# Longitudinal Clinical and Physiological Evaluation of Post-COVID-19 Conditions in Residents of Quebec

Maryam Nayyerabadi[1], Arpita Chakravarti[1], Chantal Massé[1], Marie-Lorna Paul[1], Joanie Houle[1], Amina M. Boubekeur[1], Charlotte DuSablon[1], Valérie Boudreau[1], Danijela Bovan[1], Emma Darbinian[1], Sandra Vinci[1], Pierre-Olivier Hétu[2], Johanne Poudrier[1], Suhani Patel[1], Estefania Rivera-Conde[1], Diana Munoz[1], Thao Huynh [3], Emilia Liana Falcone[1];

[1:] Montreal Clinical Research Institute (IRCM), [2] :Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM), [3] :Impact-Quebec COVID-19 (IQ-19)

## Introduction

- The WHO defines long COVID or post-COVID-19 conditions (PCC) as the presence of at least 1 symptom in individuals with a probable or confirmed history of SARS-CoV-2 infection, at least 3 months from the onset of COVID-19 that cannot be explained by an alternative diagnosis.
- It is estimated that 14.8% of Canadians who got COVID-19 will have persistent symptoms beyond 12 weeks post-infection.
- The manifestations of PCC are varied and can impact several different organ systems
- Although over 200 symptoms have been associated with PCC, some of the most common ones include: loss of taste or smell, sore throat, headache, muscle or joint pain, dyspnea, chest pain, anxiety and depression
- Studies have highlighted the increased risk of neuropsychological, cardiovascular, renal and metabolic sequelae for at least 12 months after SARS-CoV2 infection.
- To date, few studies have comprehensively evaluated long-term clinical and physiological sequelae of COVID-19 in Quebec residents.

## Aim

**By conducting a prospective longitudinal cohort study, we aimed to gather comprehensive data on the sequelae of PCC over a 12-month period. This approach allowed us to track changes in symptoms and complications in different organ systems over time to provide valuable insights into the diverse and lasting impacts of COVID-19 on individuals' health in Quebec.**

## Methods

**Participant Selection:**

- Inclusion criteria: Adults (≥ 18 years) residing in Québec with a history of previous SARS-CoV2 infection (confirmed by molecular testing or had symptoms of COVID-19 while residing with an individual who tested positive for COVID-19)
- Exclusion criteria: Known pregnancy at time of enrollment.
- Data Collection Period: February 12th, 2021 to January 26th, 2023.

**Study Schedule:**

- Baseline visit at 3 to 6 months and follow-up visit at 12 months after COVID-19 diagnosis.

**Study Procedures:**

- Case Report Form: past medical history, medications, acute COVID-19 symptoms and severity, vaccination status, survey of 49 PCC-associated symptoms, general health score (0-100%; subjectively determined by participant) and German PCC severity score(0-59; scores the severity of PCC based on 12 symptom complexes, including Chemosensory deficits, Fatigue, Exercise intolerance, and others)
- WHO-5 Well-Being Index
- Physical exam, vital signs and measurement of body mass composition by bioimpedance
- Activity level: pedometer
- Physiological Evaluations: Echocardiography, PFT, 6 MWT
- Laboratory Evaluations:
  - Saliva for SARS-CoV2 PCR testing
  - Peripheral venous blood for tests listed in Table 2.

## Results

N= 134 participants evaluated at 3-6 months and 12 months post-COVID-19.

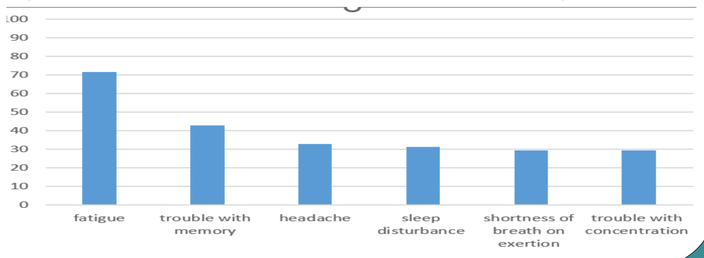


**Figure 1. prevalence of the five most common PCC symptoms at inclusion visit**

**Table 1. Clinical scores and functionality at 3-6 months vs 12 months post SARS-COV-2;** All data are presented as mean (SD), except for the severity of acute phase and frailty score, which are presented as n (%), Adj. = adjusted, NA= not applicable, SD = standard deviation, m = meter, 6MWT = 6-minute walk test, WHO =World Health Organisation.

| | 3-6 months post-SARS-COV-2 (n=134) | 12 months post-SARS-COV-2 (n=134) | *P*-value | Adj. *P*-value |
|---|---|---|---|---|
| 6MWT (m, mean (SD)) | 1339.03 (224.99) | 1348.26 (242.44) | 0.80 | NA |
| German score | 19.12 (11.09) | 17.02 (10.93) | 0.027* | 0.09 |
| General health score | 59.45 (26.75) | 68.34 (15.21) | 0.16 | NA |
| WHO-5 well-being score | 45.14 (19.61) | 51.97 (19.88) | <0.001* | <0.001* |

**Table 2. Clinical laboratory tests at 3-6 months vs 12 months post- SARS-COV-2;** All data are presented as mean (SD), † =value is reported as a dimensionless quantity, TSH = thyroid-stimulating hormone, HbA1C = hemoglobin A1C, ALT = alanine aminotransferase, AST = aspartate aminotransferase , GGT = Gamma-glutamyl Transferase , GFR = Glomerular filtration rate , NT-Pro BNP = N-terminal pro B-type Natriuretic peptide, CRP = C-reactive protein, WBC= White blood cells, RBC = Red blood cells, MCV = mean corpuscular volume, MPV = Mean Platelet Volume, PT/INR = prothrombin time/ international normalized ratio.

| | 3-6 months post-SARS-COV-2 (n=134) | 12 months post-SARS-COV-2 (n=134) | *P*-value | Adj. *P*-value |
|---|---|---|---|---|
| WBC ($10^9$/L) | 5.64 (1.42) | 5.37 (1.39) | 0.003* | 0.023* |
| Lymphocytes | 1.7 (0.49) | 1.64 (0.5) | 0.15 | NA |
| Monocytes | 0.45 (0.14) | 0.43 (0.14) | 0.06 | NA |
| Neutrophils | 3.34 (1.17) | 3.12 (1.15) | 0.006* | 0.031* |
| Eosinophils | 0.14 (0.12) | 0.14 (0.11) | 0.44 | NA |
| Basophils | 0.04 (0.11) | 0.03 (0.05) | 0.32 | NA |
| RBC ($10^{12}$/L) | 4.66 (0.46) | 4.62 (0.46) | 0.016* | 0.065 |
| Hemoglobin (g/L) | 137.89 (11.81) | 137.71 (11.3) | 0.76 | NA |
| Hematocrit† | 0.42 (0.04) | 0.41 (0.04) | 0.048* | 0.14 |
| MCV (fL) | 88.53 (4.93) | 88.76 (4.8) | 0.23 | NA |
| Platelets ($10^9$/L) | 247.73 (54.57) | 242.13 (50.82) | 0.030* | 0.09 |
| MPV (fL) | 8.9 (0.87) | 8.87 (1.01) | 0.54 | NA |
| PT/INR† | 0.99 (0.07) | 1.02 (0.07) | <0.001* | <0.00* |
| D-dimer (µg/L) | 411.19 (386.09) | 386.3 (256) | 0.37 | NA |
| Ferritin (µg/L) | 76.85 (73.61) | 70.57 (63.7) | 0.011* | 0.052 |
| Fibrinogen (g/L) | 3.36 (0.84) | 3.25 (0.64) | 0.021* | 0.08 |
| CRP (mg/L) | 6.1 (4.3) | 5.92 (3.19) | 0.57 | NA |
| Troponin (ng/L) | 2.55 (1.09) | 2.76 (1.63) | 0.25 | NA |
| Creatine kinase (U/L) | 104.78 (159.18) | 126.07 (299.69) | 0.49 | NA |
| NT-Pro BNP (ng/L) | 67.47 (55.84) | 60.16 (52.11) | 0.16 | NA |
| Total cholesterol (mmol/L) | 4.83 (1.11) | 4.85 (1.05) | 0.70 | NA |
| HDL cholesterol | 1.48 (0.37) | 1.47 (0.4) | 0.84 | NA |
| LDL cholesterol | 2.78 (0.91) | 2.79 (0.85) | 0.73 | NA |
| Non-HDL cholesterol | 3.36 (1.08) | 3.37 (0.96) | 0.82 | NA |
| Triglycerides (mmol/L) | 1.23 (0.7) | 1.27 (0.75) | 0.41 | NA |
| 25-OH Vitamin D (nmol/L) | 76.76 (30.36) | 76.74 (27.78) | 0.99 | NA |
| Vitamin B12 (pmol/L) | 266.84 (143.92) | 296.12 (163.38) | 0.015* | 0.07 |
| TSH (mUI/L) | 2.01 (1.16) | 1.9 (0.88) | 0.26 | NA |
| HbA1C† | 0.053 (0) | 0.054 (0) | <0.001* | <0.001* |
| ALT (U/L) | 18.46 (10.46) | 20.05 (12.73) | 0.07 | NA |
| AST (U/L) | 18.99 (7.12) | 19.17 (7.98) | 0.82 | NA |
| GGT (U/L) | 20.39 (13.89) | 23.1 (18.8) | 0.004* | 0.025* |
| Alkaline phosphatase (U/L) | 56.07 (18.37) | 57.73 (19.36) | 0.06 | NA |
| Total bilirubin (µmol/L) | 11.07 (5.21) | 11.65 (7.5) | 0.30 | NA |
| Albumin (g/L) | 42.89 (2.55) | 43.46 (2.51) | 0.001* | 0.011* |
| Creatinine (µmol/L) | 64.94 (13.25) | 65.3 (13.65) | 0.52 | NA |
| GFR (mL/min/1.73m²) | 101.42 (13.02) | 101 (13.71) | 0.47 | NA |
| Urea (mmol/L) | 5.37 (1.45) | 5.64 (1.51) | 0.009* | 0.052 |

**Table 3. Cardiorespiratory physiological tests at 3-6 months vs 12 months post-SARS-COV-2;** LV strain = Left ventricular strain, LV EF = Left ventricular ejection fraction, FVC = Forced vital capacity, FEV1 = Forced expiratory volume second, MMEF = 25-75 % maximal mid-expiratory flow 25-75 %.

| | 3-6 months post-SARS-COV-2 (n=134) | 12 months post-SARS-COV-2 (n=134) | P-value | Adj. P-value |
|---|---|---|---|---|
| **Echocardiography** | | | | |
| LV strain | -20.82 (1.76) | -20 (2.2) | 0.16 | NA |
| LV EF | 63.12 (3.9) | 61.11 (5.26) | 0.022* | 0.08 |
| **Pulmonary function testing** | | | | |
| FVC (L) | 3.81 (0.98) | 3.86 (0.96) | 0.27 | NA |
| FVC (%) | 95.16 (15.14) | 96.36 (12.59) | 0.34 | NA |
| FEV1 (L) | 2.85 (0.81) | 2.96 (0.86) | 0.17 | NA |
| predicted FEV1 (%) | 90.5 (20.14) | 92.88 (17.59) | 0.32 | NA |
| FEV1/FVC | 75.23 (11.5) | 75.33 (12.18) | 0.96 | NA |
| FEV1/FVC (%) | 94.58 (15.01) | 96.1 (13.62) | 0.45 | NA |
| MMEF 25-75 (%) | 2.81 (1.01) | 2.95 (1.24) | 0.27 | NA |
| Predicted MMEF 25-75 (%) | 94.43 (33.15) | 96.15 (34.45) | 0.68 | NA |

**Table 4. Evaluation of body mass composition and metabolism at 3-6 months vs 12 months post SARS-COV-2;** All data are presented as mean (SD), BMI = Body mass index, kg = kilogram, kj = kilojoules, Average MET = Average metabolic equivalent, PAL = Physical activity level.

| | 3-6 months post-SARS-COV-2 (n=134) | 12 months post-SARS-COV-2 (n=134) | *P*-value | Adj. *P*-value |
|---|---|---|---|---|
| BMI (kg/m2) | 26.81 (5.71) | 27.59 (5.8) | <0.001* | <0.001* |
| Body fat (kg) | 24.18 (11.12) | 26.06 (11.58) | <0.001* | <0.001* |
| Body fat (%) | 30.95 (9.34) | 32.58 (9.38) | <0.001* | <0.001* |
| Lean body mass (kg) | 51.92 (10.61) | 51.84 (11.34) | 0.79 | NA |
| Total energy expenditure (KJ/day) | 9268.82 (1904.25) | 8783.13 (1614.44) | 0.026* | 0.09 |
| Average MET | 1.34 (0.31) | 1.26 (0.26) | 0.003* | 0.020* |
| PAL | 1.46 (0.21) | 1.36 (0.17) | 0.003* | 0.021* |

## Conclusions

- Estimated PCC severity decreased and WHO-5 Well-being scores improved by 12 months post-COVID-19.
- Most clinical blood tests were within normal range, but there was a trend in decreased markers of inflammation by 12 months post-COVID-19.
- Despite prevalent cardiopulmonary symptoms, blood NT-Pro BNP and troponin levels, echocardiography parameters and pulmonary function tests were mostly within normal range. These findings suggest that different tests may be needed to evaluate certain end-organ sequelae in PCC.
- BMI and % body fat increased over time in association with decreased total energy expenditure. Further investigations are warranted to understand the contribution of other variables (e.g., PCC symptoms, lifestyle changes, pathophysiological processes) to these metabolic alterations.

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