# Association between self-reported functional capacity measures and postoperative myocardial injury in patients undergoing noncardiac surgeries

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#### Editorial

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# ABSTRAC T

**Background:** Self-reported functional capacity measures have an uncertain role in the pre-operative cardiovascular risk stratification.

**Aims:** This substudy aimed to evaluate whether self-reported metabolic equivalent (MET) could improve the prediction of postoperative myocardial injury (MI) over other well-established cardio-vascular risk factors.

**Methods:** This is a *post hoc* analysis of an international multicenter prospective cohort study. We recruited patients ≥45 years old who had elective elevated-risk noncardiac surgery in 45 centers across 17 countries between June 2017 and April 2020. The primary outcome was MI defined according to the Fourth Universal Definition of Myocardial Infarction. We measured the proportion of new prognostic information added by self-reported MET using multivariable logistic regression.

**Results:** In total, 860 (41.3%) patients suffered MI. In patients without systematic troponin surveillance, the odds ratio for MI with each 1-point increment in MET equaled 1.03 (95% confidence interval [CI], 0.99–1.07). The new prognostic information, according to the likelihood ratio adequacy index, accounted for 1.5%. Sensitivity analysis, including centers with >90% of patients with routine high-sensitivity troponin T monitoring, showed that MET added 21.8% of new information to the baseline model, and each additional point was associated with a lower risk of MI (odds ratio, 0.86; 95% CI, 0.81–0.91).

**Conclusions:** In elevated-risk noncardiac surgery, self-reported functional capacity measures do not significantly improve the prediction of MI; however, they add new prognostic information in centers with routine perioperative troponin monitoring.

**Key words:** cardiovascular complications, functional capacity, myocardial injury, perioperative medicine, risk assessment

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# WHAT'S NEW?

This international multicentric prospective observational study included more than 2000 patients  $\geq$ 45 years old who had elective in-patient elevated-risk noncardiac surgery. It showed that self-reported functional capacity measures did not improve the prediction of myocardial injury in the absence of systematic surveillance for this complication. Conversely, a *post hoc* analysis demonstrated that significant new prognostic information was provided by self-reported functional capacity measures in the centers with routine high-sensitivity troponin T monitoring. This finding is important in terms of the association between postoperative myocardial injury and patients' outcomes and the ongoing trials assessing measures to prevent this complication.

# INTRODUCTION

Aside from its potential to improve the patient's condition, every surgery is inherently associated with a risk of intraoperative and postoperative complications. Despite significant advances in surgical and anesthetic techniques over the last decades, postoperative complications after noncardiac procedures occur frequently and are related to increased mortality. Cardiovascular complications, including myocardial injury (MI), are most common and most significantly related to worse outcomes, which is strongly linked to short-term mortality in this population [1, 2].

Taking into account the ever-increasing age and the number of comorbidities among surgical candidates, precise cardiovascular risk stratification becomes one of the pillars of contemporary peri-operative medicine [3]. At the same time, evidence of the clinical utility of the most widely used clinical indices is contradictory, even for major cardiovascular events [4]. Unfortunately, none of the currently available tools designed to estimate the risk of MI have been externally validated yet [5].

The recommendations for including subjective evaluation of the functional capacity of the patient in pre-operative risk assessment differ depending on the guidelines [6-8]. A recent large observational cohort study weakened the recommendation for objective measurement of functional capacity using exercise testing in the pre-operative risk stratification [9]. It remains uncertain whether metabolic equivalents (METs) estimated with a structured guestionnaire could predict postoperative MI reliably. The MET: REevaluation for Peri-operative cArdlac Risk (MET-REPAIR) was a large prospective cohort study that assessed the predictive value of self-reported METs and other self-reported measures of functional capacity for a variety of cardiovascular events in patients at elevated cardiovascular risk after noncardiac surgery. Considering the low utility of functional capacity assessment in predicting major cardiovascular events, we hypothesized that its potential to predict MI will be limited as well [10].

The primary objective of this substudy was to evaluate whether self-reported METs could improve the prediction of postoperative MI over other well-established cardiovascular risk factors. Secondary objectives were to evaluate the added value of simpler measures of functional capacity in this context as well as to estimate the incidence of MI and its association with short-term mortality and incidence of major adverse cardiovascular events (MACE).

# METHODS

# Study design and setting

This was a substudy of MET-REPAIR (ClinicalTrials.gov ID: NCT03016936), an international multicenter prospective cohort study [11]. Patients included in this cohort were enrolled between June 2017 and April 2020 in the 45 centers (17 countries) that reported that they had systematic troponin surveillance protocols in the survey conducted at the beginning of the study. All patients signed written informed consent except for the centers in which the local ethical board provided written exemption from this requirement. Local or national Principal Investigators were responsible for obtaining ethical approval. The study protocol complied with the Helsinki Declaration and its amendments.

#### **Study population**

The pre-operative centers screened their surgical schedules for potential study participants. There were the following inclusion criteria for the MET-REPAIR study:

- 1. Patients scheduled for in-patient noncardiac surgery;
- Patients aged ≥45 years and undergoing elective elevated-risk noncardiac surgery as defined by either an Revised Cardiac Risk Index (RCRI) ≥2 or the National Surgical Quality Improvement Program Myocardial Infarction & Cardiac Arrest (NSQIP MICA) >1%; OR patients aged ≥65 years and undergoing elective intermediate or high-risk procedures.

The exclusion criteria were as follows:

- 1. Non-elective surgery, i.e., planned for ≤72 hours after diagnosis of the condition that made surgery necessary;
- Acute coronary syndrome or uncontrolled congestive heart failure within 30 days of the planned surgery;
- 3. Stroke within 7 days of the planned surgery;
- 4. Outpatient surgery;
- Patients unable to ambulate due to congenital or longstanding illnesses or conditions (e.g., paraplegics, polio). (Patients undergoing orthopedic surgery were NOT excluded);
- 6. Patients unable to complete the study questionnaire;
- 7. Patients unable to consent or unwilling to participate;
- 8. Previous enrolment in MET-REPAIR.

An additional criterion for this substudy was perioperative troponin surveillance. Notably, centers were not required to perform peri-operative troponin surveillance in all patients. Hence, the proportion of patients with peri-operative troponin monitoring differed across centers.

# Definition and assessment of endpoints

The main outcome was MI defined according to the Fourth Universal Definition of Myocardial Infarction, i.e., elevated cardiac troponin values with at least one value above the 99<sup>th</sup> percentile upper reference limit after surgery during hospitalization [12]. The troponin monitoring depended on the local protocol and differed in sampling time points, assays used, and population submitted to systematic sampling. The centers followed their local protocol for management in cases of MI. The study protocol did not include any mandatory additional tests in the case of elevated troponin levels, and further management was left to the treating clinician's decision.

We additionally assessed an association of MI both with 30-day mortality and 30-day MACE defined as a composite of intra- or postoperative in-hospital cardiovascular mortality, non-fatal cardiac arrest, acute myocardial infarction, stroke, and congestive heart failure requiring transfer to a higher unit of care or resulting in prolongation of stay in intensive care unit/intermediate care for ≥24 hours. The outcome was adjudicated by the local Principal Investigators based on standardized definitions after a review of in-hospital records and documents obtained during the 30-day follow-up.

Patients were followed up until hospital discharge or in-hospital death or up to 30 days if the length of stay exceeded 30 days.

## Measures of self-reported functional capacity

The primary measure of self-reported functional capacity was METs estimated using a 10-item questionnaire [13]. Patients completed the questionnaire  $\leq$ 30 days before surgery. As predefined, in the primary analyses, we used the METs defined according to the question corresponding to the highest level of exertion that was answered with "yes" without any preceding "no" to represent the patient's functional capacity. This rule was also applied if responses to any questions were missing. We additionally assessed maximal METs, defined as the question corresponding to the highest level of exertion that was answered with "yes" regardless of answers to previous questions. If at least one answer was missing, the patient was not included in the analysis (n = 5).

Secondary measures used in the analyses were the patient's:

- 1. Ability to climb stairs (number of floors);
- 2. Level of dependency;
- Self-perceived own cardiovascular fitness compared to their peers;
- 4. Their daily and weekly physical activity patterns.

# Statistical analysis

Categorical variables were given as counts and percentages and compared using the  $\chi^2$  or Fischer's tests. Continuous

variables were reported as medians (interquartile ranges) or means (standard deviations) and compared using Mann–Whitney or Student's t-test as appropriate. Survival analysis was performed using a log-rank test and displayed as Kaplan–Meier curves. Patients lost to follow-up were censored on the day of discharge.

We used logistic regression to model MI. The baseline model included established cardiovascular risk factors: sex, age, coronary artery disease, diabetes mellitus, hypertension, peripheral vascular disease, chronic heart failure, chronic kidney disease requiring dialysis, history of cerebrovascular disease, and chronic obstructive pulmonary disease, as well as surgery risk category. We built six models by adding each of the evaluated functional capacity measures to the baseline model. The association between MI and categories in each tool was expressed as an odds ratio with 95% confidence intervals. For each model, including the functional capacity measure, we calculated the area under the receiver operating curve (AUROC) and compared it with the AUROC of the model, including only clinical variables with DeLong's test.

Additionally, we calculated the proportion of new information added by functional capacity measurement tools in addition to other predictors included in the model. We divided the likelihood ratio  $\chi^2$  test of each expanded model (LRa) by the likelihood ratio  $\chi^2$  test of the base-line model (LRb) to calculate the adequacy of the base model, which was later subtracted from one to calculate the proportion of new information from each functional capacity measure.

Fraction of new information = 
$$1 - \frac{LRa}{LRb}$$

We performed *post hoc* sensitivity analysis including the only 3 centers with more than 90% of patients undergoing high-sensitivity troponin T monitoring in the perioperative period. Due to a very low number of totally dependent patients in the sensitivity analysis cohort, we did not perform analyses with dependency level as functional capacity measurement.

This was a complete case analysis. Missingness maps for explanatory variables and variables included in the multivariable analysis are presented in the Supplementary material, *Figure S1*. A two-sided *P*-value <0.05 was considered statistically significant. All statistical analyses were performed using R version 4.0.3 (2020-10-10).

# RESULTS

#### Study population

Of 15 767 patients included in the MET-REPAIR study, we identified 2084 patients who fulfilled the inclusion criteria (Figure 1). Patient characteristics stratified and tested for differences based on the occurrence of MI are shown in Table 1.



Figure 1. Study flow chart

#### **Relationship between METs and MI**

The incidence of MI was 41.3% (860/2084). The median self-reported MET was 5 (interquartile range [IQR] 5–9), and the median maximal self-reported MET was 8 (IQR 6–9) — see the Supplementary material, *Figure S2*. Combined with established cardiovascular risk factors in a logistic regression model, self-reported METs (OR, 1.03; 95% CI, 0.99–1.07) and maximal self-reported METs (OR, 1.02; 95% CI, 0.98–1.07) provided no or very little additional prognostic information on MI and did not improve the calibration of the model (Table 2). The non-linear relationships between MI and self-reported METs are presented in Figure 2.

## Prognostic value of other self-reported measures

*Figure S2* presents the distribution of patients across categories in different tools used to assess their pre-operative functional capacity (i.e., number of floors that the patient can climb, level of dependency, patient's cardiorespiratory fitness compared to peers, and self-reported pattern of daily activity). The prognostic value of evaluated measures is summarized in Table 2.

# Diagnosis and prognosis of MI

Of 860 patients with MI, there were 5 cases of non-fatal ST-segment elevation myocardial infarctions (0.6%),

30 cases of non-fatal non-ST-segment elevation myocardial infarctions (3.5%), and 3 cases of fatal myocardial infarctions (0.3%) in a total of 38 patients. Patients who developed myocardial infarction more often suffered from congestive heart failure (39.5% vs. 18.1%; P = 0.002), peripheral vascular disease (34.2% vs. 13.1%; P = 0.001), and coronary artery disease (52.6% vs. 32.8%; P = 0.02) compared to those who suffered MI not meeting myocardial infarction criteria. The incidence of MI was 28.0% (23/82), 43.3% (517/1195), and 39.7% (320/807) for low-risk, intermediate-risk, and high-risk surgeries, respectively. The incidence of MI varied significantly depending on the procedure site (Figure 3; Supplementary material, Table S1). Information regarding troponin assays used in this study and the median maximal postoperative troponin values in patients who suffered MI are summarized in the Supplementary material, Table S2.

Occurrence of MI was associated with higher 30-day mortality (4.4% vs. 1.5%; log-rank *P* <0.001), higher incidence of 30-day MACE (7.2% vs., 1.7%; log-rank *P* <0.001), and a longer duration of hospital stay (8.0 vs. 6.0 days; *P* <0.001). The Kaplan–Meier curves comparing 30-day mortality and 30-day MACE between the MI and non-myocardial injury groups are presented in Figure 4.

#### Table 1. Patient characteristics

| Characteristics                             | Number of patients<br>(n = 2084) | Myocardial injury<br>(n = 860) | Non-myocardial injury<br>(n = 1224) | P-value |
|---|----------------------------------|--------------------------------|-------------------------------------|---------|
| Age, mean (SD)                              | 72.6 <b>(</b> 7.3)               | 73.75 <b>(</b> 7.49)           | 71.77 <b>(</b> 7.13)                | <0.001  |
| Female, n (%)                               | 808 (38.8)                       | 282 (32.8)                     | 526 (43.0)                          | < 0.001 |
| Functional status, n (%)                    |                                  |                                |                                     |         |
| Independent                                 | 1 710 (82.1)                     | 656 (76.4)                     | 1 054 (86.1)                        | < 0.001 |
| Partially dependent                         | 348 (16.7)                       | 189 (22.0)                     | 159 (13.0)                          |         |
| Totally dependent                           | 25 (1.2)                         | 14 (1.6)                       | 11 (0.9)                            |         |
| Surgical risk category <sup>a</sup> , n (%) |                                  |                                |                                     |         |
| Low risk                                    | 82 (3.9)                         | 23 (2.7)                       | 59 (4.8)                            | 0.01    |
| Moderate risk                               | 1 195 (57.3)                     | 517 (60.1)                     | 678 (55.4)                          |         |
| High risk                                   | 807 (38.7)                       | 320 (37.2)                     | 487 (39.8)                          |         |
| ASA scale, n (%)                            |                                  |                                |                                     |         |
| 1   | 18 (0.9)                         | 3 (0.3)                        | 15 (1.2)                            | <0.001  |
| 11  | 664 (31.9)                       | 180 (20.9)                     | 484 (39.6)                          |         |
| 111   | 1 330 (63.9)                     | 637 (74.1)                     | 693 (56.7)                          |         |
| IV  | 71 (3.4)                         | 40 (4.7)                       | 31 (2.5)                            |         |
| Diabetes, n (%)                             | 531 (25.5)                       | 241 (28.0)                     | 290 (23.7)                          | 0.03    |
| Hypertension, n (%)                         | 1 541 (74.0)                     | 663 (77.1)                     | 878 (71.8)                          | 0.008   |
| Chronic heart failure, n (%)                | 337 (16.2)                       | 164 (19.1)                     | 173 (14.1)                          | 0.003   |
| Coronary artery disease, n (%)              | 614 (29.5)                       | 290 (33.7)                     | 324 (26.5)                          | < 0.001 |
| Myocardial infarction, n (%)                | 281 (13.5)                       | 142 (16.5)                     | 139 (11.4)                          | 0.001   |
| History of PCI, n (%)                       | 366 (17.6)                       | 192 (22.3)                     | 174 (14.2)                          | < 0.001 |
| History of CABG, n (%)                      | 155 (7.4)                        | 85 (9.9)                       | 70 (5.7)                            | 0.001   |
| Peripheral vascular disease, n (%)          | 300 (14 4)                       | 121 (14 1)                     | 179 (14.6)                          | 0.77    |
| History of stroke/TIA, n (%)                | 206 (9.9)                        | 90 (10.5)                      | 116 (9 5)                           | 0.51    |
| Active cancer, n (%)                        | 1 100 (52 8)                     | 457 (53 1)                     | 643 (52.6)                          | 0.83    |
| COPD n (%)                                  | 284 (13.6)                       | 130 (15 1)                     | 154 (12.6)                          | 0.11    |
| History of dialysis. n (%)                  | 31 (1.5)                         | 24 (2.8)                       | 7 (0.6)                             | <0.001  |
| Surgery site n (%)                          | 51 (115)                         | 2 (210)                        | , (0.0)                             | 101001  |
| Anorectal                                   | 10 (0 5)                         | 6 (0 7)                        | 4 (0,3)                             | <0.001  |
| Aortic                                      | 176 (8.4)                        | 89 (10 3)                      | 87 (7 1)                            | 101001  |
| Bariatric                                   | 1 (0 0)                          | 0 (0 0)                        | 1 (0,1)                             |         |
| Brain                                       | 75 (3.6)                         | 27 (3.1)                       | 48 (3.9)                            |         |
| ENT (not thyroid/parathyroid)               | 141 (6.8)                        | 70 (8 1)                       | 71 (5.8)                            |         |
| Foregut/Hepatopancreatobiliary              | 366 (17.6)                       | 156 (18.1)                     | 210 (17.2)                          |         |
| Gallbladder, appendix, adrenal and spleen   | 37 (1.8)                         | 6 (0 7)                        | 31 (2.5)                            |         |
| Hernia (ventral, inquinal, femoral)         | 23 (1.1)                         | 2 (0.2)                        | 21 (1.7)                            |         |
| Intestinal                                  | 214 (10.3)                       | 67 (7.8)                       | 147 (12.0)                          |         |
| Neck  | 9(0.4)                           | 3 (0 3)                        | 6 (0.5)                             |         |
| Obstetric/Gynecologic                       | 55 (2.6)                         | 10 (1.2)                       | 45 (3.7)                            |         |
| Orthopedic and non-vascular extremity       | 183 (8.8)                        | 59 (6.9)                       | 124 (10.1)                          |         |
| Other abdominal                             | 150 (7.2)                        | 68 (7.9)                       | 82 (6.7)                            |         |
| Peripheral vascular                         | 163 (7.8)                        | 62 (7.2)                       | 101 (8.3)                           |         |
| Skin  | 11 (0.5)                         | 8 (0.9)                        | 3 (0.2)                             |         |
| Spine                                       | 144 (6.9)                        | 79 (9.2)                       | 65 (5.3)                            |         |
| Non-esophageal thoracic                     | 126 (6.0)                        | 67 (7.8)                       | 59 (4.8)                            |         |
| Urology                                     | 200 (9.6)                        | 81 (9.4)                       | 119 (9.7)                           |         |
| Smoking status, n (%)                       | (>>>)                            | (***)                          |                                     |         |
| Active                                      | 334 (16.2)                       | 142 (16.7)                     | 192 (15.8)                          | 0.052   |
| Former                                      | 617 (29.9)                       | 276 (32.4)                     | 341 (28.1)                          |         |
| Never                                       | 1 114 (53.9)                     | 433 (50.9)                     | 681 (56.1)                          |         |
| Self-reported MET, median (IOR)             | 5 (5–9)                          | 5 (5-9)                        | 5 (5-9)                             | 0.91    |
| Maximal self-reported MET, median (IOR)     | 8 (6–9)                          | 8 (5-9)                        | 8 (6–9)                             | 0.84    |

<sup>a</sup>Risk categories based on 2014 European Society of Cardiology/European Society of Anaesthesiology guidelines on noncardiac surgery

Abbreviations: ASA, American Society of Anesthesiology; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; ENT, ear, nose and throat; IQR, interquartile range; MET, metabolic equivalent; PCI, percutaneous coronary intervention; SD, standard deviation; TIA, transient ischemic attack

Table 2. Summary of multivariable analysis, fraction of new information and comparison of the receiver operating curve (AUROC) with baseline model (AUROC = 0.641) from different self-reported functional capacity measures

| Measure                                     | OR (95% CI)       | Fraction of new infor-<br>mation | AUROC,<br><i>P</i> -value vs. baseline<br>model |
|---|-------------------|----------------------------------|---|
| Self-reported METS (continuous)             | 1.03 (0.99 –1.07) | 1.5%                             | 0.642 ( <i>P</i> = 0.79)                        |
| Maximal self-reported METS (continuous)     | 1.02 (0.98 - 1.07 | 0.2%                             | 0.642 ( <i>P</i> = 0.86)                        |
| Number of climbed floors                    |                   |                                  |   |
| <1  | 1.41 (0.95–2.10)  | 5.5%                             | 0.645   |
| 1   | 1.06 (0.74–1.51)  |                                  | (P = 0.37)                                      |
| 2   | 1.17 (0.85–1.61)  |                                  |   |
| 3   | 1.37 (0.98–1.92)  |                                  |   |
| 4   | 1.02 (0.71–1.47)  |                                  |   |
| >4  | Reference         |                                  |   |
| Dependency level                            |                   |                                  |   |
| Independent                                 | Reference         | 15.5%                            | 0.652   |
| Partially dependent                         | 1.82 (1.42–2.34)  |                                  | ( <i>P</i> = 0.06)                              |
| Totally dependent                           | 1.78 (0.79–4.05)  |                                  |   |
| Cardiorespiratory fitness compared to peers |                   |                                  |   |
| Lower                                       | 1.35 (1.08–1.68)  | 6.6%                             | 0.646   |
| Same  | Reference         |                                  | ( <i>P</i> = 0.30)                              |
| Higher                                      | 1.23 (0.98–1.54)  |                                  |   |
| Pattern of daily activity                   |                   |                                  |   |
| Inactive                                    | 0.80 (0.60–1.05)  | 12.8%                            | 0.650<br>( <i>P</i> = 0.11)                     |
| Low activity                                | 0.62 (0.47-0.81)  |                                  |   |
| 20–60 min/week                              | 0.63 (0.44–0.90)  |                                  |   |
| 1–3 h/week                                  | 1.03 (0.76–1.40)  |                                  |   |
| >3 h/week                                   | Reference         |                                  |   |

Abbreviation: CI, confidence interval; METS, metabolic equivalents; OR, odds ratio

# Sensitivity analysis

The sensitivity analysis included 1214 patients recruited in 3 centers, with >90% of patients undergoing peri-operative high-sensitivity troponin T monitoring. The incidence of MI in this subgroup was 58.2% (706/1214), while in patients recruited in centers with a lower troponin monitoring coverage, the MI rate was 17.7% (154/870). In this analysis, self-reported METs added 21.8% of new prognostic information about the MI to the baseline model, and each additional point was associated with a lower risk of MI (OR, 0.86; 95% CI, 0.81–0.91). The summary of multivariable analyses, the proportion of added information, and AU-ROCs are presented in the Supplementary material, *Table S3*. The non-linear association between the incidence of MI and self-reported METs is illustrated in Figure 2.

# DISCUSSION

In this multicenter prospective cohort study including more than 2000 patients at increased peri-operative cardiovascular risk undergoing noncardiac surgery, we showed that self-reported functional capacity assessed using a 10-item questionnaire does not improve the prediction of MI over established cardiovascular risk factors and is outperformed by simpler tools. However, sensitivity analysis indicated that using the same questionnaire in centers with common high-sensitivity troponin monitoring provided valuable prognostic information on MI. This might be explained by the fact that MI will only be sufficiently detected with routine monitoring because it escapes algorithms based on clinical attention. Finally, we confirmed that MI is a common complication related to poorer short-term outcomes.

Myocardial injury, despite being asymptomatic in almost 70% of cases, accounts for 16% of short-term mortality in patients undergoing noncardiac surgery [14]. The incidence of MI in our study exceeded 40% and was 2-4 times higher compared to previous reports. It was particularly high in centers with >90% routine high-sensitivity troponin T monitoring coverage (60%) but relatively low in centers with a lower number of patients with troponin monitoring (17.7%). There are several factors at least partially explaining this difference. First, the MI definition in this study was based on the Fourth Definition of Myocardial Infarction, which is markedly more liberal than the one used in the previous cohorts [12, 15–17]. Second, contrary to the VISION study, this sample consisted of patients with increased cardiovascular risk, hence a particularly high incidence of complications. This study has corroborated several previous reports and suggested an association between MI and increased short-term mortality and MACE incidence [14, 16-22].

Despite the significant impact of MI on patient outcomes, peri-operative medicine practitioners remain unequipped with reliable predictive tools. Their development is becoming more and more important in light of the emerging evidence on effective treatments as well as ongoing trials assessing ways to prevent this complication (NCT05279651) [23]. Commonly used peri-operative cardiac risk assessment indices such as RCRI and NISQIP MICA



Figure 2. Non-linear relationship between self-reported metabolic equivalents (METS) and myocardial injury incidence

Figures represent non-linear relationships between myocardial injury incidence and (A) self-reported METS and (B) maximal MET. Median values of self-reported METS (= 5) and maximal MET (= 8) were selected as reference values. The black line represents OT while the grey area represents a 95% confidence interval (CI)

perform unsatisfactorily in the era of high-sensitivity troponin assays and routine peri-operative troponin monitoring [24, 25]. Our recent article showed a lack of association between preoperative electocardiogram abnormalities and MI in high-risk patients [26]. The approach to functional capacity as another element of risk stratification varies in the current peri-operative assessment guidelines for noncardiac surgery. The 2014 American College of Cardiology/American Heart Association guidelines suggest that patients with poor functional capacity (METs <4) may warrant cardiac imaging stress testing depending on the patient- and procedure-related risk. Conversely, the authors of the guidelines issued in 2022 by the European Society of Cardiology endorsed by the European Society of Anaesthesiology and Intensive Care decided to shift from self-reported MET assessment toward the patient's declaration of his/her ability to climb  $\geq 2$  flights of stairs. Importantly, all recommendations on using functional capacity in pre-operative risk assessment are based on

low- or moderate-quality evidence [6, 7, 27]. The Canadian Cardiovascular Society did not issue any recommendations on the role of functional capacity assessment in this clinical context due to the low quality of evidence, based mainly on several small prospective studies and one large retrospective study showing contradictory results on the association between functional capacity and postoperative complications [8, 28, 29].

New evidence eventually emerged in 2018 when Wijeysundera et al. [9] published the results of a prospective study including more than 1400 patients undergoing major noncardiac surgery. This study showed no association between postoperative complications and the patient's functional capacity assessed subjectively by the clinician. The Duke Activity Status Index (DASI) score was associated with 30day death or myocardial infarction and 30-day death or MI and showed significant risk reclassification for the latter outcome, but it did not improve discrimination expressed by the receiver operating characteristic area under the curve



Figure 3. The incidence of myocardial injury stratified by different sites of surgery

After stratification by site of the surgery the median myocardial injury incidence was 39.5% (IQR 31.83–50.35). The *P*-value for difference in myocardial injury incidence between surgery sites was <0.001



**Figure 4.** Kaplan–Meier curve for 30-day mortality and MACE Abbreviation: MACE, major adverse cardiovascular events

[9]. The findings of this METREPAIR substudy are in line with those findings as the discrimination for MI of models including self-reported measures of functional capacity were not improved. Moreover, the inclusion of self-reported METs added as little as 1.5% of new information to the model with well-established cardiovascular risk factors. To account for selection bias, we performed sensitivity analysis limited to centers that performed peri-operative high-sensitivity troponin T monitoring in >90% of METREPAIR participants. In such circumstances, all measures of self-reported functional capacity significantly improved predictive value (receiver operating characteristic area under the curve) over clinical risk factors. However, the effect size was limited, and discrimination remained modest.

In our opinion, the poor performance of self-reported METs in the prediction of MI is multifactorial. First, objective measurement of peak oxygen consumption and anabolic threshold did not improve pre-operative risk assessment, therefore weakening the hypothesized link between functional capacity and postoperative outcome [9]. Second, the correlation between self-reported functional capacity and fitness measured objectively using cardiopulmonary exercise testing is moderate [13]. Finally, a questionnaire based on daily life activities is not specific for the detection of functional limitations related to cardiovascular systems and may overestimate potential cardiovascular risk in patients with other medical problems such as osteoarthritis, hernias, or spinal stenosis, which is well reflected by particularly low self-reported METs in these surgical categories in our study.

Both the MET subsection of the MET-REPAIR questionnaire and the DASI guestionnaire offer insight into patients' functional capacity by comprehensively assessing their ability to perform everyday activities and therefore are rather complex indices containing 10 and 12 items, respectively [13, 30]. Our study shows that each of the simpler functional capacity measures added more new prognostic value to the baseline model compared to the MET-REPAIR questionnaire, thus suggesting their potential as predictors of peri-operative MI. The highest proportion of new prognostic information was found for patients' dependency status, which has already been linked to postoperative outcomes in patients undergoing noncardiac surgery [31]. Moreover, lower self-perceived cardiorespiratory fitness compared to peers was related to a higher risk of MI, which is in line with previous reports linking this measure to cardiovascular disease and mortality in a non-surgical context [32].

Finally, we found no statistically significant association between the ability to climb stairs and the incidence of MI. However, the inability to ascend even one floor was related to an over 40% increase in the risk of MI, with a confidence interval ranging from 0.95 to 2.10. This is at least partially in line with the accumulating evidence on the association between major short- and long-term postoperative cardiovascular complications and pre-operative self-reported ability to climb stairs, which is now one of the recommended measures of functional capacity in the peri-operative management guidelines [10, 27, 33]. One should note that none of the simpler tools improves model discrimination assessed with AUROC, and the direction of their association is counterintuitive in some instances, e.g., lower pre-operative activity is related to lower incidence of MI. To conclude, less complex functional capacity measures seem to add more new information over well-established risk factors in predicting MI compared to the MET subsection of the MET-REPAIR questionnaire. However, their clinical utility in this clinical context requires further research.

We believe that significant differences between the results in the main analysis and the sensitivity analysis

warrant attention from both clinicians and researchers. For the first group, it is an important signal that, assuming appropriate monitoring of MI, self-reported METs could potentially become a simple and useful predictive tool in patients undergoing noncardiac surgery. For the latter group, it demonstrates an urgent need to perform a study focused on the role of self-reported functional capacity in predicting postoperative MI in this population. Such a study should be based on a large cohort of patients in whom perioperative high-sensitivity troponin monitoring is performed routinely to minimize the risk of overlooking these largely asymptomatic complications, and only then will we be able to clarify the issue of the predictive value of self-reported functional capacity in this clinical scenario.

The main strength of this article is a large sample of patients undergoing noncardiac surgery in whom self-reported functional capacity measurement was performed. We are, however, aware of several limitations of this study. First, we did not gather data on pre-operative troponin levels, which prevented us from differentiating acute and chronic postoperative troponin elevation. Second, we used the MI definition included in the Fourth Universal Definition of Myocardial Infarction, which resulted in an exceedingly high incidence of this complication. Third, there was no universal troponin surveillance protocol in this study, and we could not determine the exact number and timing of postoperative troponin measurements. Thus, there is a significant risk of bias related to a potentially large inter-center heterogeneity. To address this issue, we performed sensitivity analysis including only centers with routine high-sensitivity troponin T measurement; however, readers should be aware that such an approach only partially reduces the aforementioned heterogeneity. This study was performed between 2017 and 2020, and therefore the approach to perioperative troponin monitoring did not reflect the current guidelines according to which the vast majority of our cohort would require high-sensitivity troponin measurements before and at 24 hours and 48 hours after the procedure [27]. Fifth, this study cohort represented approximately 13% of the total MET-REPAIR cohort which may have increased the risk of selection bias. Finally, data on troponin assay were available only in patients in whom MI was diagnosed, and we could not perform additional sensitivity analyses in different subgroups depending on troponin assay (particularly high-sensitivity vs. standard sensitivity assays).

# CONCLUSION

This prospective observational study, including patients with increased cardiovascular risk undergoing noncardiac surgery, demonstrated that self-reported functional capacity has limited predictive value when MI is not sought systematically. It showed that some of the simpler tools appear to outperform a dedicated 10-item questionnaire in this regard, albeit the discrimination of the model remains limited. However, the *post hoc* sensitivity analysis suggested that in centers with routine perioperative high-sensitivity troponin monitoring self-reported functional capacity could be a useful tool in this clinical context. Finally, this study confirms that MI is a common postoperative complication related to higher 30-day mortality and MACE incidence.

#### Supplementary material

Supplementary material is available at https://journals. viamedica.pl/polish\_heart\_journal.

#### Article information

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