

## RESEARCH ARTICLE

# Continuously monitored vital signs for detection of myocardial injury in high-risk patients – An observational study

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## Abstract

**Background:** Patients are at risk of myocardial injury after major non-cardiac surgery and during acute illness. Myocardial injury is associated with mortality, but often asymptomatic and currently detected through intermittent cardiac biomarker screening. This delays diagnosis, where vital signs deviations may serve as a proxy for early signs of myocardial injury. This study aimed to assess the association between continuous monitored vital sign deviations and subsequent myocardial injury following major abdominal cancer surgery and during acute exacerbation of chronic obstructive pulmonary disease. **Methods:** Patients undergoing major abdominal cancer surgery or admitted with acute exacerbation of chronic obstructive pulmonary disease had daily troponin measurements. Continuous wireless monitoring of several vital signs was performed for up to 96 h after admission or surgery. The primary exposure was cumulative duration of peripheral oxygen saturation (SpO<sub>2</sub>) below 85% in the 24 h before the primary outcome of myocardial injury, defined as a new onset ischaemic troponin elevation assessed daily. If no myocardial injury occurred, the primary exposure was based on the first 24 h of measurement. **Results:** A total of 662 patients were continuously monitored and 113 (17%) had a myocardial injury. Cumulative duration of SpO<sub>2</sub> < 85% was significantly associated with myocardial injury (mean difference 14.2 min [95% confidence interval -4.7 to 33.1 min];  $p = .005$ ). Durations of hypoxaemia (SpO<sub>2</sub> < 88% and SpO<sub>2</sub> < 80%), tachycardia (HR > 110 bpm and HR > 130 bpm) and tachypnoea (RR > 24 min<sup>-1</sup> and RR > 30 min<sup>-1</sup>) were also significantly associated with myocardial injury ( $p < .04$ , for all).

Helge B. D. Sørensen, Eske K. Aasvang and Christian S. Meyhoff shared last authorship.

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**Conclusion:** Duration of severely low SpO<sub>2</sub> detected by continuous wireless monitoring is significantly associated with myocardial injury in high-risk patients admitted to hospital wards. The effect of early detection and interventions should be assessed next.

#### KEYWORDS

acute exacerbation of chronic obstructive pulmonary disease, continuously monitoring, hypoxaemia, myocardial injury, noncardiac surgery, tachycardia, tachypnoea, vital signs

#### Editorial Comment

In this observational study, wireless continuous monitoring of vital signs was assessed in major abdominal surgery cases on hospital wards and cases with exacerbation of COPD. Duration of hypoxaemia, tachycardia and tachypnoea were associated with myocardial injury evaluated with high-sensitive troponin measurements. The findings highlight the need to facilitate high-frequency monitoring of vital signs on wards on selected patient cohorts using advanced methods to identify opportunities for earlier intervention to try to detect and reverse this type of clinical decline on the ward. [Correction added on March 30, after first online publication: The Editorial Comment was corrected in this version.]

## 1 | INTRODUCTION

Patients admitted with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and patients undergoing major abdominal surgery, are two large groups of hospitalized patients with increased risk of cardiovascular complications.<sup>1-4</sup> However, these patient groups are currently not monitored for myocardial infarction (MI) on a routine basis. In current clinical practice, cardiac biomarkers are measured if patients present ischaemic symptoms, but approximately 65% of MIs in non-cardiac surgical patients are asymptomatic, requiring cardiac biomarker screening.<sup>1,2,5,6</sup> The term Myocardial Injury after Non-cardiac Surgery (MINS) has been introduced as post-operative patients commonly have elevated troponin levels without fulfilling the diagnostic criteria for MI.<sup>1</sup> MINS includes MI as well as other ischaemic myocardial injuries and is associated with almost 10% risk of 30-day mortality.<sup>1,7</sup> About one-half of patients admitted with AECOPD without ischaemic symptoms have elevated troponin levels suggestive of myocardial injury, which is an independent predictor of all-cause mortality.<sup>8</sup>

Although daily screening of cardiac biomarkers can detect myocardial injury, it has a risk of 24 h delay from onset, but deviations of vital signs may serve as early predictors.<sup>9</sup> Post-operative hypoxaemia is associated with increased troponin; and peri-operative hypotension, hypertension and tachycardia are associated with MINS.<sup>10-12</sup> Troponin elevations are related to tachycardia during admission for AECOPD, and the association of troponin elevations to mortality is considerably modified by tachycardia.<sup>13-15</sup> Today, vital signs are monitored with several hours between measurements in escalation protocols beginning with monitoring every 12 h, permitting unrecognized deterioration between measurements. Continuous monitoring can detect these deteriorations, which might predict myocardial injury.<sup>16,17</sup>

This study aimed to assess the association between continuously monitored vital signs and myocardial injury in patients admitted with

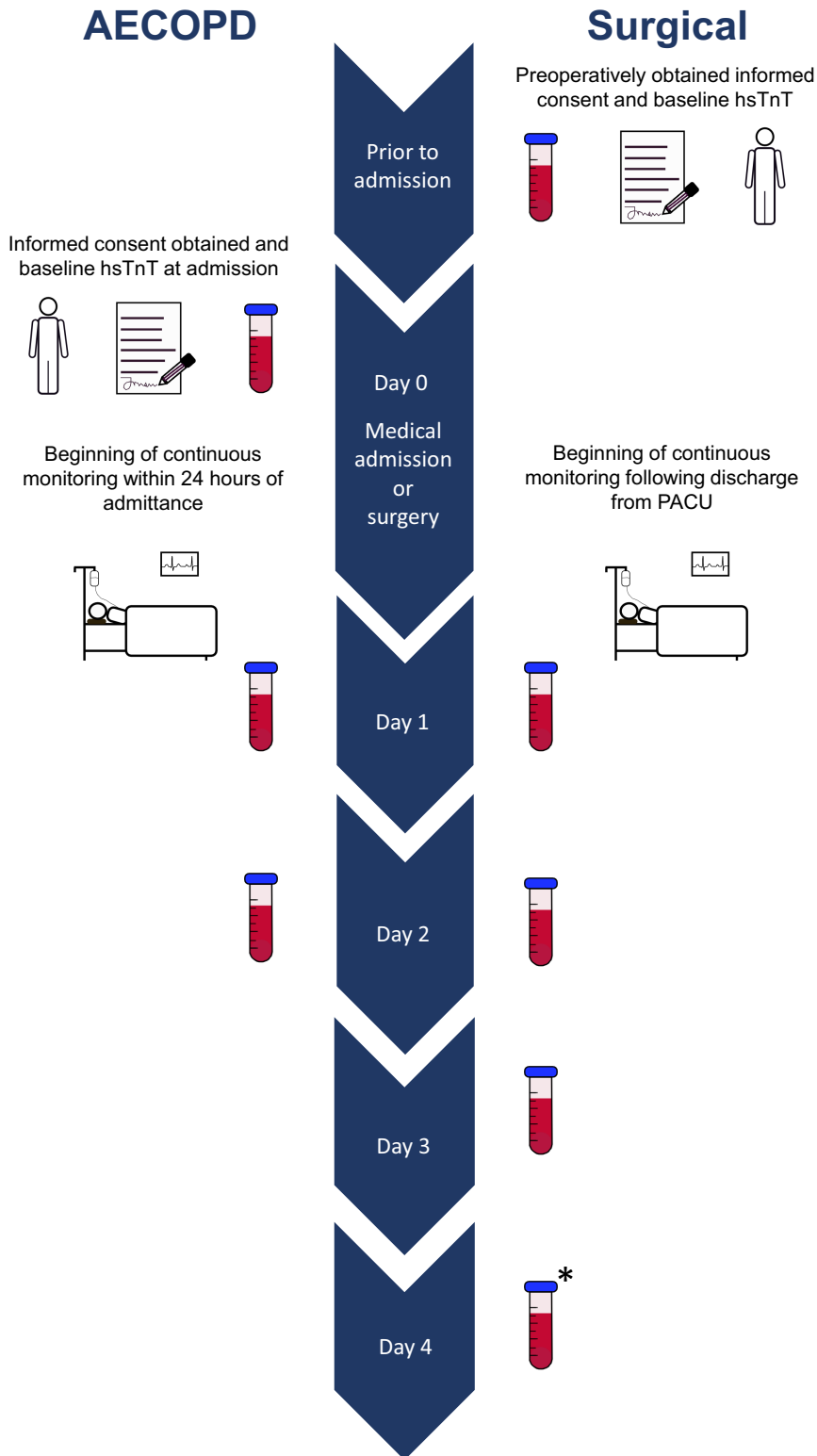
AECOPD and following major abdominal cancer surgery. We hypothesized that the cumulative duration of peripheral oxygen saturation below 85% was associated with myocardial injury.

## 2 | METHODS

We conducted a prospective observational cohort study. Data were collected from two studies of the WARD-Project (Wireless Assessment of Respiratory and circulatory Distress) (NCT03660501 and NCT03491137). Both studies were approved by the Danish Data Protection Agency (2012-58-0004), and ethical approvals were provided by the Ethical Committees of The Capital Region of Denmark, Copenhagen, Denmark (protocol number 18026653, 12 September 2018 and 17033535, 8 February 2018). The study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) 2007 checklist. [Figure 1](#) illustrates an overview of the study period.

### 2.1 | Patient enrolment

Patients were included at Bispebjerg Hospital (departments of emergency medicine, pulmonary medicine and abdominal surgery) and Rigshospitalet (department of abdominal surgery) in Denmark from February 2018 until September 2020 after written informed consent. Investigators determined eligibility. Patients were eligible if they were either adults admitted with AECOPD as admission diagnosis, or above 60 years and undergoing major abdominal cancer surgery with an expected duration of more than 2 h (i.e., oesophageal, ventricular, pancreatic or colorectal cancer surgery), based on the scheduled programme of the surgical team. Eligibility also required the possibility of the investigator to include the patient prior to surgery or within 24 h of AECOPD admittance to achieve a baseline hsTnT and set up monitoring equipment. AECOPD patients



**FIGURE 1** Study period overview.  
\*If elevated at day 3. AECOPD, acute exacerbation of chronic obstructive pulmonary disease; hsTnT, high-sensitive cardiac troponin T; PACU, post-anaesthesia care unit

also needed an expected admittance longer than 24 h from inclusion, based on clinical and paraclinical presentation and staffs' assessment. Patients were excluded if: not expected to be able to cooperate, active therapy was withdrawn (palliative care admission), they had pacemaker/ Implantable Cardioverter Defibrillator, allergy to plaster, plastic or silicone due to monitoring devices and for surgical patients a Mini-Mental State Examination less than 24, equal to predementia or worse.

## 2.2 | Data collection

AECOPD patients were monitored within 24 h of admittance, and surgical patients were monitored immediately after discharge from the post-anaesthesia care unit (PACU) to the general ward, both cohorts for a maximum of 96 h or until discharged if sooner. Monitoring was made using the following three devices from the WARD

project sensor network, all of which have been validated<sup>18</sup>: (1) Nonin WristOx 3150 (Nonin Medical inc., Minnesota, USA) measuring peripheral oxygen saturation (SpO<sub>2</sub>) with a sampling frequency of 1 per second. (2) Isansys Lifetouch patch (Isansys Lifecare, Oxfordshire, United Kingdom) measuring heart rate (HR) continuously and respiratory rate (RR) with a 1-minute sampling frequency derived from a single-lead ECG. (3) Meditech BlueBP-05 (Meditech Ltd., Hungary), measuring non-invasive systolic and diastolic blood pressure (SBP and DBP) every 30 min during daytime and 60 min during nighttime. Study personnel made daily visits to change batteries, control equipment and ensure compliance. Vital signs were transmitted by Bluetooth to a bedside gateway, from which it was transmitted to a local server by Wi-Fi, blinded to patients and ward staff. Artefacts of continuous monitoring were detected and removed before analysis as following: The HR measurement was automatically detected as R-peak intervals in the Lifetouch patch's ECG signal, 10 s of ECG was measured every minute, from which the quality of the ECG-signal was assessed. All raw data were transmitted, and after a filtration process, the quality of the 10-s segment was determined using a correlation analysis between each QRS-complex and a template of the average QRS-complex created from the previous segment. The segment was denoted as artefactual when correlation was low, and the corresponding values of HR and RR were excluded from the analysis. HR and RR were also excluded if the ECG had RS-amplitudes of the QRS-complexes less than 5 mV. HR was registered as 1-min mean HR of the R-peak intervals. R-peak intervals <20 ms or >4000 ms were excluded from the analysis. SpO<sub>2</sub> was registered as a 1-minute mean and changes larger than 4% per second were excluded. No extrapolation or assumption of vital signs were made. Plasma concentration of high-sensitive cardiac troponin T (hsTnT, Cobas 8000, e801 module, Diagnostics Roche) was measured when informed consent was obtained, as a baseline value. Measuring of hsTnT occurred the following 2 days for AECOPD patients, and at post-operative days 1–3 for surgical patients, both primarily at morning rounds. The responsible physician was contacted in case of elevated levels of hsTnT, and further treatment was at the physician's discretion. If elevated at post-operative day 3, another measurement was made at day 4, if hospitalized.

## 2.3 | Variables

Exposure variables were cumulative duration of vital sign deviations at a *priori* cut-off values during the 24 h before the first ischaemic hsTnT measurement. If no ischaemic hsTnT was present, the first 24 h of continuous monitoring before a non-ischaemic hsTnT measurement was used. Measured vital signs were: SpO<sub>2</sub>, HR, SBP, DBP and RR, of which the primary exposure variable was cumulative duration in minutes of SpO<sub>2</sub> < 85%, in the aforementioned 24 h. The exposure variables of SPB and DBP were accumulated number of events due to the measuring frequency. The primary outcome was the frequency of patients with myocardial injury within 3 days and was established *a priori*. It was defined as a hsTnT elevation of 20–64 ng

L<sup>-1</sup> with an absolute change of ≥5 ng L<sup>-1</sup>, or a hsTnT level ≥65 ng L<sup>-1</sup>, both evaluated as due to ischaemic aetiology.<sup>19</sup> Non-ischaemic causes were sepsis, acute renal failure, chronic renal insufficiency, life-threatening tachycardia, pulmonary embolism, recent cardioversion or recent cardiac arrest. If chronically elevated hsTnT was present at baseline, a change of >20% was regarded as new myocardial injury.<sup>19</sup> Secondary *a priori* outcome was peak hsTnT level within 3 days. The study also included *a priori* exploratory analyses of combinations of dichotomized exposure variables (i.e. micro events of vital sign deviations) and their association with myocardial injury. One micro event in each vital sign category were chosen and were defined as having five or more consecutive minutes of the following: hypoxaemia, SpO<sub>2</sub> < 85%; bradycardia, HR < 40 bpm; bradypnoea, RR < 11 min<sup>-1</sup> and tachypnoea, RR > 24 min<sup>-1</sup>. Micro events of hypotension were defined as 60 consecutive minutes of SBP < 90 mmHg and hypertension SBP > 180 mmHg and tachycardia HR > 130 bpm for ≥30 min. Lastly, the study included post-hoc analyses of the main outcome of cumulative duration of SpO<sub>2</sub> < 85%, in the two separate groups of AECOPD and major abdominal cancer surgery.

## 2.4 | Statistical analyses

Patients were divided into groups of myocardial injury and no myocardial injury. By Wilcoxon Rank-Sum Test, the exposure of cumulative duration of vital sign deviations were compared with myocardial injury. We describe the mean difference between groups for duration of vital sign deviations to account for a large part of vital sign deviations occurring rarely (thus, median duration being 0). The analysis of the main outcome of cumulative duration of SpO<sub>2</sub> < 85% was repeated according to subgroups of AECOPD and major abdominal cancer surgery. The exploratory analyses of combinations of micro events were planned as hypothesis generating. Patients having 0, 1, 2 or ≥3 different micro events and their frequency of myocardial injury and median peak hsTnT were illustrated. A *p*-value < .05 was considered statistically significant. Statistical analysis was performed using SAS Studio (Version 3.71; SAS Institute, Cary, NC).

## 3 | RESULTS

Of 1881 patients screened, 677 patients were included, of which 185 patients were admitted with AECOPD, and 492 patients had undergone major abdominal cancer surgery. Of these patients, 11 had no troponin measurements (e.g., due to haemolysed samples or early discharge), two patients had no vital sign monitoring and two patients had no vital sign monitoring in the 24 h before a troponin measurement, all of which were thus excluded, leaving a total sample of 662 patients for analyses (Figure 2). A total of 28,713 h of continuous monitoring were included, with an average of 43 h of measurements per patient. Patients had a median recorded monitoring time of 19 h (IQR 17 to 21) of the 24 h chosen *a priori* for the primary analyses. Monitoring time was similar in the two groups

(median 19.9 h for the myocardial injury group and 18.7 for the no myocardial injury group).

Myocardial injury occurred in 113 (17%) of the 662 patients (Table 1). Thirty-two patients had myocardial injury without continuous vital sign measurements during the preceding 24 h, and were included in reports of the primary outcome, but not in analyses including exposures. The frequencies of deviating micro events in the analysed 24 h ranged from 0.5% (SBP < 70 mmHg) to 63% (SpO<sub>2</sub> < 88% for 10 min) across groups (Table 2).

Cumulative duration of SpO<sub>2</sub> < 85% was significantly associated with subsequent myocardial injury (mean difference 14.2 min [-4.7 to 33.1]; *p* = .005, Table 3). Cumulative durations of hypoxaemia (SpO<sub>2</sub> < 88%, SpO<sub>2</sub> < 85% and SpO<sub>2</sub> < 80%), tachycardia (HR > 110 bpm and HR > 130 bpm), tachypnoea (RR > 24 min<sup>-1</sup> and RR > 30 min<sup>-1</sup>) and bradypnoea (RR < 11 min<sup>-1</sup>, but not RR < 5 min<sup>-1</sup>) were significantly associated with myocardial injury, the latter being an inverse association (Table 3). The cumulative durations of the remaining 11 vital sign deviations were not significantly associated with myocardial injury (*p* > .05 for all). The primary analysis of cumulative duration of SpO<sub>2</sub> < 85% was not significantly associated with

myocardial injury when repeated in post-hoc subgroups of major abdominal cancer surgery and AECOPD; mean difference 5.2 min (-14.2 to 24.6), *p* = .14 and 12.4 min (-21.0 to 45.9) *p* = .26 respectively. Micro events of hypoxaemia, tachycardia and tachypnoea appeared to be more frequent in the myocardial injury group, whereas micro events of the respiratory rate below 11 min<sup>-1</sup> but not below 5 min<sup>-1</sup> appeared to be less frequent, though neither were tested for significance (Table 2). The number of specific micro events and frequency of both myocardial injury and median peak hsTnT are illustrated in Figure 3. For patients with 0 and ≥3 different micro events, the frequency of myocardial injury was 14.2% and 17.5% and the median peak hsTnT was 15 and 22 ng L<sup>-1</sup> respectively.

## 4 | DISCUSSION

We found a significant association between cumulative duration of SpO<sub>2</sub> < 85% measured continuously and myocardial injury. Furthermore, cumulative durations of hypoxaemia (SpO<sub>2</sub> < 88% and SpO<sub>2</sub> < 80%), tachycardia (HR > 110 bpm and HR > 130 bpm) and

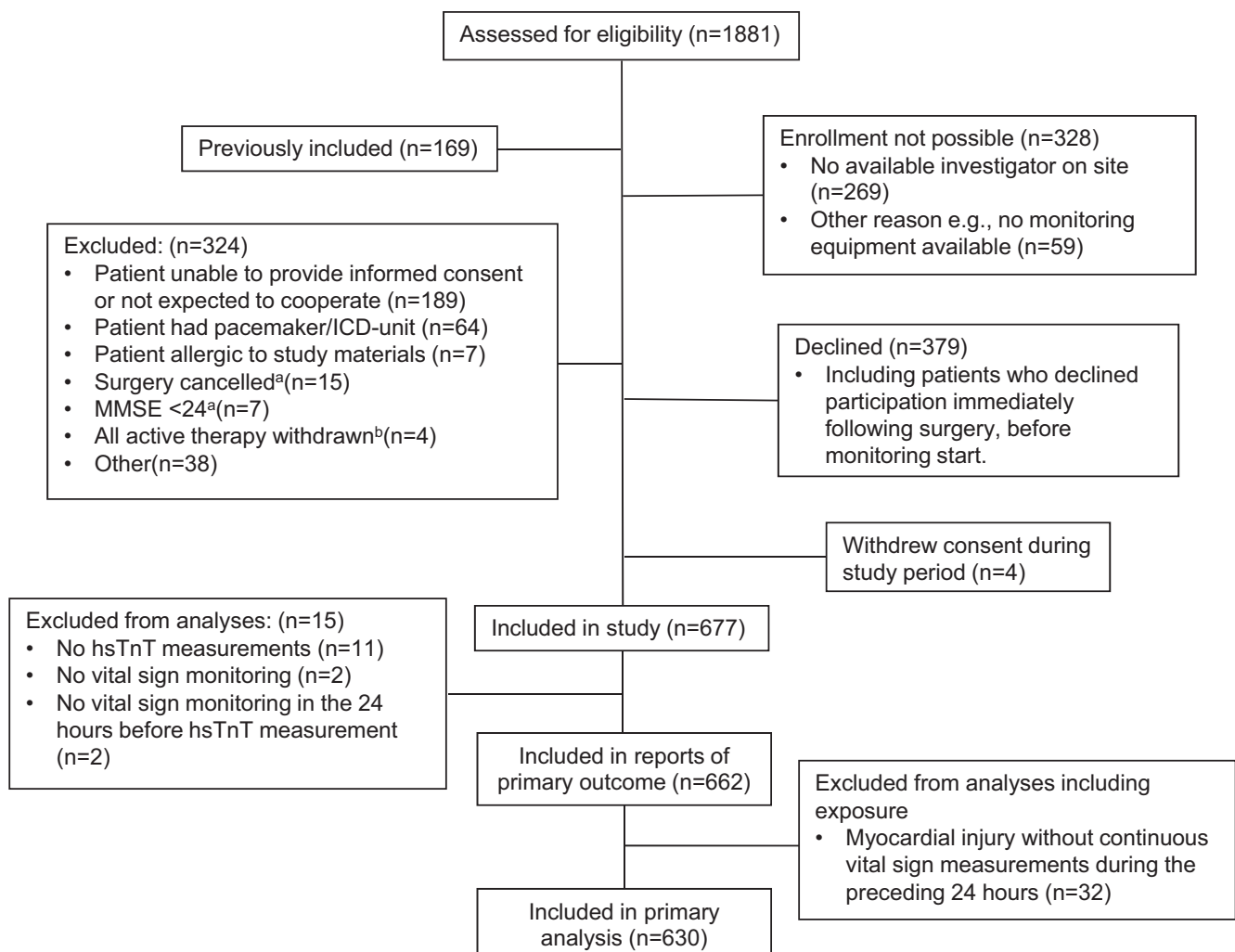


FIGURE 2 Title: Flow diagram of patient inclusion. <sup>a</sup>Surgical patients only; <sup>b</sup>AECOPD patients only. ICD, Implantable Cardioverter Defibrillator; MMSE, Mini-Mental State Examination

**TABLE 1** Baseline variables in patients with and without myocardial injury during medical admission or post-operative

	Myocardial injury (n = 113)	No myocardial injury (n = 549)
Age	74 (62 to 87)	70 (60 to 85)
Male	67 (59%)	314 (57%)
Surgical patients	77 (68%)	408 (74%)
AECOPD patients	36 (32%)	141 (26%)
BMI, kg m <sup>-2a</sup>	25 (19 to 34)	25 (19 to 34)
Daily smoker		
Never smoker	18 (16%)	142 (26%)
Previous smoker	67 (59%)	301 (55%)
Current smoker	28 (25%)	106 (19%)
Alcohol consumption		
None	28 (25%)	146 (27%)
Below recommendations <sup>b</sup>	64 (57%)	298 (54%)
Above recommendations <sup>b</sup>	21 (19%)	105 (19%)
ASA classification <sup>c</sup>		
ASA I	0 (0%)	21 (5.1%)
ASA II	29 (38%)	226 (55%)
ASA III	48 (62%)	157 (38%)
ASA IV	0 (0%)	4 (0.9%)
History of Myocardial infarction	9 (8.0%)	22 (4.0%)
History of Diabetes Mellitus	30 (27%)	87 (16%)
History of Chronic Heart Failure	11 (10%)	22 (4.0%)
FEV1/FVC <sup>d</sup>	0.52 (0.31 to 0.79)	0.52 (0.32 to 0.78)
SBP, mmHg (at inclusion)	135 (107 to 176)	135 (107 to 172)
DBP, mmHg (at inclusion)	72 (54 to 90)	76 (56 to 95)
SpO <sub>2</sub> , % (at inclusion)	97 (92 to 100)	97 (92 to 100)

Note: Values are number (percentage) or median (5–95% range).

Abbreviations: ASA, American Association of Anaesthesiology; BMI, Body mass index; FVC, Forced vital capacity; FEV1, Forced expiratory volume in 1 second; SBP, Systolic blood pressure; SpO<sub>2</sub>, Peripheral oxygen saturation.

<sup>a</sup>Data missing in two cases.

<sup>b</sup>As recommended by the Danish Health Authority: 24 g/day for men or 12 g/day for women.

<sup>c</sup>Surgical patients only.

<sup>d</sup>AECOPD patients only, based on last recording in electronic health records, available in 160 cases.

tachypnoea (RR > 24 min<sup>-1</sup> and RR > 30 min<sup>-1</sup>) were significantly associated with myocardial injury. We also found the cumulative duration of bradypnoea (RR < 11 min<sup>-1</sup>, but not RR < 5 min<sup>-1</sup>) to occur significantly less in patients with myocardial injury. The association of SpO<sub>2</sub> < 85% and myocardial injury was not significant in

subgroup analyses of AECOPD and major abdominal cancer surgery, which indicates a weaker association than reported, and the results should therefore be interpreted with caution. Our study examined two different patient populations, but it is assumable that the pathophysiology of myocardial injury is largely identical across these two high-risk hospitalized patient groups.

#### 4.1 | Hypoxaemia

Our results are consistent with a study by Bojesen et al.<sup>10</sup> of 87 post-operative patients following minimally invasive surgery using continuous pulse oximetry and troponin I measurement. They found a significant association between peak troponin I above the detection limit of 15 ng L<sup>-1</sup> and time spent below SpO<sub>2</sub> 88%. The study investigated hypoxaemia during the total monitoring time, not the isolated exposure occurring up to troponin I elevation, nor accounted for non-ischaemic aetiology, which contrasts with our study. Another study by Chan et al.<sup>11</sup> included 1106 patients and found a significantly longer mean post-operative cumulative duration of SpO<sub>2</sub> < 80% in patients with cardiac complications than patients without cardiac complications. On the contrary, results from 202 AECOPD admissions in 99 patients, showed no significant association between the partial pressure of oxygen in arterial blood and hsTnT though both were measured only once at admission.<sup>15</sup>

#### 4.2 | Tachycardia

Troponin T levels and tachycardia have also been significantly associated in previous studies of AECOPD patients measured at admission.<sup>13,15</sup> Pre-operative tachycardia has been associated with MINS, and studies of intra-operative tachycardia and myocardial injury have shown conflicting results.<sup>12,20–22</sup> Our results indicate an association between post-operative tachycardia and myocardial injury.

#### 4.3 | Hypotension

The lack of association between blood pressure and myocardial injury supports previous findings by Høiseith et al.,<sup>14</sup> who found no association between MAP and hsTnT in patients admitted with AECOPD. On the contrary, we could not confirm previous associations between post-operative hypotension and cardiac events.<sup>23–25</sup> Sessler et al. examined 9,186 patients at post-operative days 1–4 based on routine ward measurements.<sup>23</sup> They found that a composite of myocardial infarction and mortality was associated with hypotension, but blood pressure was assumed unchanged until next measurement 4–6 h later, potentially overestimating the duration. Another study of 2766 patients in surgical intensive care units found significant associations between the lowest recorded MAP and a composite outcome of MINS and mortality.<sup>24</sup> Troponin measurements were non-mandatory and possibly ordered more

	Myocardial injury (n = 81 <sup>a</sup> )	No myocardial injury (n = 549)
<b>Hypoxaemia</b>		
SpO <sub>2</sub> < 92%	49 (60%)	305 (56%)
Event duration of ≥60 min		
SpO <sub>2</sub> < 88%	51 (63%)	277 (50%)
Event duration of ≥10 min		
SpO <sub>2</sub> < 85% (primary exposure variable)	45 (56%)	247 (45%)
Event duration of ≥5 min		
SpO <sub>2</sub> < 80%	49 (60%)	221 (40%)
Event duration of ≥1 min		
<b>Bradycardia</b>		
Heart rate < 40 bpm	3 (3.7%)	17 (3.1%)
Event duration of ≥5 min		
Heart rate < 30 bpm	4 (4.9%)	14 (2.6%)
Event duration of ≥1 min		
<b>Tachycardia</b>		
Heart rate > 110 bpm	21 (26%)	72 (13%)
Event duration of ≥60 min		
Heart rate > 130 bpm	9 (11%)	23 (4.2%)
Event duration of ≥30 min		
<b>Hypotension</b>		
SBP < 90 mmHg	13 (16%)	79 (14%)
Event duration of ≥60 min		
SBP < 70 mmHg	1 (1.2%)	3 (0.5%)
One measurement		
MAP < 70 mmHg	25 (31%)	187 (34%)
Event duration of ≥60 min		
MAP < 60 mmHg	11 (14%)	81 (15%)
One measurement		
<b>Hypertension</b>		
SBP > 180 mmHg	8 (10%)	48 (8.8%)
Event duration of ≥60 min		
SBP > 220 mmHg	2 (2.5%)	4 (0.7%)
One measurement		
MAP > 120 mmHg	9 (11%)	53 (10%)
Event duration of ≥60 min		
MAP > 130 mmHg	7 (8.6%)	43 (7.8%)
One measurement		
<b>Bradypnoea</b>		
Respiratory rate < 11 min <sup>-1</sup>	13 (16%)	166 (30%)
Event duration of ≥5 min		
Respiratory rate < 5 min <sup>-1</sup>	3 (3.7%)	22 (4.0%)
Event duration of ≥1 min		
<b>Tachypnoea</b>		
Respiratory rate > 24 min <sup>-1</sup>	16 (20%)	81 (15%)
Event duration of ≥5 min		
Respiratory rate > 30 min <sup>-1</sup>	15 (19%)	60 (11%)
Event duration of ≥1 min		

**TABLE 2** Number of patients with micro events 24 h before myocardial injury compared with the first 24 h of monitoring before a non-*ischaemic* hsTnT measurement

Note: Values are number (percentage).

Abbreviations: HR, Heart Rate; hsTnT, high-sensitive cardiac troponin T; MAP, Mean arterial pressure; Peripheral oxygen saturation; RR, Respiratory rate SBP, Systolic blood pressure; SpO<sub>2</sub>.

<sup>a</sup>Thirty-two patients had myocardial injury without continuous vital sign measurements during the preceding 24 h.

**TABLE 3** Vital sign deviations 24 h before myocardial injury compared with the first 24 h of monitoring before a non-ischaemic hsTnT measurement

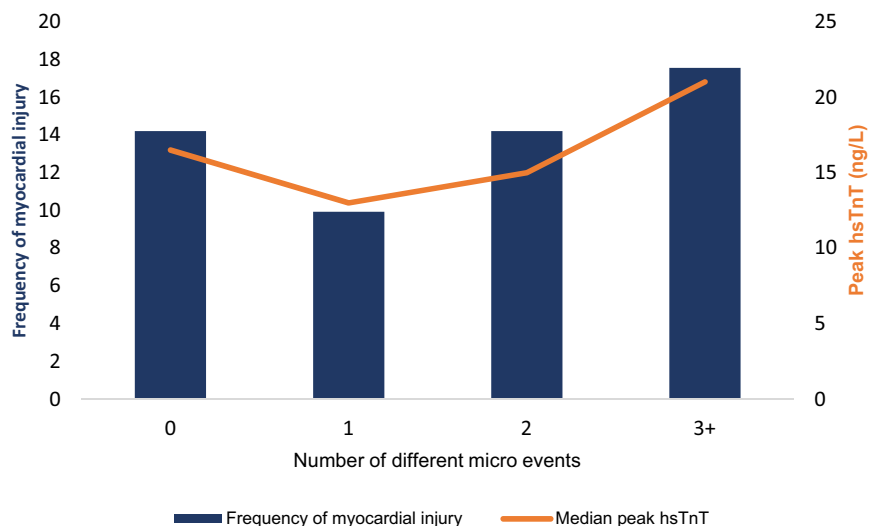
<i>n</i> = 630 <sup>a</sup>	<i>p</i> -value	Mean difference (95% CI) in minutes
<b>Hypoxaemia</b>		
SpO <sub>2</sub> < 92%	.14	37.9 (-27.5 to 103.2)
SpO <sub>2</sub> < 88%	.013	33.9 (-5.5 to 73.4)
SpO <sub>2</sub> < 85% (primary exposure variable)	.005	14.2 (-4.7 to 33.1)
SpO <sub>2</sub> < 80%	.0001	1.3 (-3.2 to 5.7)
<b>Bradycardia</b>		
HR < 40 bpm	.26	2.3 (-0.9 to 5.5)
HR < 30 bpm	.28	0.5 (-0.4 to 1.3)
<b>Tachycardia</b>		
HR > 110 bpm	.007	39.4 (-3.2 to 82.0)
HR > 130 bpm	.04	7.2 (-3.1 to 17.5)
<b>Hypotension<sup>b</sup></b>		
SBP < 90 mmHg	.96	-0.34 (-0.8 to 0.1)
SBP < 70 mmHg	.45	0.01 (-0.02 to 0.03)
MAP < 70 mmHg	.44	-0.7 (-2.0 to 0.6)
MAP < 60 mmHg	.76	-0.2 (-0.5 to 0.1)
<b>Hypertension<sup>b</sup></b>		
SBP > 180 mmHg	.54	0.3 (-0.2 to 0.9)
SBP > 220 mmHg	.12	0.07 (-0.1 to 0.3)
MAP > 120 mmHg	.52	0.1 (-0.3 to 0.6)
MAP > 130 mmHg	.69	0.2 (-0.2 to 0.5)
<b>Bradypnoea</b>		
RR < 11 min <sup>-1</sup>	<.0001	-32.9 (-57.0 to 7.8)
RR < 5 min <sup>-1</sup>	.90	-0.02 (-0.2 to 0.1)
<b>Tachypnoea</b>		
RR > 24 min	.04	20.4 (-9.3 to 50.1)
RR > 30 min <sup>-1</sup>	.04	3.0 (-3.6 to 9.5)

Abbreviations: HR, Heart Rate; hsTnT, high-sensitive cardiac troponin T; MAP, Mean arterial pressure; RR, Respiratory rate; SBP, Systolic blood pressure; SpO<sub>2</sub>, Peripheral oxygen saturation.

<sup>a</sup>Thirty-two patients had myocardial injury without continuous vital sign measurements during the preceding 24 h.

<sup>b</sup>Blood pressure variables were accumulated number of events due to measuring frequency.

**FIGURE 3** Frequency of patients with myocardial injury and median peak hsTnT, both stratified by number of different micro events. Micro events were defined as dichotomized deviations specified as 5 or more consecutive minutes of the following: hypoxaemia, SpO<sub>2</sub> < 85%; bradycardia, HR < 40 bpm; bradypnoea, RR < 11 min<sup>-1</sup> and tachypnoea, RR > 24 min<sup>-1</sup>. Micro events of hypotension were defined as 60 consecutive minutes of SBP < 90 mmHg and hypertension SBP > 180 mmHg and tachycardia HR > 130 bpm for ≥30 min. SpO<sub>2</sub>, Peripheral oxygen saturation; hsTnT, high-sensitive cardiac troponin T





often in sicker patients, prone to hypotension and adverse events. Peak hsTnT have also been associated with lowest recorded post-operative MAP, though not significant in the general ward, and not accounting for pre-operative hsTnT.<sup>25</sup>

#### 4.4 | Other deviations

Tachypnoea is a common predictor of patient deterioration. Our results further indicate an association between respiratory rate and myocardial injury, which could be due to the severity of respiratory distress in AECOPD patients. Brekke et al. found the same association in AECOPD at admission, though it did not reach significance in multivariate regression.<sup>13</sup> Additionally, an association between MINS and severe, but not mild or moderate, obstructive sleep apnoea, has been found in a post-hoc analysis.<sup>11</sup> Intra-operative hypertension has previously been associated with MINS, and intra-operative bradycardia to reduced MINS.<sup>12</sup> These deviations could be of longer duration in the general ward due to unawareness and therefore be expected to cause more harm, but no such correlation was found in our study.

Interestingly, our exploratory analysis of combinations of different micro events does not indicate that deviations of more categories are associated with an increased risk of myocardial injury or peak hsTnT. It would seem biologically plausible that autonomic compensatory mechanisms can maintain adequate oxygenation and perfusion during single category deviations compared with multiple deviations. Our contrary findings could perhaps be explained by acutely ill patients being more prone to equipment removal and thus falsely elevate frequency of myocardial injury and peak hsTnT in the group without deviating vital signs.

The major strength of this study was the comprehensive data of multiple continuous vital signs in two common high-risk groups of hospitalized patients combined with thorough screening for myocardial injury. Deviating vital signs did not result in interventions since data were blinded to ward staff, and durations are therefore clinically representative. The study shows the ability of wireless continuous monitoring to detect otherwise overlooked deviations, of significant clinical impact. The current study also comes with some limitations. First, it is unknown, at which point during the 24-h gap between troponin measurements, the event of myocardial injury occurs. Thus, we do not know whether we reported vital signs 1-h pre-event and 23-h post-event or vice versa, thereby risking a reverse causality bias. Second, the study did not account for supplemental oxygen therapy, but since data were blinded to ward staff, the SpO<sub>2</sub> measurements should be representative of the general high-risk inpatient population. Third, confounders were excluded according to the definition of MINS,<sup>19</sup> but potential other confounders like bleeding and/or anaemia were not considered. The chosen cut-off values in this study are arbitrary; however, they are based on the clinically evaluated and implemented Early Warning Score regimen and previous studies. Fourth, data were not extrapolated; and thus, the extent of deviations may have been underestimated due to periods with missing data.

The aetiology of myocardial injury is not always clear. Both a type I (coronary thrombus) and type II (oxygen supply/demand mismatch) aetiology have been proposed, but coronary angiographic studies suggest a mainly type II aetiology during AECOPD and in peri-operative myocardial infarction.<sup>26-32</sup> The associations of hypoxaemia, tachycardia and respiratory rate with myocardial injury found in our study support the theory of type II aetiology to largely contribute to myocardial injury. Additional studies of specific combinations of vital sign deviations prior to myocardial injury or further diagnostic examinations such as coronary angiography in patients with myocardial injury are warranted for further understanding of the pathophysiology. For now, preventive measures for myocardial injury are very sparse. Potentially, the findings from the current study can be useful for future clinical trials, testing the clinical effect of alarms based on these deviations in a clinical support system. This may allow the clinician to react and treat, and thus perhaps prevent or attenuate myocardial injury. In conclusion, we found that cumulative duration of SpO<sub>2</sub> below 85% was significantly associated with myocardial injury in high-risk hospitalized patients during admission for AECOPD or after major abdominal cancer surgery. Durations of hypoxaemia, tachycardia and tachypnoea were associated with myocardial injury, whereas bradypnoea occurred less commonly. The effect of early detection and interventions from continuous wireless monitoring should be assessed.

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#### CONFLICT OF INTEREST

The WARD founders have created a start-up company, WARD247 ApS, with the aim of pursuing the regulatory and commercial activities of the WARD-project. WARD247 ApS has obtained license agreement for any WARD-project software and patents. One patent has been filed: "Wireless Assessment of Respiratory and circulatory Distress (WARD) – Clinical Support System (CSS) – an automated clinical support system to improve patient safety and outcomes." None of the above entities influenced the study design, conduct, analysis, or reporting.

#### PRESENTATION OF PRELIMINARY DATA

None.

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