Methods

Study design and population

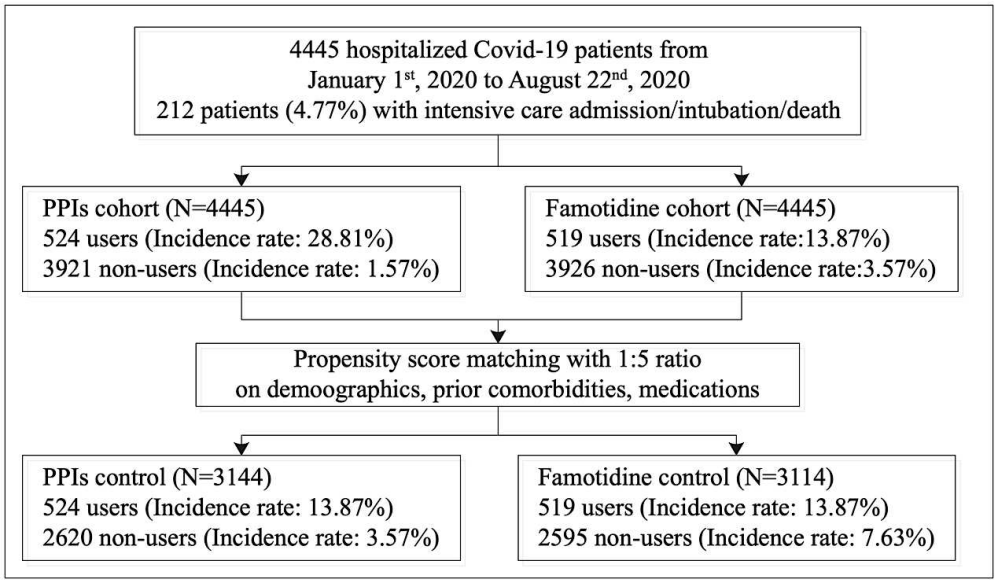
This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. This was a retrospective, territory-wide cohort study of patients with confirmed COVID-19 between 1st January 2020 and 22nd August 2020 in Hong Kong. The patients were identified from the Clinical Data Analysis and Reporting System (CDARS), a territory-wide database that centralizes patient information from individual local hospitals to establish comprehensive medical data, including clinical characteristics, disease diagnosis, laboratory results, and drug treatment details. Patients demographics, prior comorbidities, hospitalization characteristics before admission due to COVID-19, medication prescriptions, laboratory examinations of complete blood counts, biochemical tests, diabetes mellitus tests, cardiac function tests, c-reactive protein, and blood gas tests were extracted. The list of ICD-9 codes for medication items for each drug class, comorbidity identification, codes of intubation procedure are show below in **Supplementary Tables 1, 2 and 3**, respectively.

Outcomes and statistical analysis

The primary outcome was a composite of need for intensive care admission, intubation or all-cause mortality. Mortality data were obtained from the Hong Kong Death Registry, a population-based official government registry with the registered death records of all Hong Kong citizens linked to CDARS. The need for ICU admission and intubation were extracted directly from CDARS.

Descriptive statistics are used to summarize baseline clinical characteristics of all patients with COVID-19 and based on the occurrence of the primary outcome. Continuous variables were presented as median (95% confidence interval [CI] or interquartile range [IQR]) and categorical variables were presented as count (%). The Mann-Whitney U test was used to compare continuous variables. The $\chi 2$ test with Yates' correction was used for 2×2 contingency data. Propensity score matching approach was conducted to generate control groups for comparison with famotidine cohort and PPIs cohort, respectively, both with 1:5 ratio based on demographics, past comorbidities, and medications except for famotidine and PPIs. Univariate Cox regression was used to identify significant risk predictors for the primary outcome. Hazard ratios (HRs) with corresponding 95% CIs and p values were reported. All significance tests were two-tailed and considered significant if the P-value was less than 0.05. Statistical analyses were performed using RStudio software (Version: 1.1.456) and Python (Version: 3.6).

Supplementary Figures



Supplementary Figure 1. Flow diagram for patient identification with outcomes.

Supplementary Tables

Supplementary Table 1. Drugs prescribed for COVID-19 patients

ACEI
LISINOPRIL, PERINDOPRIL TERTBUTYLAMINE, PERINDOPRIL, RAMIPRIL, ENALAPRIL MALEATE, CAPTOPRIL, CAPTOPRIL TABLET, CAPTOPRIL, CAPTOPRIL TABLET 12.5MG--->, CAPTOPRIL, PERINDOPRIL ARGININE, PERINDOPRIL, CAPTOPRIL *FOR ORAL SOLUTION*, CAPTOPRIL, PERINDOPRIL, MALEATE, ARGININE
ARB
LOSARTAN POTASSIUM, IRBESARTAN, TELMISARTAN, CANDESARTAN CILEXETIL, CANDESARTAN, IRBESARTAN 300MG + HYDROCHLOROTHIAZ, IRBESARTAN, MICARDIS PLUS 40/12.5 (OR EQUIV), MICARDIS, MICARDIS PLUS 40/12.5 (OR EQUIV), MICARDIS, CO-DIOVAN 80/12.5 (OR EQUIV), DIOVAN, VALSARTAN, IRBESARTAN 150MG + HYDROCHLOROTHIAZ, IRBESARTAN, LOSARTAN K 50MG + HYDROCHLOROTHIAZI, LOSARTAN, LOSARTAN K 100MG + HYDROCHLOROTHIAZ, CO-DIOVAN 160/12.5 (OR EQUIV), SPARSENTAN/IRBESARTAN (CLINICAL TRI, IRBESARTAN, LOSARTAN OWN STOCK, LOSARTAN, CILEXETIL
Steroid
PREDNISOLONE, PROMETHAZINE COMPOUND, PROMETHAZINE HCL, PREDNISOLONE (SODIUM PHOSPHATE), METHYLPREDNISOLONE SODIUM SUCCINATE
Kaletra
KALETRA 100/25 (OR EQUIV), KALETRA (OR EQUIV)
RIBAVIRIN
INTERFERON BETA-1B
HYDROXYCHLOROQUINE
HYDROXYCHLOROQUINE SULPHATE
Calcium channel blockers
AMLODIPINE (BESYLATE), OLMESARTAN/NORVASC 40MG/5MG, DILTIAZEM HCL, NIFEDIPINE, VERAPAMIL HCL, FELODIPINE
Beta blockers
ATENOLOL, BISOPROLOL FUMARATE, METOPROLOL TARTRATE, METOPROLOL, CARVEDILOL, PROPRANOLOL HCL
Diuretics for heart failure
SPIRONOLACTONE, FRUSEMIDE (FUROSEMIDE), METOLAZONE
Diuretics for hypertension
AMILORIDE HCL, HYDROCHLOROTHIAZIDE, INDAPAMIDE (NATRILIX SR) SUSTAINED, INDAPAMIDE, DYAZIDE (OR EQUIV)
Nitrates
ISOSORBIDE DINITRATE, ISOSORBIDE, DINITRATE

Other Antihypertensive drugs
METHYLDOPA, DOXAZOSIN (MESYLATE) GITS, TERAZOSIN HCL
Proton pump inhibitors
Omeprazole, Lansoprazole, Dexlansoprazole, Esomeprazole, Pantoprazole, Rabeprazole, Ilaprazole

Supplementary Table 2. Codes for Comorbidities of COVID-19 Patients

Comorbidity	Codes
Respiratory	786.09, 518.81, 780.53, 137, E912, 465.9, 518.81, 518.81, 79.6, 518.81, 519.8, 780.59, 799.1, 780.57, 518.82, 480.1, 786.3, 519.8, 997.3, 165.9, 519.9, 648.91, 162.9, 162.3, 197, 162.5, 162.4, 486, 518.89, 496, 162.8, 415.1, V10.11, 518, 162.9, 11.96, 482.1, 507, 513, 11.9, 511.8, 511.1, 11.94, 516.8, 793.1, 482.4, 507, 515, 197, 11.93, 482, 482.83, 518.4, 482.3, 482.2, 415.1, 502, 518.89, 235.7, 793.1, 934.8, 516.9, 136.3, 38.49, 506, 112.4, 487, 481, 117.9, 38.2, 518, 11.95, 79.89, 518.1, 480.9, 505, 516.8, 495.9, 518.3, 11.23, 416.8, 513, 397.1, 117.3, 483, 508, 998.81, 416, 514, 861.21, 502, 934.8, 480.8, 648.93, 11.2, 492.8, 484.6, 78.5, 484.1, 516.3, 415.1, 416.9, 415, 416.9, 429.89, 415, 747.49, 745, 417, 770.7, 427.5, 416.9, 416, 416.8, 746.02, 573.8, 642.9, 416, 747.3, 747.3, 770.3, 779.8, 515, 424.3, 416, 417.8, 747.3, 747.3, 745.4, 518.81, 786.09, V12.6, 478, 748.5, 162.9, 996.84, 748.5, 748.6, V42.1, 748.5, 11.05, 162, 518, 747.42, 518.89, 748.5, 517.2
Renal	198.7, 189, 189, 585.9, V56.0, 189.1, 584.9, 189.1, 593.9, 189, 189, 189.8, 239.5, 189, 583.81, 593.9, 591, V10.52, 250.4, 591, 255.4, 590.8, 586, 585.1, 591, 189, 591, 239.7, 788, 996.39, 189.1, 588.9, 592, 996.39, 250.4, 593.2, 255.4, 572.4, 194, 255, 453.3, 198, 585.9, 996.39, 996.39, 590.1, 591, 591, 223, 591, 584.9, 585.9, 250.41, 996.39, 581.9, 227, 593.5, 583.89, 593.89, 404.93, 255.5, 788.9, 250.43, 227, 405.92, 592, 753.12, 996.39, E879.1, V42.0, 592, 580.89, 403.9, 593.9, V59.4, 585.9, 580.9, 250.41, 996.39, 585.9, 794.4, 584.8, 584.5, 255.9, 441.4, V58.49, 404.11, 593.9, 592, 585, 759.1, 753.11, E879.1, 753.15, 585.9, 274, 588.8, 403.91, 404.9, 404.91, 404.92, 403, 404.01, 779.8, 250.4, 227, 227, 227, 404.93, 996.81, 593.89, 753.8, 593.2, 592, 753, 996.81, 223, 589.1, 996.81, 582.9, 585.9, 996.81, 753.1, 753.3, E878.0, 593.9, 753.3, 753.17, 583.9, 593.9, 589, 866
Endocrine	202.8, 200.1, 200.12, 201.9, 204, 202.88, 200.18, 196, 204.01, 785.6, 200.11, 200.13, 202.8, 785.6, 202.85, 202.81, 202.8, 202.8, 196, 196.9, 202.8, 202.82, 785.6, 202.8, 202, 202.87, V10.79, 785.6, 202.84, 202.01, 196.8, 457.1, 12.1, 785.6, V10.79, 196.5, 196.2, 238.7, 196.1, 200.14, 457.2, 238.7, V10.61, 201.9, 457, 202.8, 289.3, 245.2, 238.7, 785.6, 457.9, 785.6, 202.93, 196.9, 202.97, 757, V10.71, 288.8, 204.1, 202.83, 457.1, 289.3, 785.6, V77.9, 237.4, 239.7, 198.89, 623.5, 259.9, 200.2, V10.71

Diabetes mellitus	251.2, 362.01, 362.02, 250.4, 250.82, 790.2, 790.6, 250.5, 250.5, 250.6, 357.2, 790.2, 250, 250.4, 250.6, 250.8, 250.51, 250.5, 250.8, 250.82, 250.51, 250.51, V77.1, 250.12, 251.2, 250.12, 250.5, 250.83, 251.2, 250.41, 251.1, 250.52, 250.5, 648.81, 250.43, 250.53, 250.53, 250.81, 250.22, 250.13, 250.22, 250.83, 250.41, 250.5, 250.52, 250.52, 250.82, 253.5, V18.0, 588.1
Hypertension	401.9, 401.9, 250.82, 790.6, 401.9, 401.9, 250.82, 796.2, 402.9, 250.83, 405.99, 642.93, 642.01, 642.91, 401.9, E942.6, 405.09, 403.9, 437.2, 401, 401.1, 401, 642.33, 348.2, 779.8, 365.04, 572.3, 416, 416, 405.91, 416.8, 642.3
Gastrointestinal	153.3, 154.1, 153.9, 569.89, 154, 153.1, 578.9, 560.9, 569.3, 537.89, 558.9, 562.1, 153.6, 239, 532.3, 569.89, 532.7, 535.6, 558.9, 38.42, 569.89, 8.45, 153.2, 569.49, 79.89, 532.9, V58.11, 569, 154.1, 41.4, 537.89, 152.1, 578.9, V10.05, 787.8, 197.4, 535.5, V10.06, 9, 569.83, 569.6, 153.4, 560.9, 537.3, 41.04, 569.84, 239, 569.81, 8.8, 535, 560.9, 532, V45.89, V12.72, 532.4, V10.09, 560.81, 235.2, 38.49, 8.45, 235.2, 532.9, 569.81, 537.89, 557.9, 569.41, 997.4, 14.8, 787.99, 8.46, 535.5, 569.41, 997.4, 578.9, 569.82, 537.9, 560.1, 569.82, 557.9, 211.3, 556.9, 562, 558.9, 578.9, 536.9, 8.46, 535.6, 566, V71.9, 569.49, 564.3, V44.4, 569.89, 564.8, 8.46, 569.83, 997.4, 997.4, 997.4, 562.11, 211.2, 9.1, 211.3, 8.47, 8.5, 211.3, 569.83, 532.1, 535.61, 560, 569.83, 565.1, 619.1, 152.9, 568, 566, 569.43, 152, 8.46, 562.11, 8.61, 569.83, 569.83, 569.81, 596.1, 535.5, 151.4, 151.9, 151.5, 151.8, 151.1, 456.8, 531.7, 535.4, 531.3, V15.2, 537.89, 211.1, 531.9, V10.04, 235.2, 531, 531.4, 456.8, 535.1, 151.3, 230.2, 151.6, 535, 211.1, 536.3, 535, V10.04, 535.51, 578.9, 531.1, 535.1, 456.8, 531.5, 537.84, 535.01, 530.7, 535.1, 535.2, 535.5, 537.6, 202.83, 535.1, 531.4, 558.9, 558.9, 558, 569.85, 153, 555.1, 562.1, 562.13, 562.11, 562.12, 569.83, V76.49, 560.2, 230.4, 569.3, 154
Stroke	434.11, 434.91, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.91, 436, 435, 430, 431, 432, 432.1, 432.9, 853, 852, 852.01, 852.02, 852.03, 852.04, 852.05, 852.06, 852.07, 852.08, 852.09, 852.2, 852.21, 852.22, 852.23, 852.24, 852.25, 852.26, 852.27, 852.28, 852.29, 852.4, 852.41, 852.42, 852.43, 852.44, 852.45, 852.46, 852.47, 852.48, 852.49, I64, 992, 992, 434.01, 433, 331, 851, 434, 434.1, 348.5, 747.81, 414.9, 457.9, 720, 681.1, 473.9, 290.3, 524.02, 720, 414.9, 215.3

Supplementary Table 3. Codes for Identifying Patients Needing Intubation

Procedure	Codes and Description
Intubation	Cont invasive mech vent->96 hours (96.72:0)
	Cont invasive mech vent-<96 hours (96.71:0)
	Invasive mechanical ventilation (96.70:0)
	Endotracheal intubation (96.04:0)
	Respiratory tract intubation (96.05:0)

Supplementary Table 4. Baseline clinical characteristics of patients with or without proton pump inhibitor (PPI)/famotidine use.
* for p≤ 0.05, ** for p ≤ 0.01, *** for p ≤ 0.001

Characteristics	PPIs/Famotidine use (N=908) Median (IQR);Max;N or Count(%)	No PPIs/famotidine use (N=3537) Median (IQR);Max;N or Count(%)	P value
Composite outcome	173(19.05%)	39(1.10%)	<0.0001***
Duration to outcome, days	25(15-40);206; n=908	28(18-130);234; n=3537	<0.0001***
Demographics			
Male gender	476(52.42%)	1753(49.56%)	0.3957
Age, years	62.2(51.5-71.8);98.7; n=908	39.5(26.1-56);100.6; n=3537	<0.0001***
Past comorbidities			
Cardiovascular	191(21.03%)	132(3.73%)	<0.0001***
Respiratory	896(98.67%)	3423(96.77%)	0.7325
Renal	127(13.98%)	112(3.16%)	<0.0001***
Endocrine	13(1.43%)	26(0.73%)	0.0739
Diabetes mellitus	213(23.45%)	294(8.31%)	<0.0001***
Hypertension	321(35.35%)	383(10.82%)	<0.0001***
Gastrointestinal	890(98.01%)	3401(96.15%)	0.7369
Stroke	139(15.30%)	52(1.47%)	<0.0001***
Hospitalization			
Number of hospitalizations	1(1-2);98; n=908	1(1-2);17; n=3376	0.7621
Length of hospital stay, days	17(12-26);326; n=908	12(8-17);351; n=3376	<0.0001***
Number of emergency readmissions	2(1-3);32; n=110	1(1-2);13; n=79	0.0007***

Medications			
PPIs	524(57.70%)	-	-
PPIs dosage, mg	1080(600-2430);20880; n=524	-	-
Famotidine	519(57.15%)	-	-
Famotidine dosage, mg	1040(480-2440);43520; n=519	-	-
ACEI	131(14.42%)	120(3.39%)	<0.0001***
ARB	115(12.66%)	127(3.59%)	<0.0001***
Steroid	195(21.47%)	437(12.35%)	<0.0001***
Kaletra	75(8.25%)	27(0.76%)	<0.0001***
Ribavirin	338(37.22%)	789(22.30%)	<0.0001***
Interferon beta-1B	663(73.01%)	1202(33.98%)	<0.0001***
hydroxychloroquine	28(3.08%)	64(1.80%)	0.0266*
Calcium channel blockers	325(35.79%)	430(12.15%)	<0.0001***
Beta blockers	184(20.26%)	144(4.07%)	<0.0001***
Diuretics for heart failure	132(14.53%)	61(1.72%)	<0.0001***
Diuretics for hypertension	7(0.77%)	8(0.22%)	0.0284*
Nitrates	28(3.08%)	9(0.25%)	<0.0001***
Other antihypertensives	87(9.58%)	63(1.78%)	<0.0001***
Complete blood count tests			
MCV, fL	87.7(84.2-91.2);110.6; n=670	86.5(82.6-89.7);104.5; n=2269	0.2531
Basophil, x10^9/L	0.01(0-0.02);0.19; n=820	0.01(0-0.02);0.2; n=2864	0.9721
Eosinophil, x10^9/L	0.004(0-0.06);1.25; n=848	0.042(0-0.1);2.25; n=2991	<0.0001***
Lymphocyte, x10^9/L	1.1(0.752-1.5);4.66; n=849	1.49(1.09-1.93);16.99; n=2999	<0.0001***

Monocyte, x10^9/L	0.5(0.358-0.658);3.26; n=849	0.5(0.38-0.62);2.32; n=2999	0.8753
Neutrophil, x10^9/L	3.5(2.6-4.69);27.17; n=849	3.2(2.37-4.256);15.82; n=2999	0.1231
WBC, x10^9/L	5.39(4.23-6.63);29.64; n=859	5.43(4.36-6.79);23.9; n=3059	0.3589
MCH, g/dL	29.9(28.5-31.1);36.8; n=859	29.6(28.2-30.7);35.1; n=3059	0.7827
Platelet, x10^9/L	197(158-241.75);778; n=858	224(183-279);722; n=3059	<0.0001***
RBC, x10^12/L	4.51(4.14-4.8785);6.97; n=859	4.74(4.38-5.12);7.45; n=3060	0.1123
HCT, L/L	0.39(0.36-0.42);0.52; n=749	0.41(0.38-0.43);0.53; n=2636	0.2315
Biochemical tests			
Potassium, mmol/L	3.8(3.5-4.1);5.9; n=744	3.8(3.6-4.1);5.74; n=2251	0.8762
Urate, mmol/L	0.3245(0.26-0.45);0.621; n=50	0.285(0.235-0.3633);0.635; n=77	0.0515
Albumin, g/L	38(33.1-42);144.5; n=746	41(38-44.4);146; n=2255	0.0823
Sodium, mmol/L	138(135-140.6);147.49; n=745	139(137-140.8);149.42; n=2257	0.6261
Urea, mmol/L	4.53(3.4-6.1);39.6; n=745	3.77(3.02-4.7);41.95; n=2255	<0.0001***
Protein, g/L	72.3(68.2-76.7);93.2; n=634	74.1(70.9-77.9);92.7; n=2049	0.2561
Creatinine, umol/L	74.3(61.4-91);1280; n=745	68.6(58-82);361; n=2257	<0.0001***
Alkaline phosphatase, U/L	66(55-83);932; n=740	64.25(53-80);550; n=2248	0.0877
Aspartate transaminase, U/L	30(22.1-49);1807.4; n=312	25(20.7-38);863; n=680	<0.0001***
Alanine aminotransferase, U/L	25(17-39);380; n=610	22.25(16-34);583; n=1816	0.0001**
Bilirubin, umol/L	8(6-12);235; n=739	7.6(5.4-10.4);104.2; n=2248	<0.0001***
Glucose, mmol/L	6.1(5.3-7.6);29.3; n=758	5.5(4.98-6.5);26.8; n=2187	<0.0001***
Diabetes mellitus tests			
HbA1c, g/dL	13.1(11.5-14.2);17.5; n=859	13.5(12.2-14.7);18.1; n=3060	<0.0001***

Cholesterol, mmol/L	3.7(2.5-4.6);7.6; n=297	4(2.9-5);9.7; n=366	0.005**
D-dimer, ng/mL	371.3(199.04-826.2);11200; n=226	270(154.5-476.8);6579.9; n=579	<0.0001***
High sensitive troponin-I, ng/L	5.5(2.13-11.96);3876.3; n=363	2.7405(0.86-5.31);115.3; n=868	<0.0001***
Lactate dehydrogenase, U/L	230(185-300);1116; n=730	189.95(161.2-227.1);1374; n=2426	<0.0001***
APTT, second	31.3(27.6-34.7);120; n=596	30.8(27.7-34.4);55.2; n=1457	0.4293
Prothrombin Time/INR, second	12(11.4-12.7);43.4; n=424	12(11.5-12.6);31.7; n=1031	0.6661
C-reactive protein, mg/dL	1.18(0.31-4.08);34; n=858	0.31(0.1-0.89);29.82; n=2996	<0.0001***
Blood gas tests			
HCO3/Bicarbonate, mmol/L	23.1(20.25-25.2);32.8; n=115	22.8(19.85-25);29.5; n=52	0.6745
Base excess, mmol/L	-0.7(-3-1.4);9.5; n=304	-0.2(-2.25-1.9);7.2; n=208	0.0272*
Blood pCO2, kPa	4.825(4.09-5.59);10.94; n=304	5.01(4.24-5.85);8.32; n=209	0.1842
Blood pH	7.42(7.37-7.47);7.612; n=304	7.42(7.38-7.47);7.541; n=209	0.8438
Calcium, mmol/L	1.135(1.06-1.175);1.33; n=28	1.125(1.115-1.19);1.31; n=8	0.4235

Supplementary Table 5. Baseline clinical characteristics of patients with or without proton pump inhibitor (PPI) use before and after propensity score matching (1:5)

* for p≤ 0.05, ** for p ≤ 0.01, *** for p ≤ 0.001

Characteristics	After 1:5 matching			Before matching		
	PPIs (N=524) Median (IQR);Max;N or Count(%)	No PPIs (N=2620) Median (IQR);Max;N or Count(%)	P value	PPIs (N=524) Median (IQR);Max;N or Count(%)	No PPIs (N=3921) Median (IQR);Max;N or Count(%)	P value
Demographics						
Male gender	307(58.58%)	1494(57.02%)	0.7612	307(58.58%)	1922(49.01%)	0.0228*
Age, years	65.2(57.1-73.9);98.7; n=524	62.6(54.4-70.3);100.6; n=2620	<0.0001***	65.2(57.1-73.9);98.7; n=524	41(27.1-57.6);100.6; n=3921	<0.0001***
Past comorbidities						
Cardiovascular	136(25.95%)	430(16.41%)	<0.0001***	136(25.95%)	187(4.76%)	<0.0001***
Respiratory	516(98.47%)	2581(98.51%)	0.9775	516(98.47%)	3803(96.99%)	0.8441
Renal	102(19.46%)	333(12.70%)	0.0006***	102(19.46%)	137(3.49%)	<0.0001***
Endocrine	10(1.90%)	50(1.90%)	1.0000	10(1.90%)	29(0.73%)	0.0159*
Diabetes mellitus	136(25.95%)	650(24.80%)	0.7089	136(25.95%)	371(9.46%)	<0.0001***
Hypertension	209(39.88%)	1026(39.16%)	0.8732	209(39.88%)	495(12.62%)	<0.0001***
Gastrointestinal	510(97.32%)	2551(97.36%)	0.9774	510(97.32%)	3781(96.42%)	0.9149
Stroke	90(17.17%)	319(12.17%)	0.0089**	90(17.17%)	101(2.57%)	<0.0001***
Hospitalization						
Episodes number	1(1-2);98; n=524	1(1-2);17; n=2513	0.7826	1(1-2);98; n=524	1(1-2);17; n=3760	<0.0001***

Length of hospital stay, days	19(13-29.5);326; n=524	13(10-19);134; n=2513	<0.0001***	19(13-29.5);326; n=524	12(8-17);351; n=3760	<0.0001***
Emergency readmission times	2(1-3);32; n=88	1(1-2);13; n=130	0.01*	2(1-3);32; n=88	1(1-2);13; n=101	0.0005***
Medications						
PPIs dosage, mg	1080(600-2430);20880; n=524	-	-	1080(600-2430);20880; n=524	-	-
Famotidine	135(25.76%)	615(23.47%)	0.4117	135(25.76%)	384(9.79%)	<0.0001***
Famotidine dosage, mg	680(280-1810);43520; n=135	1560(920-4000);24320; n=615	<0.0001***	680(280-1810);43520; n=135	1200(600-2520);24320; n=384	0.0006***
ACEI	91(17.36%)	376(14.35%)	0.1481	91(17.36%)	160(4.08%)	<0.0001***
ARB	75(14.31%)	367(14.00%)	0.9274	75(14.31%)	167(4.25%)	<0.0001***
Steroid	115(21.94%)	441(16.83%)	0.0245*	115(21.94%)	517(13.18%)	<0.0001***
Kaletra	71(13.54%)	69(2.63%)	<0.0001***	71(13.54%)	31(0.79%)	<0.0001***
Ribavirin	204(38.93%)	864(32.97%)	0.0766	204(38.93%)	923(23.53%)	<0.0001***
Interferon beta-1B	401(76.52%)	1925(73.47%)	0.6012	401(76.52%)	1464(37.33%)	<0.0001***
hydroxychloroquine	21(4.00%)	100(3.81%)	0.9401	21(4.00%)	71(1.81%)	0.0022**
Calcium channel blockers	217(41.41%)	1054(40.22%)	0.7774	217(41.41%)	538(13.72%)	<0.0001***
Beta blockers	119(22.70%)	474(18.09%)	0.0508	119(22.70%)	209(5.33%)	<0.0001***
Diuretics for heart failure	115(21.94%)	234(8.93%)	<0.0001***	115(21.94%)	78(1.98%)	<0.0001***

Diuretics for hypertension	7(1.33%)	35(1.33%)	1.0000	7(1.33%)	8(0.20%)	0.0002***
Nitrates	19(3.62%)	91(3.47%)	0.9701	19(3.62%)	18(0.45%)	<0.0001***
Other antihypertensives	70(13.35%)	227(8.66%)	0.0034**	70(13.35%)	80(2.04%)	<0.0001***
Complete blood count tests						
MCV, fL	87.745(84.6-91.2);110.6; n=404	87.4(83.8-91);102.1; n=2056	0.1132	87.745(84.6-91.2);110.6; n=404	86.6(82.7-89.835);104.5; n=2535	<0.0001***
Basophil, x10^9/L	0.01(0-0.02);0.13; n=464	0.01(0-0.02);0.19; n=2366	0.1429	0.01(0-0.02);0.13; n=464	0.01(0-0.02);0.2; n=3220	0.0041**
Eosinophil, x10^9/L	0.009(0-0.0445);1.25; n=486	0.01(0-0.08);0.953; n=2445	0.6216	0(0-0.0445);1.25; n=486	0.04(0-0.1);2.25; n=3353	<0.0001***
Lymphocyte, x10^9/L	1(0.7-1.43);3.2; n=486	1.2(0.88-1.6);16.99; n=2445	<0.0001***	1(0.7-1.43);3.2; n=486	1.42(1.05-1.9);16.99; n=3362	<0.0001***
Monocyte, x10^9/L	0.5(0.3605-0.68);3.26; n=486	0.5(0.39-0.68);2.1; n=2445	0.4243	0.5(0.3605-0.68);3.26; n=486	0.5(0.3795-0.62);2.32; n=3362	0.5017
Neutrophil, x10^9/L	3.805(2.74-5.0985);27.17; n=486	3.36(2.46-4.4);15.82; n=2445	<0.0001***	3.805(2.74-5.0985);27.17; n=486	3.2(2.37-4.235);15.82; n=3362	<0.0001***
WBC, x10^9/L	5.6(4.4-7.12);29.64; n=493	5.2(4.16-6.6);23.9; n=2458	0.0007***	5.6(4.4-7.12);29.64; n=493	5.4(4.3-6.7);23.9; n=3425	0.0149*
MCH, g/dL	30.1(28.7-31.2);36.8; n=493	29.9(28.4-31.1);34.7; n=2458	0.0697	30.1(28.7-31.2);36.8; n=493	29.65(28.2-30.7);36.1; n=3425	<0.0001***
Platelet, x10^9/L	194.5(151.5-240);778; n=492	200(162-246.5);670; n=2458	0.0592	194.5(151.5-240);778; n=492	220(180-276);773; n=3425	<0.0001***

RBC, x10^12/L	4.49(4.05-4.83);6.08; n=493	4.59(4.23-4.99);7.24; n=2458	<0.0001***	4.49(4.05-4.83);6.08; n=493	4.7195(4.37-5.1);7.45; n=3426	<0.0001***
HCT, L/L	0.39(0.35-0.42);0.516; n=441	0.399(0.37-0.42);0.501; n=2037	0.0002**	0.391(0.353-0.42);0.516; n=441	0.404(0.376-0.433);0.5287; n=2944	<0.0001***
Biochemical tests						
Potassium, mmol/L	3.8(3.5-4.1);5.9; n=426	3.88(3.5-4.2);5.59; n=2036	0.0512	3.8(3.5-4.1);5.9; n=426	3.8(3.6-4.1);5.74; n=2569	0.1035
Urate, mmol/L	0.32(0.25-0.47);0.62; n=38	0.31(0.23-0.4);0.64; n=119	0.5785	0.32(0.25-0.47);0.62; n=38	0.3(0.24-0.38);0.64; n=89	0.2521
Albumin, g/L	36.1(31-40.73);144.5; n=426	39(35-43.1);146; n=2038	<0.0001***	36.1(31-40.725);144.5; n=426	41(37.7-44.1);146; n=2575	<0.0001***
Sodium, mmol/L	137.7(134.53-140.6);147.49; n=427	138(135.7-140.2);147; n=2039	0.0141	137.7(134.53-140.6);147.49; n=427	139(137-140.7);149.42; n=2575	<0.0001***
Urea, mmol/L	5(3.8-7.01);39.6; n=427	4.4(3.5-5.6);25.53; n=2039	<0.0001***	5(3.8-7.01);39.6; n=427	3.8(3.04-4.75);41.95; n=2573	<0.0001***
Protein, g/L	71.7(67-76);93.2; n=354	73(69-77);92.7; n=1813	<0.0001***	71.7(67-76);93.2; n=354	74(70.7-77.9);92.7; n=2329	<0.0001***
Creatinine, umol/L	79(63-99.75);1280; n=427	75.2(64-90.4);461; n=2039	0.0033**	79(63-99.75);1280; n=427	69(58-82);461; n=2575	<0.0001***
Alkaline phosphatase, U/L	67(56-85);872; n=423	66(56-80);932; n=2010	0.1316	67(56-85);872; n=423	64.4(53-80);932; n=2565	0.0122*
Aspartate transaminase, U/L	32.8(24-53.8);1713; n=195	29(21.9-44);1807.4; n=704	0.0037**	32.8(24-53.8);1713; n=195	26(21-38);1807.4; n=797	<0.0001***

Alanine aminotransferase, U/L	29(18-42);380; n=361	26(19-40);197.2; n=1619	0.1306	29(18-42);380; n=361	22(16-33.5);583; n=2065	<0.0001***
Bilirubin, umol/L	8.7(6-12);235; n=423	8.2(6.3-12);104.2; n=2009	0.7284	8.7(6-12);235; n=423	7.6(5.4-10.7);104.2; n=2564	<0.0001***
Glucose, mmol/L	6.4(5.5-8);29.3; n=445	6(5.3-7.5);26.5; n=2091	0.0015**	6.4(5.5-8);29.3; n=445	5.5(5-6.6);26.8; n=2500	<0.0001***
Diabetes mellitus tests						
HbA1c, g/dL	13.1(11.5-14.3);17.5; n=493	13.2(11.265-14.3);17.4; n=2458	0.9348	13.1(11.5-14.3);17.5; n=493	13.5(12.2-14.6);18.1; n=3426	<0.0001***
Cholesterol, mmol/L	3.671(2.31-4.7);7.436; n=199	3.7(1.895-4.53);9.718; n=807	0.7603	3.671(2.31-4.7);7.436; n=199	3.94(2.885-4.9);9.718; n=464	0.009**
D-dimer, ng/mL	455.765(190-878.5);11200; n=138	400(190-810.51);4340; n=551	0.5681	455.765(190-878.5);11200; n=138	280(163.5-494.01);6579.87; n=667	<0.0001***
High sensitive troponin-I, ng/L	6.56(2.43-17.75);3876.3; n=226	4.9(2.55-8.48);93.6; n=760	0.0003***	6.56(2.4-17.75);3876.3; n=226	3(0.95-5.73);115.3; n=1005	<0.0001***
Lactate dehydrogenase, U/L	247(198-341);1096; n=428	214.5(182-268);1374; n=1998	<0.0001***	247(198-341);1096; n=428	191(162.9-231);1374; n=2728	<0.0001***
APTT, second	31.4(27.7-34.9);120; n=375	30.8(27.5-34.2);55.2; n=1551	0.1717	31.4(27.7-34.9);120; n=375	30.9(27.6-34.4);55.2; n=1678	0.2798
Prothrombin Time/INR, second	12.1(11.5-12.9);28.5; n=278	11.9(11.4-12.5);26.8; n=1006	0.0013**	12.1(11.5-12.9);28.5; n=278	12(11.4-12.6);43.4; n=1177	0.0172
C-reactive protein, mg/dL	1.8(0.5-6);34; n=491	0.9(0.3-2.9);34; n=2450	<0.0001***	1.77(0.479-5.975);34; n=491	0.311(0.1-0.972);33.99; n=3363	<0.0001***
Blood gas tests						

HCO3/Bicarbonate, mmol/L	23(20.7-24.9);32.8; n=98	23.6(20-24.8);29.5; n=103	0.6535	23(20.7-24.9);32.8; n=98	23.6(19.8-25.3);29.5; n=69	0.9948
Base excess, mmol/L	-0.9(-3-1.2);9.5; n=253	-0.1(-2.4-1.95);7.2; n=391	0.0028**	-0.9(-3-1.2);9.5; n=253	-0.1(-2.1-1.9);7.2; n=259	0.0021**
Blood pCO2, kPa	4.8(4.03-5.62);10.94; n=253	4.68(4.08-5.55);7.72; n=391	0.5422	4.8(4.03-5.6);10.9; n=253	4.9(4.3-5.8);8.3; n=260	0.1698
Blood pH	7.423(7.371-7.473);7.612; n=253	7.4435(7.394-7.469);7.57; n=396	0.005**	7.42(7.4-7.5);7.6; n=253	7.43(7.4-7.5);7.6; n=260	0.5672
Calcium, mmol/L	1.135(1.06-1.175);1.33; n=28	1.13(1.125-1.15);1.17; n=4	0.8194	1.14(1.06-1.18);1.33; n=28	1.13(1.12-1.19);1.31; n=8	0.4235

Supplementary Table 6. Baseline clinical characteristics of patients with or without famotidine use before and after propensity score matching (1:5)

* for p≤ 0.05, ** for p ≤ 0.01, *** for p ≤ 0.001

Characteristics	After 1:5 matching			Before matching		
	Famotidine (N=519) Median (IQR);Max;N or Count(%)	No famotidine (N=2595) Median (IQR);Max;N or Count(%)	P value	Famotidine (N=519) Median (IQR);Max;N or Count(%)	No famotidine (N=3926) Median (IQR);Max;N or Count(%)	P value
Demographics						
Male gender	242(46.62%)	1234(47.55%)	0.8508	242(46.62%)	1987(50.61%)	0.3410
Age, years	60.4(47.7-70.1);97.6; n=519	58.1(45.2-67.2);96.6; n=2595	0.0052**	60.4(47.7-70.0472);97.6; n=519	42.3(27.5-58.9);100.6; n=3926	<0.0001***
Past comorbidities						
Cardiovascular	98(18.88%)	359(13.83%)	0.014*	98(18.88%)	225(5.73%)	<0.0001***
Respiratory	512(98.65%)	2560(98.65%)	1.0000	512(98.65%)	3807(96.96%)	0.8210
Renal	57(10.98%)	242(9.32%)	0.3290	57(10.98%)	182(4.63%)	<0.0001***
Endocrine	7(1.34%)	35(1.34%)	1.0000	7(1.34%)	32(0.81%)	0.3360
Diabetes mellitus	121(23.31%)	528(20.34%)	0.2451	121(23.31%)	386(9.83%)	<0.0001***
Hypertension	171(32.94%)	799(30.78%)	0.5162	171(32.94%)	533(13.57%)	<0.0001***
Gastrointestinal	508(97.88%)	2540(97.88%)	1.0000	508(97.88%)	3783(96.35%)	0.8393
Stroke	83(15.99%)	227(8.74%)	<0.0001***	83(15.99%)	108(2.75%)	<0.0001***
Hospitalization						

Episodes number	1(1-2);17; n=519	1(1-2);25; n=2515	0.0004***	1(1-2);17; n=519	1(1-2);98; n=3765	<0.0001***
Length of hospital stay, days	17(11.5-25);178; n=519	13(9-20);199; n=2515	<0.0001***	17(11.5-25);178; n=519	12(8-18);351; n=3765	<0.0001***
Emergency readmission times	2(1-3);10; n=45	1(1-2);13; n=169	0.0502	2(1-3);10; n=45	1(1-2);32; n=144	0.0639
Medications						
PPIs	135(26.01%)	557(21.46%)	0.0824	135(26.01%)	389(9.90%)	<0.0001***
PPIs dosage, mg	1040(540-2040);20880; n=135	1280(720-2960);19320; n=557	0.0188*	1040(540-2040);20880; n=135	1120(640-2600);19320; n=389	0.2851
Famotidine dosage, mg	1040(480-2440);43520; n=519	-	-	1040(480-2440);43520; n=519	-	-
ACEI	72(13.87%)	295(11.36%)	0.1767	72(13.87%)	179(4.55%)	<0.0001***
ARB	60(11.56%)	274(10.55%)	0.5990	60(11.56%)	182(4.63%)	<0.0001***
Steroid	110(21.19%)	486(18.72%)	0.3138	110(21.19%)	522(13.29%)	<0.0001***
Kaletra	28(5.39%)	92(3.54%)	0.0739	28(5.39%)	74(1.88%)	<0.0001***
Ribavirin	185(35.64%)	858(33.06%)	0.4531	185(35.64%)	942(23.99%)	<0.0001***
Interferon beta-1B	366(70.52%)	1768(68.13%)	0.6725	366(70.52%)	1499(38.18%)	<0.0001***
hydroxychloroquine	13(2.50%)	64(2.46%)	0.9168	13(2.50%)	79(2.01%)	0.5751
Calcium channel blockers	172(33.14%)	849(32.71%)	0.9322	172(33.14%)	583(14.84%)	<0.0001***
Beta blockers	98(18.88%)	368(14.18%)	0.0238	98(18.88%)	230(5.85%)	<0.0001***
Diuretics for heart failure	51(9.82%)	218(8.40%)	0.3795	51(9.82%)	142(3.61%)	<0.0001***

Diuretics for hypertension	3(0.57%)	15(0.57%)	1.0000	3(0.57%)	12(0.30%)	0.5492
Nitrates	12(2.31%)	60(2.31%)	1.0000	12(2.31%)	25(0.63%)	0.0003***
Other antihypertensives	33(6.35%)	146(5.62%)	0.6077	33(6.35%)	117(2.98%)	0.0002***
Complete blood count tests						
MCV, fL	87.4(83.5-91.3);105.4; n=360	87.5(84.3-90.9);110.6; n=1920	0.4499	87.4(83.5-91.3);105.4; n=360	86.7(83-89.9);110.6; n=2579	0.0216*
Basophil, x10^9/L	0.009(0-0.02);0.19; n=469	0.01(0-0.02);0.13; n=2308	0.0411*	0.009(0-0.02);0.19; n=469	0.01(0-0.02);0.2; n=3215	<0.0001***
Eosinophil, x10^9/L	0.01(0-0.07);0.8; n=482	0.01(0-0.08);1.16; n=2398	0.7821	0.01(0-0.0655);0.8; n=482	0.04(0-0.1);2.25; n=3357	<0.0001***
Lymphocyte, x10^9/L	1.13(0.8-1.55);4.66; n=483	1.22(0.9-1.62);14.8; n=2398	0.0005***	1.13(0.8-1.55);4.66; n=483	1.41(1.016-1.9);16.99; n=3365	<0.0001***
Monocyte, x10^9/L	0.48(0.33-0.64);1.45; n=483	0.5(0.38-0.68);1.7; n=2398	0.0218*	0.48(0.33-0.64);1.45; n=483	0.5(0.38-0.63);3.26; n=3365	0.1153
Neutrophil, x10^9/L	3.4(2.4-4.32);15.9; n=483	3.3(2.4-4.5);17.97; n=2398	0.4735	3.4(2.4-4.32);15.9; n=483	3.27(2.4-4.38);27.17; n=3365	0.7461
WBC, x10^9/L	5.16(4.029-6.26);17.9; n=489	5.32(4.3-6.7);23.9; n=2421	0.0145*	5.16(4.029-6.26);17.9; n=489	5.47(4.38-6.8);29.64; n=3429	0.0002***
MCH, g/dL	29.8(28.1-31);36.8; n=489	29.9(28.6-31);35.9; n=2421	0.1682	29.8(28.1-31);36.8; n=489	29.7(28.3-30.7);35.9; n=3429	0.2134
Platelet, x10^9/L	199(160-241.75);773; n=488	206(166-257);778; n=2420	0.0128*	199(160-241.75);773; n=488	220(179-276);778; n=3429	<0.0001***

RBC, x10^12/L	4.51(4.17-4.89);6.97; n=489	4.61(4.27-4.96);7.3; n=2421	0.0015**	4.51(4.17-4.89);6.97; n=489	4.7(4.4-5.1);7.45; n=3430	<0.0001***
HCT, L/L	0.39(0.36-0.42);0.49; n=420	0.4(0.37-0.43);0.51; n=2012	0.1521	0.39(0.36-0.42);0.49; n=420	0.40(0.38-0.43);0.53; n=2965	<0.0001***
Biochemical tests						
Potassium, mmol/L	3.8(3.5-4.1);5.67; n=432	3.8(3.5-4.1);5.9; n=1937	0.8758	3.8(3.5-4.1);5.67; n=432	3.8(3.59-4.1);5.9; n=2563	0.4478
Urate, mmol/L	0.37(0.31-0.45);0.621; n=25	0.31(0.24-0.39);0.635; n=120	0.0355*	0.37(0.3056-0.45);0.621; n=25	0.2875(0.2375-0.3685);0.635; n=102	0.0038**
Albumin, g/L	39(35-42.3);141.36; n=434	39(34.75-43.6);146; n=1936	0.0462*	39(35-42.25);141.36; n=434	41(37-44.1);146; n=2567	<0.0001***
Sodium, mmol/L	138(135.1-140.35);147.49; n=432	138.6(136-141);147; n=1941	0.0366*	138(135.1-140.35);147.49; n=432	139(137-140.7);149.42; n=2570	<0.0001***
Urea, mmol/L	4.3(3.22-5.6);36.2; n=432	4.3(3.3-5.5);39.6; n=1940	0.8508	4.3(3.22-5.6);36.2; n=432	3.9(3.1-4.845);41.95; n=2568	<0.0001***
Protein, g/L	72.9(68.8-77.3);93.2; n=373	73.84(70-77);92.24; n=1690	0.0768	72.9(68.8-77.3);93.2; n=373	74(70.4-77.5);92.7; n=2310	0.0007***
Creatinine, umol/L	71.05(61-86.5);1280; n=432	73(59-87.7);530; n=1941	0.9300	71.05(61-86.5);1280; n=432	69.75(58-84);1216.2; n=2570	0.0058**
Alkaline phosphatase, U/L	65(54-80);932; n=430	65(54.05-78);282; n=1923	0.5686	65(54-80);932; n=430	65(53.95-80);550; n=2558	0.9157
Aspartate transaminase, U/L	29(22-49);1807.4; n=173	28(21-41);427.6; n=724	0.1007	29(22-49);1807.4; n=173	26.1(21-39);863; n=819	0.0056**

Alanine aminotransferase, U/L	23(16-36.3);380; n=348	25(18-38);275; n=1553	0.0113*	23(16-36.3);380; n=348	23(16-35);583; n=2078	0.8508
Bilirubin, umol/L	7.8(5.8-11.8);56.5; n=429	8(6-11.1);179.7; n=1923	0.7129	7.8(5.8-11.8);56.5; n=429	7.8(5.5-10.8);235; n=2558	0.1297
Glucose, mmol/L	5.9(5.3-7.4);26.5; n=425	6(5.3-7.4);29.29; n=2026	0.7784	5.86(5.26-7.4);26.5; n=425	5.58(5-6.7);29.29; n=2520	<0.0001***
Diabetes mellitus tests						
HbA1c, g/dL	13(11.4-14.1);17.1; n=489	13.3(11.6-14.3);17.7; n=2421	0.0228*	13(11.4-14.1);17.1; n=489	13.5(12.2-14.665);18.07; n=3430	<0.0001***
Cholesterol, mmol/L	3.8(2.8-4.6);7.6; n=159	3.7(1.9-4.6);8.7; n=638	0.4579	3.8(2.8-4.6);7.559; n=159	3.9(2.6-4.9);9.718; n=504	0.4820
D-dimer, ng/mL	369(220.5-743.6);6544.8; n=124	360(185.4-699.8);11200; n=559	0.2653	369(220.5-743.6);6544.8; n=124	280(152.7-540.01);11200; n=681	0.0006***
High sensitive troponin-I, ng/L	4.8(2-10);400.2; n=200	4.5(1.9-10);3876.3; n=790	0.4090	4.772(2-10);400.2; n=200	3(1-6.29);3876.3; n=1031	<0.0001***
Lactate dehydrogenase, U/L	219(180.5-281.5);1116; n=411	210(174-266);874; n=1994	0.0063**	219(180.5-281.5);1116; n=411	194(164-236);1374; n=2745	<0.0001***
APTT, second	31.6(27.9-34.8);66.4; n=319	30.2(27.1-33.6);120; n=1480	0.0005***	31.6(27.9-34.8);66.4; n=319	30.8(27.6-34.4);120; n=1734	0.1432
Prothrombin Time/INR, second	12(11.35-12.55);43.4; n=220	11.9(11.4-12.5);31.7; n=968	0.9726	12(11.35-12.55);43.4; n=220	12(11.5-12.6);31.7; n=1235	0.2356
C-reactive protein, mg/dL	0.81(0.26-2.864);34; n=492	0.61(0.24-2.2);28.4; n=2400	0.0608	0.81(0.26-2.864);34; n=492	0.314(0.11-1.18);29.818; n=3362	<0.0001***

Blood gas tests						
HCO3/Bicarbonate, mmol/L	23.8(19.9-26);30.7; n=45	23(21.3-24.8);31; n=151	0.4424	23.8(19.9-26);30.7; n=45	22.65(20.25-24.65);32.8; n=122	0.2187
Base excess, mmol/L	-0.4(-2.7-1.65);6.1; n=135	-0.8(-2.2-1.9);9.5; n=413	0.9523	-0.4(-2.7-1.65);6.1; n=135	-0.5(-2.5-1.5);9.5; n=377	0.6725
Blood pCO2, kPa	4.8(4.1-5.7);10.9; n=135	4.8(4.1-5.5);10.7; n=414	0.9430	4.78(4.07-5.675);10.94; n=135	4.895(4.15-5.73);10.65; n=378	0.6196
Blood pH	7.4(7.4-7.5);7.6; n=135	7.4(7.39-7.5);7.6; n=414	0.4179	7.42(7.38-7.5);7.6; n=135	7.42(7.38-7.47);7.6; n=378	0.8737
Calcium, mmol/L	1.1(0.99-1.2);1.2; n=8	1.17(1.1-1.19);1.3; n=32	0.0484*	1.095(0.99-1.15);1.19; n=8	1.135(1.1-1.185);1.33; n=28	0.1227

Supplementary Table 7. Composite risk of meeting the primary outcome among hospitalized Covid-19 patients after propensity score matching (1:5).

* for p≤ 0.05, ** for p ≤ 0.01, *** for p ≤ 0.001

Characteristics	Famotidine vs Control HR [95% CI]	P value	PPIs vs Control HR [95% CI]	P value
PPIs/Control	-	-	6.32[5.02, 7.95]	<0.0001***
PPIs dosage, mg	-	-	1.00[1.00, 1.00]	<0.0001***
Famotidine/Control	1.98[1.47, 2.66]	<0.0001***	-	-
Famotidine dosage, mg	1.00[1.00, 1.00]	0.009**	-	-
Demographics				
Male gender	1.69[1.33, 2.14]	<0.0001***	2.47[1.83, 3.35]	<0.0001***
Age, years	1.05[1.05, 1.06]	<0.0001***	1.06[1.05, 1.07]	<0.0001***
Past comorbidities				
Cardiovascular	1.91[1.50, 2.42]	<0.0001***	2.23[1.63, 3.04]	<0.0001***
Respiratory	3.34[1.23, 9.09]	0.0183*	2.46[0.60, 10.13]	0.214
Renal	2.89[2.28, 3.66]	<0.0001***	4.06[2.97, 5.54]	<0.0001***
Endocrine	1.25[0.59, 2.64]	0.563	2.14[0.88, 5.21]	0.0927.
Diabetes mellitus	1.73[1.38, 2.18]	<0.0001***	1.95[1.44, 2.64]	<0.0001***
Hypertension	2.13[1.70, 2.65]	<0.0001***	2.42[1.83, 3.22]	<0.0001***
Gastrointestinal	2.05[1.07, 3.93]	0.0304*	1.93[0.70, 5.35]	0.204
Stroke	2.14[1.66, 2.76]	<0.0001***	2.26[1.61, 3.19]	<0.0001***
Hospitalizations				
Episodes number	1.04[1.02, 1.05]	<0.0001***	1.18[1.13, 1.23]	<0.0001***

Length of hospital stay, days	1.01[1.01, 1.02]	<0.0001***	1.02[1.02, 1.03]	<0.0001***
Emergency readmission times	1.06[1.00, 1.13]	0.070	1.11[0.99, 1.25]	0.076
Medications				
ACEI	2.55[2.01, 3.23]	<0.0001***	2.98[2.18, 4.09]	<0.0001***
ARB	0.68[0.48, 0.97]	0.0349*	1.08[0.70, 1.65]	0.738
Steroid	0.79[0.57, 1.08]	0.135	0.51[0.32, 0.80]	0.0032**
Kaletra	16.44[12.85, 21.04]	<0.0001***	23.15[17.17, 31.22]	<0.0001***
Ribavirin	1.05[0.82, 1.33]	0.717	0.84[0.62, 1.14]	0.266
Interferon beta-1B	3.21[2.25, 4.57]	<0.0001***	3.42[2.21, 5.27]	<0.0001***
Hydroxychloroquine	1.57[1.00, 2.44]	0.049*	3.80[2.33, 6.19]	<0.0001***
Calcium channel blockers	1.92[1.54, 2.39]	<0.0001***	2.39[1.80, 3.18]	<0.0001***
Beta blockers	1.61[1.26, 2.07]	0.0002***	1.76[1.27, 2.44]	0.0008***
Diuretics for heart failure	7.20[5.77, 8.98]	<0.0001***	11.03[8.29, 14.67]	<0.0001***
Diuretics for hypertension	2.13[1.13, 3.99]	0.019*	10.27[4.82, 21.88]	<0.0001***
Nitrates	0.49[0.22, 1.11]	0.0876.	0.64[0.21, 2.01]	0.446
Other antihypertensives	1.49[1.10, 2.02]	0.0109*	2.55[1.71, 3.80]	<0.0001***
Complete blood count tests				
MCV, fL	1.02[1.00, 1.03]	0.0663.	1.03[1.01, 1.06]	0.0077**
Basophil, x10^9/L	1.97[0.01, 405.50]	0.803	1341[3.96, 453873.00]	0.0154*
Eosinophil, x10^9/L	0.07[0.01, 0.43]	0.0038**	0.02[0.00, 0.24]	0.0021**
Lymphocyte, x10^9/L	0.33[0.25, 0.42]	<0.0001***	0.26[0.19, 0.36]	<0.0001***
Monocyte, x10^9/L	2.35[1.65, 3.36]	<0.0001***	2.14[1.21, 3.79]	0.0094**
Neutrophil, x10^9/L	1.24[1.21, 1.27]	<0.0001***	1.28[1.24, 1.32]	<0.0001***

WBC, x10^9/L	1.17[1.14, 1.20]	<0.0001***	1.18[1.15, 1.22]	<0.0001***
MCH, g/dL	1.01[0.97, 1.05]	0.562	1.05[0.99, 1.11]	0.095
Platelet, x10^9/L	1.00[1.00, 1.00]	0.0009***	1.00[0.99, 1.00]	0.0004***
RBC, x10^12/L	0.58[0.49, 0.69]	<0.0001***	0.57[0.45, 0.71]	<0.0001***
HCT, L/L	0.01[0.00, 0.06]	<0.0001***	0.00[0.00, 0.09]	0.0007***
Biochemical tests				
Potassium, mmol/L	1.22[0.95, 1.56]	0.124	1.57[1.12, 2.19]	0.0086**
Urate, mmol/L	88.32[4.95, 1575]	0.0023**	0.92[0.03, 29.11]	0.964
Albumin, g/L	0.99[0.98, 1.00]	0.026*	0.99[0.98, 1.00]	0.0845.
Sodium, mmol/L	0.98[0.95, 1.01]	0.212	0.93[0.90, 0.97]	0.0004***
Urea, mmol/L	1.11[1.10, 1.13]	<0.0001***	1.15[1.12, 1.17]	<0.0001***
Protein, g/L	0.93[0.91, 0.95]	<0.0001***	0.93[0.90, 0.95]	<0.0001***
Creatinine, umol/L	1.00[1.00, 1.00]	<0.0001***	1.00[1.00, 1.01]	<0.0001***
Alkaline phosphatase, U/L	1.00[1.00, 1.01]	<0.0001***	1.00[1.00, 1.01]	<0.0001***
Aspartate transaminase, U/L	1.00[1.00, 1.00]	<0.0001***	1.00[1.00, 1.00]	<0.0001***
Alanine aminotransferase, U/L	1.01[1.00, 1.01]	<0.0001***	1.01[1.01, 1.01]	<0.0001***
Bilirubin, umol/L	1.02[1.01, 1.02]	<0.0001***	1.03[1.02, 1.03]	<0.0001***
Glucose, mmol/L	1.15[1.12, 1.18]	<0.0001***	1.15[1.11, 1.19]	<0.0001***
Diabetes mellitus tests				
HbA1c, g/dL	0.93[0.91, 0.95]	<0.0001***	0.95[0.93, 0.98]	0.0003***
Cholesterol, mmol/L	1.02[0.92, 1.13]	0.692	0.98[0.86, 1.12]	0.743
D-dimer, ng/mL	1.00[1.00, 1.00]	<0.0001***	1.00[1.00, 1.00]	<0.0001***
High sensitive troponin-I, ng/L	1.001[1.0, 1.01]	0.205	1.00[1.00, 1.00]	<0.0001***

Lactate dehydrogenase, U/L	1.00[1.00, 1.00]	<0.0001***	1.006[1.005, 1.006]	<0.0001***
APTT, second	1.04[1.03, 1.05]	<0.0001***	1.04[1.03, 1.05]	<0.0001***
Prothrombin Time/INR, second	1.11[1.06, 1.17]	<0.0001***	1.06[1.01, 1.11]	0.0129*
C-reactive protein, mg/dL	1.10[1.09, 1.12]	<0.0001***	1.12[1.11, 1.14]	<0.0001***
Blood gas tests				
HCO3/Bicarbonate, mmol/L	0.94[0.88, 1.00]	0.0504	0.92[0.86, 0.99]	0.0215*
Base excess, mmol/L	0.88[0.85, 0.91]	<0.0001***	0.92[0.88, 0.96]	0.0003***
Blood pCO2, kPa	0.87[0.77, 0.98]	0.0179*	0.92[0.81, 1.05]	0.213
Blood pH	0.04[0.01, 0.21]	0.0002***	0.28[0.03, 2.34]	0.24
Calcium, mmol/L	0.86[0.01, 91.97]	0.950	4.61[0.02, 860.40]	0.567

Supplementary Table 8. Baseline clinical characteristics of patients with or without proton pump inhibitor (PPI) use before and after propensity score matching (1:1)

* for p≤ 0.05, ** for p ≤ 0.01, *** for p ≤ 0.001

Characteristics	After 1:1 matching			Before matching		
	PPIs (N=524) Median (IQR);Max;N or Count(%)	No PPIs (N=524) Median (IQR);Max;N or Count(%)	P value	PPIs (N=524) Median (IQR);Max;N or Count(%)	No PPIs (N=3921) Median (IQR);Max;N or Count(%)	P value
Demographics						
Male gender	307(58.58%)	298(56.87%)	0.8101	307(58.58%)	1922(49.01%)	0.0228*
Age, years	65.2(57.1-73.9);98.7; n=524	63.1(54.6-71.3);100.6; n=524	0.0067**	65.2(57.1-73.9);98.7; n=524	41(27.1-57.6);100.6; n=3921	<0.0001***
Past comorbidities						
Cardiovascular	136(25.95%)	96(18.32%)	0.0212*	136(25.95%)	187(4.76%)	<0.0001***
Respiratory	516(98.47%)	516(98.47%)	1.0000	516(98.47%)	3803(96.99%)	0.8441
Renal	102(19.46%)	80(15.26%)	0.1541	102(19.46%)	137(3.49%)	<0.0001***
Endocrine	10(1.90%)	10(1.90%)	1.0000	10(1.90%)	29(0.73%)	0.0159*
Diabetes mellitus	136(25.95%)	124(23.66%)	0.5506	136(25.95%)	371(9.46%)	<0.0001***
Hypertension	209(39.88%)	212(40.45%)	0.9475	209(39.88%)	495(12.62%)	<0.0001***
Gastrointestinal	510(97.32%)	510(97.32%)	1.0000	510(97.32%)	3781(96.42%)	0.9149
Stroke	90(17.17%)	69(13.16%)	0.1424	90(17.17%)	101(2.57%)	<0.0001***
Hospitalization						
Episodes number	1(1-2);98; n=524	1(1-2);6; n=506	<0.0001***	1(1-2);98; n=524	1(1-2);17; n=3760	<0.0001***

Length of hospital stay, days	19(13-29.5);326; n=524	13(10-19);76; n=506	<0.0001***	19(13-29.5);326; n=524	12(8-17);351; n=3760	<0.0001***
Emergency readmission times	2(1-3);32; n=88	1(1-2);3; n=38	0.1583	2(1-3);32; n=88	1(1-2);13; n=101	0.0005***
Medications						
PPIs dosage, mg	2000(720-3960);20880; n=524	-	-	1080(600-2430);20880; n=524	-	-
Famotidine	135(25.76%)	122(23.28%)	0.5111	135(25.76%)	384(9.79%)	<0.0001***
Famotidine dosage, mg	2000(480-3580);43520; n=135	2120(1200-3680);17200; n=122	0.0942	680(280-1810);43520; n=135	1200(600-2520);24320; n=384	0.0006***
ACEI	91(17.36%)	85(16.22%)	0.7361	91(17.36%)	160(4.08%)	<0.0001***
ARB	75(14.31%)	75(14.31%)	1.0000	75(14.31%)	167(4.25%)	<0.0001***
Steroid	115(21.94%)	90(17.17%)	0.1283	115(21.94%)	517(13.18%)	<0.0001***
Kaletra	71(13.54%)	30(5.72%)	0.0001***	71(13.54%)	31(0.79%)	<0.0001***
Ribavirin	204(38.93%)	179(34.16%)	0.3013	204(38.93%)	923(23.53%)	<0.0001***
Interferon beta-1B	401(76.52%)	394(75.19%)	0.8885	401(76.52%)	1464(37.33%)	<0.0001***
hydroxychloroquine	21(4.00%)	20(3.81%)	0.9952	21(4.00%)	71(1.81%)	0.0022**
Calcium channel blockers	217(41.41%)	212(40.45%)	0.8839	217(41.41%)	538(13.72%)	<0.0001***
Beta blockers	119(22.70%)	98(18.70%)	0.2213	119(22.70%)	209(5.33%)	<0.0001***
Diuretics for heart failure	115(21.94%)	64(12.21%)	0.0006***	115(21.94%)	78(1.98%)	<0.0001***

Diuretics for hypertension	7(1.33%)	7(1.33%)	1.0000	7(1.33%)	8(0.20%)	0.0002***
Nitrates	19(3.62%)	19(3.62%)	1.0000	19(3.62%)	18(0.45%)	<0.0001***
Other antihypertensives	70(13.35%)	54(10.30%)	0.2063	70(13.35%)	80(2.04%)	<0.0001***
Complete blood count tests						
MCV, fL	87.745(84.6-91.2);110.6; n=404	87.3(83.7-90.9);102.1; n=422	0.1897	87.745(84.6-91.2);110.6; n=404	86.6(82.7-89.835);104.5; n=2535	<0.0001***
Basophil, x10^9/L	0.01(0-0.02);0.13; n=464	0.01(0-0.01);0.1; n=479	0.0549	0.01(0-0.02);0.13; n=464	0.01(0-0.02);0.2; n=3220	0.0041**
Eosinophil, x10^9/L	0.001(0-0.05);1.25; n=486	0.01(0-0.08);0.8; n=499	0.0046**	0(0-0.0445);1.25; n=486	0.04(0-0.1);2.25; n=3353	<0.0001***
Lymphocyte, x10^9/L	1(0.7-1.4);3.2; n=486	1.2(0.9-1.6);13.7; n=499	<0.0001***	1(0.7-1.43);3.2; n=486	1.42(1.05-1.9);16.99; n=3362	<0.0001***
Monocyte, x10^9/L	0.5(0.4-0.7);3.3; n=486	0.5(0.4-0.6515);2.1; n=499	0.2388	0.5(0.3605-0.68);3.26; n=486	0.5(0.3795-0.62);2.32; n=3362	0.5017
Neutrophil, x10^9/L	3.8(2.7-5.1);27.2; n=486	3.5(2.5-4.5);13.4; n=499	0.0015**	3.805(2.74-5.0985);27.17; n=486	3.2(2.37-4.235);15.82; n=3362	<0.0001***
WBC, x10^9/L	5.6(4.4-7.12);29.64; n=493	5.4(4.3-7.1);23.9; n=503	0.2212	5.6(4.4-7.12);29.64; n=493	5.4(4.3-6.7);23.9; n=3425	0.0149*
MCH, g/dL	30.1(28.7-31.2);36.8; n=493	29.9(28.3-31.1);34.7; n=503	0.1515	30.1(28.7-31.2);36.8; n=493	29.65(28.2-30.7);36.1; n=3425	<0.0001***
Platelet, x10^9/L	194.5(151.5-240);778; n=492	200(159.5-243);593; n=503	0.2793	194.5(151.5-240);778; n=492	220(180-276);773; n=3425	<0.0001***

RBC, x10^12/L	4.49(4.05-4.83);6.08; n=493	4.59(4.23-5.03);6.79; n=503	<0.0001***	4.49(4.05-4.83);6.08; n=493	4.7195(4.37-5.1);7.45; n=3426	<0.0001***
HCT, L/L	0.39(0.35-0.42);0.516; n=441	0.4(0.372-0.423);0.5; n=419	0.0007***	0.391(0.353-0.42);0.516; n=441	0.404(0.376-0.433);0.5287; n=2944	<0.0001***
Biochemical tests						
Potassium, mmol/L	3.8(3.5-4.1);5.9; n=426	3.9(3.5-4.18);5.1; n=438	0.0641	3.8(3.5-4.1);5.9; n=426	3.8(3.6-4.1);5.74; n=2569	0.1035
Urate, mmol/L	0.32(0.25-0.47);0.62; n=38	0.37(0.24-0.41);0.62; n=23	0.6180	0.32(0.25-0.47);0.62; n=38	0.3(0.24-0.38);0.64; n=89	0.2521
Albumin, g/L	36.1(31-40.73);144.5; n=426	39(35-43.15);146; n=436	<0.0001***	36.1(31-40.725);144.5; n=426	41(37.7-44.1);146; n=2575	<0.0001***
Sodium, mmol/L	137.7(134.5-140.6);147.5; n=427	138.13(136-141);146; n=438	0.0012**	137.7(134.53-140.6);147.49; n=427	139(137-140.7);149.42; n=2575	<0.0001***
Urea, mmol/L	5(3.8-7.01);39.6; n=427	4.7(3.6-5.8);25.53; n=438	0.0003***	5(3.8-7.01);39.6; n=427	3.8(3.04-4.75);41.95; n=2573	<0.0001***
Protein, g/L	71.7(67-76);93.2; n=354	72.8(68.9-76.5);90.1; n=390	0.0074**	71.7(67-76);93.2; n=354	74(70.7-77.9);92.7; n=2329	<0.0001***
Creatinine, umol/L	79(63-99.8);1280; n=427	75.1(62-91);361; n=438	0.0228*	79(63-99.75);1280; n=427	69(58-82);461; n=2575	<0.0001***
Alkaline phosphatase, U/L	67(56-85);872; n=423	68.4(57.1-80);932; n=429	0.7464	67(56-85);872; n=423	64.4(53-80);932; n=2565	0.0122*
Aspartate transaminase, U/L	32.8(24-53.8);1713; n=195	30(22-45);1807.4; n=142	0.1366	32.8(24-53.8);1713; n=195	26(21-38);1807.4; n=797	<0.0001***

Alanine aminotransferase, U/L	29(18-42);380; n=361	25(17.1-37.5);130; n=350	0.0381*	29(18-42);380; n=361	22(16-33.5);583; n=2065	<0.0001***
Bilirubin, umol/L	8.7(6-12);235; n=423	8(6.4-11.1);36.8; n=429	0.3679	8.7(6-12);235; n=423	7.6(5.4-10.7);104.2; n=2564	<0.0001***
Glucose, mmol/L	6.4(5.5-8);29.29; n=445	5.9(5.3-7.4);19.28; n=424	0.0013**	6.4(5.5-8);29.3; n=445	5.5(5-6.6);26.8; n=2500	<0.0001***
Diabetes mellitus tests						
HbA1c, g/dL	13.1(11.5-14.3);17.5; n=493	13.3(11.2-14.4);17.2; n=503	0.8845	13.1(11.5-14.3);17.5; n=493	13.5(12.2-14.6);18.1; n=3426	<0.0001***
Cholesterol, mmol/L	3.7(2.3-4.7);7.436; n=199	3.8(2-4.4);7.6; n=177	0.5051	3.671(2.31-4.7);7.436; n=199	3.94(2.885-4.9);9.718; n=464	0.009**
D-dimer, ng/mL	455.8(190-878.5);11200; n=138	472.3(230.5-794.6);4340; n=122	0.8792	455.765(190-878.5);11200; n=138	280(163.5-494.01);6579.87; n=667	<0.0001***
High sensitive troponin-I, ng/L	6.6(2.4-17.8);3876.3; n=226	5.4(2.3-8.7);93.6; n=164	0.0068**	6.56(2.4-17.75);3876.3; n=226	3(0.95-5.73);115.3; n=1005	<0.0001***
Lactate dehydrogenase, U/L	247(198-341);1096; n=428	215(186-268);1116; n=421	<0.0001***	247(198-341);1096; n=428	191(162.9-231);1374; n=2728	<0.0001***
APTT, second	31.4(27.7-34.9);120; n=375	31.5(28.4-34.6);55.2; n=314	0.8648	31.4(27.7-34.9);120; n=375	30.9(27.6-34.4);55.2; n=1678	0.2798
Prothrombin Time/INR, second	12.1(11.5-12.9);28.5; n=278	12(11.5-12.5);26.8; n=206	0.0858	12.1(11.5-12.9);28.5; n=278	12(11.4-12.6);43.4; n=1177	0.0172
C-reactive protein, mg/dL	1.8(0.5-6.0);34; n=491	0.9(0.3-3.2);28.1; n=500	<0.0001***	1.77(0.479-5.975);34; n=491	0.311(0.1-0.972);33.99; n=3363	<0.0001***
Blood gas tests						

HCO3/Bicarbonate, mmol/L	23(20.7-24.9);32.8; n=98	23.6(18.45-25.3);29.5; n=26	0.5172	23(20.7-24.9);32.8; n=98	23.6(19.8-25.3);29.5; n=69	0.9948
Base excess, mmol/L	-0.9(-3-1.2);9.5; n=253	0(-2.35-2.2);6.1; n=87	0.0273*	-0.9(-3-1.2);9.5; n=253	-0.1(-2.1-1.9);7.2; n=259	0.0021**
Blood pCO2, kPa	4.8(4.03-5.62);10.94; n=253	4.77(4.24-5.76);7.72; n=87	0.6467	4.8(4.03-5.6);10.9; n=253	4.9(4.3-5.8);8.3; n=260	0.1698
Blood pH	7.42(7.37-7.47);7.61; n=253	7.433(7.38-7.46);7.54; n=88	0.4239	7.42(7.4-7.5);7.6; n=253	7.43(7.4-7.5);7.6; n=260	0.5672
Calcium, mmol/L	1.13(1.06-1.17);1.33; n=28	-	-	1.14(1.06-1.18);1.33; n=28	1.13(1.12-1.19);1.31; n=8	0.4235

Supplementary Table 9. Baseline clinical characteristics of patients with or without famotidine use before and after propensity score matching (1:1)

* for p≤ 0.05, ** for p ≤ 0.01, *** for p ≤ 0.001

Characteristics	After 1:1 matching			Before matching		
	Famotidine (N=519) Median (IQR);Max;N or Count(%)	No famotidine (N=519) Median (IQR);Max;N or Count(%)	P value	Famotidine (N=519) Median (IQR);Max;N or Count(%)	No famotidine (N=3926) Median (IQR);Max;N or Count(%)	P value
Demographics						
Male gender	242(46.62%)	250(48.16%)	0.8085	242(46.62%)	1987(50.61%)	0.3410
Age, years	60.4(47.7-70.1);97.6; n=519	58.0 (46.8-68.1);96.6; n=519	0.0501	60.4(47.7-70.0472);97.6; n=519	42.3(27.5-58.9);100.6; n=3926	<0.0001***
Past comorbidities						
Cardiovascular	98(18.88%)	78(15.02%)	0.1893	98(18.88%)	225(5.73%)	<0.0001***
Respiratory	512(98.65%)	512(98.65%)	1.0000	512(98.65%)	3807(96.96%)	0.8210
Renal	57(10.98%)	53(10.21%)	0.7930	57(10.98%)	182(4.63%)	<0.0001***
Endocrine	7(1.34%)	7(1.34%)	1.0000	7(1.34%)	32(0.81%)	0.3360
Diabetes mellitus	121(23.31%)	107(20.61%)	0.4434	121(23.31%)	386(9.83%)	<0.0001***
Hypertension	171(32.94%)	166(31.98%)	0.8619	171(32.94%)	533(13.57%)	<0.0001***
Gastrointestinal	508(97.88%)	508(97.88%)	1.0000	508(97.88%)	3783(96.35%)	0.8393
Stroke	83(15.99%)	55(10.59%)	0.0316*	83(15.99%)	108(2.75%)	<0.0001***
Hospitalization						
Episodes number	1(1-2);17; n=519	1(1-2);25; n=505	0.0026**	1(1-2);17; n=519	1(1-2);98; n=3765	<0.0001***

Length of hospital stay, days	17(11.5-25);178; n=519	13(9-20);120; n=505	<0.0001***	17(11.5-25);178; n=519	12(8-18);351; n=3765	<0.0001***
Emergency readmission times	2(1-3);10; n=45	1(1-1);13; n=34	0.01318	2(1-3);10; n=45	1(1-2);32; n=144	0.0639
Medications						
PPIs	135(26.01%)	124(23.89%)	0.5878	135(26.01%)	389(9.90%)	<0.0001***
PPIs dosage, mg	2440(800-4120);20880; n=135	2960(1100-4040);10000; n=124	0.6272	1040(540-2040);20880; n=135	1120(640-2600);19320; n=389	0.2851
Famotidine dosage, mg	1280(520-3320);43520; n=519	-	-	1040(480-2440);43520; n=519	-	-
ACEI	72(13.87%)	62(11.94%)	0.4708	72(13.87%)	179(4.55%)	<0.0001***
ARB	60(11.56%)	57(10.98%)	0.8686	60(11.56%)	182(4.63%)	<0.0001***
Steroid	110(21.19%)	100(19.26%)	0.5798	110(21.19%)	522(13.29%)	<0.0001***
Kaletra	28(5.39%)	22(4.23%)	0.4940	28(5.39%)	74(1.88%)	<0.0001***
Ribavirin	185(35.64%)	178(34.29%)	0.7985	185(35.64%)	942(23.99%)	<0.0001***
Interferon beta-1B	366(70.52%)	357(68.78%)	0.8348	366(70.52%)	1499(38.18%)	<0.0001***
hydroxychloroquine	13(2.50%)	13(2.50%)	1.0000	13(2.50%)	79(2.01%)	0.5751
Calcium channel blockers	172(33.14%)	178(34.29%)	0.8293	172(33.14%)	583(14.84%)	<0.0001***
Beta blockers	98(18.88%)	83(15.99%)	0.3429	98(18.88%)	230(5.85%)	<0.0001***
Diuretics for heart failure	51(9.82%)	46(8.86%)	0.7044	51(9.82%)	142(3.61%)	<0.0001***

Diuretics for hypertension	3(0.57%)	3(0.57%)	1.0000	3(0.57%)	12(0.30%)	0.5492
Nitrates	12(2.31%)	12(2.31%)	1.0000	12(2.31%)	25(0.63%)	0.0003***
Other antihypertensives	33(6.35%)	32(6.16%)	0.9940	33(6.35%)	117(2.98%)	0.0002***
Complete blood count tests						
MCV, fL	87.4(83.5-91.3);105.4; n=360	87.6(84.1-90.55);102.1; n=383	0.6515	87.4(83.5-91.3);105.4; n=360	86.7(83-89.9);110.6; n=2579	0.0216*
Basophil, x10^9/L	0.009(0-0.02);0.2; n=469	0.01(0-0.02);0.1; n=461	0.0299*	0.009(0-0.02);0.19; n=469	0.01(0-0.02);0.2; n=3215	<0.0001***
Eosinophil, x10^9/L	0.01(0-0.07);0.8; n=482	0.01(0-0.1);0.67; n=485	0.0059**	0.01(0-0.0655);0.8; n=482	0.04(0-0.1);2.25; n=3357	<0.0001***
Lymphocyte, x10^9/L	1.13(0.8-1.55);4.66; n=483	1.21(0.9-1.63);3.24; n=485	0.0032**	1.13(0.8-1.55);4.66; n=483	1.41(1.016-1.9);16.99; n=3365	<0.0001***
Monocyte, x10^9/L	0.48(0.33-0.64);1.45; n=483	0.5(0.39-0.67);1.39; n=485	0.0532	0.48(0.33-0.64);1.45; n=483	0.5(0.38-0.63);3.26; n=3365	0.1153
Neutrophil, x10^9/L	3.4(2.4-4.32);15.9; n=483	3.32(2.4-4.45);17.97; n=485	0.7966	3.4(2.4-4.32);15.9; n=483	3.27(2.4-4.38);27.17; n=3365	0.7461
WBC, x10^9/L	5.16(4.03-6.26);17.9; n=489	5.34(4.3-6.8);19.95; n=489	0.0702	5.16(4.029-6.26);17.9; n=489	5.47(4.38-6.8);29.64; n=3429	0.0002***
MCH, g/dL	29.8(28.1-31);36.8; n=489	29.8(28.7-31);34.6; n=489	0.3479	29.8(28.1-31);36.8; n=489	29.7(28.3-30.7);35.9; n=3429	0.2134
Platelet, x10^9/L	199(160-241.75);773; n=488	203(164-253);597.2; n=489	0.1917	199(160-241.75);773; n=488	220(179-276);778; n=3429	<0.0001***

RBC, x10^12/L	4.51(4.17-4.89);6.97; n=489	4.6(4.28-4.93);7.24; n=489	0.0303*	4.51(4.17-4.89);6.97; n=489	4.7(4.4-5.1);7.45; n=3430	<0.0001***
HCT, L/L	0.39(0.36-0.42);0.49; n=420	0.40(0.37-0.42);0.51; n=416	0.0021**	0.39(0.36-0.42);0.49; n=420	0.40(0.38-0.43);0.53; n=2965	<0.0001***
Biochemical tests						
Potassium, mmol/L	3.8(3.5-4.1);5.67; n=432	3.8(3.5-4.11);5.9; n=398	0.8513	3.8(3.5-4.1);5.67; n=432	3.8(3.59-4.1);5.9; n=2563	0.4478
Urate, mmol/L	0.37(0.31-0.45);0.62; n=25	0.32(0.24-0.39);0.54; n=27	0.0973	0.37(0.3056-0.45);0.621; n=25	0.2875(0.2375-0.3685);0.635; n=102	0.0038**
Albumin, g/L	39(35-42.25);141.36; n=434	38.9(34.6-43);146; n=399	0.4241	39(35-42.25);141.36; n=434	41(37-44.1);146; n=2567	<0.0001***
Sodium, mmol/L	138(135.1-140.4);147.5; n=432	138.91(136.4-141);146; n=398	0.0352*	138(135.1-140.35);147.49; n=432	139(137-140.7);149.42; n=2570	<0.0001***
Urea, mmol/L	4.3(3.22-5.6);36.2; n=432	4.4(3.3-5.5);15.19; n=397	0.9255	4.3(3.22-5.6);36.2; n=432	3.9(3.1-4.845);41.95; n=2568	<0.0001***
Protein, g/L	72.9(68.8-77.3);93.2; n=373	73(69.95-77.2);88.9; n=343	0.5548	72.9(68.8-77.3);93.2; n=373	74(70.4-77.5);92.7; n=2310	0.0007***
Creatinine, umol/L	71.05(61-86.5);1280; n=432	72(59-85.5);250; n=398	0.8335	71.05(61-86.5);1280; n=432	69.75(58-84);1216.2; n=2570	0.0058**
Alkaline phosphatase, U/L	65(54-80);932; n=430	62(53-79);275.9; n=395	0.2198	65(54-80);932; n=430	65(53.95-80);550; n=2558	0.9157
Aspartate transaminase, U/L	29(22-49);1807.4; n=173	28(22.85-40.5);139; n=156	0.2748	29(22-49);1807.4; n=173	26.1(21-39);863; n=819	0.0056**

Alanine aminotransferase, U/L	23(16-36.3);380; n=348	26(18.15-41.25);201; n=327	0.0031**	23(16-36.3);380; n=348	23(16-35);583; n=2078	0.8508
Bilirubin, umol/L	7.8(5.8-11.8);56.5; n=429	8(5.8-11);59.7; n=395	0.8474	7.8(5.8-11.8);56.5; n=429	7.8(5.5-10.8);235; n=2558	0.1297
Glucose, mmol/L	5.9(5.26-7.4);26.5; n=425	5.9(5.2-7.5);29.3; n=407	0.8077	5.86(5.26-7.4);26.5; n=425	5.58(5-6.7);29.29; n=2520	<0.0001***
Diabetes mellitus tests						
HbA1c, g/dL	13(11.4-14.1);17.1; n=489	13.5(11.8-14.3);17.4; n=489	0.0365*	13(11.4-14.1);17.1; n=489	13.5(12.2-14.7);18.1; n=3430	<0.0001***
Cholesterol, mmol/L	3.8(2.8-4.6);7.559; n=159	3.71(2-4.6);7.0; n=136	0.4988	3.8(2.8-4.6);7.559; n=159	3.9(2.6-4.9);9.718; n=504	0.4820
D-dimer, ng/mL	369(220.5-743.6);6544.8; n=124	416(241-810.51);11200; n=125	0.6954	369(220.5-743.6);6544.8; n=124	280(152.7-540.01);11200; n=681	0.0006***
High sensitive troponin-I, ng/L	4.8(2-10);400.2; n=200	4.5(2.2-10);3876.3; n=181	0.7649	4.772(2-10);400.2; n=200	3(1-6.29);3876.3; n=1031	<0.0001***
Lactate dehydrogenase, U/L	219(180.5-281.5);1116; n=411	210(171-260);779; n=399	0.0105*	219(180.5-281.5);1116; n=411	194(164-236);1374; n=2745	<0.0001***
APTT, second	31.6(27.9-34.8);66.4; n=319	30.3(27.5-33.9);120; n=311	0.0511	31.6(27.9-34.8);66.4; n=319	30.8(27.6-34.4);120; n=1734	0.1432
Prothrombin Time/INR, second	12(11.4-12.6);43.4; n=220	11.9(11.5-12.6);28.5; n=219	0.8448	12(11.35-12.55);43.4; n=220	12(11.5-12.6);31.7; n=1235	0.2356
C-reactive protein, mg/dL	0.8(0.3-2.9);34; n=492	0.6(0.25-2.4);23.4; n=482	0.1259	0.81(0.26-2.9);34; n=492	0.31(0.11-1.2);29.8; n=3362	<0.0001***
Blood gas tests						

HCO3/Bicarbonate, mmol/L	23.8(19.9-26);30.7; n=45	23.5(21-25.15);27.7; n=32	0.5350	23.8(19.9-26);30.7; n=45	22.7(20.3-24.7);32.8; n=122	0.2187
Base excess, mmol/L	-0.4(-2.7-1.65);6.1; n=135	-0.4(-1.9-2.1);6.4; n=89	0.3969	-0.4(-2.7-1.65);6.1; n=135	-0.5(-2.5-1.5);9.5; n=377	0.6725
Blood pCO2, kPa	4.78(4.07-5.68);10.94; n=135	5.18(4.32-5.51);10.65; n=89	0.5976	4.8(4.1-5.7);10.9; n=135	4.9(4.2-5.73);10.65; n=378	0.6196
Blood pH	7.42(7.38-7.48);7.61; n=135	7.42(7.39-7.47);7.61; n=89	0.5616	7.4(7.4-7.5);7.6; n=135	7.42(7.4-7.47);7.6; n=378	0.8737
Calcium, mmol/L	1.095(0.99-1.15);1.19; n=8	1.17(1.02-1.18);1.33; n=9	0.2270	1.095(0.99-1.15);1.19; n=8	1.135(1.1-1.185);1.33; n=28	0.1227

Supplementary Table 10. Composite risk of meeting the primary outcome among hospitalized Covid-19 patients after propensity score matching (1:1).

* for p≤ 0.05, ** for p ≤ 0.01, *** for p ≤ 0.001

Characteristics	Famotidine vs Control HR [95% CI]	P value	PPIs vs Control HR [95% CI]	P value
PPIs/Control	-	-	11.76[7.77, 17.79]	<0.0001***
PPIs dosage, mg	-	-	1.00[1.00, 1.00]	<0.0001***
Famotidine/Control	1.81[1.35, 2.43]	<0.0001***	-	-
Famotidine dosage, mg	1.00[1.00, 1.00]	0.155	-	-
Demographics				
Male gender	1.79[1.33, 2.42]	0.0001***	2.09[1.44, 3.04]	0.0001***
Age, years	1.04[1.03, 1.05]	<0.0001***	1.07[1.05, 1.08]	<0.0001***
Past comorbidities				
Cardiovascular	1.60[1.18, 2.16]	0.0023**	2.32[1.57, 3.43]	<0.0001***
Respiratory	2.63[0.64, 10.79]	0.179	2.12[0.29, 15.42]	0.459
Renal	2.85[2.13, 3.82]	<0.0001***	3.52[2.36, 5.26]	<0.0001***
Endocrine	2.00[0.89, 4.52]	0.0945.	2.10[0.67, 6.64]	0.205
Diabetes mellitus	1.79[1.34, 2.40]	<0.0001***	2.33[1.60, 3.38]	<0.0001***
Hypertension	2.03[1.54, 2.69]	<0.0001***	2.78[1.94, 3.98]	<0.0001***
Gastrointestinal	0.87[0.42, 1.80]	0.714	0.74[0.27, 2.02]	0.551
Stroke	1.71[1.23, 2.38]	0.0014**	2.78[1.85, 4.17]	<0.0001***
Hospitalizations				
Episodes number	1.02[1.00, 1.04]	0.0233*	1.15[1.10, 1.21]	<0.0001***

Length of hospital stay, days	1.01[1.01, 1.01]	<0.0001***	1.02[1.02, 1.03]	<0.0001***
Emergency readmission times	1.03[0.96, 1.11]	0.418	1.02[0.84, 1.23]	0.876
Medications				
ACEI	2.20[1.61, 2.99]	<0.0001***	2.96[1.99, 4.42]	<0.0001***
ARB	0.99[0.67, 1.47]	0.959	1.19[0.70, 2.02]	0.519
Steroid	0.85[0.59, 1.23]	0.396	0.45[0.26, 0.81]	0.0072**
Kaletra	8.74[6.53, 11.69]	<0.0001***	18.19[12.42, 26.64]	<0.0001***
Ribavirin	0.94[0.71, 1.26]	0.699	0.79[0.54, 1.16]	0.227
Interferon beta-1B	2.81[1.81, 4.36]	<0.0001***	2.88[1.73, 4.78]	<0.0001***
Hydroxychloroquine	1.29[0.70, 2.37]	0.417	4.04[2.17, 7.54]	<0.0001***
Calcium channel blockers	1.90[1.43, 2.51]	<0.0001***	2.78[1.93, 3.99]	<0.0001***
Beta blockers	1.45[1.06, 1.99]	0.021*	1.97[1.32, 2.93]	0.0009***
Diuretics for heart failure	6.08[4.60, 8.04]	<0.0001***	9.59[6.68, 13.75]	<0.0001***
Diuretics for hypertension	2.70[1.20, 6.08]	0.0169*	5.46[1.73, 17.19]	0.0038**
Nitrates	0.24[0.06, 0.96]	0.0434*	0.70[0.17, 2.82]	0.612
Other antihypertensives	1.37[0.94, 2.00]	0.0977.	2.79[1.69, 4.61]	<0.0001***
Complete blood count tests				
MCV, fL	1.01[0.99, 1.03]	0.282	1.04[1.01, 1.08]	0.013*
Basophil, x10^9/L	957.2[2.3, 394292.0]	0.0255*	5512.0[6.45, 4713864.0]	0.0124*
Eosinophil, x10^9/L	0.29[0.05, 1.83]	0.188	0.03[0.00, 0.47]	0.0132*
Lymphocyte, x10^9/L	0.38[0.28, 0.53]	<0.0001***	0.24[0.16, 0.37]	<0.0001***
Monocyte, x10^9/L	1.29[0.78, 2.13]	0.319	2.88[1.40, 5.90]	0.004**
Neutrophil, x10^9/L	1.19[1.16, 1.23]	<0.0001***	1.29[1.23, 1.35]	<0.0001***

WBC, x10^9/L	1.16[1.12, 1.19]	<0.0001***	1.24[1.18, 1.30]	<0.0001***
MCH, g/dL	1.00[0.95, 1.05]	0.888	1.05[0.98, 1.13]	0.153
Platelet, x10^9/L	1.00[1.00, 1.00]	0.0376*	0.998[0.995, 1.000]	0.0808.
RBC, x10^12/L	0.68[0.55, 0.85]	0.0006***	0.45[0.34, 0.59]	<0.0001***
HCT, L/L	0.01[0.00, 0.21]	0.00267**	0.00[0.00, 0.017]	<0.0001***
Biochemical tests				
Potassium, mmol/L	1.75[1.29, 2.38]	0.0003***	1.39[0.93, 2.08]	0.11
Urate, mmol/L	3.52[0.13, 95.37]	0.455	0.90[0.01, 61.40]	0.961
Albumin, g/L	1.00[0.99, 1.00]	0.231	0.99[0.98, 1.00]	0.126
Sodium, mmol/L	0.97[0.94, 1.01]	0.0958.	0.93[0.89, 0.97]	0.0012**
Urea, mmol/L	1.09[1.07, 1.11]	<0.0001***	1.13[1.10, 1.16]	<0.0001***
Protein, g/L	0.93[0.91, 0.95]	<0.0001***	0.93[0.90, 0.97]	<0.0001***
Creatinine, umol/L	1.00[1.00, 1.00]	<0.0001***	1.003[1.002, 1.004]	<0.0001***
Alkaline phosphatase, U/L	1.00[1.00, 1.00]	<0.0001***	1.004[1.002, 1.005]	<0.0001***
Aspartate transaminase, U/L	1.00[1.00, 1.00]	<0.0001***	1.002[1.001, 1.002]	<0.0001***
Alanine aminotransferase, U/L	1.01[1.00, 1.01]	0.0016**	1.011[1.007, 1.016]	<0.0001***
Bilirubin, umol/L	1.02[1.01, 1.03]	<0.0001***	1.02[1.00, 1.05]	0.0361*
Glucose, mmol/L	1.12[1.08, 1.17]	<0.0001***	1.14[1.09, 1.19]	<0.0001***
Diabetes mellitus tests				
HbA1C, g/dL	0.94[0.92, 0.97]	<0.0001***	0.94[0.91, 0.97]	0.000158***
Cholesterol, mmol/L	0.96[0.85, 1.08]	0.45	0.95[0.81, 1.12]	0.531
D-dimer, ng/mL	1.00[1.00, 1.00]	<0.0001***	1.000[1.000, 1.000]	<0.0001***
High sensitive troponin-I, ng/L	1.0[0.9996, 1.001]	0.588	1.0[0.9995, 1.001]	0.912

Lactate dehydrogenase, U/L	1.00[1.00, 1.00]	<0.0001***	1.005[1.004, 1.006]	<0.0001***
APTT, second	1.03[1.02, 1.05]	<0.0001***	1.04[1.02, 1.05]	<0.0001***
Prothrombin Time/INR, second	1.13[1.07, 1.19]	<0.0001***	1.05[0.99, 1.11]	0.119
C-reactive protein, mg/dL	1.11[1.09, 1.13]	<0.0001***	1.12[1.10, 1.15]	<0.0001***
Blood gas tests				
HCO3/Bicarbonate, mmol/L	0.94[0.88, 1.00]	0.0642.	0.92[0.84, 1.01]	0.0752.
Base excess, mmol/L	0.86[0.83, 0.90]	<0.0001***	0.92[0.87, 0.98]	0.0062**
Blood pCO2, kPa	0.91[0.80, 1.03]	0.144	0.87[0.74, 1.03]	0.101
Blood pH	0.04[0.01, 0.27]	0.001**	1.12[0.08, 16.17]	0.935
Calcium, mmol/L	11.2[0.10, 1225.0]	0.313	423.3[0.31, 574342.0]	0.1