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ORIGINAL ARTICLE

Inverse Relationship of Maximal Exercise Capacity to Hospitalization Secondary to Coronavirus Disease 2019

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Abstract

Objective: To investigate the relationship between maximal exercise capacity measured before severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and hospitalization due to coronavirus disease 2019 (COVID-19).

Methods: We identified patients (≥18 years) who completed a clinically indicated exercise stress test between January 1, 2016, and February 29, 2020, and had a test for SARS-CoV-2 (ie, real-time reverse transcriptase polymerase chain reaction test) between February 29, 2020, and May 30, 2020. Maximal exercise capacity was quantified in metabolic equivalents of task (METs). Logistic regression was used to evaluate the likelihood that hospitalization secondary to COVID-19 is related to peak METs, with adjustment for 13 covariates previously identified as associated with higher risk for severe illness from COVID-19.

Results: We identified 246 patients (age, 59±12 years; 42% male; 75% black race) who had an exercise test and tested positive for SARS-CoV-2. Among these, 89 (36%) were hospitalized. Peak METs were significantly lower (P<.001) among patients who were hospitalized (6.7±2.8) compared with those not hospitalized (8.0±2.4). Peak METs were inversely associated with the likelihood of hospitalization in unadjusted (odds ratio, 0.83; 95% CI, 0.74-0.92) and adjusted models (odds ratio, 0.87; 95% CI, 0.76-0.99).

Conclusion: Maximal exercise capacity is independently and inversely associated with the likelihood of hospitalization due to COVID-19. These data further support the important relationship between cardiorespiratory fitness and health outcomes. Future studies are needed to determine whether improving maximal exercise capacity is associated with lower risk of complications due to viral infections, such as COVID-19.

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Respiratory viral infections, like severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), cause a systemic inflammatory response that places a substantial burden on the cardiopulmonary system. Higher cardiorespiratory fitness (eg, exercise capacity) is reflective of a greater cardiopulmonary reserve and the body's ability to respond to an insult as well as inversely related to risk for adverse outcomes among individuals diagnosed with a chronic disease.[1-6] Fitness is moderated by age, genomics, and presence of chronic disease and is heavily influenced by physical activity, especially structured exercise training.[6,7] In addition to improving fitness, cardiorespiratory (eg, aerobic type) exercise training improves immune function, reduces chronic low-grade inflammation, and lowers the risk of respiratory infections.[8,9]

Numerous studies have identified factors associated with worsening clinical outcomes among patients with coronavirus disease 2019 (COVID-19), including preexisting

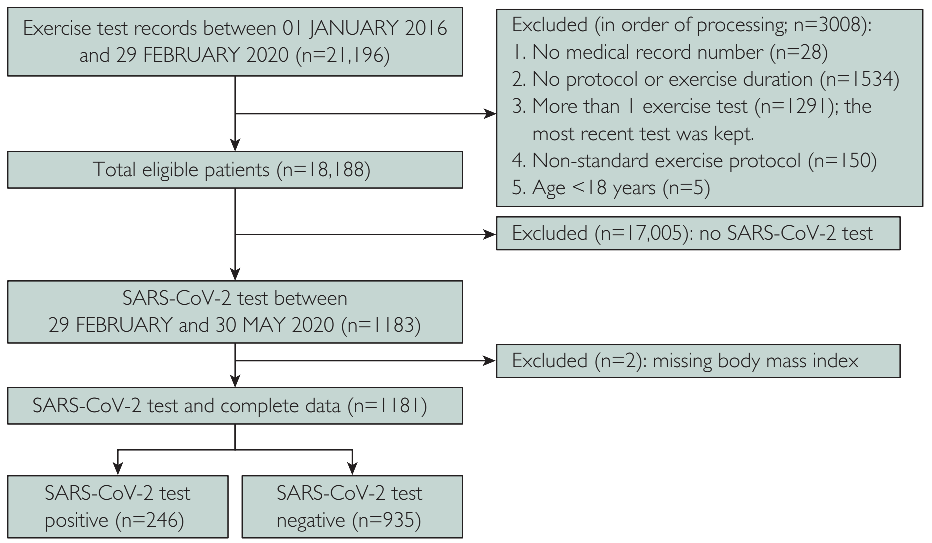

FIGURE 1. Development of the cohort. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

comorbidities (eg, pulmonary disease, heart disease),[10] lifestyle factors (eg, smoking, obesity),[10-12] and demographic characteristics (eg, male sex, older age).[10,11] Yet to be described among patients who test positive for the disease is the association between maximal exercise capacity and risk of COVID-19–related complications.

The purpose of this retrospective study was to investigate the relationship between maximal exercise capacity measured during a clinically indicated exercise stress test performed before SARS-CoV-2 infection and hospitalization due to COVID-19. We hypothesized that maximal exercise capacity would be independently and inversely related to hospitalization due to COVID-19.

METHODS

Study Overview

For this retrospective observational study, we included adults (≥18 years) who completed a clinically indicated exercise stress test on a treadmill between January 1, 2016, and February 29, 2020, within the Henry Ford Medical Group and had a test for SARS-CoV-2 between February 29 and May 30, 2020. Hospitalizations were identified through a minimum of 30 days after the SARS-CoV-2 test, and discharge disposition was queried through July 31, 2020. Patients were identified by a query of the clinical reporting system used to create exercise stress test reports (details later; Figure 1). Patients were excluded if the exercise protocol or exercise test duration was incomplete. When more than one test was available for a given patient, only the most recent test was included. SARS-CoV-2 was detected using real-time reverse transcriptase polymerase chain reaction tests. This study was approved by the Henry Ford Health System Institutional Review Board, and informed consent was waived.

Exercise Stress Tests

Exercise tests types were electrocardiography only, electrocardiography plus echocardiography (eg, stress echo), and cardiopulmonary exercise tests. Tests were supervised by clinical exercise physiologists, nurses, and cardiovascular technicians. Before the test, cardiovascular risk factors and relevant medical history were reviewed by staff using the medical record and patient interview. Exercise tests were conducted consistent with American Heart Association guidelines.[13] The supervising clinician selected the exercise protocol; the Bruce and modified Bruce protocols were most often chosen. Patients were verbally encouraged to provide a sign- or symptom-limited maximal effort. A preliminary report that included demographic characteristics, cardiovascular risk factors, relevant medical history, and rest and exercise data was created by the supervising clinician using a clinical reporting system (*syngo* Dynamics, Siemens Medical Solutions). This report was subsequently reviewed by a reading cardiologist and uploaded to the medical record (Epic, Epic Systems Corporation).

Covariate Data

Demographic, clinical, rest, and exercise data collected at the time of the exercise test were extracted from the clinical reporting system used to create the exercise test report for the medical record. These data were complemented with data from the health system's electronic data warehouse, which contains clinical (outpatient and inpatient), laboratory, financial, and medication data from the electronic medical record. By use of *International Classification of Diseases, Tenth Revision* codes (Supplemental Table 1, available online at http://www.mayoclinicproceedings.org), clinical data were extracted from the data warehouse for patients who completed an exercise test and had a test for SARS-CoV-2. These data included hypertension, diabetes mellitus, heart failure, myocardial infarction, coronary artery bypass graft surgery, percutaneous coronary intervention, cerebrovascular accident, chronic obstructive pulmonary disease, asthma, chronic kidney disease, and liver disease. History of any cancer was identified from the Henry Ford Cancer Institute's tumor registry. Body mass index was calculated on the basis of the most recent height and weight available from the electronic medical record before the SARS-CoV-2 test. If either was unavailable, data from the exercise test were used. Tobacco smoking was based on patient interview at the time of the exercise test.

Quantifying Maximal Exercise Capacity

Consistent with landmark studies by Bruce et al[14] and Blair et al,[7] maximal exercise capacity was quantified in metabolic equivalents of task (METs) as estimated from total exercise duration using protocol-specific equations. The equations were developed with data from exercise tests in which oxygen uptake was measured by open-circuit spirometry (eg, cardiopulmonary exercise test). These cardiopulmonary exercise tests were performed during a 5-year period before the exercise tests included in this analysis. Details about these tests and the equations to estimate METs are provided in Supplemental Tables 2 and 3 and Supplemental Figures 1 to 4 (available online at http://www.mayoclinicproceedings.org).

Statistical Analyses

Between-group comparisons were made using 2-sided *t*-test and χ^2 test for continuous and nominal data, respectively. Logistic regression was used to calculate the odds ratio (OR) and 95% CI for SARS-CoV-2 infection on the basis of peak METs (continuous variable). Logistic regression was also used to evaluate the likelihood that hospitalization secondary to COVID-19 is related to peak METs (in both quartiles and continuous). For our primary analysis, logistic regression was used with peak METs as a continuous variable with adjustment for conditions based on those that the Centers for Disease Control and Prevention identified as representing definite or possible increased risk for severe illness from COVID-19.[15] The included covariates were age 65 years or older at the time of the SARS-CoV-2 test, sex, history of asthma, cancer, cerebrovascular accident, chronic kidney disease, chronic obstructive pulmonary disease, coronary heart disease (ie, coronary artery disease, myocardial infarction, or coronary revascularization), diabetes mellitus (type 1 or 2), heart failure, hypertension, obesity (body mass index $\geq$30 $kg \cdot m^{-2}$), and tobacco smoking. Liver disease was not present in our cohort. The α level was $<.05$. Continuous data are

TABLE 1. Characteristics of Patients Who Tested Positive for SARS-CoV-2[a,b]

Variable	All patients (N=246)	Hospitalized: No (n=157)	Hospitalized: Yes (n=89)	*P*
Male sex	104 (42)	59 (38)	45 (51)	.06
Age at SARS-CoV-2 test (y)	59±12	57±11	63±13	<.001
Race				
Black	184 (75)	119 (76)	65 (73)	.76
White	44 (18)	26 (17)	18 (20)	
Other	18 (7)	12 (8)	6 (7)	
Body mass index ($kg \cdot m^{-2}$)	32±7	33±7	32±7	.22
Medical history				
Hypertension	166 (68)	98 (62)	68 (76)	.03
Obesity	148 (60)	100 (64)	48 (54)	.14
Diabetes mellitus (type 1 or 2)	86 (35)	47 (30)	39 (44)	.04
Asthma	39 (16)	23 (15)	16 (18)	.59
Tobacco smoking	36 (15)	24 (15)	12 (14)	.85
Cancer	26 (11)	12 (8)	14 (16)	.054
Coronary heart disease	25 (10)	11 (7)	14 (16)	.046
Chronic kidney disease	15 (6)	4 (3)	11 (12)	.004
Heart failure	14 (6)	5 (3)	9 (10)	.04
Cerebrovascular accident	12 (5)	8 (5)	4 (5)	>.99
COPD	9 (4)	4 (3)	5 (6)	.29
Medications				
Antilipemic	97 (39)	49 (31)	48 (54)	.001
Calcium channel blockade	74 (30)	39 (25)	35 (39)	.02
β-Blockade	63 (26)	30 (19)	33 (37)	.002
Diuretic	66 (27)	34 (22)	32 (36)	.02
Inhaler	58 (24)	34 (22)	24 (27)	.35
Antihyperglycemic	49 (20)	26 (17)	23 (26)	.10
Insulin	46 (19)	23 (15)	23 (26)	.04
Angiotensin receptor blockade	38 (15)	21 (13)	17 (19)	.27
Antiplatelet/coagulant	36 (15)	13 (8)	23 (26)	<.001
ACE inhibitor	34 (14)	18 (12)	16 (18)	.18

[a]ACE = angiotensin-converting enzyme; COPD = chronic obstructive pulmonary disease; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
[b]Data are presented as mean ± SD or number (% of group).

presented as mean ± standard deviation unless noted otherwise. Statistical analyses were performed using IBM SPSS Statistics v24.

RESULTS

We identified 1181 adult patients who had an exercise stress test, a test for SARS-CoV-2, and complete data to be included in the analysis (Figure 1). Exercise test indications were chest pain (n=665 [56%]); shortness of breath or fatigue (n=191 [16%]); abnormal electrocardiogram or abnormal finding on functional study (n=86 [7%]); heart failure evaluation (n=66 [6%]); heart rate or rhythm evaluation (n=59 [5%]); presurgical evaluation, screening for cardiovascular disorder, or assessment of exercise capacity (n=44 [4%]); known coronary heart disease (n=42 [4%]); and other (n=28 [2%]). Maximal exercise capacity was 7.5±2.8 METs. Median time between the exercise test and the SARS-CoV-2 test was 2.1 years (25th-75th percentile, 1.1-3.1 years). Age at the time of the SARS-CoV-2 test was 59±12 years; 21% (n=246) tested positive for SARS-CoV-2. There was no association between peak METs (continuous variable) and the likelihood of SARS-CoV-2 infection (unadjusted OR, 1.00; 95% CI, 0.95-1.05).

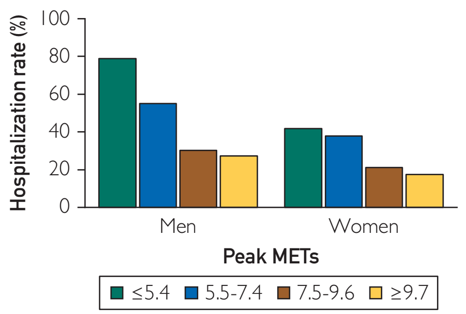

FIGURE 2. Unadjusted rate of hospitalization among patients with coronavirus disease 2019 (COVID-19) by quartiles of peak metabolic equivalents of task (METs).

Characteristics of the 246 patients who tested positive for SARS-CoV-2 are shown in Table 1. Among these patients, 89 (36%) were hospitalized. Compared with those who were not hospitalized for COVID-19, patients who were hospitalized were significantly older and more likely to have hypertension, diabetes mellitus, coronary heart disease, chronic kidney disease, and heart failure. Hospitalized patients were also more likely to be prescribed an antilipemic medication, calcium channel blocker, β-blocker, diuretic, insulin, and antiplatelet/coagulant. Among the hospitalized patients, median length of stay was 13 days (range, 1-57 days); 28 (11%) were admitted to the intensive care unit (median stay, 6 days; range, 1-27 days), 8 (3%) were put on a ventilator, and 13 (5%) died. There was no significant difference in mean METs (P=.98) between patients with and patients without severe illness, defined as intensive care unit stay, ventilator support, or death.

Among all patients who tested positive for SARS-CoV-2, the most frequently used exercise test protocol was Bruce (n=201 [82%]), followed by modified Bruce (n=27 [11%]) and two other treadmill protocols that increase workload at a slower rate (n=18 [7%]). Reasons for stopping the tests were general fatigue (n=138 [56%]), dyspnea (n=84 [34%]), patient request (n=7 [3%]), and other (n=17 [7%]). Peak METs were significantly lower (P<.001) among patients who were hospitalized (6.7±2.8) compared with those not hospitalized (8.0±2.4).

The unadjusted rate of hospitalization due to COVID-19 by sex and quartiles of peak METs is shown in Figure 2. Based on unadjusted logistic regression, there was a significant trend for lower likelihood of hospitalization across these quartiles for all patients combined (P=.001) and in men (P=.003) but not in women (P=.09). Among all patients, the unadjusted OR of hospitalization in the lowest fitness quartile (≤5.4 METs) was 3.88 (95% CI, 1.71-8.77) compared with the highest fitness quartile (≥9.7 METs).

Results from the logistic regression analysis with the covariates sorted by their Wald χ^2 are shown in Table 2. Peak METs (continuous variable) were inversely associated with the likelihood of hospitalization in unadjusted and adjusted models. Each unit higher of peak METs was independently associated with a 13% (adjusted OR, 0.87; 95% CI, 0.76-0.99) lower odds of hospitalization. There was no significant interaction for peak METs by sex (P=.99), age younger than 65 years vs 65 years or older (P=.95), or obese vs not obese (P=.08). As shown in Figure 3, there is a steady decline in the predicted probability of hospitalization with increasing peak METs, with a nadir near 13 METs.

DISCUSSION

In a diverse cohort of patients who tested positive for SARS-CoV-2, we showed an independent and inverse association between maximal exercise capacity and likelihood of hospitalization for COVID-19, a finding consistent with our hypothesis. One MET higher of exercise capacity was associated with 13% lower odds for hospitalization. This might be the first report of maximal exercise capacity as a predictor of hospitalization due to viral infection.

Cardiorespiratory fitness or exercise capacity directly reflects the integrated function of multiple organ systems. As such, it is an important measure of overall health and the body's ability to respond to internal and external stressors,[6] such as COVID-19. Akin to this is the practice of measuring exercise capacity before surgery to categorize a

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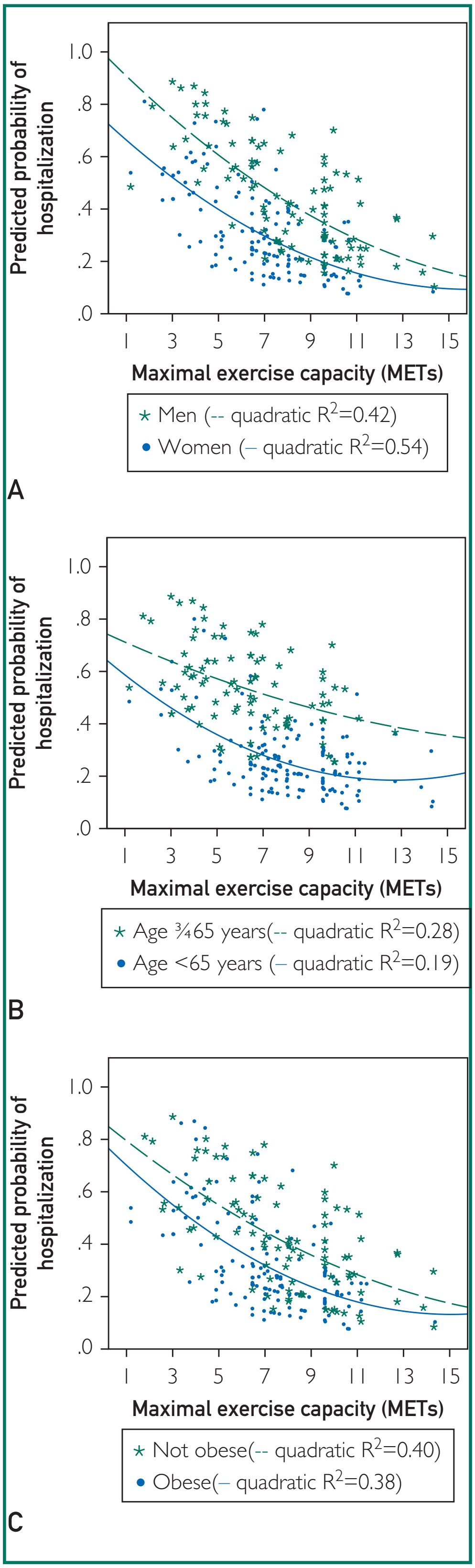

FIGURE 3. Predicted probability of hospitalization among patients with coronavirus disease 2019 (COVID-19) associated with peak metabolic equivalents of task (METs) by sex (A), age (B), and obesity (C). Predicted probability is based on the adjusted logistic regression (Table 2).

patient's ability to tolerate the perioperative "cardiopulmonary burden" associated with general anesthesia and the sustained increase in oxygen demand after surgery.[2,5] COVID-19 represents another burden or stressor on the cardiopulmonary system, providing a potential physiologic explanation for the observed inverse association between maximal exercise capacity and risk for hospitalization. Finally, this association is consistent with previous findings in patients referred for an exercise stress test[16,17] and those with a chronic disease, including coronary artery disease,[3] chronic kidney disease,[1] and heart failure.[4]

There is an additional physiologic rationale for our findings, and it involves first appreciating that an individual's exercise capacity is greatly influenced by physical activity and exercise training habits. Although genetics, age, and the presence of chronic disease also influence exercise capacity, the volume of exercise that one routinely engages in is associated with risk of infection, modeled as a J-shaped curve.[8,9] Specifically, moderate-intensity aerobic-type exercise enhances immune function above that observed with sedentary behavior, and repeated high-intensity exercise performed for a prolonged duration may impair immune function and increase the risk for infection.[8,9] In summary, regular moderate- to vigorous-intensity aerobic exercise is an important contributor to exercise capacity and favorably influences biologic pathways that are involved with the body's response to an infection.[9]

The implications of our findings are important for several reasons. First, like smoking and obesity, exercise capacity is a modifiable factor that could be a target for preventive strategies (eg, regular exercise) aimed at attenuating

TABLE 2. Results From Logistic Regression Analysis to Assess the Relationship Between Peak METs Achieved During a Clinically Indicated Exercise Stress Test and Likelihood of Hospitalization Secondary to COVID-19

Variable	β	SE	Wald χ^2	*df*	*P*	OR	OR 95% CI Lower	OR 95% CI Upper
Unadjusted model								
METs	−0.19	0.06	11.98	1	.001	0.83	0.74	0.92
Constant	0.84	0.42	3.98	1	.046	2.31	—	—
Adjusted model								
METs	−0.14	0.07	4.18	1	.04	0.87	0.76	0.99
Age ≥65 years	0.72	0.34	4.54	1	.03	2.06	1.06	4.00
Male sex	0.65	0.33	4.00	1	.045	1.92	1.01	3.63
Asthma	0.62	0.40	2.36	1	.12	1.85	0.84	4.07
Obesity	−0.42	0.32	1.69	1	.19	0.66	0.35	1.24
Chronic kidney disease	0.76	0.69	1.21	1	.27	2.13	0.55	8.20
Diabetes mellitus (type 1 or 2)	0.33	0.32	1.08	1	.30	1.39	0.75	2.59
COPD	0.75	0.73	1.05	1	.31	2.12	0.50	8.94
Coronary heart disease	0.39	0.49	0.65	1	.42	1.48	0.57	3.83
Cancer	0.36	0.46	0.57	1	.44	1.43	0.58	3.52
Hypertension	0.25	0.34	0.54	1	.46	1.28	0.66	2.50
Cerebrovascular accident	−0.31	0.68	0.21	1	.65	0.74	0.20	2.77
Tobacco smoking	−0.20	0.43	0.21	1	.65	0.82	0.36	1.90
Heart failure	0.14	0.68	0.05	1	.83	1.16	0.31	4.36
Constant	−0.38	0.71	0.28	1	.60	0.69	—	—

COPD = chronic obstructive pulmonary disease; METs = metabolic equivalents of task; OR = odds ratio; SE = standard error.

disease-specific complications. Second, exercise capacity was one of the strongest predictors of hospitalization among patients positive for SARS-CoV-2 (Wald χ^2, 4.18; Table 2) and could be used for risk stratification. Third, the association we identified may be an important consideration for future trials that investigate factors associated with disease-specific complications. Such trials might consider exercise capacity as a covariate or an unmeasured confounder.

Our study is not without limitations. First, we acknowledge the possibility of residual confounding due to unmeasured behavioral or clinical characteristics. Important among these, we do not have data on physical activity or tobacco smoking habits between the time of the exercise test and SARS-CoV-2 infection. Second, exercise capacity may have changed between the time of the exercise tests and SARS-CoV-2 infection (median, 2.1 years). However, in a previous study, we reported[18] that during a median of 3.8 years between two exercise tests, there was minimal change in exercise capacity among men (median, 0.3 METs; 25th-75th percentile, −2.1 to 0.6 METs). Similar values were observed in women. Third, as a retrospective study, we risk misclassification of chronic disease status, especially among patients who were not hospitalized because these patients might have obtained additional health care at another health system. Strengths of this study include the racially diverse cohort and the inclusion of several covariates that are currently thought to have increased risk due to SARS-CoV-2.

Although the risk of viral infections associated with change in fitness or changes in physical activity habits is beyond the scope of this analysis, these data reinforce several important public health messages. First, both volume of physical activity and exercise capacity are inversely related to risk of infection, incident chronic disease, and health outcomes among individuals with and without chronic disease.[6,19] Second, change in both physical activity and exercise capacity is inversely associated with health outcomes.[6,19] Third, increasing physical activity, especially through structured exercise training, is the primary means for most people to increase exercise capacity.[19] Collectively, these support the importance of identifying alternative avenues that allow individuals to maintain and preferably to increase physical activity levels when normal activities might be restricted by local health authorities in response to a public health crisis, as has occurred in many regions during the COVID-19 pandemic.

CONCLUSION

Maximal exercise capacity determined from an exercise stress test before SARS-CoV-2 infection is independently and inversely associated with the likelihood of hospitalization due to COVID-19. These data further support the important relationship between cardiorespiratory fitness and health outcomes. Patients should be encouraged to regularly engage in aerobic exercise to maintain or to improve their exercise capacity. Future studies are needed to determine whether improving exercise capacity is associated with lower risk of complications due to viral infections, such as COVID-19.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **COVID-19** = coronavirus disease 2019; **METs** = metabolic equivalents of task; **OR** = odds ratio; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2

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REFERENCES

1. DeOreo PB. Hemodialysis patient-assessed functional health status predicts continued survival, hospitalization, and dialysis-attendance compliance. *Am J Kidney Dis*. 1997;30(2):204-212.
2. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64(22):e77-e137.
3. Keteyian SJ, Brawner CA, Savage PD, et al. Peak aerobic capacity predicts prognosis in patients with coronary heart disease. *Am Heart J*. 2008;156(2):292-300.
4. Keteyian SJ, Patel M, Kraus WE, et al. Variables measured during cardiopulmonary exercise testing as predictors of mortality in chronic systolic heart failure. *J Am Coll Cardiol*. 2016;67(7):780-789.
5. Older PO, Levett DZH. Cardiopulmonary exercise testing and surgery. *Ann Am Thorac Soc*. 2017;14(suppl 1):S74-S83.
6. Ross R, Blair SN, Arena R, et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation*. 2016;134(24):e653-e699.
7. Blair SN, Kohl HW 3rd, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. *JAMA*. 1989;262(17):2395-2401.
8. Gleeson M, Walsh NP. The BASES expert statement on exercise, immunity, and infection. *J Sports Sci*. 2012;30(3):321-324.
9. Nieman DC. Coronavirus disease-2019: a tocsin to our aging, unfit, corpulent, and immunodeficient society. *J Sport Health Sci*. 2020;9(4):293-301.
10. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA*. 2020;323(20):2052-2059.
11. Sanchis-Gomar F, Lavie CJ, Mehra MR, Henry BM, Lippi G. Obesity and outcomes in COVID-19: when an epidemic and pandemic collide. *Mayo Clin Proc*. 2020;95(7):1445-1453.
12. Sharma A, Garg A, Rout A, Lavie CJ. Association of obesity with more critical illness in COVID-19. *Mayo Clin Proc*. 2020;95(9):2040-2042.
13. Fletcher GF, Ades PA, Kligfield P, et al. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation*. 2013;128(8):873-934.
14. Bruce RA, Kusumi F, Hosmer D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. *Am Heart J*. 1973;85(4):546-562.
15. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19). https://www.cdc.gov/coronavirus/2019-ncov/index.html.
16. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med*. 2002;346(11):793-801.
17. Al-Mallah MH, Juraschek SP, Whelton S, et al. Sex Differences in cardiorespiratory fitness and all-cause mortality: the Henry Ford ExercIse Testing (FIT) Project. *Mayo Clin Proc*. 2016;91(6):755-762.
18. Brawner CA, Al-Mallah MH, Ehrman JK, Qureshi WT, Blaha MJ, Keteyian SJ. Change in maximal exercise capacity is associated with survival in men and women. *Mayo Clin Proc*. 2017;92(3):383-390.
19. US Department of Health and Human Services. *2018 Physical Activity Guidelines for Americans*. 2nd ed. Washington, DC: US Department of Health and Human Services; 2018.