Science Letter

Prediction of postoperative cardiopulmonary complications via assessment of heart rate recovery after submaximal exercise testing

Risk prediction is a fundamental component of peri-operative medicine. Cardiopulmonary exercise testing to maximal effort is considered the gold standard, objective measure of cardiopulmonary fitness [1]. Its use is limited due to cost, availability and contraindications in patients with certain comorbidities. Submaximal exercise tests such as the 6-minute walk test (6MWT) are a cost-effective, well-tolerated alternative, but their results can be influenced by patient effort [2].

Heart rate recovery may present a useful, objective alternative to determine functional capacity following submaximal exercise tests. Heart rate recovery is a robust surrogate for cardiac vagal activity, which is associated with exercise capacity, cardiovascular morbidity and all-cause mortality [3]. Heart rate recovery 1, the reduction in heart rate over 1 min following exercise cessation, is a validated marker for peri-operative risk prediction after maximal testing [4]. However, previous work has demonstrated that heart rate recovery 1 after submaximal exercise may be effort dependent [5].

We devised a novel heart rate recovery quantification parameter, heart rate recovery-area under the curve (HRR-AUC), which exhibits greater reproducibility and reduced effort dependence compared with existing markers across different exercise intensities in healthy volunteers [5]. The applicability of HRR-AUC in the surgical population remains unknown, however. We sought to explore the association between existing (heart rate recovery 1, 6MWT distance) and novel (HRR-AUC) quantifiers of functional capacity with cardiopulmonary complications and duration of high dependency unit (HDU) stay in patients undergoing lung resection surgery. We performed a planned, secondary analysis of data collected during the BNP for prediction of outcome following lung resection surgery (PROFILES) study; a multicentre, prospective, observational cohort study recruiting patients presenting for lung cancer resection. We retrospectively reviewed a subgroup of patients who, between October 2018 and August 2019, underwent heart rate recovery determination after 6MWTs during pre-operative surgical assessment.

The 6MWTs were performed in accordance with American Thoracic Society guidelines and modified to include heart rate recovery determination. Heart rate was recorded using a portable ECG monitor (Avant 4000, Nonin Medical, Plymouth, MN, USA) at 30-s intervals for 6 min immediately after exercise cessation and plotted on heart rate vs. time curves. The HRR-AUC was calculated as the area under the heart rate vs. time curve throughout the 6-min recovery period using the composite trapezoid rule.

The primary outcome was the association between heart rate recovery 1, HRR-AUC and distance achieved at 6MWT, with cardiopulmonary complications 30 days after surgery as defined by the European Society of Thoracic Surgeons `Silver-book´ definitions [6]. Duration of HDU stay was explored as a secondary outcome, with prolonged stay defined as > 24 h postoperatively [7].

Mean heart rate recovery 1, HRR-AUC and 6MWT distance were compared between patients with and without cardiopulmonary complications and prolonged HDU stays using Student's t-test. Area under the receiver operating characteristic curves (AUROCCs) were calculated to explore the predictive strength of 6MWT distance, heart rate recovery 1 and HRR-AUC for cardiopulmonary complications.

The PROFILES study recruited a subgroup of 36 patients for 6MWT and heart rate recovery testing, 29 of whom had complete data for analysis. Ten (34%) patients developed cardiopulmonary complications. Baseline characteristics of this sub-cohort are summarised in online Supporting Information Table S1.

The HRR-AUC was significantly elevated in patients with cardiopulmonary complications (55.2 bpm*min) compared with those without (38.9 bpm*min), as shown in Fig. 1a (95%CI 0.13–32.5, p = 0.048). There were no differences in mean heart rate recovery 1 (15.1 bpm vs. 14.8 bpm; [95%CI -7.8–8.4], p = 0.937, Fig. 1b) or 6MWT distance (408 cm vs. 387 cm; [95%CI -64.8–107.0], p = 0.616, Fig. 1c) between patients with and without cardiopulmonary complications.

The HRR-AUC was found to be predictive of 30-day cardiopulmonary complications, with an AUROCC of 0.72

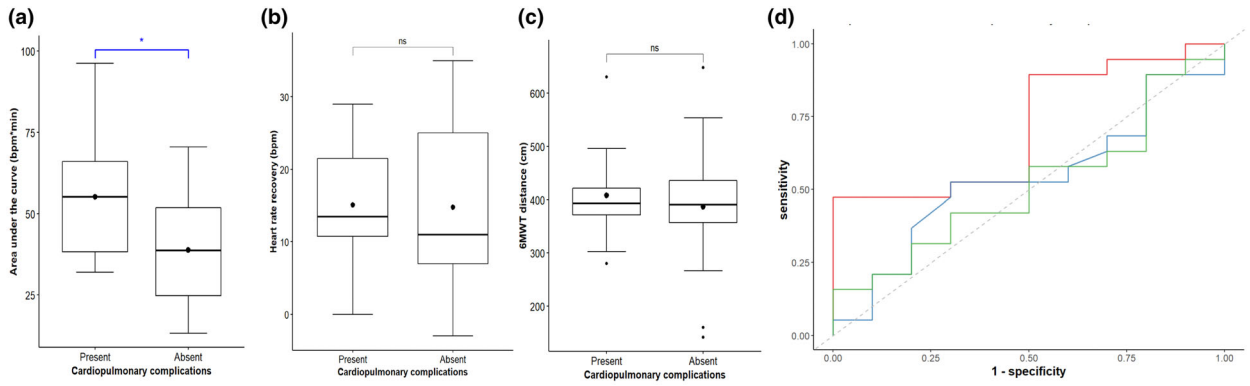

Figure 1 Association between (a) heart rate recovery-area under the curve (HRR-AUC), (b) heart rate recovery (HRR)1 and (c) 6-minute walk test (6MWT) distance in patients with (n = 10) and without (n = 19) postoperative cardiopulmonary complications, accompanied by (d) area under receiver operating characteristic curves (AUROCC) for prediction of 30-day cardiopulmonary complications. Data in (a)–(c) are presented as median with error bars showing IQR. Mean is depicted as large, filled circle. * = $p < 0.05$, ns = $p > 0.05$. Data in (d) presented as AUROCC curves for HRR-AUC, red; HRR1, blue and 6MWT, green.

(95%CI 0.52–0.9). Heart rate recovery 1 and 6MWT distance appeared to show no discrimination (AUROCC = 0.53 [95% CI 0.30–0.76] and 0.52 [95%CI 0.29–0.74], respectively), as illustrated in Fig. 1d.

Seven patients (24%) had a prolonged HDU stay. There were no differences in mean heart rate recovery 1 ($p = 0.371$), 6MWT distance ($p = 0.447$) or HRR-AUC ($p = 0.093$) between patients with normal and prolonged stays.

We found that HRR-AUC differed significantly in patients with and without 30-day cardiopulmonary complications, whilst the 6MWT and heart rate recovery 1 showed no difference. The wide confidence intervals of the AUROCCs reflect the small sample size and exploratory nature of this study.

There was no difference in heart rate recovery 1 and 6MWT distance between patients with or without cardiopulmonary complications or prolonged HDU stays. These findings reinforce our group's previous work [5] and work by Orini et al. [8], which highlight the limitations of heart rate recovery 1 in the submaximal exercise setting. Heart rate recovery 1 relies on heart rates recorded in the first minute of recovery, ignoring potentially useful trends beyond that timescale. The HRR-AUC considers the entirety of the 6 min and accounts for the natural inflections and deflections seen on a heart rate recovery profile, potentially explaining its greater intra-individual reproducibility after submaximal exercise tests [5].

In summary, our findings suggest that pre-operative HRR-AUC differs significantly in patients with cardiopulmonary complications and shows predictive capability for 30-day cardiopulmonary complications compared with 6MWT and heart rate recovery 1 in patients undergoing lung resection surgery. The HRR-AUC offers a promising alternative to conventional pre-operative fitness predictors. A larger, multicentre trial is needed to further explore the predictive capability of HRR-AUC in clinical practice and compare this with validated risk assessment questionnaires such as the Duke Activity Status Index.

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Supporting Information

Additional supporting information may be found online via the journal website.

Table S1. Patient characteristics of the study cohort.