Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Telephone Screening of Cognitive Status (TICS) in severe COVID-19 patients: Utility in the era of social isolation

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Dear Editor,

Although several neurological syndromes have been described in COVID-19, little is known about cognitive dysfunction in this setting [1]. The social isolation, such as we are experiencing now due to the SARS-CoV-2 pandemic, is a significant limitation to cognitive assessment in these patients. Thus, alternative methods to assess cognitive function in large, community-dispersed populations containing an unknown proportion of individuals with cognitive impairment are desirable. Additionally, screening assessment methods must be inexpensive and accessible to researchers from countries with low socio-economic resources.

The main objective of this pilot study is evaluate the feasibility of an easy, remote assessment of cognitive status and quality of life (QOL) in severe COVID-19 surviving patients. The Telephone Screening of Cognitive Status (TICS) is a validated instrument for dementia screening in large populations, assessing in less than 30 min many essential cognitive functions such as orientation, memory, concentration, naming, comprehension, calculation, reasoning, and judgment [2]. The TICS has excellent interrater reliability ($r = 0.97$) and high sensitivity (85%) and specificity (83%) for the detection of dementia when compared with a brief, in-person neuropsychological examination [3]. The EuroQol is a validated instrument to assess the QOL through the evaluation of mobility, self-care, main activity, social relationship, pain, and mood [4].

We selected severe COVID-19 patients admitted to an intensive care unit from March to May 2020. In all cases, SARS-CoV-2 RNA was detected by RT-qPCR through nasal and oropharyngeal swabs. For this study, we considered severe COVID-19 cases those who needed mechanical ventilation. The Local Ethical Committee at INI/FIOCRUZ approved this study.

After discharge, a telephone contact inviting patients to participate in the study was made by one of the principal investigators. The test was then scheduled for a second time for those who agreed to participate. Briefly, TICS is a short cognitive battery that asses several cognitive domains. The TICS was administered according to published procedures and followed a standardized script [2]. It includes the following items: (1) Name and complete date; (2) Space orientation; (3) Counting backward; (4) 10-word list learning exercise and then a delayed recall of that word list; (5) Subtractions; (6) Responsive naming; (7) Repetition; (8) Current President and Vice President; (9) Finger tapping, and (10) Word opposites. The total score is 41 points and we followed the procedures for scoring the TICS according to the original report. Thus, a score of 33 or more indicates normal cognition, between 26 and 32 points ambiguous, from 21 to 25 points indicates mild cognitive impairment (MCI), and $\leq$ 20 points suggest a moderate to severe cognitive impairment [2]. Additionally, we evaluated patients' QOL using the EuroQol instrument, a standardized non-disease-specific instrument for describing and valuing health-related QOL [4]. The final score is a composite of multiple domains which contain information about mobility, self-care, main activity, social relationship, pain, and mood.

From March to May 2020, 98 COVID-19 patients were admitted to the intensive care unit. Among those, 14 patients died, and 48 had not undergone mechanical ventilation. The remaining 36 COVID-19 patients were invited to participate. After the first telephone contact we included 23 individuals. During hospitalization, delirium was diagnosed in 91.3% of these patients, although most patients were younger than 55 years old: only 4 out of 23 patients were older than 65 years, while 14 were younger than 55 years old.

The median interval between discharge and the first contact was 83 days (37 to 115 days) and from first contact to TICS was 15 days (6 to 21 days). The main reasons for not including the other patients were not being available to be tested and the presence of previous cognitive impairment or some neurological disease that prevented remote testing by telephone. The main clinical characteristics of patients are in Table 1.

In this pilot study, most patients were male and had one or more risk factors associated with COVID-19 lethality, such as systemic hypertension, obesity, and diabetes. TICS lasted an average of 15 min to be administered, with the longest items being subtraction and delayed word recall. Only one of the investigators in this pilot study (ABS) performed TICS.

No patient had a final TICS score $\leq$ of 20 points, indicative of severe cognitive impairment. MCI was diagnosed in three patients, while in six

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Table 1
Clinical characteristics of 23 severe COVID-19 patients submitted to the Telephone Screening Cognitive Status (TICS).

	General (n 23)	Group 1 (n 14)	Group 2 (n 6)	Group 3 (n 3)	*p*-Value
Age (years)	53.6 ± 11,7	51.6 ± 13.5	55.3 ± 8.8	59.3 ± 7.8	0.303
Male/Female	18/5	11/3	6/0	2/1	–
Risk factor[1]	18/23	11/14	4/6	3/3	0.520*
MV (days)[2]	7.4 ± 6.1	7.6 ± 7.1	8.1 ± 7.8	5.3 ± 3.78	0.778
ICU (days)[3]	12.3 ± 7	13 ± 8.2	12.8 ± 4.7	8 ± 3.4	0.322
Delirium[4]	21/23	12/14	6/6	3/3	0.495*
Schooling (years)	12.7 ± 3.5	14 ± 3.3	12.5 ± 1.7	7 ± 1.7	0.009
TICS[5]	31.9 ± 1.2	34.6 ± 1.2	30 ± 2.0	23.3 ± 1.5	0.000

Group 1 - patients with TICS score ≥ 32; Group 2 – patients with TICS score between 26 and 32; Group 3 – patients with TICS score between 21 and 25.

[1] Presence of one of the following comorbidities: blood hypertension, diabetes, obesity.

[2] Days of mechanical ventilation.

[3] Days in intensive care unit.

[4] Presence of delirium during hospitalization.

[5] Total score in TICS. Values are expressed in mean ± SD.

an ambiguous result was detected. The majority of patients had normal cognitive assessments (14 out of 23 individuals). As expected, poor schooling was associated with worse TICS performance. The mean EuroQol score was 71.9 ± 27.5 (final composite score assessing multiple domains, namely mobility, self-care, main activity, social relationships, pain, and mood). Patients with mild cognitive impairment in TICS tended to have a low EuroQol score (median of 50 points) compared to patients with ambiguous and with normal TICS performance (median of 85 points in each group); this difference was not statistically significant (*p* 0.062, Kruskall-Wallis test).

This pilot study's main objective was to evaluate TICS' utility in the COVID era setting. In this respect, we see that it is an easy and cost-effective tool to screen cognitive dysfunction in severe COVID patients. In this small cohort, MCI was detected in 13% and an ambiguous performance in TICS (i.e., between 26 and 32 points) in 26% of severe COVID-19 surviving patients. These patients were referred for a face-to-face evaluation with a cognition specialist as soon as possible.

Given that human-to-human transmission of SARS-CoV-2 is obvious, we conducted a telephone assessment of cognition of surviving COVID-19 patients to minimize the contact between medical staff and patients with COVID-19. This first neuropsychological assessment can be useful to select those patients who deserve further, complete neuropsychological evaluation in the future.

Self-reported memory problems can be observed in patients who survived acute respiratory distress syndrome and can persist up to five years after, affecting significantly the QOL [5]. Although anxiety, depression, and post-traumatic stress syndrome are also common in acute respiratory distress syndrome patients, contributing to cognitive impairment, there is evidence suggesting that cognitive deficits occur independently of psychological problems and are associated with the severity of infection [6]. The same psychological problems are now observed in COVID-19 patients and the same could be applied in these patients [7].

During the pandemic of SARS in 2002, many surviving patients complained of poor concentration and memory, indicating possible cognitive impairment [8]. However, it remains unknown whether SARS-CoV-2 infection is also associated with cognitive dysfunction. In the only report assessing specifically this matter, Zhou et al. described that COVID-19 patients exhibited a mild cognitive dysfunction in sustained attention domains in an iPad-based online neuropsychological test [9]. Unfortunately, electronic cognitive assessment is not available on a large scale, especially in low-income communities.

The main limitation of this study is the lack of a control group. However, in this preliminary pilot study, we intended only to assess the feasibility of TICS to evaluate cognitive performance in COVID-19 patients. Further studies with more patients and a control group are being developed.

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