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ORIGINAL ARTICLE

Immediate postoperative high-sensitivity troponin T concentrations and long-term patient-reported health-related quality of life

A prospective cohort study

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BACKGROUND Myocardial injury after noncardiac surgery is associated with mortality and major adverse postoperative cardiovascular events. The effect of postoperative troponin concentrations on patient-reported health-related quality of life (HRQoL) is unknown.

OBJECTIVE The study examined the association between immediate postoperative troponin concentrations and self-reported HRQoL 1 year after surgery.

DESIGN Prospective cohort study.

SETTING Single-centre tertiary care hospital in the Netherlands between July 2012 and 2015.

PATIENTS Patients aged at least 60 years undergoing moderate and major noncardiac surgery.

INTERVENTION None.

MAIN OUTCOME MEASURES HRQoL total score was assessed with the EuroQol five-dimensional questionnaire. Tobit regression analysis was used to determine the association between postoperative troponin concentrations and 1-year HRQoL. Peak high-sensitivity troponin T values were divided into four categories: less than 14, 14 to 49, 50 to 149 and at least 150 ng l^{-1}.

RESULTS A total of 3085 patients with troponin measurements were included. 2634 (85.4%) patients were alive at 1-year follow-up of whom 1297 (49.2%) returned a completed questionnaire. The median score for HRQoL was 0.82 (0.85, 0.81, 0.77 and 0.71 per increasing troponin category). Multivariable analysis revealed betas of −0.06 [95% confidence interval (CI) −0.09 to −0.02], −0.11 (95% CI −0.18 to −0.04) and −0.18 (95% CI −0.29 to −0.07) for troponin levels of 14 to 49, 50 to 149 and at least 150 ng l^{-1} when compared with values less than 14 ng l^{-1}. Other independent predictors for lower HRQoL were chronic obstructive pulmonary disease, female sex, peripheral arterial disease and increasing age.

CONCLUSION Higher levels of postoperative troponin measured immediately after surgery were independently associated with lower self-reported HRQoL total score at 1-year follow-up.

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Introduction

A substantial number of patients undergoing intermediate to high-risk noncardiac surgery develop peri-operative myocardial injury,[1–3] detected by an elevated troponin level.[4] Postsurgical troponin concentrations have been shown to be independently associated with early and late mortality and also major adverse cardiovascular events (MACE).[1,2,5,6]

Physical wellbeing following surgery is traditionally evaluated by using clinical measures such as surgical outcome and mortality, but patient-reported outcome measures (PROMs) are increasingly being regarded as important.[7] Health-related quality of life (HRQoL) is such a PROM, measuring the impact of disease on physical and mental health. The EuroQol questionnaire is a worldwide, validated tool to assess this nondisease-specific health status.[8,9] It is mostly used within diseases to assess treatment effect, but if used as a generic measure, it holds the promise to be a generalised measurable

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outcome for patients with different diseases. Adverse cardiovascular outcomes are known to affect quality of life and vice versa.[10] Moreover, cardiac biomarkers are independently associated with deterioration of quality of life in nonsurgical patients.[14,15] The relationship between postsurgical troponin concentrations and adverse clinical outcome is well known, but its relation with HRQoL has not been evaluated before. Extending previous findings of troponin measurements with PROMs can further emphasise their clinical value and could help guide the allocation of healthcare resources. In this study, we assess the relationship between postoperative troponin release and HRQoL at 1-year follow-up after intermediate to high-risk noncardiac surgery.

Methods

Study design, setting and participants

The current study is nested within an observational cohort registry of patients aged at least 60 years undergoing intermediate-to-high risk noncardiac surgery at the Erasmus University Medical Centre, Rotterdam, the Netherlands between July 2012 and July 2015, who have been described previously.[1,11,12] This registry was reviewed by the Medical Ethical Committee of Erasmus University, Rotterdam, who approved the noninterventional character of the study (MEC-2013-397). The study was conducted in compliance with the Helsinki declaration[13] and strengthening the reporting of observational studies in epidemiology criteria[14] for observational studies.

Troponin measurements were routinely obtained on postoperative days 1, 2 and 3, unless discharged earlier. Previous medical history and clinical characteristics were collected retrospectively from medical records. Information on MACE and HRQoL was obtained 1 year after surgery by sending out written questionnaires. Data on quality of life were not available for patients who did not respond or died within the first year and consequently, these patients were not included in the final analysis.

Endpoints and measurements

Postoperative troponin measurements

Troponin measurement on the first 3 days after surgery is standard clinical care in patients aged 60 years and older undergoing intermediate-to-high risk noncardiac surgery at the Erasmus University Medical Centre. The Roche fifth-generation Elecsys high-sensitivity troponin T assay is used. For analysis, troponin levels were divided into four categories, as previously published.[1,11,12] The first category ($<14\,ng\,l^{-1}$) is considered normal, based on the manufacturer's 99th percentile of a normal population.[15] The second (14 to $49\,ng\,l^{-1}$) was based on the $0.03\,ng\,ml^{-1}$ threshold of the fourth-generation assay's abnormal elevations, which is equivalent to $50\,ng\,l^{-1}$ of the fifth assay.[16] The highest threshold was extrapolated from the highest threshold in the Vascular events In noncardiac Surgery patIents cOhort evaluatioN study,[2] which was 10 times the threshold of an abnormal troponin elevation, that is $140\,ng\,l^{-1}$ for the fifth generation, rounding off to $150\,ng\,l^{-1}$.

Troponin concentrations at least $50\,ng\,l^{-1}$ were evaluated for meeting the diagnostic criteria of the third universal definition of postoperative myocardial infarction (MI).[4]

Questionnaires

Follow-up data for MACE and quality of life were acquired 1 year after the date of surgery, either through questionnaires sent out by postal mail or, in case of a nonresponse, by telephone interview. The questionnaires consisted of a structured investigation of the patients' own report on MACE[1] combined with the EuroQol five-dimensional questionnaire (EQ-5D-5L) to assess present health status and HRQoL. For MACE, all patient-reported events were checked in the electronic hospital patient information system if possible, or through contacting the general practitioner and other hospitals. In case of a total nonresponse, the electronic hospital patient information system was used as best alternative possible for data collection on MACE. This was done for all participants in the cohort and the date of the last review or consultation was used to calculate clinical follow-up time.

Major adverse cardiovascular events

MACE was defined as the composite endpoint of MI, angina (stable and unstable), coronary revascularisation (both percutaneous coronary intervention or coronary artery bypass graft) or cerebrovascular accident (CVA) at 1-year follow-up, all for which hospital admission was required.[1]

Health-related quality of life

The primary endpoint of the current study was HRQoL at 1-year follow-up. For the assessment of HRQoL, the (validated) Dutch version of the EQ-5D-5L was used and was sent out 1 year after surgery.[8] The EQ-5D-5L is a PROM widely used around the world.[17] It covers five domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and each domain has five answer categories (no problems to severe problems). HRQoL total score was calculated from the five dimensions of the EQ-5D-5L, with a standard set of population-based weights validated for the Netherlands.[8] Calculated index scores range from 1 (best health state) to −0.446 for the worst health state possible, with negative scores reflecting a health state worse than death. A mean difference of 0.037 to 0.069 in EQ-5D-5L is considered clinically relevant.[18] Additionally, the EuroQol visual analogue scale (EQ-VAS) score was assessed. The EQ VAS records the patient's overall current state of health on a vertical visual analogue scale, where the endpoints are labelled from 100 (the best health you can imagine) to 0 (the worst health you can imagine). The EQ VAS

provides a quantitative measure of the patient's perception of their overall state of health.

Statistical analysis

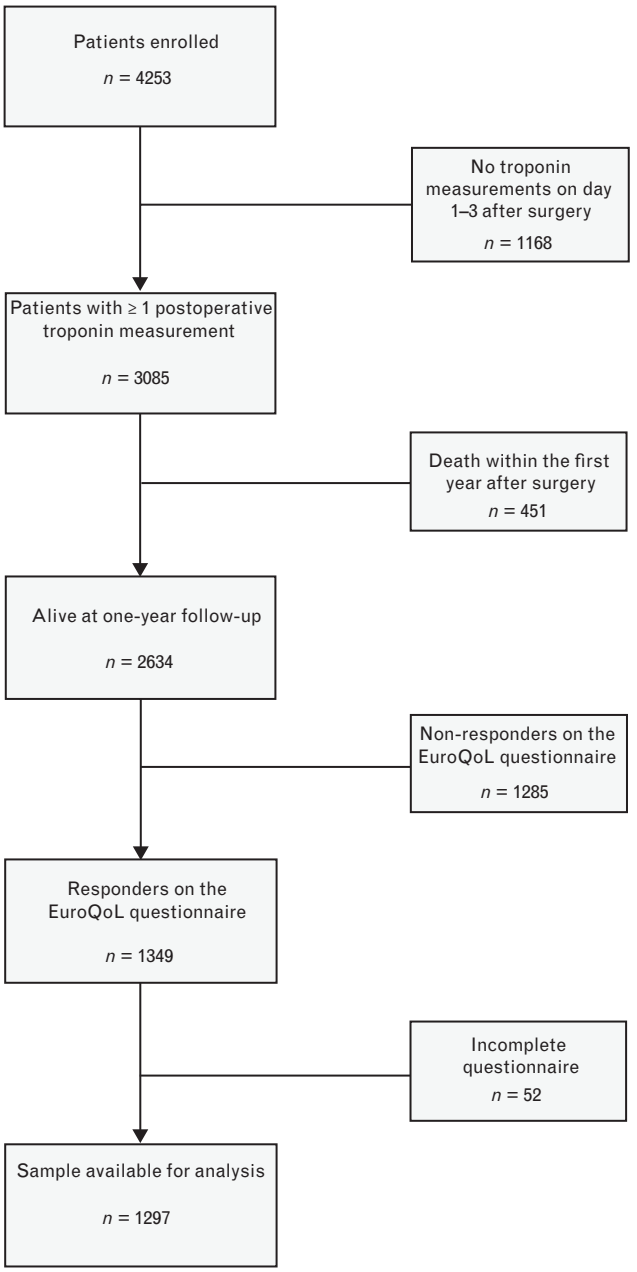
Descriptive statistics are presented as numbers (%). Continuous data are given as median [IQR]. Baseline characteristics were stratified by troponin categories and compared using Pearson's χ^2 analyses or Fisher's exact test for categorical data, and the Kruskal–Wallis test for continuous data. The Kernel density estimation plot was used to visualise the distribution of HRQoL total scores per troponin category. Sensitivity analysis was performed to compare baseline characteristics between responders and nonresponders to the questionnaire. To investigate the influence of troponin concentrations higher than the reference category (i.e. values $<14\,ng\,l^{-1}$) on HRQoL total score, Tobit regression was performed and right-censored at 1. This censoring was performed because of skewed data on the one hand and a maximum performance limit of 1 on the other; a defined boundary which can be silently exceeded by individual performance.[19,20] Regression coefficients are presented along with their 95% confidence interval (CI). Multivariable analysis included all baseline characteristics [sex, age, coronary heart disease, diabetes, CVA, chronic obstructive pulmonary disease (COPD), renal failure, peripheral arterial disease (PAD), chronic heart failure, type of surgery and emergency surgery], as the model was not limited by the number of confounding factors. Sensitivity analysis was performed to assess the effect of MACE on patient-reported HRQoL total score. For all tests, a probability value for significance of less than 0.05 (two-sided) was used. All statistical analyses were performed with SPSS statistical software, version 24 (SPSS Inc., Chicago, Illinois, USA) or R Statistical Software, version 1.0.153 (Free Software Foundation Inc., Boston, MA, USA) for Kernel Density Plot, Tobit Regression[21] and Likert-Scale Plot.[22]

Results

Study population

From the 1st July 2012 to the 1st 2015, 3085 consecutive patients with postoperative troponin measurements were enrolled. Within the first year 451 (14.6%) patients died, leaving 2634 patients eligible for study (Fig. 1). Of these, 1297 (49.2%) returned a completed questionnaire on quality of life at a median follow-up duration of 1.3 [1.2 to 1.6] years after surgery. The response rate between patients with and without troponin elevation was 49.5 vs. 50.3%, respectively. In the nonresponders, histories of CVA (17.3 vs. 14.3%, $P=0.03$), COPD (16.4 vs. 11.5%, $P<0.001$) and diabetes mellitus (27.5 vs. 19.8%, $P<0.001$) were more frequent when compared with the responders. The incidence of MACE did not differ between responders and nonresponders (5.0 vs. 5.4%, $P=0.67$) at 1-year follow-up.

Fig. 1



Flowchart of study sample.

Overall, in the final study sample the median age was 69 [64 to 74] years and male sex was predominant (60.1%) (Table 1). A history of cardiovascular diseases and subsequent medical therapy was more frequently observed in higher categories of postoperative troponin release. With increasing levels of peak troponin concentrations, time to discharge was prolonged and fewer people were discharged home (Table 1). In 105 (8.1%) patients with postoperative troponin measurements at least $50\,ng\,l^{-1}$, 23 (21.9%) could be classified as postoperative MI.

Table 1 Baseline characteristics stratified by troponin category

hsTnT values (ng l^{-1})	<14 (*n* = 635)	14 to 49 (*n* = 557)	50 to 149 (*n* = 79)	≥150 (*n* = 26)	*P* value
Age (years)	66 [63 to 71]	72 [66 to 77]	72 [67 to 76]	74 [66 to 76]	<0.001
Sex (male)	317 (49.9)	386 (69.3)	56 (70.9)	20 (76.9)	<0.001
Hypertension	299 (47.1)	322 (57.8)	51 (64.6)	16 (61.5)	<0.001
Coronary artery disease	76 (12.0)	131 (23.5)	25 (31.6)	16 (61.5)	<0.001
Myocardial infarction	40 (6.3)	78 (14.0)	17 (21.5)	10 (38.5)	<0.001
Cerebrovascular accident	68 (10.7)	92 (16.5)	17 (21.5)	8 (30.8)	<0.001
PAD	57 (9.0)	72 (12.9)	12 (15.2)	1 (3.8)	0.056
COPD	54 (8.5)	75 (13.5)	18 (22.8)	2 (7.7)	<0.001
Diabetes mellitus	100 (15.7)	121 (21.7)	27 (34.2)	9 (34.6)	<0.001
Current or history of heart failure	9 (1.4)	42 (7.5)	6 (7.6)	6 (23.1)	<0.001
Renal failure	13 (2.0)	57 (10.2)	30 (38.0)	6 (23.1)	<0.001
Medication use					
Beta-blockers	184 (29.0)	239 (42.9)	40 (50.6)	15 (57.7)	<0.001
Statins	237 (37.3)	288 (51.7)	41 (51.9)	18 (69.2)	<0.001
ACE inhibitor	119 (18.7)	144 (25.9)	23 (29.1)	11 (42.3)	0.001
Aspirin	159 (25.0)	215 (38.6)	37 (46.8)	16 (61.5)	<0.001
Oral anticoagulants	36 (5.7)	82 (14.7)	14 (17.7)	5 (19.2)	<0.001
Diuretics	138 (21.7)	174 (31.2)	34 (43.0)	10 (38.5)	<0.001
Insulin	29 (4.6)	45 (8.1)	17 (21.5)	6 (23.1)	<0.001
Type of surgery					0.028
General	79 (12.4)	70 (12.6)	6 (7.6)	4 (15.4)	
Orthopaedics	110 (17.3)	92 (16.5)	15 (19.0)	2 (7.7)	
Urology/Gynaecology	138 (21.7)	85 (15.3)	10 (12.7)	2 (7.7)	
Vascular	139 (21.9)	163 (29.3)	24 (30.4)	7 (26.9)	
Other	169 (26.6)	147 (26.4)	24 (30.4)	11 (42.3)	
Emergency surgery	19 (3.0)	23 (4.1)	17 (21.5)	8 (30.8)	<0.001
Length of surgery (min)	212 [165 to 296]	201 [157 to 272]	193 [148 to 244]	200 [43 to 250]	0.029
Type of anaesthesia					0.242
General	614 (96.7)	531 (95.3)	75 (94.9)	25 (96.2)	
Combined general and epidural	63 (9.9)	37 (6.6)	6 (7.6)	4 (15.4)	
Spinal	15 (2.4)	23 (4.1)	2 (2.5)	0 (0.0)	
Regional	50 (7.9)	42 (7.5)	6 (7.6)	0 (0.0)	
Hospital admission (days)	5 [3 to 8]	7 [4 to 12]	10 [6 to 14]	12 [8 to 26]	<0.001
Discharged home	593 (93.4)	487 (87.4)	62 (78.5)	20 (76.9)	<0.001

ACE, angiotensin-converting-enzyme inhibitors; hsTnT, high-sensitivity troponin T. Values presented are number (proportion) or median [IQR]. Renal failure is defined as creatinine values more than 177 μmol l^{-1}. COPD, chronic obstructive pulmonary disease; PAD, peripheral arterial disease.

Health-related quality of life

Overall, the median score for HRQoL using the EQ-5D-5L was 0.82 [0.68 to 0.91] and 80 [65 to 90] for the EQ-VAS score, 1 year postoperatively. A shift towards lower HRQoL scores for higher troponin category was observed (Table 2, Fig. 2, Appendix A, http://links.lww.com/EJA/A317). For patients with values less than 14 ng l^{-1}, the majority reported no problems in all domains except for pain and/or discomfort (Fig. 3). In this domain, the severity of reported symptoms was increased and this was seen across all troponin categories. Increase in severity of the symptom reported for other domains accrued stepwise with increasing troponin categories. For the 65 patients experiencing MACE during follow-up, median HRQoL total score was 0.77 [0.63 to 0.85] compared with 0.82 [0.69 to 0.92] for patients without MACE ($P = 0.004$). The same trend was observed for the EQ-VAS score; median 70 [50 to 80] compared with 80 [65 to 90] ($P = 0.025$) for patients with and without MACE, respectively (Table 2).

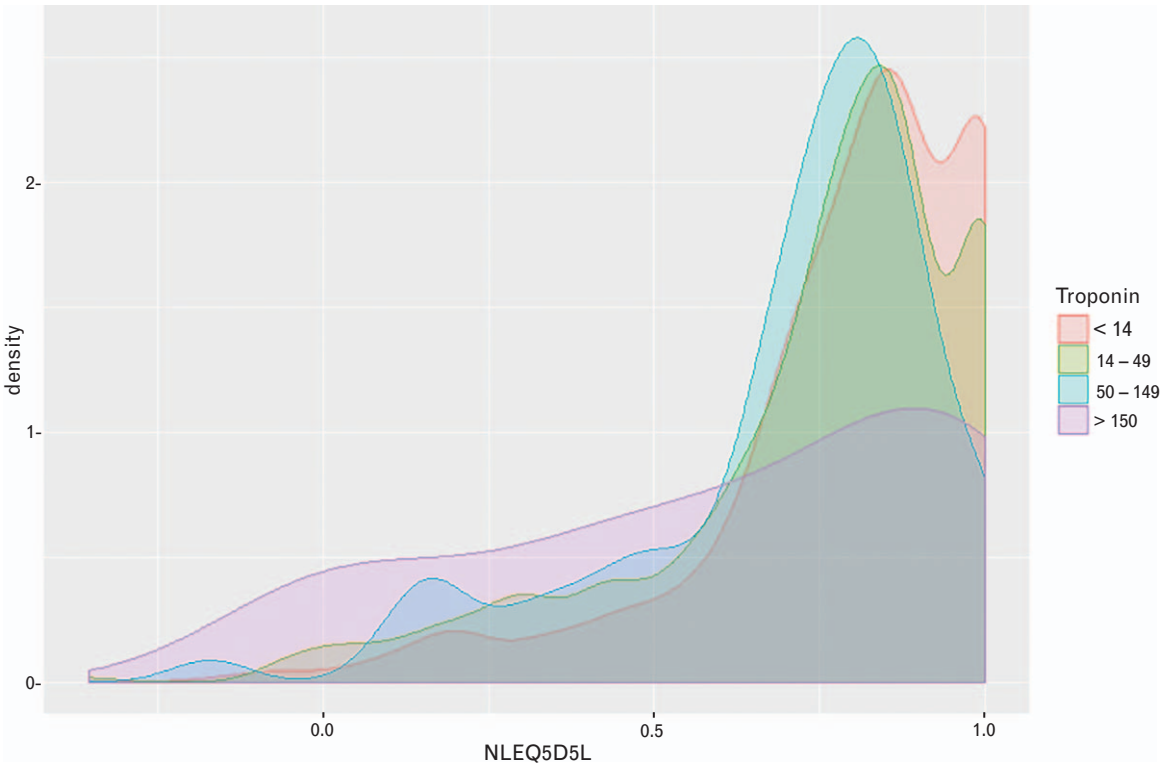
For HRQoL, Tobit regression analysis revealed a significant stepwise impairment for HRQoL with β −0.07 (95% CI −0.10 to −0.04), −0.13 (95% CI −0.20 to −0.06) and −0.19 (95% CI −0.30 to −0.07) for increasing troponin category, respectively (Table 3). When adjusted for the previous medical history, results were β −0.06 (−0.09 to 0.02), −0.11 (−0.18 to 0.04) and −0.18 (−0.29 to 0.07) per increasing troponin category, respectively (Table 3). Other independent predictors for lower HRQoL were COPD, female sex, PAD and increasing age. Sensitivity analyses in patient without MACE revealed similar β for impairment.

Discussion

In this study, we analysed the association between postoperative troponin release and self-reported HRQoL at 1-year follow-up in patients who underwent intermediate-to-high risk noncardiac surgery. Our results demonstrate that increased troponin levels are independently associated with HRQoL and that there is an inverse association between categories of troponin concentration and reported health status 1 year after surgery.

In our study cohort with a median age of 69 years, we found a median HRQoL total score of 0.82. For reference,

Fig. 2



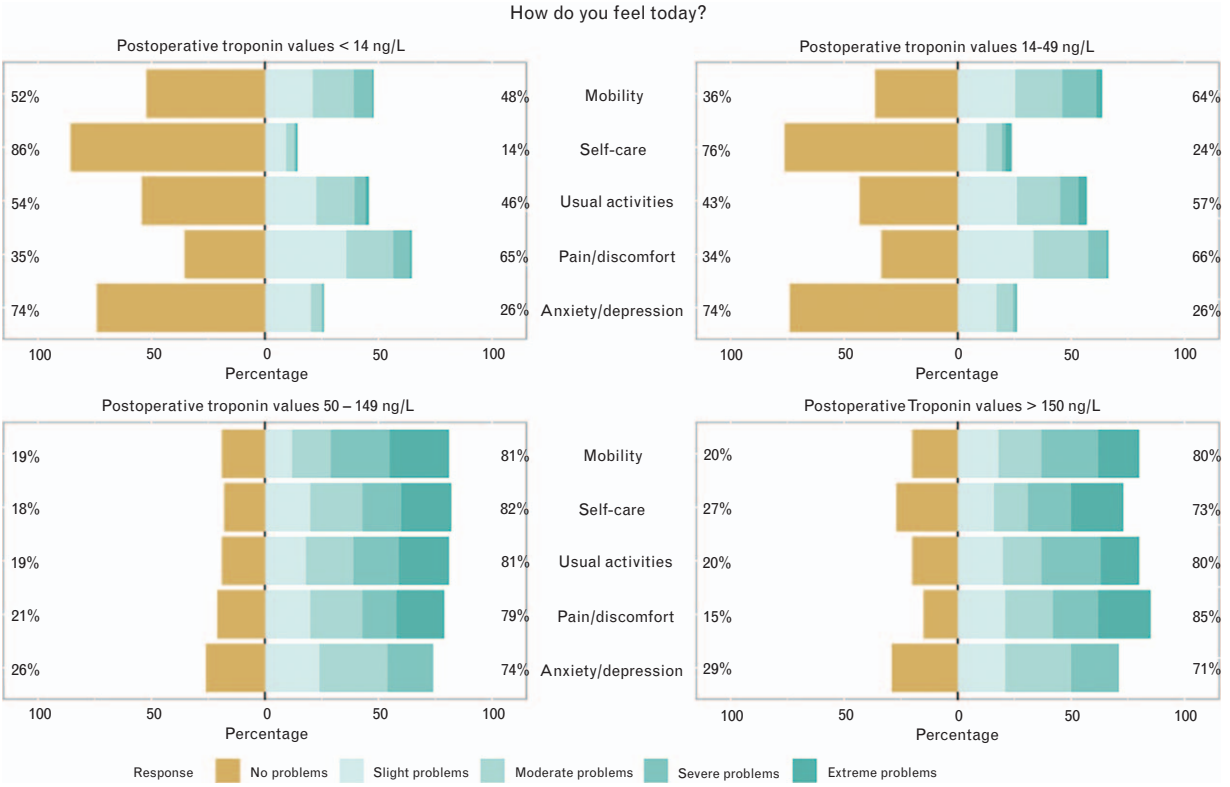
Kernel density estimation plot of the distributions of the health-related quality-of-life total score stratified by troponin category.

the EQ-5D-5L index norm for the general population in the Netherlands aged 60 to 70 years is set at 0.84.[8] When scores are stratified by troponin category, patients with no elevation (i.e. the reference category of $<14\,ng\,l^{-1}$) have similar values. A decrement towards 0.71 is seen when postoperative troponin concentrations increase. Mitchell *et al.*[23] investigated the relative impact of several diseases on health status in a nonsurgical cohort. Compared with healthy individuals, they found lower health status for major (chronic) health conditions like heart disease, diabetes, depression and cancer. More importantly, they showed that in terms of disease severity, HRQoL decreased as disease severity increased. The same trend is seen in our results. After adjustment for previous medical history, HRQoL total score fell with increasing levels of troponin concentrations when compared with values in the reference category of less than $14\,ng\,l^{-1}$. Furthermore, relationships for known independent predictors of impaired HRQoL other than troponin, like female sex, COPD, CVA, PAD and increasing age were identified in our study.[8,24–27]

The cardiac biomarker troponin has proven its value in the field of cardiology. Postoperative measurements are increasingly incorporated into current clinical practice because of their prognostic capability for both adverse cardiovascular events and mortality following surgery.[1,3,28] To these we now add these clinical outcome measures derived from the patients' own perceptions of health. However, how to respond clinically to elevated troponin levels remains a topic of debate. McCarthy *et al.*[15] explored the differential diagnosis in nonsurgical patients with increased troponins, with myocardial ischaemia as the most common cause of abnormal concentration. It has been frequently suggested that coronary artery disease (CAD) is attributable to myocardial oxygen supply–demand mismatch in surgical patients.[29,30] With its increasing incidence worldwide and with the character of a chronic disease, CAD will continue to affect physical, psychological and social wellbeing. In ischaemic heart disease patients, increased myocardial ischaemia leads to a lower quality of life.[26,31] In haemodialysis patients, a similar association was observed. High troponin T levels were independently associated with deterioration in the physical domains of HRQoL.[32] In the current study, an increase in severity of the symptom reported domains, also accrued stepwise with increasing troponin categories.

We have previously shown that time to MACE was inversely related to higher troponin concentrations.[1] Moreover, time to discharge was prolonged and fewer people were discharged home. When observing baseline

Fig. 3



Likert-scale plot for the five dimensions of the EuroQol five-dimensional questionnaire stratified by troponin category. The scale displays percentages of answers for each dimension, with 'no problems' on the left side and 'slight', 'moderate', 'severe' and 'extreme' on the right side (with a darker colour green reflecting more severe symptoms).

characteristics, a higher prevalence of cardiovascular comorbidity was seen across higher concentrations. It is likely that the occurrence of MACE has negatively influenced HRQoL.[31] However, in sensitivity analyses, deterioration of HRQoL scores in the absence of MACE is also observed at follow-up. Therefore, it is probable that the degree of myocardial injury signals the severity of underlying cardiovascular burden, which influences perceived quality of life. Next to having prognostic capabilities, troponin levels measured immediately after noncardiac surgery might serve as an indicator for lower quality of life.

There are some limitations to this study. First, we have only a single measurement of HRQoL, preventing us from commenting on the course of peri-operative change, which could have added valuable information on the quality of life after surgery. This also accounts for troponin measurements. High pre-operative troponin concentrations could reflect chronic cardiovascular comorbidity and this is known to correlate with lower perceived quality of life. On the contrary, routine pre-operative troponin measurements were not available in the cohort and their influence could therefore not be assessed. Second, the literature does not provide nondisease-specific guidelines for cut-off values to make the EQ-5D-5L Total Score manageable for daily clinical practice. We used EQ-5D-5L as a continuous score to prevent information loss through dichotomisation of the results (as proposed for the EQ-5D3L). Whether the effect of

Table 2 **Comparison of symptom reports on the EuroQol questionnaire stratified by troponin category**

hsTnT values (ng l^{-1}) HRQoL	<14 (*n* = 635)	14 to 49 (*n* = 557)	50 to 149 (*n* = 79)	≥150 (*n* = 26)	*P* value
Total score	0.85 [0.72 to 1.00]	0.81 [0.66 to 0.90]	0.77 [0.64 to 0.86]	0.71 [0.38 to 1.0]	<0.001
EQ-VAS	80 [69 to 90]	75 [60 to 85]	70 [55 to 80]	63 [50 to 80]	<0.001

Values are presented as median [IQR]. EQ-VAS, EuroQol visual analogue scale; HRQoL, health-related quality of life; hsTnT, high-sensitivity troponin T.

Table 3 Censored Tobit regression for health-related quality of life total score

HRQoL	Univariable ß (95% CI)	Multivariable ß (95% CI)
Troponin		
$<14\,ng\,l^{-1}$	ref	ref
14 to $49\,ng\,l^{-1}$	−0.07 (−0.10 to −0.04)	−0.06 (−0.09 to −0.02)
50 to $149\,ng\,l^{-1}$	−0.13 (−0.20 to −0.06)	−0.11 (−0.18 to −0.04)
$>150\,ng\,l^{-1}$	−0.19 (−0.30 to −0.07)	−0.18 (−0.29 to −0.07)
Type of surgery		
General	ref	ref
Orthopaedic	0.16 (0.10 to 0.21)	0.13 (0.08 to 0.19)
Urology/Gynaecology	0.19 (0.13 to 0.24)	0.15 (0.10 to 0.20)
Vascular	0.14 (1.10 to 0.19)	0.17 (0.12 to 0.22)
Other	0.07 (0.02 to 0.12)	0.05 (0.002 to 0.10)
Sex (female)	−0.07 (−0.11 to −0.04)	−0.08 (−0.11 to −0.05)
Age	−0.01 (−0.01 to −0.004)	−0.003 (−0.005 to −0.0004)
Hypertension	−0.06 (−0.06 to −0.06)	−0.027 (−0.058 to 0.005)
CAD	−0.07 (−1.10 to −0.04)	−0.032 (−0.07 to 0.01)
Cerebrovascular accident	−0.09 (−0.13 to −0.06)	−0.07 (−0.11 to −0.03)
Peripheral arterial disease	−0.07 (−0.10 to −0.04)	−0.12 (−0.17 to −0.06)
Renal failure	0.006 (−0.026 to 0.039)	0.09 (0.02 to 0.15)
COPD	−0.16 (−0.19 to −0.12)	−0.11 (−0.16 to −0.07)
Diabetes	−0.05 (−0.08 to −0.02)	−0.03 (−0.06 to 0.01)
Congestive heart failure	−0.07 (−0.10 to −0.04)	0.001 (−0.07 to 0.08)
Emergency surgery	−0.03 (−0.06 to −0.003)	−0.01 (−0.08 to 0.06)

Univariable and adjusted ß coefficients from Tobit regression of HRQoL total score. Total number of observations: 1297. The model is right-censored at 1, as this is the maximum HRQoL total score. Total number of censored observations: 292. Regression coefficients represent the mean change in HRQoL. CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HRQoL, health-related quality of life.

myocardial injury on HRQoL is mediated via the development of adverse cardiac events which cause a decrease in HRQoL, or by the degree of myocardial damage, is difficult to determine. The presence of cardiovascular comorbidity is taken into account in the regression model; however, residual confounding can still be present. Third, an issue with working with utility values is that values are scaled, ranging from −0.446 to 1, and thereby at risk for a ceiling and/or floor effect.[20] The distribution (stratified per troponin category) clearly shows that the majority of patients score between 0.75 and 1. Individuals can have a maximum score of 1 while having different degrees of health performance. Therefore, we performed a Tobit regression model to assess the relationship between HRQoL and postoperative troponin concentrations.[20] As aforementioned, utility scores are associated with some uncertainty. The results of the current study can be distorted by being subject to responder bias. When measuring quality of life, patients are prone to self-selection bias. When comparing baseline characteristics for prior medial history between responders and nonresponders, the higher incidence of comorbidities like COPD and diabetes seen in the nonresponders could reflect a nonresponse bias effect.[33] The direction and extent of such bias is difficult to estimate. Last, we have no information on the occurrence of primarily surgical complications, which could influence the patients' overall experience of quality of life.

Conclusion

Higher levels of postoperative troponin concentrations measured immediately after surgery were independently associated with lower self-reported HRQoL 1-year after noncardiac surgery. These findings support the use of routine peri-operative troponin measurements. Further studies designed to improve postoperative patient-relevant outcomes in identified high-risk patients are indicated.

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Conflicts of interest: none.

Presentation: content of this article was presented at the annual meeting of the American Society of Anesthesiologists 2019.

References

1 Mol KHJM, Hoeks SE, Liem VGB, *et al.* Postoperative troponin release is associated with major adverse cardiovascular events in the first year after noncardiac surgery. *Int J Cardiol* 2019; **280**:8–13.
2 Devereaux PJ, Chan MTV, Alonso-Coello P, *et al.*, Vascular Events in Noncardiac Surgery Patients Cohort Evaluation (VISION) Study Investigators. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012; **307**:2295–2304.
3 van Waes JA, Nathoe HM, de Graaff JC, *et al.*, Cardiac Health After Surgery (CHASE) Investigators. Myocardial injury after noncardiac surgery and its association with short-term mortality. *Circulation* 2013; **127**:2264–2271.
4 Thygesen K, Alpert JS, Jaffe AS, *et al.*, ESC Committee for Practice Guidelines (CPG). Third universal definition of myocardial infarction. *Eur Heart J* 2012; **33**:2551–2567.
5 van Waes JA, Grobben RB, Nathoe HM, *et al.*, Cardiac Health After Surgery (CHASE) Investigators. One-year mortality, causes of death, and cardiac interventions in patients with postoperative myocardial injury. *Anesth Analg* 2016; **123**:29–37.

6 Ekeloef S, Alamili M, Devereaux PJ, *et al.* Troponin elevations after non-cardiac, non-vascular surgery are predictive of major adverse cardiac events and mortality: a systematic review and meta-analysis. *Br J Anaesth* 2016; **117**:559–568.
7 Black N. Patient reported outcome measures could help transform healthcare. *BMJ* 2013; **346**:f167.
8 Versteegh MM, Vermeulen KM, Evers SMAA, *et al.* Dutch tariff for the five-level version of EQ-5D. *Value Health* 2016; **19**:343–352.
9 EuroQol Group. EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* 1990; **16**:199–208.
10 Mommersteeg PMC, Denollet J, Spertus JA, *et al.* Health status as a risk factor in cardiovascular disease: a systematic review of current evidence. *Am Heart J* 2009; **157**:208–218.
11 Liem VGB, Hoeks SE, Grüne F, *et al.* Prognostic value of postoperative high-sensitivity troponin T in patients with different stages of kidney disease undergoing noncardiac surgery. *Br J Anaesth* 2018; **120**:84–93.
12 van Lier F, Wesdorp FHIM, Liem VGB, *et al.* Association between postoperative mean arterial blood pressure and myocardial injury after noncardiac surgery. *Br J Anaesth* 2018; **120**:77–83.
13 World Medical Association. World Medical Association declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; **310**:2191–2194.
14 von Elm E, Altman DG, Egger M, *et al.* Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007; **335**:806–808.
15 McCarthy CP, Raber I, Chapman AR, *et al.* Myocardial injury in the era of high-sensitivity cardiac troponin assays: a practical approach for clinicians. *JAMA Cardiol* 2019; **4**:1034–1042.
16 Giannitsis E, Kurz K, Hallermayer K, *et al.* Analytical validation of a high-sensitivity cardiac troponin T assay. *Clin Chem* 2010; **56**:254–261.
17 Devlin NJ, Brooks R. EQ-5D and the EuroQol Group: past, present and future. *Appl Health Econ Health Policy* 2017; **15**:127–137.
18 McClure NS, Sayah FA, Xie F, *et al.* Instrument-defined estimates of the minimally important difference for EQ-5D-5L index scores. *Value Health* 2017; **20**:644–650.
19 Twisk J, Rijmen F. Longitudinal Tobit regression: a new approach to analyze outcome variables with floor or ceiling effects. *J Clin Epidemiol* 2009; **62**:953–958.
20 Austin PC. A comparison of methods for analyzing health-related quality-of-life measures. *Value Health* 2002; **5**:329–337.
21 Henningsen A. *censReg: censored regression (Tobit) models*. 2017.
22 Bryer J, Speerschneider K. *Likert: analysis and visualization Likert items*. 2016.
23 Mitchell PM, Al-Janabi H, Richardson J, *et al.* The relative impacts of disease on health status and capability wellbeing: a multi-country study. *PLoS One* 2015; **10**:e0143590.
24 Hicken GJ, Lossing AG, Ameli fM. Assessment of generic health-related quality of life in patients with intermittent claudication. *Eur J Vasc Endovasc Surg* 2000; **20**:336–341.
25 de Torres JP, Casanova C, Hernández C, *et al.* Gender and COPD in patients attending a pulmonary clinic. *Chest* 2005; **128**:2012–2016.
26 De Smedt D, Clays E, Annemans L, *et al.* Health related quality of life in coronary patients and its association with their cardiovascular risk profile: results from the EUROASPIRE III survey. *Int J Cardiol* 2013; **168**:898–903.
27 Janssen B, Szende A. *Self-Reported Population Health: An International Perspective based on EQ-5D. Chapter 3 Population norms for the EQ-5D.* 2014.
28 Devereaux PJ, Biccard BM, Sigamani A, *et al.*, Writing Committee for the VISION Study Investigators. Association of postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2017; **317**:1642–1651.
29 Devereaux PJ, Duceppe E, Guyatt G, *et al.*, MANAGE Investigators. Dabigatran in patients with myocardial injury after noncardiac surgery (MANAGE): an international, randomised, placebo-controlled trial. *Lancet* 2018; **391**:2325–2334.
30 Sheth T, Chan M, Butler C, *et al.*, Coronary Computed Tomographic Angiography and Vascular Events in Noncardiac Surgery Patients Cohort Evaluation Study Investigators. Prognostic capabilities of coronary computed tomographic angiography before noncardiac surgery: prospective cohort study. *BMJ* 2015; **350**:h1907.
31 Tušek-Bunc K, Petek D. Comorbidities and characteristics of coronary heart disease patients: their impact on health-related quality of life. *Health Qual Life Outcomes* 2016; **14**:159.
32 Williams CE, Curtis BM, Randell EW, *et al.* Cardiac biomarkers and health-related quality of life in new hemodialysis patients without symptomatic cardiac disease. *Can J Kidney Health Dis* 2014; **1**:16.
33 Sedgwick P. Nonresponse bias versus response bias. *BMJ* 2014; **348**:g2573.