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

Short title: Functional capacity in the prediction of myocardial injury

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WHAT'S NEW?

This international multicentric prospective observational study including more than 2000 patients ≥45 years old having elective, in-patient, elevated-risk noncardiac surgery showed that self-reported functional capacity measures do not improve the prediction of myocardial injury in the context of no systematic surveillance towards this complication. Conversely, a post-hoc analysis revealed a significant new prognostic information provided by self-reported functional capacity measures in centres with routine high-sensitivity troponin T monitoring. This finding is important in terms of association between postoperative myocardial injury and patients' outcomes and the ongoing trials assessing measures to prevent this complication.

ABSTRACT

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

Aim: The aim of this substudy was to evaluate whether self-reported metabolic equivalent (MET) could improve the prediction of postoperative myocardial injury over other well-established cardiovascular risk factors.

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

Results: 860 (41.3%) patients suffered a myocardial injury. In patients without systematic troponin surveillance the odds ratio for myocardial injury with each 1-point increment in MET equalled 1.03 (95% confidence interval [CI], 0.99–1.07). The new prognostic information, according to the likelihood ratio adequacy index, accounted to 1.5%. Sensitivity analysis,

including centres with >90% of patients with routine high-sensitivity troponin T monitoring, revealed that MET added 21.8% of new information to the baseline model, and each additional point was associated with a lower risk of myocardial injury (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 myocardial injury, however they add new prognostic information in centres with routine perioperative troponin monitoring.

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

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 improvements in surgical and anesthetic techniques over the last decades, postoperative complications occur frequently and are related to increased mortality after noncardiac procedures. The most common and most significantly related to worse outcomes are cardiovascular complications, including myocardial injury, 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 myocardial injury 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 position of 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 questionnaire could predict postoperative myocardial injury reliably. The MET: REevaluation for Peri-operative cArdIac Risk (MET-REPAIR) is a large prospective cohort study that assesses 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 the prediction of major cardiovascular events, we hypothesized that its potential to predict myocardial injury 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 myocardial injury over other well-established cardiovascular risk factors. Secondary objectives were to evaluate the added value of simpler measures of functional capacity in this regard as well as to estimate the incidence of myocardial injury 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 multicentre prospective cohort study [11]. Patients included in this subcohort were enrolled between June 2017 and April 2020. The patients were recruited in the 45 centres (17 countries), reporting to have systematic troponin surveillance protocols in the survey conducted at the beginning of the study. All patients signed a written informed consent except for centres for which the responsible, ethical board provided written exemption from this requirement. Local or national Principal Investigators were responsible for obtaining ethical approval. The study protocol complied with Helsinki Declaration and its amendments.

Study population

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

- (1) Patients scheduled for in-patient noncardiac surgery;
- (2) Patients aged ≥45 years and undergoing elective elevated-risk noncardiac surgery as defined by either an RCRI ≥2 or NSQIP MICA >1%; OR patients aged ≥65 years of age 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 it necessary;
- (2) 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;
- (5) Patients unable to ambulate due to congenital or longstanding illnesses or conditions (e.g., paraplegics, polio). (Patients undergoing orthopedic surgery were NOT excluded);
- (6) Unable to complete the study questionnaire;
- (7) Unable to consent or unwilling to participate;
- (8) Previous enrolment in MET-REPAIR.

An additional criterion for this substudy was peri-operative troponin surveillance. Of note, it was not required for the centre to perform peri-operative troponin surveillance in all patients. Hence, the proportion of patients with peri-operative troponin monitoring differed across centres.

Definition and assessment of endpoints

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

We additionally assessed the association of myocardial injury 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 a prolongation of stay on 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 the 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;
- (3) Self-perceived own cardiovascular fitness compared to their peers;
- (4) Their daily and weekly physical activity patterns.

Statistical analysis

Categorical variables were summarized as counts and percentages and compared using the chisquare or Fischer test. Continuous variables were reported as median (interquartile range) or mean (standard deviation) and compared using Mann–Whitney or Student T test as appropriate. Survival analysis was performed using a log-rank test and presented on Kaplan–Meier curves. Patients lost to follow-up were censored on the day of discharge.

We used logistic regression to model myocardial injury. 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 myocardial injury and categories in each tool was expressed as an odds ratio with 95% confidence intervals. For each model, including 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 fraction of new information added by functional capacity measurement tools on top of other predictors included in the model. We divided the likelihood ratio chi-square test of each expanded model (LRa) by the likelihood ratio chi-square test of the baseline model (LRb) to calculate the adequacy of the base model, which was later subtracted from one to calculate the fraction of new information from each functional capacity measure.

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

We performed a *post hoc* sensitivity analysis including the only 3 centres with more 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 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 myocardial injury are shown in Table 1.

Relationship between METs and myocardial injury

The incidence of myocardial injury 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 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 myocardial injury and did not improve the calibration of the model (Table 2). Non-linear relationships between myocardial injury 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 myocardial injury

Of 860 patients with myocardial injury, there were 5 non-fatal ST-elevation myocardial infarctions (0.6%), 30 non-fatal non-ST-elevation myocardial infarctions (3.5%), and 3 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 myocardial injury not meeting myocardial infarction criteria. The incidence of myocardial injury was 28.0% (23/82), 43.3% (517/1195), and 39.7% (320/807) for low-risk, intermediate-risk, and high-risk surgeries. The incidence of myocardial injury 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 myocardial injury are summarized in Supplementary material, *Table S2*.

Occurrence of myocardial injury 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). Kaplan–Meier curves comparing 30-day mortality and 30-day MACE between myocardial injury and non-myocardial injury groups are presented in Figure 4.

Sensitivity analysis

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

DISCUSSION

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

Myocardial injury, despite being asymptomatic in almost 70% of cases, contributes to approximately 16% of short-term mortality in patients undergoing noncardiac surgery [14]. The incidence of myocardial injury in our study exceeds 40% and is 2–4 times higher compared to previous reports. It was particularly high in centres with >90% routine high-sensitivity troponin T monitoring coverage (60%) but relatively low in centres with a lower number of patients with troponin monitoring (17.7%). There are several factors at least partially explaining this difference. First, the myocardial injury 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 consists of patients with increased cardiovascular risk, hence a particularly high incidence of complications. This study corroborates several previous reports and suggests an association between myocardial injury and increased short-term mortality and MACE incidence [14, 16–22].

Despite the significant impact of myocardial injury on patients` outcomes, perioperative medicine practitioners remain unequipped with reliable predictive tools. Their development is becoming more and more important in the 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 perform unsatisfactorily in the era of high-sensitivity troponin assays and routine peri-operative troponin monitoring [24, 25]. Our recent paper showed lack of association between preoperative ECG abnormalities and myocardial injury 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

decided to shift from self-reported METs assessment towards the ability to climb ≥ 2 flights of stairs declared by the patient. Importantly, all recommendations pertaining to the utilisation of 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 recommendation 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 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 DASI score was associated with 30-day death or myocardial infarction and 30-day death or myocardial injury 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 [9]. The findings of this METREPAIR substudy are in line with those findings as the discrimination for myocardial injury 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 a model with well-established cardiovascular risk factors. To account for selection bias, we performed a sensitivity analysis limited to centres which performed perioperative 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 myocardial injury 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 living 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 METs subsection of the MET-REPAIR questionnaire and DASI questionnaire 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 myocardial injury. The highest fraction 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 myocardial injury, 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 myocardial injury. However, the inability to climb even one floor was related to an over 40% increase in the risk of myocardial injury, with a confidence interval ranging from 0.95 to 2.10. The latter 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 myocardial injury. To conclude, less complex functional capacity measures seem to add more new information over well-established risk factors to the prediction of myocardial injury compared to the METs 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 the researchers. For the first group, it is an important signal that, assuming appropriate monitoring towards myocardial injury, 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 prediction of postoperative myocardial injury in this population. Such 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 this largely asymptomatic complications and only then we

will be able to clarify the issue of predictive value of self-reported functional capacity in this clinical scenario.

The main strength of this paper 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 preoperative troponin level, which prevented us from differentiating acute and chronic postoperative troponin elevation. Second, we used the myocardial injury definition included in the 4th 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 are unable to determine the exact number and timing of postoperative troponin measurements. Thus, there is a significant risk of bias related to a potentially large inter-centre heterogeneity in this aspect. To address this issue we performed a sensitivity analysis including only centres with routine high-sensitivity troponin T measurement, however the readers should be aware that such approach only partially reduces the aforementioned heterogeneity. This study was performed between 2017 and 2020 and therefore the approach to perioperative troponin monitoring does not reflect the current guidelines according to which vast majority of our cohort would require high-sensitivity troponin measurements before and at 24 h and 48 h after the procedure [27]. Fifth, this susbstudy cohort represents approximately 13% of the total MET-REPAIR cohort which may increase the risk of the selection bias. Finally, data on troponin assay is available only in patients in whom the myocardial injury was diagnosed, and we are unable to 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, proved that self-reported functional capacity has limited predictive value when myocardial injury is not sought for in a systematic manner. It revealed 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 suggests that in centres with routine perioperative high-sensitivity troponin monitoring self-reported functional capacity may be a useful tool in this clinical context. Finally, this study confirms that myocardial injury 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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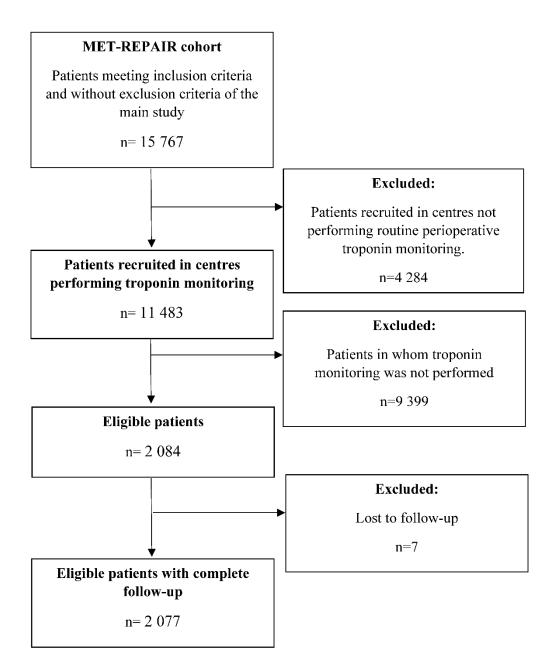


Figure 1. Study flow chart

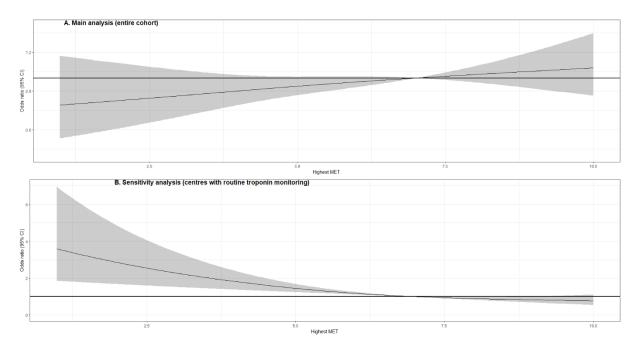


Figure 2. Non-linear relationship between self-reported metabolic equivalents (METS) and myocardial injury incidence

Figures represent non-linear relationships between myocardial injury incidence and ($\bf A$) self-reported METS and ($\bf B$) 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



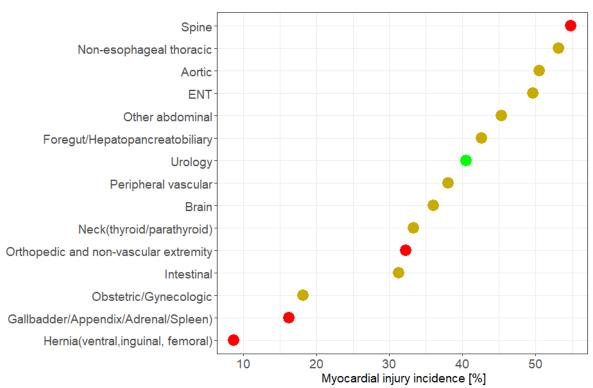


Figure 3. The incidence of myocardial injury stratified by different sites of surgery After stratification by site of the surgery the median myocardial injury incidence was 39.5% (IQR, 31.83–50.35). The *P*-value for difference in myocardial injury incidence between surgery sites was

< 0.001

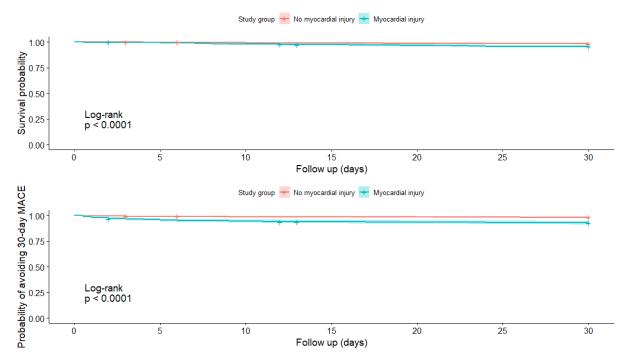


Figure 4. Kaplan–Meier curve for 30-day mortality and MACE Abbreviations: MACE, major adverse cardiovascular events

 Table 1. Patient characteristics

Characteristics	Number of patients	Myocardial injury	No myocardial injury	<i>P</i> -value
	(n = 2084)	(n = 860)	(n = 1224)	
Age, mean (SD)	72.6 (7.3)	73.75 (7.49)	71.77 (7.13)	< 0.001
Female, n (%)	808 (38.8)	282 (32.8)	526 (43.0)	< 0.001
Functional status, n (%)				< 0.001
Independent	1 710 (82.1)	656 (76.4)	1 054 (86.1)	
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 ^a , n (%)				0.01
Low risk	82 (3.9)	23 (2.7)	59 (4.8)	
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(%)				< 0.001
Ι	18 (0.9)	3 (0.3)	15 (1.2)	
II	664 (31.9)	180 (20.9)	484 (39.6)	
III	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 (%)				< 0.001
Anorectal	10 (0.5)	6 (0.7)	4 (0.3)	
Aortic	176 (8.4)	89 (10.3)	87 (7.1)	
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, inguinal, 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(%)				0.052
Active	334 (16.2)	142 (16.7)	192 (15.8)	
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 (IQR)	5 (5–9)	5 (5–9)	5 (5–9)	0.91
Maximal self-reported MET, median (IQR)	8 (6–9)	8 (5–9)	8 (6–9)	0.84

^aRisk categories based on 2014 European Society of Cardiology/European Society of Anaesthesiology guidelines on non-cardiac 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	AUROC,
		new	P-value vs.
		information	baseline
			model
Self-reported METS (continuous)	1.03 (0.99 to 1.07)	1.5%	0.642
		1.3%	(P = 0.79)
Maximal self-reported METS	1.02 (0.98 to 1.07	0.204	0.642
(continuous)		0.2%	(P = 0.86)
Number of climbed floors			
<1	1.41 (0.95 to 2.10)		
1	1.06 (0.74 to 1.51)		0.645
2	1.17 (0.85 to 1.61)	5.5%	0.645
3	1.37 (0.98 to 1.92)		(P = 0.37)
4	1.02 (0.71 to 1.47)		
>4	Reference		
Dependency level			
Independent	Reference	15.5%	0.652
Partially dependent	1.82 (1.42 to 2.34)	13.370	(P = 0.06)
Totally dependent	1.78 (0.79 to 4.05)		
Cardiorespiratory fitness compared to			
peers			0.646
Lower	1.35 (1.08 to 1.68)	6.6%	(P = 0.30)
Same	Reference		(I = 0.30)
Higher	1.23 (0.98 to 1.54)		
Pattern of daily activity			
Inactive	0.80 (0.60 to 1.05)		
Low activity	0.62 (0.47 to 0.81)	12.8%	0.650
20-60 min/week	0.63 (0.44 to 0.90)	12.070	(P = 0.11)
1–3 h/week	1.03 (0.76 to 1.40)		
>3 h/week	Reference		

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