ambulatory surgery have a very low risk of major complications and are unlikely to benefit from preoperative stress testing. Our study, therefore, focused on individuals who had reasonable opportunities to undergo, and potentially benefit from, preoperative stress testing.

Our study also has several limitations. Firstly, we could not compare outcomes from different stress tests (for example, exercise treadmill testing and nuclear perfusion). The American College of Cardiology and American Heart Association guidelines recommend exercise electrocardiography testing as the test of choice, with the use of other modalities on the basis of factors such as resting electrocardiogram abnormalities, patient physique or build, and function tolerance.5 Given that these factors are not recorded in administrative databases, yet might be prognostically important, comparison on the basis of testing modality would be biased by residual confounding.

Secondly, our study was observational in design; hence, our results demonstrate an association between preoperative testing and survival, but do not prove causation. None the less, randomised trials of preoperative stress testing also have limitations. A trial of stress testing in intermediate risk patients would probably not be feasible. On the basis of the one year mortality rate of approximately 8.9% among intermediate risk patients in our study, roughly 31 100 participants would be required to detect a 10% relative risk reduction in a randomised trial (two tailed α of 0.05 and 80% power). Conversely, a randomised trial in high risk patients would also be large, but potentially feasible. On the basis of the 15.5% one year mortality rate among high risk participants in our study, approximately 4000 high risk individuals would be required to detect a 20% relative risk reduction (two tailed α of 0.05 and 80% power).

Thirdly, our data sources could not account for individuals who underwent preoperative coronary revascularisation on the basis of high risk findings on preoperative stress testing but subsequently died before their planned non-cardiac surgeries. These deaths before surgery are unlikely to affect our results significantly. In the stress testing arm of the cohort matched by propensity scores, 335 (1.1%) individuals subsequently underwent either percutaneous coronary intervention or coronary artery bypass graft surgery before the planned non-cardiac procedures. If the mortality rate associated with preoperative coronary revascularisation is assumed to be 2%,41 42 46 seven individuals may have undergone stress testing and revascularisation but died before their planned non-cardiac surgeries. These individuals would have been missing from our matched cohort, which included only patients who actually underwent non-cardiac surgery. None the less, even if these seven missing deaths were included in our analyses, the proportion of patients dead at one year in the stress testing arm of the matched...
These benefits largely applied to patients who were at high risk for cardiac complications on the basis of three or more clinical risk factors.

In contrast, stress testing was associated with only minor benefits for intermediate risk patients (one or two risk factors) and with harm in low risk individuals.

Conclusions

Non-invasive cardiac stress testing before elective intermediate to high risk non-cardiac surgery is associated with improved one year survival and reduced hospital stay. These benefits principally apply to patients at high risk for cardiac complications on the basis of clinical risk factors. Our results are generally supportive of the current American College of Cardiology and American Heart Association guidelines for preoperative cardiac evaluation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Non-invasive cardiac stress testing can help risk stratify surgical patients for perioperative cardiac complications and thereby better inform clinical care.

Current consensus based guidelines recommend non-invasive stress testing before surgery, but only in individuals with clinical risk factors for cardiac complications.

The effect of preoperative stress testing on postoperative clinical outcomes is unclear.

WHAT THIS STUDY ADDS

Preoperative stress testing was associated with reduced one year mortality, hospital stay, and hospital mortality.

These benefits largely applied to patients who were at high risk for cardiac complications on the basis of three or more clinical risk factors.

In contrast, stress testing was associated with only minor benefits for intermediate risk patients (one or two risk factors) and with harm in low risk individuals.
