BJA Open, 9 (C): 100255 (2024)

BJA Open

doi: 10.1016/j.bjao.2023.100255
Advance Access Publication Date: 17 January 2024
Original Research Article

ORIGINAL RESEARCH ARTICLE

Preoperative aerobic fitness and perioperative outcomes in patients undergoing cystectomy before and after implementation of a national lockdown

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Data were presented in part and virtually at the international conference for Evidence Based Perioperative Medicine (EBPOM) Ireland | Chicago, 21–23 September 2021.

Abstract

Background: Lower fitness is a predictor of adverse outcomes after radical cystectomy. Lockdown measures during the COVID-19 pandemic affected daily physical activity. We hypothesised that lockdown during the pandemic was associated with a reduction in preoperative aerobic fitness and an increase in postoperative complications in patients undergoing radical cystectomy.

Methods: We reviewed routine preoperative cardiopulmonary exercise testing (CPET) data collected prior to the pandemic (September 2018 to March 2020) and after lockdown (March 2020 to July 2021) in patients undergoing radical cystectomy. Differences in CPET variables, Postoperative Morbidity Survey (POMS) data, and length of hospital stay were compared.

Results: We identified 267 patients (85 pre-lockdown and 83 during lockdown) who underwent CPET and radical cystectomy. Patients undergoing radical cystectomy throughout lockdown had lower ventilatory anaerobic threshold (9.0 [7.9–10.9] *vs* 10.3 [9.1–12.3] ml kg^{-1} min^{-1}; P=0.0002), peak oxygen uptake (15.5 [12.9–19.1] *vs* 17.5 [14.4–21.0] ml kg^{-1} min^{-1}; P=0.015), and higher ventilatory equivalents for carbon dioxide (34.7 [31.4–38.5] *vs* 33.4 [30.5–36.5]; P=0.030) compared with pre-lockdown. Changes were more pronounced in males and those aged >65 yr. Patients undergoing radical cystectomy throughout lockdown had a higher proportion of day 5 POMS-defined morbidity (89% *vs* 75%, odds ratio [OR] 2.698, 95% confidence interval [CI] 1.143–6.653; P=0.019), specifically related to pulmonary complications (30% *vs* 13%, OR 2.900, 95% CI 1.368–6.194; P=0.007) and pain (27% *vs* 9%, OR 3.471, 95% CI 1.427–7.960; P=0.004), compared with pre-lockdown on univariate analysis.

Conclusions: Lockdown measures in response to the COVID-19 pandemic were associated with a reduction in fitness and an increase in postoperative morbidity among patients undergoing radical cystectomy.

Keywords: aerobic fitness; COVID-19 lockdown; CPET; postoperative morbidity; radical cystectomy

Received: 3 August 2023; **Accepted:** 16 December 2023

Limited preoperative aerobic fitness and cardiopulmonary function are associated with perioperative morbidity,[1] increased healthcare resource utilisation,[2,3] and postoperative mortality[4,5] among patients undergoing major elective surgery. Peak oxygen consumption (VO_2 peak), ventilatory anaerobic threshold (AT), and ventilatory equivalents for carbon dioxide measured at AT (V_E/VCO_2) by cardiopulmonary exercise testing (CPET) are objective markers that predict perioperative complications.[6,7]

In response to the COVID-19 pandemic, mandatory stay-at-home (lockdown) policies were implemented in the UK throughout 2020–1.[8] This has inadvertently led to reductions in self-reported physical activity. Longitudinal evaluation of physical activity patterns in England in 35 915 adults demonstrated that one-third of the individuals had decreased levels of physical activity after the first national lockdown.[9] Similar studies reported decreases in physical activity and increases in sedentary behaviours across several populations.[10] Older patients with comorbidities (obesity, hypertension, lung disease) were disproportionately affected compared with younger adults.[11]

Patients undergoing radical cystectomy for malignancy represent a high-risk group with multiple comorbidities[12] who are at risk of significant perioperative morbidity.[13] Poor functional capacity and frailty are also increasingly common in this patient group and are associated with increased morbidity and mortality.[14,15] As such, preoperative CPET is routinely performed in patients undergoing radical cystectomy at our centre.

We hypothesised that the implementation of nationally mandated lockdowns adversely affected preoperative aerobic fitness in patients undergoing high-risk surgery, with associated adverse effects on postoperative morbidity. Our primary objective was to ascertain differences in objective markers of aerobic fitness between patients undergoing radical cystectomy before and after the national lockdown. Markers of aerobic fitness included ventilatory AT, VO_2 peak, and V_E/VCO_2 at AT. Secondary outcomes included day 5 Postoperative Morbidity Survey (POMS)-defined morbidity and length of hospital stay (LOHS).

Methods

Ethics approval

This study was deemed a service evaluation by the local research department (Joint Research Office) and by using the NHS Health Research Authority decision tool. Specific ethics approval was therefore not required. Caldicott Guidelines relating to data collection and confidentiality were maintained. Patients provided written informed consent for subsequent review of the results of their CPET to be stored on an institutional database. Local Research Ethics Committee approval was given for the collection of CPET data on an institutional database (Reference: 19/LO/1371).

Patients and setting

We conducted a single-centre, retrospective, observational study at University College London Hospitals NHS Foundation Trust. We included patients who underwent radical cystectomy for malignancy and had routine preoperative CPET between September 2018 and July 2021. Preoperative CPET performed before the implementation of the first national lockdown (March 2020) was classified as 'pre-lockdown', and preoperative CPET performed from March 2020 to July 2021 was classified as 'lockdown'. The 'lockdown' group encompassed patients presenting for CPET during the: first national lockdown (March–June 2020); minimal lockdown restrictions (July–September 2020); re-imposing of restrictions (September–October 2020); second national lockdown (November 2020); tiered system re-introduction (December 2020); third national lockdown (January–March 2021); phased exit from lockdown (March–July 2021).

Perioperative care pathway

Pre-lockdown patients attended a face-to-face cystectomy clinic for discussion of their diagnosis and treatment options. Patients under consideration for surgery subsequently attended a face-to-face 'One-Stop-Shop' Enhanced Recovery Clinic where CPET was performed. This pathway has been established at our hospital since 2016.[16] As a high-volume bladder cancer centre, we continued to treat patients throughout lockdown, safely delivering the same complex cystectomy service.[17] Throughout lockdown, the first face-to-face clinic was replaced by a telephone clinic to limit hospital footfall.

Cardiopulmonary exercise testing

All patients referred for radical cystectomy underwent routine preoperative CPET. Testing was performed in accordance with the Perioperative Exercise Testing and Training Society (POETTS) guidelines.[6,18] A symptom-limited incremental ramp protocol to volitional exhaustion was performed on an electromagnetically braked cycle ergometer (Lode Corival 906900; Groningen, The Netherlands). Breath-by-breath gas exchange was analysed by a metabolic cart (Metalyzer® 3B; CORTEX Biophysik GmbH, Leipzig, Germany), calibrated prior to each use. A suitable ramp was selected to achieve 8–12 min of incremental exercise and was based on physiologist experience taking into consideration patient weight, age, sex, activity levels, and on-the-day haemoglobin concentration. Testing consisted of rest (3 min), unloaded cycling (3 min), ramped exercise (~8–12 min), and recovery (3 min).

Oxygen uptake (VO_2) and carbon dioxide production (VCO_2), ventilatory frequency, tidal volume, and end-tidal gas tensions were recorded. Ventilatory equivalents for oxygen (V_E/VO_2) and carbon dioxide (V_E/VCO_2) were derived. Values for V_E/VCO_2 were recorded at the AT. VO_2 peak was defined as the highest average VO_2 over the last 30 s of ramped exercise. We determined AT using a combination of the V-slope method, changes in ventilatory equivalent, and end-tidal profiles as per POETTS guidance.[18] VO_2 peak and AT were adjusted for body mass (ml kg^{-1} min^{-1}). All tests were independently interpreted by two clinical exercise physiologists and further verified by a CPET-experienced consultant anaesthetist.

Patient characteristics (age, sex, BMI), comorbidities, ASA grade, smoking status, type of surgery, type of urinary diversion, postoperative care destination, and length of stay (hospital, HDU/ICU, ward) were recorded. Postoperative complications were prospectively recorded using the POMS data,[19] routinely collected in our institution. We described morbidity as a dichotomous non-weighted outcome for any positive score in each of the nine POMS domains on postoperative day 5. Patients who left hospital before day 5 were assumed to have no POMS-defined complications.

Statistical methods

All statistical analysis and graph preparation was performed using GraphPad Prism (v9.5.1; GraphPad Software, San Diego, CA, USA). The Shapiro–Wilk test was used to assess normality. Data were presented as mean (SD) and median (inter-quartile range [IQR]) for parametric and non-parametric continuous data, respectively. Categorical data were presented as number (%). Between-group comparisons were performed using the unpaired *t*-test for parametric continuous variables or the Mann–Whitney *U*-test for non-parametric continuous variables. The χ^2 or Fisher's exact test were used for categorical variables, as appropriate. Subgroup analyses by sex and age (≤65 or >65 years) for AT, VO_2 peak, and V_E/VCO_2 were performed to identify any groups of patients whose fitness levels were disproportionately affected. Two-sided tests were used throughout with statistical significance set at $P \leq 0.05$. Odds ratios (ORs) and 95% confidence intervals (CIs) are presented as OR (95% CI). Kaplan–Meier curves were constructed to assess differences in LOHS with the log-rank (Mantel–Cox) test to compare the time-to-event distributions. Differences were presented as hazard ratio (HR) with 95% CIs, HR (95% CI).

Results

Between September 2018 and July 2021, 267 patients attended the 'One-Stop-Shop' clinic of which 168 patients underwent preoperative CPET and subsequent radical cystectomy. Of the patients undergoing radical cystectomy, 85 patients (51%) were assessed pre-lockdown and 83 patients (49%) throughout lockdown. There was no difference in the proportion of patients who did not undergo radical cystectomy (59 [42%] throughout lockdown *vs* 40 [32%] pre-lockdown; $P=0.107$). Characteristics for patients undergoing CPET and radical cystectomy are presented in Table 1.

There were no differences in the mode of surgery ($P=0.245$), planned postoperative care destination ($P=0.211$), or the type of urinary diversion ($P=0.634$) when comparing pre-lockdown with lockdown (Table 2). The time to surgery was shorter in the lockdown group ($P=0.0001$).

Compared with pre-lockdown, patients presenting throughout lockdown had lower median (IQR) for AT (9.0 [7.9–10.9] *vs* 10.3 [9.1–12.3]; $P=0.0002$) and VO_2 peak (15.5 [12.9–19.1] *vs* 17.5 [14.4–21.0]; $P=0.015$). The median (IQR) for V_E/VCO_2 was higher throughout lockdown compared with

Table 1 Baseline characteristics of patients undergoing CPET and radical cystectomy classified into the pre-lockdown and lockdown groups. Values are median (inter-quartile range), mean (SD), or number (proportion). ASA-PS, American Society of Anesthesiologists Physical Status classification; BMI, body mass index; COPD, chronic obstructive pulmonary disease; P-POSSUM, Portsmouth Physiological and Operative Severity Score for the enumeration of mortality and morbidity.

	Pre-lockdown group ($n=85$)	Lockdown group ($n=83$)	P-value
Age (yr)	68 (62–73)	68 (60–74)	0.938
BMI (kg m^{-2})	26.5 (23.9–30.5)	26.8 (24.3–30.6)	0.636
Sex, *n* (%)			
Male	68 (80)	58 (70)	
ASA-PS, *n* (%)			
ASA 1–2	40 (47)	25 (30)	
ASA 3	42 (49)	50 (60)	
ASA 4	3 (4)	8 (10)	
Smoking status, *n* (%)			
Never	30 (35)	22 (27)	
Former	43 (51)	45 (54)	
Current	12 (14)	16 (19)	
Myocardial infarction, *n* (%)	4 (5)	4 (5)	
Ischaemic heart disease, *n* (%)	7 (8)	4 (5)	
Congestive heart failure, *n* (%)	0 (0)	0 (0)	
Peripheral vascular disease, *n* (%)	7 (8)	6 (7)	
Cerebral vascular disease, *n* (%)	2 (2)	5 (6)	
Dementia, *n* (%)	0 (0)	0 (0)	
COPD, *n* (%)	12 (14)	4 (5)	
Diabetes mellitus, *n* (%)	14 (17)	15 (18)	
P-POSSUM			
Physiological score	18 (15–20)	17 (15–19)	0.107
Operative score	15 (15–17)	15 (15–16)	0.958
Creatinine (mg dl^{-1})	0.87 (0.72–1.05)	0.84 (0.76–1.02)	0.890
Blood pressure (mm Hg)			
Systolic	138 (21)	142 (24)	0.302
Diastolic	77 (12)	77 (10)	0.764
Clinical tumour staging, *n* (%)			
T≤1	39 (46)	37 (45)	
T2	32 (38)	32 (39)	
T3	10 (12)	11 (13)	
T4	4 (5)	3 (4)	
N0	76 (89)	78 (94)	
N≥1	9 (11)	5 (6)	
M0	83 (98)	83 (100)	
M≥1	2 (2)	0 (0)	
Neo-adjuvant chemotherapy, *n* (%)	39 (46)	25 (30)	
COVID-19, *n* (%)	0 (0)	5 (6)	

Table 2 Comparison of surgical mode, postoperative care destination, urinary diversion, and time to surgery between the pre-lockdown and lockdown group. Values are number (proportion) and median (inter-quartile range). HDU, high-dependency unit; ICU, intensive care unit.

	Pre-lockdown group (*n*=85)	Lockdown group (*n*=83)	*P*-value
Mode of surgery			0.245
Open	12 (14)	7 (8)	
Laparoscopic	73 (86)	76 (92)	
Postoperative care destination			0.211
HDU/ICU	80 (94)	82 (99)	
Ward	5 (6)	1 (1)	
Urinary diversion			0.634
Ileal conduit	68 (80)	71 (86)	
Orthotopic neobladder	13 (15)	9 (11)	
Other	4 (5)	3 (4)	
Time to surgery (days)	44 (23–65)	24 (14–42)	0.0001

pre-lockdown (34.7 [31.4–38.5] *vs* 33.4 [30.5–36.5]; *P*=0.030; Fig 1).

Compared with patients presenting pre-lockdown, there was a higher proportion of patients with any POMS-defined morbidity on day 5 throughout lockdown (89% *vs* 75%, OR 2.698 [95% CI 1.143–6.653]; *P*=0.019). Within the nine individual domains of POMS-defined morbidity, there was a greater proportion of patients scoring in the POMS pulmonary domain (30% *vs* 13%, OR 2.900 [95% CI 1.368–6.194]; *P*=0.007) and pain domain (27% *vs* 9%, OR 3.471 [95% CI 1.427–7.960]; *P*=0.004). There were no differences in the proportion of any of the other POMS domains (Table 3). A greater need for post-operative mobility support (58% *vs* 34%, OR 2.648 [95% CI 1.393–4.985]; *P*=0.002) throughout lockdown was observed. No differences in the proportion of CCU re-admissions (13% *vs* 8%; *P*=0.219) or unplanned return to theatre (6% *vs* 8%; *P*=0.766) existed throughout lockdown. A greater proportion of patients presenting throughout lockdown remained in hospital on day 5 compared with pre-lockdown (*P*<0.0001). Compared with pre-lockdown, LOHS was 2 days greater in patients presenting throughout lockdown (10.0 [7.0–16.0] *vs* 8.0 [6.0–14.0]; *P*=0.002, effect size 0.33).

The difference in LOHS was assessed by Kaplan–Meier analysis of the time to event distribution (Fig 2). The log-rank (Mantel–Cox) test demonstrated that the LOHS distributions were not significantly different, $\chi^2(1)=2.774$, *P*=0.096 corresponding HR of 1.269 (95% CI 0.9361–1.720).

In the pre-lockdown group, there was a single patient with a 112-day LOHS who acted as an outlier: this was associated with 10 unplanned returns to theatre. Of the other six patients pre-lockdown and five patients throughout lockdown who had an unplanned return to theatre, all had fewer than two returns. When this outlier was excluded from the Kaplan–Meier analysis, the median (IQR) LOHS for the pre-lockdown group was 7.5 (6.0–13.75) days. Analysis of the

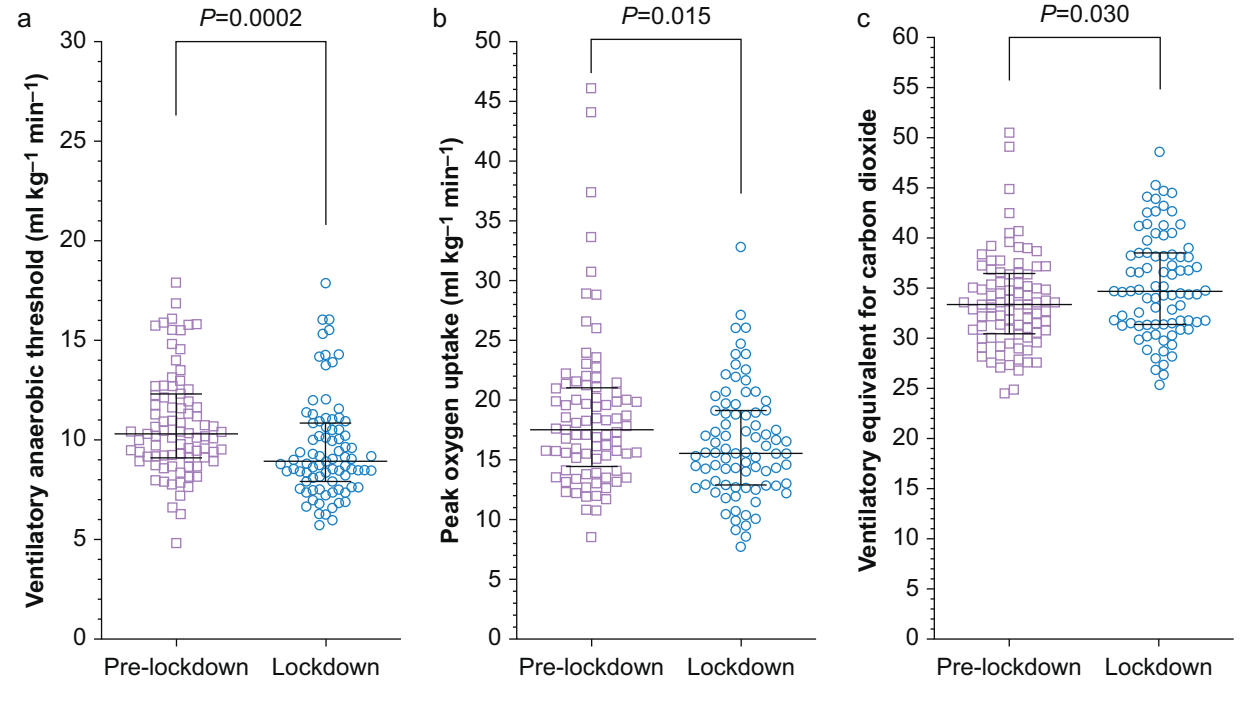

Fig 1. Comparison of objectively measured cardiorespiratory fitness variables in patients undergoing radical cystectomy in the pre-lockdown group *vs* lockdown group for (a) ventilatory anaerobic threshold, (b) peak oxygen uptake, and (c) ventilatory equivalent for carbon dioxide. Data are presented as individual values with median (long horizontal line) and inter-quartile range (short vertical lines). Purple squares indicate pre-lockdown data and blue circles indicate lockdown data. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 3 Day 5 Postoperative Morbidity Survey (POMS)-defined morbidity and postoperative length of stay data pre-lockdown and during lockdown. Values are presented as median (inter-quartile range) or number (proportion). CCU, critical care unit; HDU, high-dependency unit; ICU, intensive care unit.

	Pre-lockdown group (*n*=85)	Lockdown group (*n*=83)	P-value
Day 5 morbidity			
Inpatient	71 (84)	83 (100)	< 0.0001
Any POMS	64 (75)	74 (89)	0.019
Any pulmonary	11 (13)	25 (30)	0.007
Any infectious	29 (34)	36 (43)	0.218
Any renal	27 (32)	23 (28)	0.566
Any gastrointestinal	39 (46)	42 (51)	0.540
Any cardiovascular	3 (4)	4 (5)	0.718
Any neurological	1 (1)	1 (1)	0.999
Any wound	40 (47)	48 (58)	0.162
Any haematological	2 (2)	4 (5)	0.440
Any pain	8 (9)	22 (27)	0.004
Mobility support	29 (34)	48 (58)	0.002
Unplanned return to theatre	7 (8)	5 (6)	0.766
CCU re-admission	6 (8)	11 (13)	0.219
Length of stay (days)			
HDU/ICU	2.0 (1.0–3.0)	1.0 (1.0–4.0)	0.571
Ward	6.0 (5.0–10.0)	8.0 (5.0–12.0)	0.015
Total hospital stay	8.0 (6.0–14.0)	10 (7.0–16.0)	0.002

time to event distribution difference with this patient excluded demonstrated that the difference in LOHS became significant, $\chi^2(1)=4.615$, $P=0.032$, and patients in the lockdown group had HR of 1.360 (95% CI 1.001–1.998).

In the subgroup analyses by sex and age, we identified groups of patients whose fitness levels were disproportionately affected (Table 4). A decrease in AT was observed throughout lockdown for males ($P=0.006$) and females ($P=0.050$). Males also had a lower VO_2 peak ($P=0.039$) and higher V_E/VCO_2 at AT ($P=0.015$). The primary outcome, AT, was also lower in the lockdown group when patients were stratified by age. Patients over 65 yr old had a lower AT ($P=0.0001$). Patients throughout

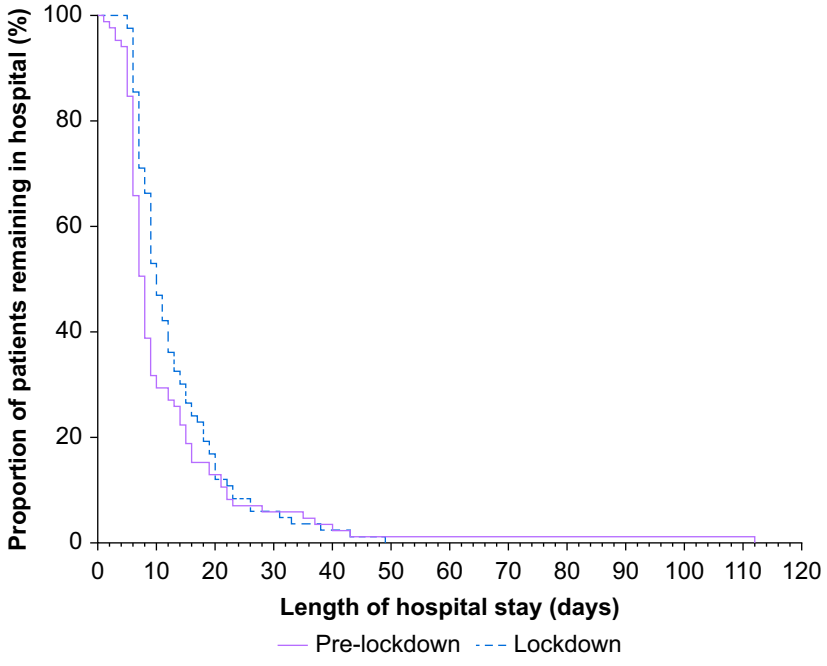

Fig 2. Kaplan–Meier curve indicating length of hospital stay after radical cystectomy comparing all patients operated pre-lockdown (purple solid line) with all patients operated throughout lockdown (blue broken line). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 4 Subgroup comparison of objectively measured cardiorespiratory fitness variables between the pre-lockdown and lockdown group by sex and age. Data are presented as median (inter-quartile range).

	Pre-lockdown group (n=85)	Lockdown group (n=83)	P-value
Anaerobic threshold (ml kg^{-1} min^{-1})			
Male	10.4 (9.3–12.5)	9.3 (8.2–11.1)	0.006
Female	10.1 (8.1–11.3)	8.5 (6.8–9.4)	0.050
≤65 yr	10.2 (8.9–13.1)	9.4 (8.4–11.4)	0.235
>65 yr	10.4 (9.1–12.1)	8.6 (7.6–10.2)	< 0.0001
Peak oxygen uptake (ml kg^{-1} min^{-1})			
Male	18.3 (15.5–21.4)	16.3 (13.8–20.0)	0.039
Female	15.3 (13.3–17.8)	14.4 (11.0–16.8)	0.648
≤65 yr	19.0 (15.7–22.8)	17.1 (14.3–20.7)	0.203
>65 yr	16.7 (14.1–20.0)	14.9 (12.7–17.5)	0.018
Ventilatory equivalent for CO_2			
Male	33.2 (30.1–36.5)	35.2 (31.5–39.2)	0.015
Female	33.4 (31.7–36.1)	34.0 (31.4–36.9)	0.884
≤65 yr	31.5 (29.2–34.4)	31.6 (30.2–34.7)	0.382
>65 yr	34.8 (31.7–37.5)	37.2 (34.3–40.5)	0.013

lockdown over 65 yr old also had a lower VO_2 peak (P=0.018) and higher V_E/VCO_2 at AT (P=0.013). No difference was identified in any patients aged 65 yr or younger.

Discussion

These data are the first, to our knowledge, to assess the impact of COVID-19 restrictions on objectively measured preoperative aerobic fitness levels and postoperative outcomes in complex major surgery. In patients undergoing radical cystectomy, we observed reductions in CPET-defined preoperative aerobic fitness and an increased likelihood of developing POMS-defined morbidity on day 5.

Decreased preoperative aerobic fitness reflects the expected consequences of reduced physical activity throughout lockdown. Numerous observational studies report associations between the implementation of restrictions and changes in physical activity behaviours,[9–11,20] including increased sedentary time.[10] Strain and colleagues[21] analysed a nationally representative dataset using the 'Sport England Active Lives Survey' to assess changes in non-occupational moderate-to-vigorous physical activity levels. They report a substantial decline after restrictions were introduced, such that the odds of reporting any activity in 2020 were 30% lower than in 2016–9. McCarthy and colleagues[22] compared smartphone-tracked movement in the UK, observing a 37% reduction in weekly physical activity minutes with a median reduction of 57 min below baseline in the first week of lockdown. As physical activity and sedentary time are associated with cardio-respiratory fitness,[23,24] measures that directly restrict time spent being active will have adversely affected cardio-respiratory fitness.

Physical activity affects many physiological variables, including aerobic capacity, and fuel metabolism.[25] Reductions in patient activity would therefore have a detrimental effect on aerobic fitness. Four weeks of physical inactivity reduces endurance capacity by up to 41%.[26] In studies investigating the effects of short-term physical inactivity in habitually active participants, cardio-respiratory fitness and lower limb lean mass significantly declined within 14 days, a decrease of 2.2 ml kg^{-1} min^{-1} in VO_2 peak being reported (comparable with the decrement noted in this study).[27] Patients with bladder cancer often have additional treatment-related and cancer-related barriers to maintaining physical activity levels, such as management of urinary symptoms and therapy-related fatigue.[28] These barriers, in combination with the adverse effect of lockdowns on physical activity, likely contribute towards the reduction in cardio-respiratory fitness reported in this study.

We observed a higher V_E/VCO_2 at AT in the lockdown group, reflecting an increase in the number of individuals with impaired gas exchange. The relationship of ventilation to carbon dioxide production mirrors the ventilation-to-perfusion relationship.[6] Smoking and physical inactivity are both associated with decrements in cardiac structure and function.[29] Two-thirds of the study population were current/ex-smokers; this, in combination with inactivity during lockdown, may have contributed to the uncoupling of this relationship and the observed higher V_E/VCO_2. A significant proportion of patients undergoing elective cancer surgery demonstrate ventilatory inefficiency despite the lack of cardiorespiratory risk factors.[5] Physical activity has also been shown to attenuate the age-related decline in lung function, particularly in current/ex-smokers.[30] Consequently, reduction in physical activity throughout lockdown may have mitigated the protective effects of physical activity on lung health in the lockdown group.

The proportion of any POMS-defined morbidity pre-lockdown was 75% which is comparable with published data.[19,31] In comparison, the odds of developing any POMS-defined morbidity during lockdown were ~2.7 times that of pre-lockdown. We observed differences in ASA grade and cardio-respiratory fitness in our lockdown group compared with the pre-lockdown group. The relationship between cardio-respiratory fitness and outcomes is well described in patients undergoing radical cystectomy.[32,33] We are unable to determine the reasons for higher ASA grades in the lockdown group as comorbidity proportions were similar. We hypothesise that the increase in ASA grade reflects the decrease in observed cardio-respiratory fitness, as estimated by CPET in the lockdown group, influencing the assessment of ASA grade. With fewer patients undergoing neoadjuvant chemotherapy throughout lockdown, we would expect greater cardio-respiratory fitness as neoadjuvant chemotherapy reduces aerobic fitness.[34] Lower cardio-respiratory fitness in this group supports the notion of lockdown deconditioning. Fewer patients undergoing neoadjuvant chemotherapy and increased theatre capacity for radical cystectomy (reduction in non-cancer services) may also account for the shorter time to surgery.

The odds of developing POMS-defined pulmonary morbidity in the lockdown group were ~2.9 times higher than pre-lockdown, reflecting both reductions in cardio-respiratory fitness and, specifically, increases in V_E/VCO_2 at AT. Recent pooled analysis of patients undergoing cancer surgery demonstrated that before surgery (1) higher VO_2 peak was associated with absence of postoperative complications or pulmonary complications and (2) V_E/VCO_2 values were significantly lower in patients with no pulmonary complications.[35] In patients with bladder cancer, the V_E/VCO_2 at AT is positively correlated with cardio-pulmonary complications and length of stay.[32] In our study, the lockdown group demonstrated a higher V_E/VCO_2, lower AT, lower VO_2 peak, and experienced a higher proportion of any POMS-defined morbidity and POMS-defined pulmonary morbidity.

We also report a greater need for mobility support on day 5 after surgery in the lockdown group. Periods of inactivity adversely impact muscle mass and function in older adults,[36] possibly explaining the greater mobility requirement. We did not observe a statistically significant difference in LOHS distribution in the lockdown group, although a trend to increased length of stay in the lockdown group was observed (Mann–Whitney *U*-test [P=0.002] with moderate effect size [0.33]). This may reflect the multitude of factors that are known to influence LOHS (such as discharge planning, significant outliers in LOHS [observed in this study] and COVID-19 influences on ward staffing).

When stratified by age, older patients appeared to be disproportionately affected by lockdown. Significant reductions in all three commonly reported CPET measures (AT, VO_2 peak, and V_E/VCO_2 at AT) were limited to patients aged >65 yr. These findings are in line with other studies. Data from 9190 participants in the UK reported disproportionately reduced physical activity among adults with health issues including obesity, hypertension, and disability.[11] Impaired function, advanced age, and multimorbidity are frequent features of frailty and are increasingly common in the bladder cancer population,[14] with frailty associated with worse outcomes after bladder cancer surgery.[15] Furthermore, the rate of decline in aerobic fitness and muscle mitochondrial enzyme activity after deconditioning is faster in older patients.[37] The effects of short-term inactivity are more easily reversible in younger adults than in older adults.[38]

This study is limited by its single-centre, retrospective, and unblinded design. Clinicians were not blinded to CPET findings as CPET was used as a routine clinical tool. Clinicians interpreting the reduced CPET values may have made modifications to individual patient care. Nevertheless, this unblinded practice reflects the pragmatic use of perioperative CPET. We do not have data on the incidence of long COVID which may have implications on cardio-respiratory fitness. Before surgery, five patients (6%) had a positive laboratory confirmed diagnosis of COVID-19. Four patients had COVID-19 >7 weeks before their surgical date and none required hospitalisation. Although our site was a nominated 'COVID-19 Clean Site' for continuation of elective cancer surgery, other factors may have influenced outcomes during this time, including increased hospital pressures and staff re-allocation which would be difficult to account for. Nevertheless, all patients in this study were considered operable, having undergone the same clinical decision-making process, and the modes of surgery and care destination in both groups were comparable. Likewise, comorbidity and tumour staging were comparable between groups.

The use of prospectively collected POMS-defined morbidity data is a major strength of this study. POMS-defined morbidity is a reliable and valid measure of morbidity after major surgery,[19] including urological surgery.[39] The use of CPET to objectively measure the impact of lockdown and inactivity on cardio-respiratory fitness is another major strength. CPET-derived variables are objective markers of cardio-respiratory fitness used perioperatively.[6,18] In contrast, other studies assessing the impact of COVID-19 lockdowns are limited by the use of non-validated questionnaires and recall bias.[40] A further strength is our approach for detecting and verifying key CPET variables by two experienced exercise physiologists and an independent adjudication by an anaesthetist with an interest in exercise physiology.

In summary, we observed lower preoperative aerobic fitness levels, as measured by CPET, in patients undergoing radical cystectomy throughout lockdown compared with pre-lockdown. These changes were more pronounced in older patients. Reductions in preoperative aerobic fitness in lockdown were associated with increased likelihood of developing any POMS-defined morbidity on day 5. These data reflect findings from studies demonstrating reductions in physical activity patterns throughout lockdown and also reflect known associations between cardio-respiratory fitness and clinical outcomes after cystectomy. The wider implications of this period of inactivity on healthcare and longer-term outcomes are unknown. Future research should focus on understanding the sustained impact of reduced cardio-respiratory fitness in the older population as a result of COVID-19 lockdowns on longer-term perioperative outcomes.

Authors' contributions

Conception: NT, AD, MT, ANS, JDK, NA, RCMS, DSM, JW
Study design: NT, AD, NA, RCMS, DSM, JW
Data acquisition: NT, AD, SRM
Analysis: NT, PA, NA, RCMS, DSM, JW
Drafting article: NT, NA, RCMS, DSM, JW
Manuscript revision: all authors
Final approval: all authors

Acknowledgements

JW is funded by an IARS mentored research grant. NA acknowledges support from the Medical Research Council (Grant award MR/W030489/1).

Declarations of interest

The authors declare that they have no conflicts of interest.

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Handling editor: Phil Hopkins