

Correlation of SARS-CoV-2 Nasopharyngeal CT Values With Viremia and Mortality in Adults Hospitalized With COVID-19

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Background. Both severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viremia and nasopharyngeal viral load have been suggested to be predictors of unfavorable outcome in coronavirus disease 2019 (COVID-19). This study aimed to investigate whether nasopharyngeal viral load is correlated with viremia and unfavorable outcome.

Methods. The presence of SARS-CoV-2 RNA was determined in paired nasopharyngeal and serum samples collected at admission from patients hospitalized for COVID-19. Standardized cycle threshold values (CT values) were used as an indicator of viral load. An adjusted logistic regression was used to estimate the risk of viremia at different nasopharyngeal CT values. A Cox regression was used to estimate the risk of 60-day mortality.

Results. A total of 688 patients were included. Viremia at admission was detected in 63% (146/230), 46% (105/226), and 31% (73/232) of patients with low, intermediate, and high nasopharyngeal CT values. The adjusted odds ratios of being viremic were 4.4 (95% CI, 2.9–6.8) and 2.0 (95% CI, 1.4–3.0) for patients with low and intermediate CT values, compared with high CT values. The 60-day mortality rate was 37% (84/230), 15% (36/226), and 10% (23/232) for patients with low, intermediate, and high nasopharyngeal CT values at admission, respectively. Adjusted hazard ratios were 2.6 (95% CI, 1.6–4.2) and 1.4 (95% CI, 0.8–2.4) for patients with low and intermediate CT values compared with high CT values.

Conclusions. There was a dose-dependent correlation between nasopharyngeal CT values and viremia at admission for COVID-19. Moreover, there was an increased risk of 60-day mortality for patients with low, compared with high, nasopharyngeal CT values.

Keywords. SARS-CoV-2; COVID-19; RNAemia; viral load; viremia.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) primarily infects the respiratory tract but has also been detected in extrapulmonary tissues such as blood in patients with coronavirus disease 2019 (COVID-19) [1–3]. The nasopharyngeal viral load gradually declines after a peak at or around symptom onset [4]. The level of the initial peak is highly individual but seems to be higher in older persons [4, 5]. Viral shedding from the upper respiratory tract is prolonged in patients with severe compared with mild disease [6]. A high respiratory viral load and low cycle threshold values (CT values) at

admission predicted intubation and mortality in some studies, while other studies found no such correlation [7–10].

Detectable SARS-CoV-2 RNA in blood at admission, henceforth called viremia, is a strong predictor for developing critical disease and was associated with an 8-fold increased risk of 28-day mortality [1, 11]. Moreover, the odds of mortality increased by 40% for each additional day of viremia [12]. Disease severity, age of the tested population, and the sensitivity of the method used were associated with the proportion of patients with viremia [1, 13]. In a cohort of 123 consecutively admitted patients, 47% were viremic [9]. Moreover, viremia was detected in 2%, 27%, and 78% of patients discharged from an emergency department, patients admitted to a general ward, and patients admitted to an intensive care unit, respectively [14].

We hypothesized that impaired viral control has a role in the development of severe COVID-19 and results in a persistently high respiratory viral load and viremia. The primary aim of this study was to investigate whether a high upper respiratory tract SARS-CoV-2 viral load is correlated with viremia at admission for COVID-19. The secondary aim was to investigate the

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correlation between high upper airway viral load at admission and an unfavorable outcome.

METHODS

Study Design, Setting, and Population

The study hospital in Danderyd, Stockholm, Sweden, is a 500-bed tertiary care hospital, and the study period was March 23, 2020, to April 20, 2021. Adult patients admitted to the hospital for COVID-19 with a positive nasopharyngeal SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) –1 to 1 day from admission and a serum sample analyzed for the presence of SARS-CoV-2 within –1 to 3 days of admission were included.

Patients admitted primarily for reasons other than COVID-19, developing COVID-19 during hospitalization, being transferred to Danderyd hospital from other hospitals, or with substantial missing data were excluded.

Data on viremia as a predictor for mortality in a subgroup ($n = 227$) of the cohort have been published previously [1, 12].

Data Collection

Baseline characteristics at admission, treatments, and outcome data were extracted by reviewing electronic medical records. The highest reached level on the World Health Organization (WHO) ordinal scale of outcome (3 = hospitalized, no oxygen therapy; 4 = oxygen therapy; 5 = noninvasive ventilation [NIV] or high-flow oxygen therapy [HFO]; 6 = mechanical ventilation; 7 = mechanical ventilation and organ support; 8 = death) during hospitalization was recorded. The electronic medical records are linked to the Swedish Population Register, ensuring accurate all-cause 60-day mortality data.

RT-PCR Analyses

RT-PCR analyses for detection of SARS-CoV-2 RNA in nasopharyngeal and serum samples were performed at Karolinska University Laboratory. Serum samples were initially drawn from patients perceived to have more severe disease. From May 10, 2020, samples were routinely drawn from patients hospitalized with COVID-19 and analyzed for the presence of SARS-CoV-2 RNA. Several different RT-PCR methods were used during the study period due to varying availability of reagents.

Nasopharyngeal samples were analyzed on the cobas 6800 instrument (Roche Molecular Diagnostics, Pleasanton, CA, USA) targeting the E and ORF 1a/b genes; the GeneXpert system (Cepheid, Sunnyvale, CA, USA) targeting the E and N genes; the TaqPath assay (Thermo Fisher Scientific, MA, USA) targeting the S, N, and ORF 1a/b genes; the Amplidag platform (Mobidiag, Finland) targeting the N and ORF1a/b genes; the NeuMoDx assay (NeuMoDx Molecular, Ann Arbor, MI, USA) targeting the Nsp2 and N genes; a NeuMoDx multiplex assay targeting Nsp2; and an in-house

assay targeting the RdRp and E genes, after separate RNA extraction (MagNA Pure 96, Roche Molecular Diagnostics or MGISP-960, MGI Tech) or automated on the NeuMoDx platform. The in-house PCR was performed using a QS6 or ABI7500 instrument (Applied Biosystems, Foster City, CA, USA) in 20- μ L reactions including oligonucleotides and the TaqPath 1-step RT-qPCR Master Mix kit (Applied Biosystems, Foster City, CA, USA). The sequence of the primers and probe was as follows: E-gene fwd, GGAAGAGACA GGTACGTTAATA; E-gene rev, AGCAGTACGCACACAA TCGAA; and E-gene probe, ACACTAGCCATCCTTA CTGCGCTTCG. RdRp primers and probe were performed according to Edén et al. [15]. After a reverse transcription step at 50°C for 15 minutes followed by 2 minutes of denaturation at 95°C, 45 cycles of 2-step PCR were performed (3 seconds at 95°C, 30 seconds at 56°C).

Whole blood was drawn, and after centrifugation at 1480 g for 5 minutes, serum samples were kept at 4°C until analysis the same day or the following day. All samples were analyzed using the above-described cobas, NeuMoDx, and in-house assays. Amplification of at least 1 gene target was considered a positive test. From December 15, 2020, the same fluorophore was used for both targets of the GeneXpert assay, resulting in only 1 CT value per sample. The analyses were therefore divided into 2 time periods (GeneXpert 1 and GeneXpert 2).

Statistics

CT values from the RT-PCRs were used as an indicator of viral load, where a lower CT value implies a higher viral load. The Pearson correlation coefficient was calculated for the CT values of the different gene targets within each RT-PCR method reporting 2 or more CT values. CT values generated from different assays are not directly comparable. Therefore, CT values were standardized by subtracting them from the mean and dividing them by the standard deviation of the distribution of values within each used assay. This produced values that were better comparable between different methods. The standardized CT values were then divided into tertiles by the 33rd and 66th percentiles, representing high, intermediate, and low viral loads.

A binomial logistic regression was fitted for the main analysis regarding the risk of being viremic with different levels of nasopharyngeal CT values. Covariates identified by prior knowledge and via a Directed Acyclical Graph (DAG) were included in a multivariable model. The included covariates were age, Charlson Comorbidity Index (CCI), immunosuppression, symptom duration at admission, and SARS-CoV-2 subtype. Patients were assumed to be infected with the wild-type virus until February 21, 2021, after which the Alpha variant of concern (lineage B.1.1.7) dominated. The February cutoff was based on epidemiological data as sequencing was not part of this study. Immunosuppression was defined as intake of the equivalent of ≥ 10 mg of prednisolone for >4 weeks before

admission, ongoing chemotherapy, or treatment with rituximab, infliximab, adalimumab, or a similar profoundly immunosuppressive medication. Results are presented as adjusted odds ratios (ORs) with 95% CIs. Sensitivity analyses were performed excluding RT-PCR assays with <20 nasopharyngeal samples and including only the RT-PCR assay with the most samples.

A Kaplan-Meier curve was constructed and a Cox proportional hazards regression was fitted to estimate the risk of 60-day mortality for the secondary analysis regarding the correlation of nasopharyngeal CT values and outcome. The same covariates as in the main analysis were included in a multivariable analysis. Results are presented as adjusted hazard ratios (HRs) with 95% CIs. The assumption of proportional hazards was tested graphically by comparing curves on the log-log plot of survival. In-hospital outcome was described using the highest level reached on the WHO ordinal scale. As time to mechanical ventilation was unknown, a binomial logistic regression was fitted to estimate the risk of mechanical ventilation and/or death during hospitalization.

A *P* value <.05 was considered significant. Continuous variables are presented as medians with interquartile ranges (IQRs), and categorical variables as counts and percentages. Statistical analyses were performed using STATA, version 15.1 (StataCorp, College Station, TX, USA).

Patient Consent

The Swedish Ethical Review Authority approved the study (registration number 2020-01770). Informed consent was waived.

RESULTS

Study Population

A total of 3663 patients with COVID-19 were admitted to Danderyd Hospital during the study period. Thirty-five percent (1275/3663) had a serum sample analyzed for SARS-CoV-2 RNA, and 19% (688/3663) were included in the cohort (Figure 1). The median age (IQR) of included patients was 67 (55–78) years, and 65% (445/688) were male. Baseline characteristics are presented in Table 1. Patients with low nasopharyngeal CT values had a higher median age, shorter symptom duration at admission, lower estimated glomerular filtration rate, and more frequently received treatments for COVID-19, compared with patients with intermediate or high CT values.

Nasopharyngeal RT-PCRs

The distribution of CT values from the different RT-PCR assays is shown in Supplementary Figure 1. CT values from different gene targets on the same sample showed a very strong correlation (Supplementary Table 1). As data on some of the gene targets were missing, the gene target with complete data for each assay was chosen for standardization. The CT value ranges for

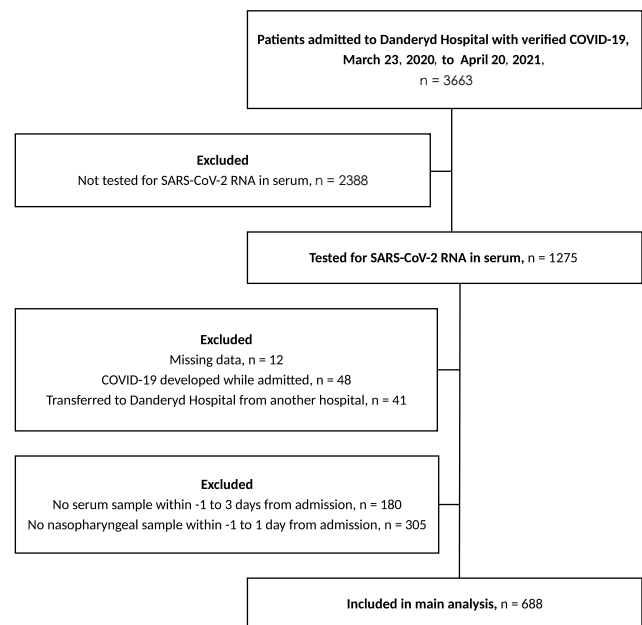


Figure 1. Flowchart. Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

the low, intermediate, and high categories were 13.5–23.7, 23.8–29.8, and 29.9–44.9 for GeneXpert 1; 11.5–20.2, 20.3–26.5, and 26.7–44.2 for GeneXpert 2; and 16.8–23.4, 23.6–27.4, and 28.1–34.3 for the in-house assay, respectively (Supplementary Table 2).

Correlation of Nasopharyngeal CT Values and Viremia

Viremia at admission was detected in 63% (146/230), 46% (105/226), and 31% (73/232) of patients with low, intermediate, and high nasopharyngeal CT values, respectively (Figure 2).

The crude ORs of being viremic at admission were 3.8 (95% CI, 2.6–5.6; *P* < .001) and 1.9 (95% CI, 1.3–2.8; *P* = .001) for patients with low and intermediate CT values, compared with high CT values, in the univariate logistic regression. After adjusting for age, CCI, immunosuppression, symptom duration, and dominant virus variant, the ORs were 4.4 (95% CI, 2.9–6.8; *P* < .001) and 2.0 (95% CI, 1.4–3.0; *P* < .001) for patients with low and intermediate CT values, compared with high CT values (Table 2). The results were concordant in a sensitivity analysis excluding CT values from RT-PCR assays with few samples and in an analysis including only values from the GeneXpert 1 assay with CT value as a continuous variable (Supplementary Table 3 and 4, Supplementary Figure 2). There was a weak but significant correlation between standardized CT values from nasopharyngeal and serum samples in viremic patients ($r = 0.12$; *P* = .03) (Supplementary Figure 3). There was also a weak but significant correlation between standardized nasopharyngeal CT values and age in both nonviremic ($r = -0.23$; *P* < .001) and viremic patients ($r = -0.39$; *P* < .001) (Supplementary Figure 4).

Table 1. Demographics, Clinical Characteristics at Admission, and Outcome Data

Variable	Full Cohort (n = 688)	Low CT Values (n = 230)	Intermediate CT Values (n = 226)	High CT Values (n = 232)
Age, y	67 (55–78)	74 (63–83)	65 (54–77)	60 (48–72)
Sex female:male	243:445 (35:65)	79:151 (34:66)	79:147 (35:65)	85:147 (37:63)
Charlson Comorbidity Index	1 (0–2)	1 (0–3)	1 (0–2)	0 (0–2)
Immunosuppression	52 (8)	21 (9)	11 (5)	20 (9)
Body mass index, kg/m ²	28 (24–32)	27 (24–31)	29 (25–32)	27 (24–31)
Estimated PaO ₂ /FiO ₂	282 (181–358)	271 (192–348)	277 (171–350)	286 (190–376)
Body temperature, °C	39 (38–39)	39 (38–39)	38 (38–39)	38 (38–39)
C-reactive protein, mg/L	85 (42–149)	81 (35–137)	85 (39–145)	101 (51–164)
Procalcitonin, µg/L	0.2 (0.1–0.5)	0.2 (0.1–0.5)	0.2 (0.1–0.4)	0.2 (0.1–0.5)
Lymphocyte count, ×10 ⁹ /L	0.8 (0.6–1.2)	0.8 (0.5–1.1)	0.8 (0.6–1.2)	0.9 (0.7–1.2)
Fibrin D-dimer, mg/L	1.0 (0.6–1.9)	1.0 (0.5–2.0)	0.9 (0.6–1.4)	1.0 (0.6–2.1)
Troponin T, ng/L	12 (7–25)	19 (10–33)	11 (8–23)	10 (6–18)
eGFR, mL/min/1.7m ²	68 (51–84)	58 (42–74)	68 (51–81)	78 (61–90)
ALT, µkat/L	0.6 (0.4–0.9)	0.5 (0.3–0.8)	0.6 (0.4–0.8)	0.6 (0.4–1.0)
Dominant virus variant				
Wild-type	562 (82)	181 (79)	185 (82)	196 (84)
Alpha variant of concern	126 (18)	48 (21)	41 (18)	37 (16)
Symptom duration, d	7 (4–10)	5 (2–7)	7 (5–10)	9 (6–11)
Days from admission to nasopharyngeal sample	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Days from admission to serum sample	1 (1–2)	1 (1–2)	1 (1–2)	1 (0–1)
Days from nasopharyngeal to serum sample	1 (1–2)	1 (1–2)	1 (1–2)	1 (0–1)
Nasopharyngeal sample analyzed with:				
Amplidiag	3 (0)	1 (0)	1 (0)	1 (0)
Cobas	11 (2)	4 (2)	3 (1)	4 (2)
GeneXpert 1	352 (51)	118 (52)	114 (50)	120 (52)
GeneXpert 2	257 (37)	86 (38)	88 (39)	83 (36)
In-house	39 (6)	12 (5)	12 (5)	15 (6)
In-house (NeuMoDx)	8 (1)	3 (1)	3 (1)	2 (1)
NeuMoDx	2 (0)	1 (0)	0 (0)	1 (0)
NeuMoDx (multiplex)	5 (1)	2 (1)	1 (0)	2 (1)
ThermoFisher	11 (2)	3 (1)	4 (2)	4 (2)
Serum sample analyzed with:				
Cobas	253 (37)	78 (34)	85 (38)	90 (39)
In-house	416 (60)	146 (64)	135 (60)	135 (58)
In-house (NeuMoDx)	19 (3)	5 (2)	6 (3)	8 (3)
Thrombosis prophylaxis	652 (95)	224 (97)	215 (95)	213 (92)
Corticosteroid treatment ^a	406 (59)	151 (66)	136 (60)	119 (51)
Remdesivir treatment	129 (19)	58 (25)	42 (19)	29 (13)
Tocilizumab treatment	3 (0)	1 (0)	0 (0)	2 (1)
Convalescent plasma treatment	115 (17)	48 (21)	38 (17)	29 (12)
Viremia	324 (47)	146 (63)	105 (46)	73 (31)
WHO ordinal scale outcome ^b	4 (4–6)	4 (4–8)	4 (4–5)	4 (3–4)
60-d mortality	142 (21)	84 (37)	35 (15)	23 (10)

Data are median (IQR) or No. (%).

Abbreviations: ALT, alanine aminotransferase; CT, cycle threshold; eGFR, estimated glomerular filtration rate; IQR, interquartile range; PaO₂/FiO₂, partial pressure of oxygen/fraction of inspired oxygen; WHO, World Health Organization.

^aEquivalent of ≥20 mg of prednisolone for ≥3 days.

^bHighest score reached during hospitalization.

Correlation of Nasopharyngeal CT Values and Outcome

The 60-day mortality rate was 37% (84/230), 15% (35/226), and 10% (23/232) for patients with low, intermediate, and high nasopharyngeal CT values at admission, respectively. A Kaplan-Meier graph of 60-day mortality is shown in [Figure 3A](#). The crude HRs for 60-day mortality were 4.3

(95% CI, 2.7–6.8; $P < .001$) and 1.6 (95% CI, 1.0–2.7; $P = .07$) for patients with low and intermediate CT values compared with high CT values in the univariate Cox regression. The adjusted HRs were 2.6 (95% CI, 1.6–4.2; $P < .001$) and 1.4 (95% CI, 0.8–2.4; $P = .19$) for patients with low and intermediate CT values compared with high CT values after adjustment

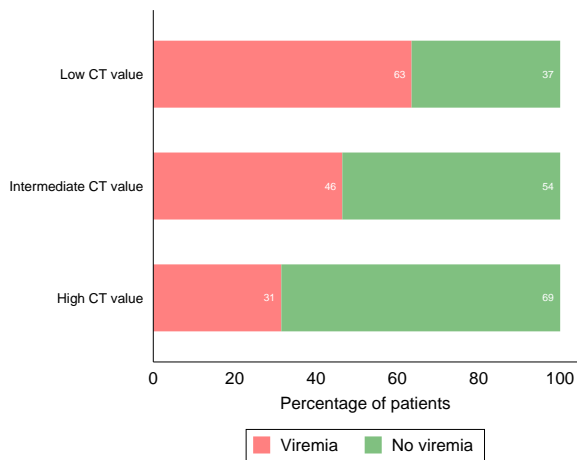


Figure 2. Proportion of patients with viremia according to nasopharyngeal cycle threshold value categories.

for age, CCI, immunosuppression, symptom duration, and dominant virus variant (Table 3).

In-hospital outcomes according to the WHO ordinal scale for different levels of nasopharyngeal CT values are shown in Figure 3B. The crude ORs for mechanical ventilation and/or in-hospital mortality were 4.8 (95% CI, 3.0–7.7; $P < .001$) and 1.7 (95% CI, 1.0–2.8; $P = .03$) for patients with low and intermediate CT values compared with high CT values in a univariate logistic regression. In the multivariate analysis, the ORs were 4.0 (95% CI, 2.4–6.6; $P < .001$) and 1.6 (95% CI, 1.0–2.7; $P = .06$) for patients with low and intermediate CT values compared with high CT values (Supplementary Table 5).

DISCUSSION

This study aimed to investigate whether high respiratory viral load at admission correlated with viremia and more severe illness. The results showed 4 times higher odds of viremia in patients with low nasopharyngeal CT values and 2 times higher odds in patients with intermediate CT values, compared with

high CT values. There thus appeared to be a dose–response correlation between respiratory viral load as indicated by nasopharyngeal CT values and the odds of viremia. Smaller studies have previously reported conflicting results. Respiratory viral load was significantly higher in patients with viremia compared with nonviremic patients in a study on 41 patients [16]. There was a strong correlation in viral RNA levels between endotracheal aspirates and plasma sampled at day 1 after intubation in 33 patients [17]. Viremia correlated with a CT value <30 in 20 repeatedly sampled patients [18]. Other studies have also shown weak or moderate correlations of viremia and respiratory RNA load [2, 13]. On the other hand, respiratory CT values and viremia or serum RNA load did not correlate in 102 patients with paired respiratory and serum samples at admission [9]. Similarly, nasopharyngeal viral load did not correlate with viremia in a study on 72 admitted patients [19]. Limitations of the previous studies included small numbers, use of CT values from respiratory samples, which can vary considerably depending on peri-analytical factors, and lack of regression analyses to take characteristics such as age and comorbidities into account. The larger number of patients, dose response, and multivariable regression analysis used in this study support the finding of a correlation between nasopharyngeal CT values and viremia. Immunosuppression, a lower Charlson Comorbidity Index, and hospitalization during the Alpha variant of concern time period were also independently associated with viremia, probably highlighting the importance of a well-functioning immune response and strain-dependent virulence in COVID-19. The correlation of a lower CCI with viremia may be due to patients with multiple comorbidities having a lower threshold before needing hospitalization without necessarily being severely ill from COVID-19.

The 2-fold higher risk of 60-day mortality and the increased risk of mechanical ventilation and/or in-hospital mortality in patients with low CT values are in line with most previous data [7, 10, 20]. Specifically, a higher CT value (indicating lower viral load) resulted in reduced odds for mortality or discharge

Table 2. Odds Ratios for Being Viremic at Admission

Variable	Univariate			Multivariate		
	OR	95% CI	<i>P</i> Value	OR	95% CI	<i>P</i> Value
Nasopharyngeal CT values						
High CT values	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Intermediate CT values	1.9	1.3–2.8	.001	2.0	1.4–3.0	<.001
Low CT values	3.8	2.6–5.6	<.001	4.4	2.9–6.8	<.001
Age, y	1.0	1.0–1.0	.10	1.0	1.0–1.0	.15
Charlson Comorbidity Index	0.9	0.8–1.0	.04	0.8	0.7–0.9	<.001
Immunosuppression	1.9	1.1–3.4	.03	2.1	1.1–3.9	.02
Symptom duration, d	1.0	1.0–1.0	.17	1.0	1.0–1.0	.90
Alpha VoC time period	1.8	1.2–2.6	.004	1.7	1.1–2.6	.01

Odds ratios with 95% CIs for being viremic calculated by binomial logistic regression.

Abbreviations: CT, cycle threshold; OR, odds ratio; VoC, variant of concern.

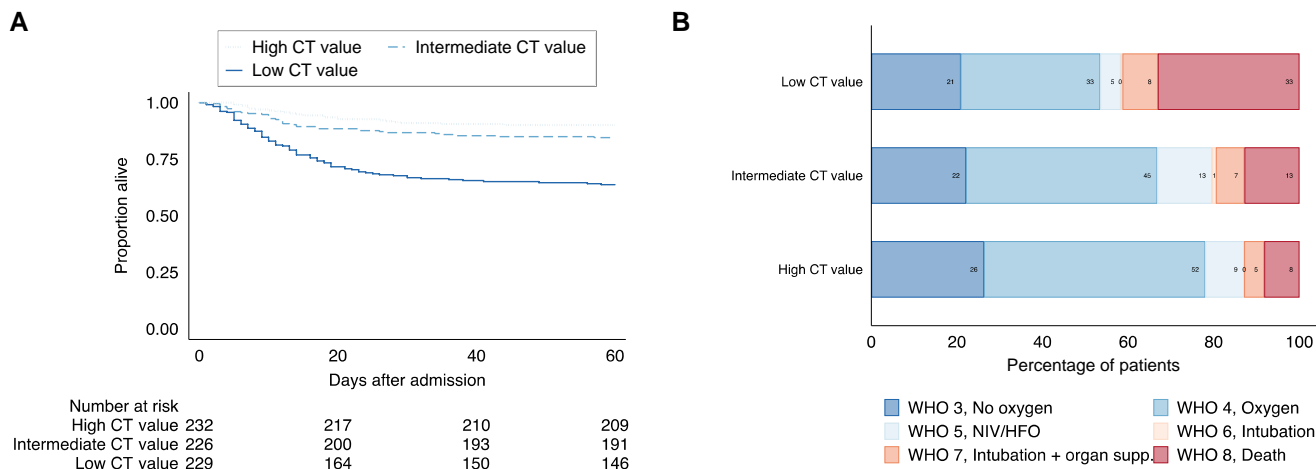


Figure 3. Sixty-day mortality and in-hospital outcomes. *A*, Kaplan-Meier curve of 60-day all-cause mortality according to nasopharyngeal CT value categories. *B*, In-hospital World Health Organization ordinal scale outcome according to nasopharyngeal CT value categories. Abbreviations: CT, cycle threshold; HFO, high-flow oxygen therapy; NIV, noninvasive ventilation; WHO, World Health Organization.

to hospice in a study including 2308 patients [7]. Moreover, respiratory viral load was associated with mortality in a study including 1145 patients, and with both mortality and intubation in a cohort of 678 patients [10, 20]. Studies finding that respiratory viral load did not predict mortality or intensive care unit care have generally been smaller [8, 9]. The clinical implication of this correlation is that nasopharyngeal CT values at admission potentially could be used in the risk assessment of patients with COVID-19. This may in turn be helpful when deciding on treatments and monitoring of patients, especially in situations with limited resources.

The causality of the relationship between low upper airway CT values, viremia, severe COVID-19, and death found in this study is not known. Previous studies have shown that the elderly have higher upper respiratory tract viral loads and are more likely to be viremic compared with younger persons [1, 4]. Patients with severe disease shed viable virus longer, and patients with immunodeficiencies (in particular

B-cell-depleted patients) have a high incidence of viremia and death [6, 21, 22]. Moreover, viremia correlates with markers of a dysregulated inflammatory response [14]. Available data thus suggest that poor viral control may be a contributing factor to high viral loads at admission, viremia, and disease severity and may represent a link to the dysregulated immune response that has been described in the pathology of COVID-19 [23]. Alternative explanations for the correlation of respiratory CT values at admission to viremia and outcome include a high exposure dose of SARS-CoV-2, a high peak viral load, or that patients with a high risk of unfavorable outcome were admitted early after symptom onset when viral loads were high. However, symptom duration was not significantly associated with viremia and outcome in the multivariable analyses of this study.

The strengths of this study include the relatively large population, no loss to follow-up of 60-day all-cause mortality, and that data from several different RT-PCR assays were used

Table 3. Hazard Ratios for 60-Day All-Cause Mortality

Variable	Univariate			Multivariate		
	HR	95% CI	P Value	HR	95% CI	P Value
Nasopharyngeal CT values						
High CT values	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Intermediate CT values	1.6	1.0–2.7	.07	1.4	0.8–2.4	.19
Low CT values	4.3	2.7–6.8	<.001	2.6	1.6–4.2	<.001
Age, y	1.1	1.0–1.1	<.001	1.0	1.0–1.1	<.001
Charlson Comorbidity Index	1.3	1.2–1.3	<.001	1.1	1.0–1.2	.007
Immunosuppression	1.8	1.1–3.0	.02	2.1	1.3–3.5	.005
Symptom duration, d	0.9	0.9–1.0	<.001	1.0	1.0–1.0	.76
Alpha VoC time period	1.1	0.7–1.7	.70	0.8	0.6–1.3	.44

HRs with 95% CIs for being viremic calculated by Cox regression.

Abbreviations: CT, cycle threshold; HR, hazard ratio; VoC, variant of concern.

with concordant results in sensitivity analyses. This is also, to our knowledge, the first study analyzing the correlation of nasopharyngeal CT values and viremia as the primary question. Limitations were that not all hospitalized patients were included and that only hospitalized patients from 1 hospital were included, which may affect the generalizability of the study. The study was conducted when the wild-type virus and the Alpha variant of concern were circulating, affecting the generalizability to other viral variants. Regarding the secondary aim of the correlation between CT values and outcome, included patients represent a convenience sample, which also may introduce a selection bias. The use of CT values as a proxy for viral load is suboptimal as it may be affected by peri-analytical factors such as sampling technique and therefore may introduce a misclassification bias. Moreover, the standardization and classification of CT values from different assays with different performance into categories is a novel approach and could introduce some inconsistency, especially for assays with few analyzed samples. However, results were consistent in sensitivity analyses.

CONCLUSIONS

There was a dose-dependent correlation between nasopharyngeal CT values and viremia at admission in this cohort of 688 patients hospitalized for COVID-19. Moreover, there was an increased risk of 60-day mortality and unfavorable in-hospital outcome for patients with low, compared with high, nasopharyngeal CT values. Low nasopharyngeal CT values at admission could potentially be used for early identification of a high-risk population.

Supplementary Data

[Supplementary materials](#) are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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