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ABSTRACT

Objectives We aimed to identify exercise tests that have been validated to support a safe discharge to home in patients with or without COVID-19.

Study design Scoping review, using PRISMA-ScR reporting standards. Medline, PubMed, AMED, Embase, CINAHL and LitCovid databases were searched between 16 and 22 February 2021, with studies included from any publication date up to and including the search date.

Intervention Short exercise tests.

Primary outcome measures Safe discharge from hospital, readmission rate, length of hospital stay, mortality. Secondary outcomes measures: safety, feasibility and reliability.

Results Of 1612 original records screened, 19 studies were included in the analysis. These used a variety of exercise tests in patients with chronic obstructive pulmonary disease, suspected pulmonary embolism and pneumocystis carinii pneumonia, heart failure or critical illness. Only six studies had examined patients with COVID-19, of these two were still recruiting to evaluate the 1 min sit-to-stand test and the 40-steps test. There was heterogeneity in patient populations, tests used and outcome measures. Few exercise tests have been validated to support discharge decisions. There is currently no support for short exercise tests for triage of care in patients with COVID-19.

Conclusions Further research is needed to aid clinical decision-making at discharge from hospital.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ First scoping review to comment on the evidence for using exercise testing within the acute assessment of COVID-19 cases.
⇒ Scoping review method following Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for Scoping Reviews reporting guidelines, comprising an extensive search in Medline, PubMed, AMED, Embase, CINAHL and LitCovid databases.
⇒ Abstracts screened by two independent authors using predefined inclusion and exclusion criteria as outlined in our study protocol. The scoping review protocol allowed for any exercise test performed in an acute hospital or primary care setting, in acute cardiopulmonary disease including COVID-19, excluding acute coronary syndrome.
⇒ The review allowed for surrogate outcomes for safe discharge including length of hospitalisation, rehospitalisation, clinical deterioration and mortality.

BACKGROUND

Oxygen saturation is a key parameter in the Early Warning Score, a tool instrumental in identifying the physiological deterioration that frequently precedes clinical deterioration in patients.[1] With the emergence of COVID-19, the feature of silent hypoxaemia gained prominence, referring to patients with severely low oxygen levels, who do not exhibit corresponding features of respiratory distress.[2 3] Understanding that patients at risk of deterioration from COVID-19 could exhibit hypoxaemia as an early indicator of future clinical deterioration,[4 5] with or without the presence of dyspnoea, has led to the integral role of oximetry in the assessment of suspected COVID-19.[6]

As well as silent hypoxia, there have been reports of patients presenting with COVID-19, who have normal oxygen saturation at rest, and develop hypoxaemia on exertion.[7] This has led to the inclusion of exercise testing in guidance for the assessment of suspected COVID-19, within primary care and emergency departments (EDs).[8 9] Emerging evidence of exertional hypoxaemia in COVID-19 as a potential indicator of future deterioration[10] has increased interest in an appropriate exercise test within the acute setting to detect exertional desaturation.

Greenhalgh *et al* used a panel of front-line clinicians to gather consensus on a risk score for suspected COVID-19 in primary care, which includes a suggestion to perform the 40 steps desaturation tests in patients with oxygen saturations above 96%.[11] This test initially appeared in NHS England guidance for ED assessment during the first wave of

the pandemic in the UK,[12] but has not been validated, although it may closely resemble non-standardised walking tests commonplace in clinical practice.

There is an urgent need to identify an appropriate rapid exercise test for the acute setting to assess exertional desaturation in the unwell patient. The test needs to distinguish patients most at risk of deterioration, while ensuring those not desaturating are safe to recover from their illness at home.

This review aims to identify where exercise tests have previously been used in the clinical setting as a discharge decision aid, or way of escalating definitive diagnosis and management in COVID-19 and other acute cardiopulmonary disease.

The review questions for the purpose of this study include:

- Which exercise tests have been validated for use in the context of COVID-19?
- Which existing exercise tests have been used as part of patient assessment in the acute setting to promote safe discharge from hospital?
- Which exercise tests have been shown to effectively demonstrate exertional desaturation and can they be applied safely to an acute setting? What degree of desaturation during an exercise test is significant in acute lung disease, for outcomes including safe discharge, hospitalisation, mortality, length of stay?

METHODS

Study design

A scoping review format was used with a protocol designed with reference to the Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for Scoping Reviews (PRISMA-ScR)[13] reporting guidelines.

The Population, Intervention, Comparator and Outcome (PICO) question for the review was: 'which exercise tests (I) can be used in the assessment of adults in acute care settings (P), in addition to usual care (C), to promote safe discharge from hospital (O)?'

Inclusion and exclusion criteria

Studies conducted in an ED, medical admissions unit, inpatient ward, intensive care unit (ICU), ambulance service and primary care were included. Adult patients presenting to acute settings with symptoms suggesting an acute coronary syndrome were excluded. 'Exercise testing' was defined as any walk, step, sit-to-stand, incremental shuttle, stair climb, bicycle ergometry or treadmill tests. Included were tests used at any part of an acute admission: on presentation (to identify the need for hospitalisation), during admission or at the time of discharge (to identify clinical stability to allow transfer to the community) as long as one of the primary or secondary outcome measures was included in the reporting. Any study publication date up to and including the search date was included in the analysis.

The primary outcome measure was safe discharge as defined by an absence of rehospitalisation or, mortality, length of hospital stay or need for further investigation. Secondary outcomes included safety, feasibility and reliability of the test in the acute setting. Randomised control trials, cohort studies, case–control studies, observational studies, and systematic reviews were screened for references of any relevant studies that met the inclusion criteria outlined. Specific exclusions are outlined further in the study protocol (online supplemental file 1).

Information sources

Our structured search included the Medline, PubMed, AMED Embase, CINAHL and LitCovid electronic databases, and ClinicalTrials.gov and Clinical Trials registry (EU) for ongoing studies. The search terms used are outlined in online supplemental file 2. The titles and abstracts of the studies identified by the search were screened independently by two review authors using the Rayyan[14] platform. Discrepancies were discussed between the two reviewers and, where necessary, a third independent reviewer was consulted. A full-text review of all included papers was then completed to confirm eligibility.

Data extraction was done by a single author. Assessment of the quality of research including risk of bias was not formally assessed within the scope of this review. The study selection was reported using the standards outlined in the PRISMA-ScR.[13] The data included was analysed in relation to the review questions and outcomes outlined, discussing COVID-19 and other acute cardiopulmonary disease separately. The results are used to discuss suitable tests for assessing exertional desaturation in the acute setting, including needs for future research.

Patient and public involvement

Patients and the public were not consulted in the design of this research; however, the results have clear implications for patients and the public, and we would anticipate patient involvement in subsequent research and clinical policy decisions arising from the findings of this review.

RESULTS

In total, 1944 records were identified by the searches, of which 339 were duplicates. Of 1612 original records screened, 17 completed studies and 2 ongoing studies were included in the analysis stage (figure 1). The demographics of the studies are summarised in table 1. Studies were from the UK (1), Europe (7), North America (4), Asia (2), South America (1) and Australia (1). Multiple different outcomes and heterogeneity of methods and populations preclude a meta-analysis. Completion rates of the chosen exercise test varied from 32% to 100% (median 99%). The most used cut-offs were 3% desaturation and desaturating below 90% in four studies each.

COVID-19

Four studies included patients with confirmed or suspected COVID-19 (table 2). Two further studies were still recruiting (online supplemental file 3). Kamran *et al*[15] assessed patients at admission for minimal desaturation,

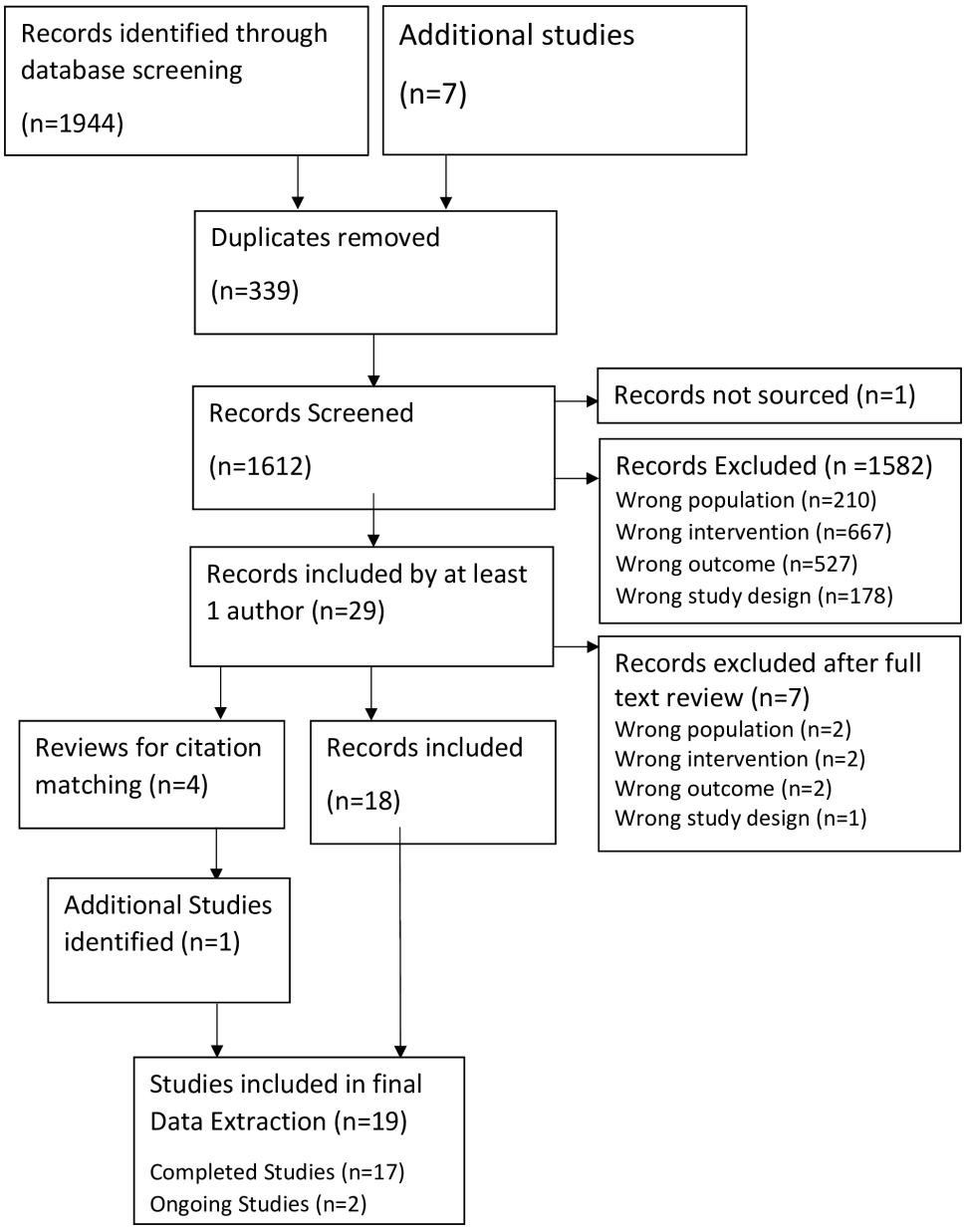

Figure 1 Consolidated Standards of Reporting Trials flow diagram showing the study selection process. In total, 1944 records were identified by the search, 1612 abstracts were screened and 19 studies were included in the final evaluation (17 completed and 2 ongoing studies).

using a 10-feet desaturation test. The mean drop in oxygen saturation following the exercise test was 3% in stable patients, 9% in patients who clinically deteriorated (p<0.001) and 15% in patients who later died (p<0.001). Overall, 52% of patients who remained stable desaturated≥3%, compared with 84% of the clinically deteriorating group and 96% of the mortality group (χ^2 square test, p<0.001). However, on multivariate Cox regression analysis, desaturation during the 10-feet test was not a significant predictor of deterioration (HR 0.99, CI 0.95 to 1.04, p=0.706).

Fuglebjerg *et al*[16] screened 47 inpatients with COVID-19 with oxygen saturation (SpO2)>94% and no fever, recruiting 26 patients without comorbid lung or cardiac disease. Overall, 50% of the participants terminated the 6 min walk test (6MWT) due to desaturation below SpO_2 90%, of whom 46% were admitted to ITU and 15% received mechanical ventilation. Only 46% of these cases were investigated further for pulmonary embolism (PE), but of those investigated, 67% tested positive for PE.

Banzi *et al*[17] assessed the feasibility of a daily rapid walk test as an admission decision tool in primary care, using 5% desaturation to trigger admission. None of the 37 patients in the study met this threshold. One patient was admitted due to a SpO_2<90% at rest and required CPAP. Due to the small sample obtained conclusions about feasibility were not reached.

Goodacre *et al*[10] retrospectively analysed 22 000 records, identifying 817 suspected or confirmed COVID-19 patients presenting to ED who had post-exertional oxygen

Table 1 Demographics of included studies

Reference	Study type	Setting	Diagnosis	Participants	Demographics
Kamran *et al*[15]	Single-centre cross-sectional study	Hospital, Pakistan	COVID-19	252	Age, median (range): 63 (29–85) Sex, %: male, 61.5
Fuglebjerg *et al*[16]	Prospective cohort study, retrospective control group	Hospital, Denmark	Cases: COVID-19 controls: IPF	Cases: 26 Controls: 204	Age, median (IQR): 59 (50–70) Sex, %: male 86.5
Banzi *et al*[17]	Pilot feasibility study	Primary care, Italy	Suspected or confirmed COVID-19	37	Age, median (range): 53.9 (23–83) Sex, %: male 27%
Goodacre *et al*[10]	Observational cohort study (mixed prospective and retrospective methodology)	Multicentre, ED, UK	Suspected or confirmed COVID-19	817	Age, mean (SD): 58.4 (24.2) Sex, %: male, 49.2, female, 49.9, not recorded 0.9 Ethnicity, %: white 58.1, Asian 8.2, black 5.8, mixed/multiple 2.2, other 5.8, not recorded 20.0
Danielsbacka *et al*[19]	Cross-sectional study	Medical admissions unit, Sweden	PE, subdivided into two groups based on vessel occlusion	50	Age, mean (SD): 54.7 (9.9) Sex, %: male, 39
McCabe *et al*[20]	Observational cohort study	Hospital, USA	Heart failure	71	Age, mean (SD): 52.6 (12.3) Sex, %: female, 42.3 Ethnicity, %
La Rovere *et al*[21]	Retrospective cohort study	Cardiology unit, Italy	Heart failure	466	Age, mean (SD): 61.3 (±11.0) Sex, %: male 35.0
Sakai *et al*[22]	Prospective cohort study	Hospital, Japan	Interstitial pneumonia	73	Age, mean: 68.5 Sex, %: male 63
Howie-Esquivel and Dracup[23]	Prospective pilot Study	Hospital, USA	Heart failure	44	Age, mean (range): 59.6 (27–100) Sex, %: male 65.9 Ethnicity, %: Caucasian/white: 50 African American/black: 29.5, Hispanic/Latino: 11.4 Asian/Pacific Islander: 9.1
Amin *et al*[24]	Prospective cohort study	ED and rapid access thrombosis clinic, Canada	Suspected PE	114	Age, mean: 52.9 Sex, %: male 36.8
Pan *et al*[25]	Prospective cohort study	ED, Canada	CCF, COPD and stable chest pain	40	Age, mean (range): 69 (53–91) Sex, %: male, 60.
José and Dal Corso*et al*[26]	Case–control study	Hospital, Brazil	Cases: acute lung disease Controls: healthy volunteers	Cases: 77 Controls: 20	Age, mean: 56 (36–68) case, 52 (41–66) control Sex, %: male 59.7
Kakavas *et al*[27]	Observational cohort study	Pulmonary unit, Greece	AECOPD	22	Age, mean (SD): 67.2 (7.2) Sex, %: male, 63.
Chouaid *et al*[28]	Prospective cohort study	Respiratory unit, France	HIV positive, suspected PCP	85	Age, median (range): 35 (25–60) Sex, %: male 90.5
Sauleda *et al*[29]	Case–control study	ED, Spain	HIV positive Cases: PCP Controls: non-PCP	Cases: 22 Controls: 23	Age, mean (SE): cases 31 (1), controls 28 (1)
Kichura *et al*[30]	Prospective cohort study	ED, USA	Heart failure	50	Age, median (SD): 66.2 (±12.5) Sex, %: male 42
Denehy *et al*[31]	Nested cohort study	ICU, Australia	ICU inpatients	144 at admission, 116 at discharge	Age, mean (SD): 60.4 (15.8) Sex, %: male, 63

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CCF, congestive cardiac failure; COPD, chronic obstructive pulmonary disease; ED, emergency department; ICU, intensive care unit; IPF, idiopathic pulmonary fibrosis; PCP, pneumocystis pneumonia; PE, pulmonary embolism.

Table 2 Exercise testing in COVID-19

Reference	Intervention	Physiological monitoring	Outcome
Kamran *et al*[15]	10-feet walk O_2 desaturation test at hospital admission	O_2 saturations using pulse oximeter, supported by ABG—≥3% desaturation cut-off used	128 stable, n (%): ► <3%: 62 (48.4) ► ≥3%: 66 (51.6) 124 clinical deterioration, n (%): ► <3%: 17 (13.7) ► ≥3%: 107 (86.3) (χ^2 p<0.0001) 49 mortality, n(%): ► <3%: 2 (4.1) ► ≥3%: 47 (96.0) (χ^2 p<0.0001)
Fuglebjerg *et al*[16]	6MWT at hospital discharge	SpO_2 using pulse oximeter—terminated early if below 90%	Early termination: 50% 46.2% of terminated tests investigated further. PE confirmed in 66.7% of those investigated further.
Banzi *et al*[17]	Daily rapid walk test as admission decision tool	SpO_2 using pulse oximeter—desaturation≥5% or <90% used to trigger hospitalisation	0% patients desaturated≥5%, 3% (1 patient) desaturated below 90%—hospitalised and required CPAP Insufficient sample size for feasibility conclusions
Goodacre *et al*[10]	Exertional test (not standardised)	SpO_2 following exertion—not standardised—≥3% desaturation considered significant	30-day adverse outcomes: Multivariable primary analysis: ► c-statistic—0.59 (95% CI 0.465 to 0.713) ► PPV of ≥3% desaturation 1.78 (95% CI 1.25 to 2.53) ► 0.67 of ≥3% desaturation (95% CI 0.46 to 0.98) Multivariable model secondary* analysis: ► c-statistic—0.67 (0.46 to 0.98) ► PPV of ≥3% desaturation—1.98 (95% CI 1.26 to 3.10) ► NPV of ≥3% desaturation—0.61 (95% CI 0.35 to 1.07)

*Excluded ages<16 years, SpO_2<94%, National Early Warning Score>3.[18]
ABG, arterial blood gas; CPAP, continuous positive airway pressure; c-stat, concordance statistic; CXR, X-ray of the chest; ITU, intensive treatment unit; 6MWT, 6 min walk test; NPV, negative predictive value; O2, oxygen; PE, pulmonary embolism; PPV, positive predictive value; SpO_2, peripheral oxygen saturation.

saturations recorded. The exertional test used was not standardised. Mean decrease in oxygen saturation was 2.9% in the adverse outcome group (needing any cardiorespiratory, renal support or death) compared with 1.9% in the no adverse outcome group, with 3% desaturation found to be optimal at predicting adverse outcome. Exertional desaturation was not found to be predictive of adverse outcomes in the primary analysis cohort (p=0.376), but a secondary analysis cohort excluding participants with a baseline SpO_2<94%, National Early Warning Score[18] of 3 or more, age below 16 years and limited ability to self-care, indicated that desaturation≥3% could be predictive of adverse outcomes in this group (p=0.019).

Other acute cardiopulmonary disease

Table 3 summarises findings in other acute cardiopulmonary disease. Five studies using a 6MWT alone were identified. A lower 6 min walk distance was linked to higher rates of vessel occlusion from pulmonary embolism,[19] as well as rehospitalisation within 30 days,[20] and 12 months[21] in heart failure patients. One study in interstitial pneumonia[22] found 4% desaturation during the 6MWT to be optimal to predict rehospitalisation within 12 months from respiratory-related events (71% sensitivity, 79% specificity). The study also found the SpO_2 recovery index; a measure of SpO_2 1 min after the 6MWT, minus the lowest recorded SpO_2 at the end of the 6MWT, showed a significant association with rehospitalisation (HR 0.30 (95% CI 0.10 to 0.90), p=0.03). However, another study[23] conducted the 6MWT in 44 patients with heart failure 24–48 hours prior to discharge but found no association between the lowest SpO_2 value and 90-day cardiac-related rehospitalisation (HR 1.01, 95% CI 0.94 to 1.08, p=0.78).

The 3 min walk test (3MWT) was used in patients with suspected PE, using SpO_2<86% for 30 s, desaturation≥2% or heart rate>100 beats per minute (bpm) as stopping criteria.[24] Overall, 66% of participants met at least one of these criteria, of whom 32% tested positive for PE. Overall, 10% of the PE group met the criteria versus 2% of the non-PE group. An SpO_2 decrease of more than or equal to 2% and heart rate increase of more than 10 bpm was 100% sensitive but only 11.9% specific for PE. A feasibility study using the 3MWT as a clinical decision tool in acute dyspnoea found that 42% of those with a poor outcome were unable to complete the 3MWT, compared with 4% of those with a good outcome.[25] A study comparing the Chester step test (CST) and modified incremental step tests (MIST) with the 6MWT found correlation with number of steps completed and reduced

Table 3 Studies of exercise testing in acute lung diseases other than COVID-19 in the acute setting

Reference	Intervention	Physiological monitoring	Outcome
Danielsbacka *et al*[19]	6MWT on the day of discharge	Masimo Rad V.5 pulse oximeter finger probe End-test SpO_2<90% cut-off used	Qanadli score for PE grading groups compared (QS2=higher degree of occlusion) Mean 6MWD (m): ► QS1 516±98.4 ► QS2 446±137.4 p=0.050 Desaturation<90%: ► QS1 16% ► QS2 17%
McCabe *et al*[20]	6MWT prior to discharge	6MWD	30-day rehospitalisation: ► Mean 6MWD (m) readmission; 536±434 ► Mean 6MWD (m) no readmission: 811±380 p=0.02
La Rovere *et al*[21]	6MWT at discharge	Distance walked (6MWD) measured (m)	Mortality: 6MWD (m), mean±SD; ► Alive 408.9±95.9 ► Deceased 311.1±102.2 p<0.0001
Sakai *et al*[22]	6MWT at discharge	Pulsox-M pulse oximeter 4% determined as optimal cut-off	12 month rehospitalisation in interstitial pneumonia: SpO_2 recovery index; ► 71.4% sensitivity ► 79.2% specificity Kaplan-Meier analysis comparing≥4% vs <4%; p<0.001
Howie-Esquivel and Dracup[23]	6MWT, inpatients	6MWD and lowest O_2 recorded with Writox (Nonin Medical) pulse oximeter	90-day cardiac rehospitalisation: Lowest O_2 value; ► HR (95% CI): 1.01 (0.94 to 1.08) p=0.78 6MWD; ► HR (95% CI): 0.99 (0.99 to 1.00) p=0.06
Amin *et al*[24]	3MWT during diagnostic workup	Criticare 504-DXP pulse oximeter Positive criteria: SpO_2<86% for 30 s, or HR>110 (CCF), >120 (COPD) for 60 s or new chest pain	65.8% of tests positive criteria: ► 32% positive for PE 10% of PE vs 2% non-PE group met criteria SpO_2 drop≥2% and HR increase>10 bpm ► 100% sensitivity (95% CI 88.7 to 100) for PE diagnosis ► 11.9% specificity (95% CI 6.6 to 21.0) for PE diagnosis
Pan *et al*[25]	3MWT prior to discharge	Nellcor Puritan Bennett (NPB-40) pulse oximeter Terminated if Borg score>7, chest pain, SpO_2<86% for 30 s or HR>120 for 60 s, or patient's request	Poor outcome* within 14-days: Walk test completed in full: ► Poor outcome 58% ► Good outcome 96% p<0.01 End-test SaO_2<90%: ► Poor outcome 25%, ► Good outcome 0% p<0.01
José and Dal Corso[26]	CST, MIST and next day 6MWT in inpatients	SpO_2 measured using a 9500 Nonin pulse oximeter	Exercise-induced desaturation (Mean; 95% CI): CST (–2%; –6 to 0) MIST (–2%; –6 to –1) Length of stay: Number of steps during CST (r=–0.23, p=0.049) Number of steps during MIST (r=–0.23, p=0.042)
Kakavas *et al*[27]	30 s and five-repetition sit-to-stand tests at discharge	Number of repetitions in 30 s and duration to five repetitions	COPD exacerbation within 12 months: 30s-STS, mean repetition±SD ► Yes 11±3 ► No 18±8 (p=0.05) 5-STS, mean duration±SD ► Yes 14.2±3.3 ► No 10.1±3.1 (p=0.05)

Continued

Table 3 Continued

Reference	Intervention	Physiological monitoring	Outcome
Chouaid *et al*[28]	Treadmill exercise test—increasing 2 min constant speed steps (2, 4, 6 and 8 km/h)	SpO_2 measured using finger pulse oximetry	22% confirmed PCP on diagnostic testing. 3% desaturation: ► 100% sensitivity for PCP ► 70%–80%† specificity for PCP SpO_2<96%: ► 100% sensitivity for PCP ► 31% specificity for PCP
Sauleda *et al*[29]	2 min pedalling on stretcher bed (40 cycles/min)	SaO_2 measured by Ohmeda 3740 pulse oximeter Positive if desaturation≥3%	Desaturation≥3%: ► 77% of PCP ► 9% non-PCP pneumonia SaO_2 decrease, mean % (SE): ► PCP: −1% p<0.01 ► Non-PCP pneumonia+2% p<0.05 Sensitivity 77%, specificity 91% Mortality: ► 100% PCP cases desaturated≥3%
Kichura *et al*[30]	3 min bike ergometry distance at admission and discharge	Distance biked recorded in metres DeskCycle Exercise Bike Pedal Exerciser (3D Innovations) used	Length of stay: Admission; r=−0.11, p=0.46 Discharge; r=−0.03, p=0.85 30-day readmission: Admission; r=−0.03, p=0.85 Discharge; r=0.02, p=0.91
Denehy et al[31]	PFIT* at admission and discharge, compared with TUG and 6MWT	Sit-to-stand assistance, marching on the spot (steps/min), shoulder flexion and knee extension strength	Discharge to home: ► PFIT, OR 1.20, p=0.01 Length of stay: ► Admission PFIT, B coefficient −2.13, p<0.001 28-day readmission ► Admission PFIT not correlated (data not presented)

*Admission to hospital, the need for BiPAP, intubation, relapse, or death.
†With or without prophylactic pentamidine.
B, beta; bpm, beats per minute; CCF, congestive cardiac failure; COPD, chronic obstructive pulmonary disease; CST, Chester step test; HR, heart rate; HRR2, heart rate recovery within 2 min; ITU, intensive treatment unit; MIST, modified incremental step test; 6MWD, 6 min walk distance; 3MWT, 3 min walk test; 6MWT, 6 min walk test; PCP, pneumocystis pneumonia; PE, pulmonary embolism; PFIT, physical function ITU test; QS1, qanadli score group 1; QS2, qanadli score group 2; r, Pearson correlation coefficient; SaO_2, oxygen saturation of arterial oxygen; SpO_2, peripheral oxygen saturation; 30s-STS, 30 s sit-to-stand test; 5-STS, 5 repetition sit-to-stand test; TUG, Timed up and go test.

length of hospital stay (CST r=−0.23, p=0.049, MIST; r=−0.23, p=0.042). Mean desaturation was 2% on all three tests. The 6MWD was found to correlate with CST (r=0.590) and MIST (r=0.64), and no adverse events were recorded.[26]

One study in acute exacerbations of chronic obstructive pulmonary disease (COPD)[27] included a 30 s sit-to-stand (30s-STS) and five repetition sit-to-stand test (5-STS) at discharge (2 hours apart). Patients who had further exacerbation of COPD within 12 months had a mean of 7 less repetitions of the 30s-STS compared those with no further exacerbations (p=0.05). Mean time to complete the 5-STS was also significantly longer in those who had further COPD exacerbation within 12 months (p=0.05). Heart rate and SpO_2 during the test were not found to be correlated with future exacerbations.

Chouaid *et al*[28] used a treadmill exercise test in the diagnostic workup of patients with HIV positive with suspected pneumocystis pneumonia (PCP). A 3% decrease in saturation during the test had 100% sensitivity for PCP and 70%–80% sensitivity, with exertional desaturation more specific for PCP than resting hypoxia.

Two studies using cycle ergometry were identified including a study in patients with HIV presenting with symptoms of pneumonia.[29] Twenty-two cases had confirmed PCP, 23 controls had other non-PCP pneumonias. Desaturation of ≥3%, was met in 77% of PCP cases, compared with 9% of non-PCP pneumonias. The mean decrease in SaO_2 was 88%–84% in the PCP group (p<0.01), compared with 91%–93% in the non-PCP group (p<0.05).

Kichura *et al*[30] used a 3 min bicycle ergometry in 50 heart failure patients presenting to ED at admission and discharge. No significant correlation between bike distance and length of hospital stay, readmission or mortality was found.

The final included study assessed inpatients at an ICU, who completed a physical function ITU test (PFIT) including a marching on the spot test, which was compared with the timed up and go test and the 6MWT.

Higher PFIT scores (ie, better function) were found to be significantly associated with discharge to home (OR 1.20, p=0.01) and reduced length of hospital stay (B coefficient −2.13, p<0.001). However, admission PFIT was not significantly associated with 28-day readmission.[31]

DISCUSSION

Principal findings

This scoping review is the first to describe the use of different exercise tests in the assessment of confirmed or suspected COVID-19. Two of the larger studies in COVID-19 excluded a high proportion of the screened population, suggesting that the test may not be safe to perform in the normal hospitalised population. The utility of an exercise test in COVID-19 to predict early deterioration, using postexertional desaturation, may be limited to mobile, high-functioning patients with stable observations at rest.

Strengths and limitations

The search included tests used at any part of an acute admission: on presentation, during admission or at the time of discharge as long as one of the primary or secondary outcome measures was included in the reporting. By including exercise testing at various timepoints during a patient's hospital journey we sought to identify suitable exercise tests which could be applied as a discharge decision tool. Inclusion of these studies has provided important insights into the safety and feasibility of exercise testing in the acute hospital setting, which are important for clinicians wishing to incorporate an exercise test as part of a discharge pathway. However, the inclusion of exercise tests performed at different points in the disease course, as well as in different settings (eg, ED vs primary care) are likely to produce variable outcomes, and therefore caution is advised in using their conclusions to estimate whether a discharge can be considered safe.

We found few results matching our inclusion criteria. We opted to exclude tests carried out in the outpatient setting, which limited the scope of literature assessed and may have led to overlooking a brief exercise test, that could be appropriate for use in COVID-19, but has not yet been tested in the acute setting. The identified literature is methodologically diverse, consisting mainly of small studies, with significant variation in the exercise test performed, condition studied and outcomes assessed. This makes drawing definitive conclusions more challenging. In addition to physiological monitoring using oxygen saturation, parameters such as the walking distance, repetitions or time taken to complete a predefined test were used in several studies: these likely measure frailty and comorbidity as well as cardiopulmonary function so may be less useful in the acute setting to predict short term outcomes, particularly in COVID-19. Some of the studies[22 27] identified used longer-term outcomes of up to 12 months that are less useful in the assessment of acute presentation with COVID-19.

Relation of findings to previous studies

The utility of exercise testing in the acute setting, particularly in terms of aiding with safe discharge, remains up for debate. A rapid systematic review on the safety and efficacy of rapid exercise tests for exertional desaturation in COVID-19 proposed the 1 min sit-to-stand test as warranting further investigation,[7] and our study has identified that an ongoing prospective trial aims to explore its use in the assessment of COVID-19 patients to predict hospitalisation and adverse events. The 1 min sit-to-stand test is validated in a range of settings,[32] including in the preoperative assessment for lung transplantation,[33] and may be more beneficial in demonstrating exertional desaturation. However, it has been noted to induce high cardiopulmonary stress and requires significant muscular strength to stand from sitting without support. This may make it unsuitable for use in a remote setting and not easy to achieve by many hospitalised patients, including the most frail. Additionally, we did not find extensive data to support the use of sit-to-stand tests in the acute setting.

New additions to the field of exercise testing such as the 10-feet desaturation test and 40-steps desaturation test are being used in COVID-19 without prior validation. Clinical practicalities favour a shorter test, although the evidence base for the longer 6MWT is more widely established. The shortest comparable test in published studies is the 10 m walk test (10MeWT), which involves walking as quickly as possible between two points on a flat surface measuring 10 m, with the time taken to complete the test recorded. Excellent intertest and test–retest reliability was found between the 10MeWT, and 6MWT in a cohort of dementia patients,[34] and the 15 m and 30 m variations of the 6MWT in stroke patients.[35] However, these tests have been used to measure gait speed, not desaturation.[36] We found no evidence of a similarly short walk test which linked desaturation to clinical deterioration or mortality. The 3MWT may offer a compromise to deliver a timely yet more highly validated test. Observations in paediatric studies indicate a quicker walking speed during the first minute of the 6MWT, as well as moderate reliability from 3 min onwards, a finding that warrants further investigation in adult patients with a range of mobility, before recommendation of a shorter walking test can be made.[37]

Implications for clinical practice

Our findings appear to substantiate previous recommendations that a desaturation of 3% or more is significant.[38] Overall, 5% or more desaturation appears to be too high a threshold in a cohort of COVID-19 patients,[17] while a threshold of 2% has only been used in combination with a change in heart rate to predict PE,[24] and not found to correlate with hospital length of stay in COPD exacerbations.[26] Meanwhile, a desaturation value between 3% and 4% appears to be the most useful in balancing sensitivity and specificity in many of the studies discussed.[15 16 29] A

cut-off SpO_2 below 90% (representing 4% desaturation, as these studies also specified a baseline saturation of 94%) has also been used with some success both in patients infected with COVID-19[14] and patients not infected with COVID-19.[25] However, given the high variability in exercise test length and intensity used, the most appropriate threshold would need to be decided on a test-by-test basis and is likely to vary according to the disease studied.

COVID-19 provides diverse physiological challenges with desaturation potentially caused by pneumonitis, thromboembolic disease or myocarditis. These different mechanisms might be difficult to differentiate by clinicians tasked with screening large cohorts of patients in the setting of a pandemic, but further research should address the combination of exercise testing with other biomarkers such as troponin, lactate dehydrogenase (LDH) or Brain Natriuretic Peptide (BNP) to gain better insights into both aetiology and risk profile. LDH has been used as a marker of severity of illness in COVID-19[39] and might describe vascular permeability or indeed myocardial strain[40] and could be explored further as a marker for safe discharge.

All tests discussed were found to be safe with none or few adverse events reported. We broadly suggest that brief tests of exertion, requiring no equipment and limited space, and therefore easy to perform remotely or in a hospital cubicle are most feasible to deliver, particularly in the context of COVID-19 pneumonitis where desaturation could be more marked in the acute phase. The drawback is that we have identified a lack of validation for the shorter exertional tests used commonly in clinical practice including the 40-steps desaturation test which is part of national guidance on the assessment of COVID-19. A shorter test may be less sensitive to detect desaturation but could have high specificity to detect COVID-19, or its complications, and a validation study to assess this is urgently indicated.

Unanswered questions for future research

We did not identify any studies within suspected COVID-19 in which different exercise test approaches were compared, or where an exertional test was part of an interventional pathway compared with usual care. This limits the recommendation of a validated test to be applied in the acute setting of assessing acute COVID-19.

Shorter tests are more practical in the acute setting, but are less validated in relation to facilitating safe discharge. One of these in widespread use is the 40-steps desaturation test, although variations in applying the test exist due to its lack of validated protocol. Since the completion of this scoping review, our group has published preliminary findings from using an on-the-spot variation of the 40-steps desaturation test in acute inpatients.[41] We observed that the 40-steps desaturation test may not be feasible in a significant proportion of acute inpatients. We were unable to recruit sufficient patients with COVID-19 within this study, therefore, larger studies in COVID-19 specifically are still required to elicit the utility of the 40-steps test within COVID-19 inpatients. A 1 min sit-to-stand test may also be suitable, but is harder to achieve, and has also not been studied in the acute setting. We found some evidence to support the use of a 3MWT, which despite being relatively brief still requires space to deliver and may be hard to complete in full by acutely unwell patients.

We found little evidence for using desaturation as a clinical decision tool in acute conditions, including COVID-19. Desaturation of 2%–4% on exertion has been associated with adverse outcomes including clinical deterioration, rehospitalisation and mortality in several small studies. However, as the literature identified differs widely in the clinical setting and timing of the exercise in relation to the disease course, the presence of desaturation on exertion should not be used in isolation to inform a safe discharge. Further research is required with clinical practicalities favouring a shorter test. The 40-steps test, which is widely used in clinical practice but is not validated for use in COVID-19, requires further exploration.

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