Putting the PASC Score to the Test: Clinical vs. Statistical Accuracy in Long COVID Diagnosis

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BACKGROUND

In the wake of the COVID-19 pandemic, one in ten people with acute COVID-19 develop a condition known as Long COVID (LC). Currently, there is no diagnostic biomarker or standardize clinical tool to confirm the diagnosis of LC, leading to underdiagnosis and stigmatization of the condition. The NIH RECOVER initiative developed a symptom-based case definition used to identify cases of LC (PASC Score)[1]. In the absence of a gold standard diagnostic test, and with multisystemic involvement, the focus was to identify the symptoms that differentiated the infected versus uninfected individuals. We examined the concordance of the PASC score in a cohort of patients followed by a specialized LC clinics.

METHODS

Participants were recruited from Long COVID Clinics in Baltimore, MD. Participants met the NAM 2024 LC definition, had at least one neuropsychiatric symptom and were aged 18 to 80. Control participants are group-matched by age, biological sex, and SARS-CoV-2 infection status. PASC score publication methods where implemented to determine presence of the following symptoms:

- **Smell or Taste:** loss/change in smell or taste
- **Post Exertional Malaise (PEM):** worsening of symptoms after even minor physical or mental effort
- **Chronic Cough**
- **Brain Fog:** Neuro-QoL SF v2.0 short form[2]
- **Thirst**
- **Palpitations**
- **Chest Pain:** SAQ-7[3], <75
- **Fatigue:** FACIT-Fatigue[4], moderate or worse
- **Sexual desire or capacity**
- **Dizziness**
- **Gastrointestinal Symptoms**
- **Abnormal movement**
- **Hair loss**

Using LC definition as the 'true' condition, we compared PASC Total ≥12 as well as comparing the presence of individual, pairs of, and triplets of symptoms. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and F1 score were calculated based on these classifications for both the overall PASC score and for individual symptoms, as well as combinations.

Our analysis highlights the importance of symptom combinations, particularly post exertional malaise (PEM), altered smell/taste, and brain fog, in improving sensitivity for Long COVID diagnosis.

RESULTS

LC cohort (n=100) had a mean age of 47.7 years, was 73% female, and 76% had >16 years of education. Healthy controls (n=18) were similar demographically.

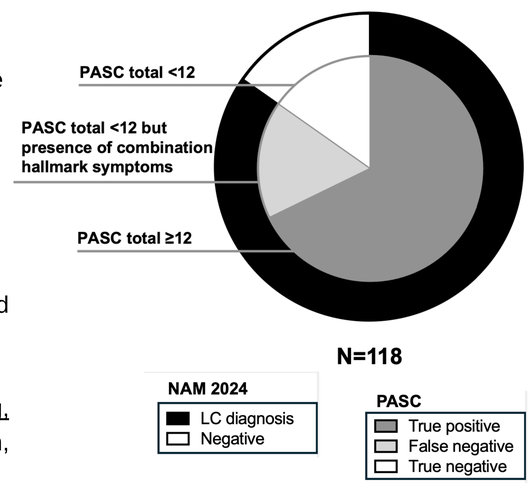
- Preexisting conditions in LC: mental health disorders (51%), asthma (32%), HTN (33%), and autoimmune disease (28%)
- 44% of LC participants reported disability: concentration and memory (75%), walking or climbing stairs (72.7%), doing errands alone (68.2%), and dressing or bathing (45.4%)
- Onset of LC symptoms: Pre Delta (30%), Delta (29%), and Omicron (41%)

RECOVER PASC Definition	Long COVID (LC) NAM 2024		
	LC	Control	Total
PASC+	80 (A: True Positive)	0 (B: False Positive)	80 (Test Positive)
PASC-intermediate	20 (C: False Negative)	18 (D: True Negative)	38 (Test Negative)
	100	18	118

- NPV was 47.37%, with F1 score of 0.889.
- The combination of hallmark symptoms loss/change of smell/taste, PEM, and brain fog had 93% sensitivity, 100% specificity, with F1 = 0.964 indicating these symptoms may be key contributors to LC identification.

LC patients with PASC score ≥12 were more likely to:

- Report autoimmune disease, asthma, and disability
- Have LC onset on pre-delta or delta variant
- Report loss/change in smell/taste, PEM, brain fog, chronic cough, thirst, palpitations, chest pain, fatigue, GI symptoms, and abnormal movements.



RESULTS (cont.)

PASC score items	LC (n=100) n/%	PASC+ (n=80) n (%)	PASC intermediate (n=20) n (%)	P-value
Smell/taste	37	34 (42.5)	3 (15)	<0.001
PEM	85	76 (95.0)	9 (45)	<0.001
Chronic cough	23	22 (27.5)	1 (5)	0.032
Brain fog	62	60 (75.0)	2 (10)	<0.001
Thirst	47	45 (56.3)	2 (10)	<0.001
Palpitations	68	65 (81.3)	3 (15)	<0.001
Chest pain	64	57 (71.3)	7 (35)	0.003
Fatigue	67	62 (77.5)	5 (25)	<0.001
Sexual desire or capacity	48	41 (51.2)	7 (35)	0.193
Dizziness	26	18 (22.5)	8 (40)	0.111
Gastrointestinal	85	73 (91.3)	12 (60)	<0.001
Abnormal movements	31	31 (38.8)	0 (0)	<0.001
Hair loss	43	36 (45.0)	7 (35)	0.419
PASC total score, M (SD)	18.3 (7.7)	20.9 (6.1)	7.7 (3.2)	<0.001

CONCLUSIONS

Long COVID is a common disabling condition for which there is no biomarker or clinical diagnostic tool, leading to underdiagnosis of the millions affected. This study is the first attempt at validating the RECOVER PASC score in a cohort of clinically diagnosed LC patients, providing insights into the iterative process needed to refine the LC definition. The validation of the RECOVER PASC score in our cohort provides insights for the iterative process needed in the ongoing refinement of the LC definition. Our analysis highlights the importance of hallmark symptom combination, altered smell/taste, and brain fog, in improving sensitivity for LC diagnosis. We call for ongoing efforts to develop a readily implementable clinical tool for LC diagnosis.

REFERENCES

1. Thaweethai T, Jolley SE, Karlson EW, et al. Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection. JAMA. 2023;329(22):1934-1946.
2. Cella D, Lai JS, Nowinski CJ, et al. Neuro-QOL: brief measures of health-related quality of life for clinical research in neurology. Neurology. 2012;78(23):1860-1867.
3. Spertus JA, Winder JA, Dewhurst TA, et al. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. Journal of the American College of Cardiology. 1995;25(2):333-341.
4. Cella D, Yount S, Rothrock N, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. Medical care. 2007;45(5 Suppl 1):S3-S11

AKNOLEDGEMENT

The work was supported by RF1 MH133411 (Rubin, Veenhuis). The authors would like to thank Drs. Serena Spudich and Shelli Farhadian for sharing their tool-Yale COVID-19 Review of Systems-version 10. The authors would also like to acknowledge the participants for without them this research would not be possible.

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