Supplementary data 1: Distribution of patients in the HCQ group and the no-HCQ group as a function of the centre, and technics used for the PCR (n=181)

	HCQ group (n=84)	No-HCQ group (n=89)	Received HCQ more than 48 h after admission (n=8)
Mondor Hospital	66	1	3
Cochin Hospital	6	25	0
Foch Hospital	11	32	0
Centre Hospitalier Sud-Francilien	1	31	5

In each department, patients were treated according to local medical consensus defined prior to the patients' admissions.

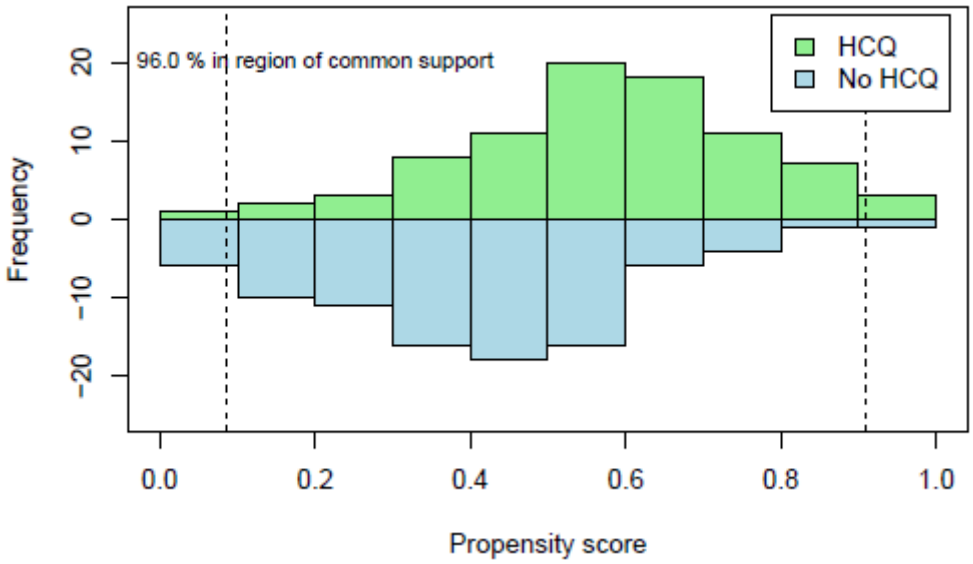
- Mondor Hospital: one patient did not receive HCQ for an unknown reason
- Cochin Hospital: No patients were treated with HCQ in unit 1 and 2, only one patient received HCQ in unit 3 because he strongly requested this treatment, and 5 patients received HCQ in unit 4 in accordance with the medical consensus in this unit.
- Foch Hospital: No patients were treated with HCQ in unit 1, 2, and 4, whereas patients in unit 3 received it.
- Centre Hospitalier Sud-Francilien patients were treated with HCQ after a change in the local medical consensus on March 26.

Mondor Hospital and Centre Hospitalier Sud-Francilien: Nasopharyngeal swabs were processed for RNA extraction with the QIAsymphony platform. Real-time RT-PCR was performed with a commercial test kit, the RealStar SARS-CoV-2 RT-PCR kit 1.0 (Altona, Hamburg, Germany) on a LightCycler® 480 plate-based real-time PCR platform, according to the manufacturer's instructions.

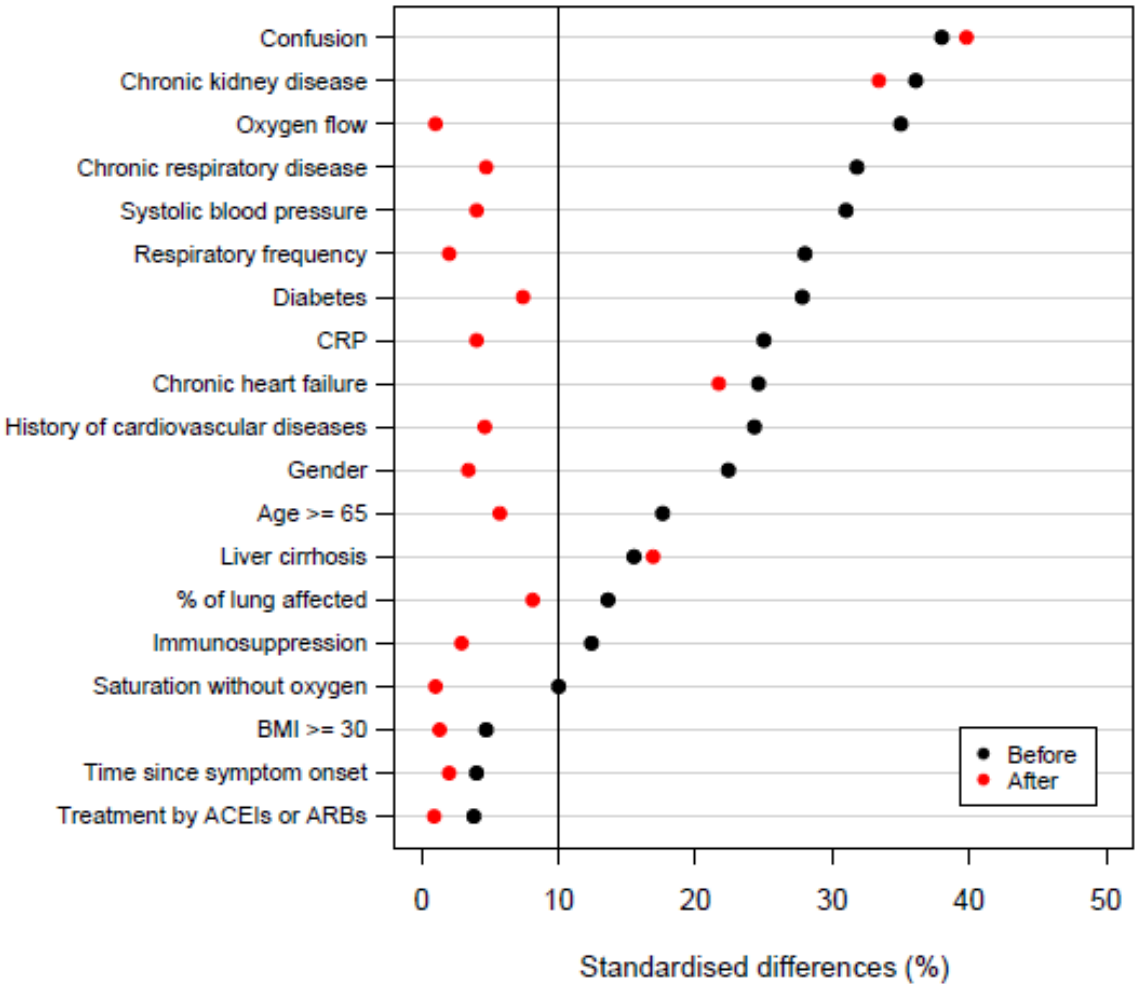
Foch Hospital: Nasopharyngeal swabs were processed for RNA extraction with the EasyMag Platform (BioMérieux, Marcy L'Etoile, France). Real-time RT-PCR was performed using a commercial test kit Allplex nCov 2019 (Seegene, Seoul, South Korea) on a CFX96 plate-based real-time PCR platform, according to the manufacturer instructions.

Cochin Hospital: Nasopharyngeal swabs were processed for RNA extraction with either the QIAsymphony or the NIMBUS platform. Real-time RT-PCR was performed using commercial test kits : either RealStar SARS-CoV-2 RT-PCR kit 1.0 (Altona, Hamburg,Germany) on a LightCycler® 480 or a QS (Applied BioSystems) platform, or the AllPlex coronavirus Seegene RT-PCR kit on the CFX96 platform (Eurobio, Evry, France).

Supplementary data 2: Propensity scores in the HCQ and no-HCQ groups (n=173)



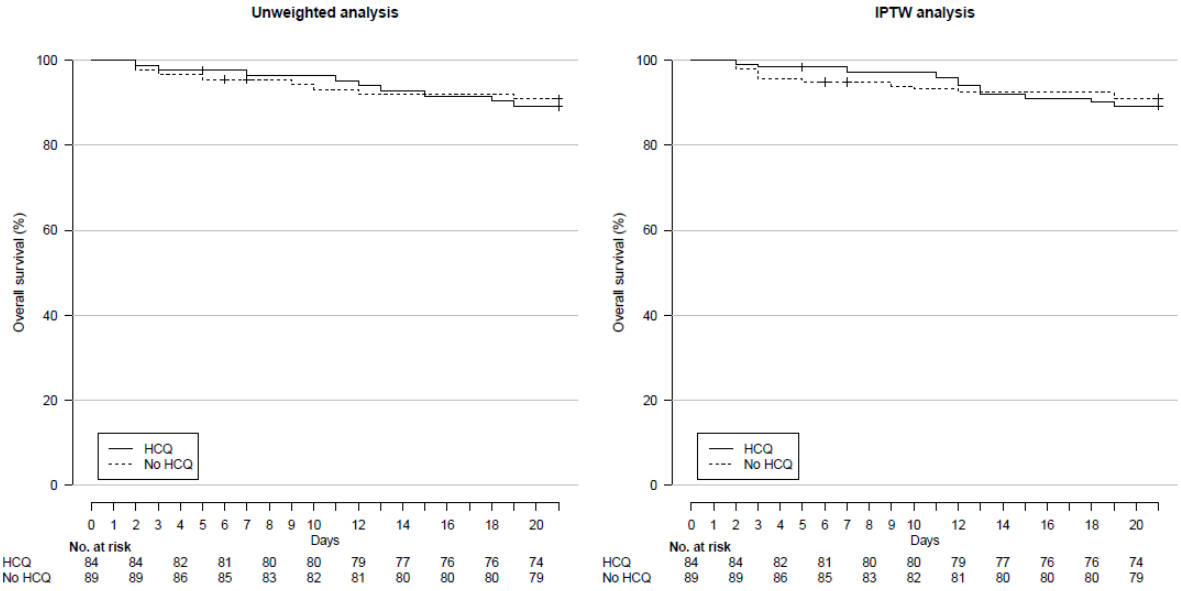
Supplementary data 3: Standardised differences of variables used to generate the propensity score (n=173)



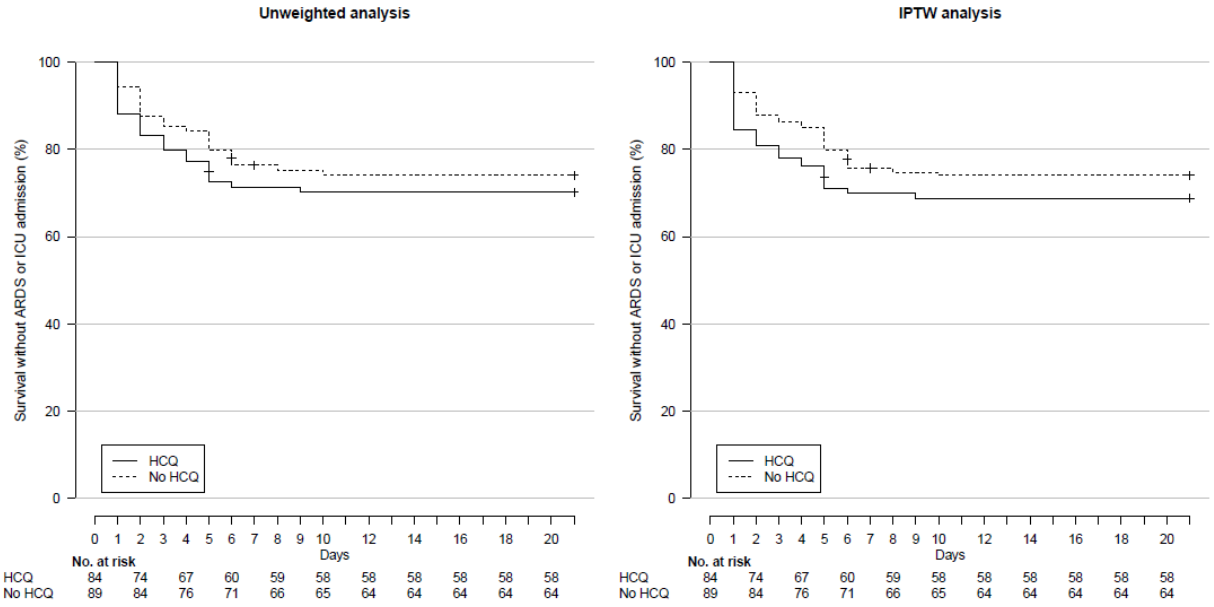
Supplementary data 4: Variables included in the final propensity score model

Variable	Type
Age	Binary (≥ 65 years old)
Gender	Binary (Male/Female)
Chronic respiratory insufficiency under oxygen therapy or asthma or cystic fibrosis or any chronic respiratory pathology likely to decompensate during a viral infection	Binary (Yes/No)
Cardiovascular disease: hypertension, stroke, coronary artery disease, cardiac surgery	Binary (Yes/No)
Insulin-dependent diabetes mellitus (DM), or DM with diabetic microangiopathy or macroangiopathy	Binary (Yes/No)
Treatment by immunosuppressive drugs (including anticancer chemotherapy) or uncontrolled HIV infection or HIV infection with CD4 cell counts < 200/µl; or a haematological malignancy)	Binary (Yes/No)
BMI	Binary (≥30 kg/m^2 or not)
Treatment by angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs)	Binary (Yes/No)
Date of symptom onset	Continuous (days)
% of lung affected on the computer tomography (CT) scan	Trinary (≥50 %, <50%, no CT-scan performed)
Respiratory frequency	Continuous (Cycles/min)
Oxygen saturation without oxygen	Continuous (%)
Systolic blood pressure	Continuous (mmHg)
Need for oxygen and oxygen flow	Continuous (L/min)
C-reactive protein (CRP)	Continuous (mg/L)

Supplementary data 5: Kaplan-Meier curves for overall survival before (left panel) and after (right panel) IPTW



Supplementary data 6: Kaplan-Meier curves for survival without ARDS before (left panel) and after (right panel) IPTW

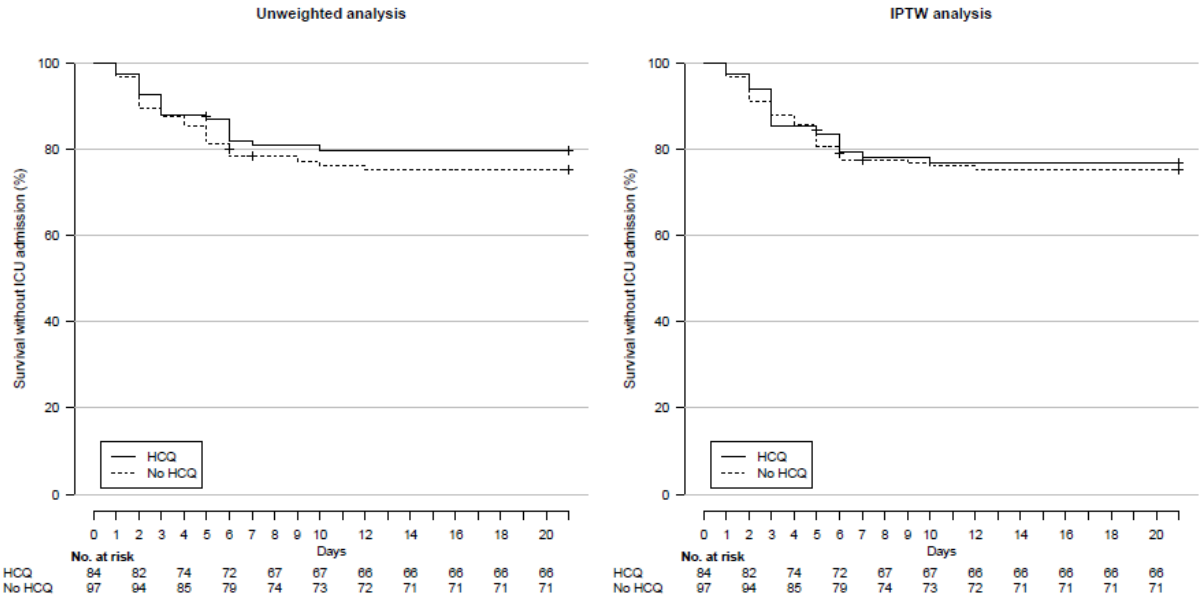


Supplementary data 7: Sensitivity analyses. All proportions are from weighted analyses. *The trimmed sample was truncated at the region of common support. **Patients who did not receive HCQ and who reached the primary outcome within the first 48 hours were randomly assigned to the HCQ group or no-HCQ group.

Outcome	Analysis	HCQ	No-HCQ	Ratio (95% CI)
		Number of events	Number of events	
Survival without transfer in ICU at day 21	**Trimmed sample***	16/81	21/85	wHR 0.9 (0.4 to 2.1)
	Accounting for events occurring during the grace period**	21/88	18/85	wHR 1.2 (0.6 to 2.4)
Overall survival at day 21	**Trimmed sample***	9/81	7/85	wHR 1.3 (0.4 to 3.7)
	Accounting for events occurring during the grace period**	10/88	7/85	wHR 1.3 (0.5 to 3.8)
Survival without ARDS at day 21	**Trimmed sample***	23/81	22/85	wHR 1.3 (0.6 to 2.6)
	Accounting for events occurring during the grace period**	29/88	19/85	wHR 1.6 (0.8 to 3.0)
Oxygen weaning at day 21	**Trimmed sample***	63/81	62/85	wRR 1.1 (0.9 to 1.3)
	Accounting for events occurring during the grace period**	67/88	65/85	wRR 1.0 (0.9 to 1.2)
Discharge from hospital at day 21	**Trimmed sample***	64/81	67/85	wRR 0.9 (0.8 to 1.2)
	Accounting for events occurring during the grace period**	68/88	70/85	wRR 0.9 (0.8 to 1.1)

Supplementary data 8: Estimation of an "intention to treat" effect (n=181). Patients who received HCQ after 48 hours are considered in the no-HCQ group. wHRs, wRRs and 95% CI are those from the IPTW analysis. Below, the Kaplan-Meier curve for the primary outcome before (left panel) and after (right panel) IPTW

	Number of events HCQ group (n=84)	**Number of events No-HCQ group (n=97)**	**Ratio (95% CI)**
Survival without transfer to ICU	17	24	wHR 0.9 (0.5 to 1.9)
Overall survival	9	8	wHR 1.3 (0.5 to 3.6)
Survival without ARDS	25	25	wHR 1.3 (0.7 to 2.4)
Oxygen weaning	66	72	wRR 1.1 (0.9 to 1.3)
Discharge to home/rehabilitation	67	77	wRR 1.0 (0.8 to 1.2)



Supplementary data 9: Estimation of an "as treated" effect (n=181). Patients who received HCQ after 48 hours are considered in the HCQ group. wHRs, wRRs and 95% CI are those from the IPTW analysis. Below, the Kaplan-Meier curve for the primary outcome before (left panel) and after (right panel) IPTW

	Number of events HCQ group (n=92)	**Number of events No-HCQ group (n=89)**	**Ratio (95% CI)**
Survival without transfer to ICU	19	22	wHR 1.0 (0.4 to 2.1)
Overall survival	9	8	wHR 1.1 (0.4 to 3.1)
Survival without ARDS	27	23	wHR 1.3 (0.7 to 2.6)
Oxygen weaning	72	66	wRR 1.1 (0.9 to 1.3)
Discharge to home/rehabilitation	73	71	wRR 0.9 (0.8 to 1.1)