Supplementary

Table S1 Baseline characteristics and physiological parameters on admission of ARDS patients treated with different corticosteroid doses

Variables	All patients (n=357)	No corticosteroid (n=72)	Low corticosteroid (n=213)	High corticosteroid (n=72)	P value
Age (years)	67 [57–75]	67 [59–79]	67 [57–76]	63.5 [55–73]	0.21
Sex, male	244 (68.35)	51 (70.83)	147 (69.01)	46 (63.89)	0.63
Smoking	101 (28.29)	15 (20.83)	71 (33.33)	15 (20.83)	0.04
APACHE II score	19 [11–28]	12 [8–26]	20 [12–28]	20 [14–31.5]	0.10
Immune deficiency	160 (44.82)	16 (22.22)	98 (46.01)	46 (63.89)	<0.001
PaO_2/FiO_2	189.5 [111–259]	217.5 [143–282]	173 [108–252]	165 [94–250]	0.008
Cause of ARDS					
Pneumonia	265 (74.23)	42 (58.33)	167 (78.40)	56 (77.78)	0.003
Sepsis	17 (4.76)	2 (2.78)	11 (5.16)	4 (5.56)	0.78
Aspiration	12 (3.36)	5 (6.94)	7 (3.29)	0 (0.00)	0.06
Trauma	10 (2.80)	4 (5.56)	4 (1.88)	2 (2.78)	0.27
Others	53 (14.85)	19 (26.39)	24 (11.27)	10 (13.89)	0.007
Any comorbidity					
Diabetes	77 (21.57)	12 (16.67)	49 (23.00)	16 (22.22)	0.52
Hypertension	144 (40.34)	34 (47.22)	83 (38.97)	27 (37.50)	0.40
Chronic liver disease	41 (11.48)	9 (12.50)	25 (11.74)	7 (9.72)	0.86
Respiratory support					
Noninvasive mechanical ventilation	281 (78.71)	59 (81.94)	162 (76.06)	60 (83.33)	0.32
Invasive mechanical ventilation	184 (51.54)	18 (25.00)	127 (59.62)	39 (54.17)	<0.001
ECMO	19 (5.32)	1 (1.39)	12 (5.63)	6 (8.33)	0.14
Physiologic parameters					
HB (g/L)	108 [91–125]	115 [94.5–125.5]	106 [87–125]	105.5 [91–124]	0.37
HCT (g/L)	32.7 [27.6–37.4]	34.6 [28.7–37.6]	32.35 [27.3–37.45]	32.65 [27.6–37.4]	0.66
WBC ($\times10^9$/L)	10.555 [6.62–14.31]	9.89 [6.645–11.60]	10.93 [6.76–14.72]	10.54 [6.53–14.59]	0.37
PLT ($\times10^9$/L)	184 [101.5–265.5]	208 [122–315]	182 [102–256]	163 [72.5–261.5]	0.11
NEUT	8.3 [5.3–12.4]	7.8 [4.6–10.2]	8.6 [6–12.9]	9.1 [5.1–13.1]	0.29
Lym	0.7 [0.4–1.1]	0.8 [0.45–1.2]	0.65 [0.4–1.1]	0.5 [0.3–1]	0.08
ESR (mm/h)	40 [16–63]	46.5 [28–63.5]	38 [12–63]	39 [13–63]	0.48
TBil (μmol/L)	11.45 [7–21.3]	11 [7.2–24.7]	11.9 [7.2–22.2]	9.95 [6.85–17.2]	0.35
Scr (μmol/L)	72 [55–108]	73.5 [56–116]	76 [56–120]	61 [49–83]	0.02
LDH (U/L)	367.5 [259–603]	287.5 [214.5–369.5]	379 [256–640]	446 [303–640]	0.002
PCT (ng/mL)	0.635 [0.14–2.89]	0.67 [0.14–3.63]	0.665 [0.14–3.16]	0.45 [0.11–1.71]	0.52
CRP (mg/L)	73.6 [29–142.8]	87.4 [32.3–128.2]	68.25 [29.05–153.9]	71.85 [29–129.7]	0.76
D-dimer (μg/mL)	4.085 [1.99–9.11]	4.285 [1.9–9.91]	4.3 [2.11–10.36]	3.23 [1.66–7.52]	0.35
PT (seconds)	13.7 [12.45–15.5]	13.55 [12.8–15.1]	13.9 [12.4–16]	13.5 [11.9–15.2]	0.26
CD19 (%)	16.8 [8.1–27.8]	13.05 [9.55–24.35]	18 [8.3–28]	20.7 [7.1–31.3]	0.33
CD3 (%)	64.7 [52.6–77.25]	70.5 [61–78.7]	63.3 [51.7–75.4]	61.35 [49.8–77.2]	0.050
CD4 (%)	35.4 [24.9–44.5]	36.9 [31.4–45.1]	35.9 [23.6–45.6]	30.8 [20.9–42.1]	0.07
CD8 (%)	23.8 [15.9–35.8]	25.8 [19.7–36.8]	22.7 [16–34.4]	23.4 [13.65–38.75]	0.44
CD4/CD8	1.4 [0.9–2.4]	1.45 [0.9–2.1]	1.4 [0.9–2.6]	1.4 [0.7–2.2]	0.77
CD56+16 (%)	11.35 [6.55–19.45]	10.2 [8.3–14.7]	12.1 [6.4–22.7]	9.7 [6–18.35]	0.59
TNF (pg/mL)	14.7 [9.7–25.3]	16.65 [9.2–26.9]	15.5 [9.95–24.95]	13.65 [9.7–24.5]	0.77
IL-1β (pg/mL)	5.55 [5–10.9]	5.3 [5–10.6]	5.85 [5–11.4]	5 [5–10]	0.52
IL-2R (U/mL)	1,450.5 [891–2,543]	1,139 [773–1,932]	1,373 [923.5–2,317]	1,726 [1,038–2,928]	0.06
IL-6 (pg/mL)	35.7 [13.1–143]	26.5 [13.4–111.5]	53.3 [14.7–168]	36.65 [9.5–104]	0.37
IL-8 (pg/mL)	57 [25–115]	41 [17–117]	62 [26–111]	62 [27–118]	0.24
IL-10 (pg/mL)	9.9 [5–24.2]	5.05 [5–11.7]	9.95 [5–24.65]	11.65 [5.1–25.7]	0.04
Clinical outcomes					
28-day mortality	193 (54.06)	33 (45.83)	107 (50.23)	53 (73.61)	0.001
In-hospital mortality	219 (61.34)	35 (48.61)	126 (59.15)	58 (80.56)	<0.001
Days of hospitalization	14 [7–24]	11.5 [5–22]	14 [7–25]	14 [9–21.5]	0.32

Data are presented as n (%) or median [IQR]. For continuous variables, one-way ANOVA or Kruskal-Wallis tests was used to calculate the P value unless otherwise noted. For categorical variables, chi-square test was used to calculate the P value unless otherwise noted. Most of the baseline characteristics were comparable between different corticosteroid groups, whereas patients with immune deficiency were unevenly distributed between the three groups. ARDS, acute respiratory distress syndrome; APACHE II, Acute Physiologic and Chronic Health Evaluation II; PaO_2, partial pressure of oxygen; FiO_2, fraction of inspired oxygen; ECMO, extracorporeal membrane oxygenation; HB, hemoglobin; HCT, hematocrit; WBC, white blood cell; PLT, platelet count; NEUT, neutrophil; Lym, lymphocyte; ESR, erythrocyte sedimentation rate; TBil, total bilirubin; Scr, serum creatinine; LDH, lactate dehydrogenase; PCT, procalcitonin; CRP, C-reactive protein; PT, prothrombin time; CD, cluster of differentiation; TNF, tumor necrosis factor; IL, interleukin; IL-2R, interleukin 2 receptor; IQR, interquartile range; ANOVA, analysis of variance.

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Table S2 Risk factors associated with 28-day mortality in different glucocorticoid doses groups

Variables	All patients (n=357)			No corticosteroid (n=72)			Low corticosteroid (n=213)			High corticosteroid (n=72)		
	Death (n=193)	No death (n=164)	P value	Death (n=33)	No death (n=39)	P value	Death (n=107)	No death (n=106)	P value	Death (n=53)	No death (n=19)	P value
Age, >67 years	101	80	0.50	22	18	0.08	58	52	0.45	21	10	0.33
Sex, male	131	113	0.84	22	29	0.47	74	73	0.96	35	11	0.53
Smoking	52	49	0.54	6	9	0.61	36	35	0.92	10	5	0.52
PaO_2/FiO_2, <100 mmHg	51	21	0.001	4	3	0.70	30	16	0.01	17	2	0.06
Diabetes	38	39	0.35	8	4	0.11	19	30	0.07	11	5	0.75
Hypertension	67	77	0.02	17	17	0.50	34	49	0.03	16	11	0.03
Chronic liver disease	27	14	0.11	5	4	0.72	15	10	0.30	7	0	0.18
Immune deficiency	102	58	0.001	13	3	0.001	51	47	0.63	38	8	0.02
HB, >112 g/L	74	80	0.07	13	21	0.50	40	50	0.17	21	9	0.56
HCT, >31.0 g/L	87	80	0.52	14	16	0.72	47	57	0.25	26	7	0.55
WBC, $>11.00\times10^9$/L	86	68	0.50	9	11	0.85	50	50	>0.99	27	7	0.34
PLT, $>184\times10^9$/L	80	83	0.08	10	24	0.02	47	52	0.36	23	7	0.60
NEUT, >5.5	102	99	0.41	16	18	0.37	55	70	0.13	31	11	0.93
Lym, >0.6	58	70	0.005	11	19	0.20	30	44	0.04	17	7	0.59
ESR, >40 mm/h	51	42	0.13	5	12	0.36	25	25	0.24	21	5	0.34
TBil, >11.4 μmol/L	91	70	0.27	14	13	0.14	55	48	0.27	22	9	0.66
Scr, >72 μmol/L	100	62	0.003	15	16	0.25	65	44	0.002	20	2	0.03
LDH, >366 U/L	93	49	<0.001	7	5	0.16	54	34	<0.001	32	10	0.40
PCT, >0.63 ng/mL	96	60	0.01	15	15	0.68	60	38	0.001	21	7	0.95
CRP, >73.6 mg/L	97	70	0.055	15	20	0.73	56	44	0.07	26	6	0.15
D-dimer, >4.08 μg/mL	103	65	0.003	18	13	0.01	62	45	0.03	23	7	0.45
PT, >13.7 seconds	93	63	0.03	15	11	0.04	57	45	0.07	21	7	0.85
CD19, >16.8%	53	49	0.44	2	10	0.25	30	32	0.31	21	7	0.86
CD3, >64.6%	43	55	0.06	7	13	0.49	19	37	0.02	17	5	0.64
CD4, >35.4%	42	53	0.10	6	14	>0.99	24	36	0.24	12	3	0.73
CD8, >22.0%	51	51	0.94	8	11	0.41	26	34	0.60	17	6	0.85
CD4/CD8, >1.4	43	50	0.35	4	11	0.70	25	32	0.76	14	7	0.48
CD56+16, >11.2%	49	42	0.38	6	7	0.12	28	30	0.56	15	5	>0.99
TNF, >14.6 pg/mL	50	47	0.39	12	11	0.04	24	31	0.67	14	5	>0.99
IL-1β, >5.5 pg/mL	48	39	0.29	10	8	0.18	25	28	0.64	13	3	0.47
IL-2R, >1,446 U/mL	60	42	0.001	8	7	0.07	28	28	0.07	24	7	0.22
IL-6, >35.7 pg/mL	40	41	0.03	10	8	0.10	29	33	0.12	1	0	>0.99
IL-8, >57 pg/mL	54	33	0.003	9	2	0.001	28	27	0.16	17	4	0.41
IL-10, >10.0 pg/mL	56	31	0.001	6	3	0.06	27	22	0.047	23	6	0.65

Data are presented as n. For continuous variables, *t*-test or Mann-Whitney *U* test was used to calculate the P value unless otherwise noted. For categorical variables, chi-square test was used to calculate the P value unless otherwise noted. PaO_2, partial pressure of oxygen; FiO_2, fraction of inspired oxygen; HB, hemoglobin; HCT, hematocrit; WBC, white blood cell; PLT, platelet count; NEUT, neutrophil; Lym, lymphocyte; ESR, erythrocyte sedimentation rate; TBil, total bilirubin; Scr, serum creatinine; LDH, lactate dehydrogenase; PCT, procalcitonin; CRP, C-reactive protein; PT, prothrombin time; CD, cluster of differentiation; TNF, tumor necrosis factor; IL, interleukin; IL-2R, interleukin 2 receptor.

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Table S3 Correlation between risk factors and 28-day mortality in different corticosteroid dose groups

Variables	All patients (n=357)		No corticosteroid (n=72)		Low Corticosteroid (n=213)		High corticosteroid (n=72)	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.01 (1.00–1.03)	0.03	1.04 (0.98–1.10)	0.19	1.02 (1.00–1.04)	0.09	1.01 (0.98–1.03)	0.51
Sex, male	0.88 (0.59–1.32)	0.54	0.95 (0.24–3.84)	0.94	0.89 (0.50–1.58)	0.68	1.05 (0.49–2.27)	0.89
Smoking	0.92 (0.60–1.40)	0.69	0.85 (0.21–3.47)	0.82	1.12 (0.64–1.94)	0.70	1.15 (0.47–2.82)	0.76
Immune deficiency	1.80 (1.27–2.54)	0.001	12.46 (2.63–58.94)	0.001	1.31 (0.81–2.10)	0.27	2.99 (1.15–7.73)	0.02
PaO_2/FiO_2, <100 mmHg	1.53 (1.04–2.56)	0.03	0.56 (0.06–4.92)	0.60	1.65 (1.00–2.72)	0.05	1.82 (0.79–4.19)	0.16
Cause of ARDS								
Pneumonia	0.71 (0.45–1.14)	0.16	2.41 (0.48–12.15)	0.29	0.84 (0.42–1.66)	0.61	0.42 (0.12–1.46)	0.17
Sepsis	1.50 (0.69–3.24)	0.30	1.94 (0.08–45.01)	0.68	1.38 (0.48–3.99)	0.55	5.17 (0.91–29.48)	0.06
Aspiration	0.40 (0.12–1.35)	0.14	1.18 (0.15–9.43)	0.88	0.27 (0.03–2.11)	0.21	–	–
Trauma	1.02 (0.40–2.60)	0.97	0.57 (0.07–4.69)	0.60	1.01 (0.12–8.39)	0.99	0.44 (0.04–5.10)	0.51
Any comorbidity								
Diabetes	0.87 (0.58–1.32)	0.52	2.15 (0.44–10.61)	0.35	0.77 (0.43–1.37)	0.37	0.69 (0.28–1.72)	0.43
Hypertension	0.77 (0.54–1.11)	0.16	1.82 (0.44–7.58)	0.41	0.75 (0.45–1.23)	0.25	0.33 (0.14–0.78)	0.01
Chronic liver disease	1.39 (0.82–2.33)	0.22	1.13 (0.23–5.44)	0.88	1.59 (0.74–3.41)	0.23	1.34 (0.42–4.29)	0.62
Physiologic parameters								
PLT	1.00 (0.99–1.00)	0.19	1.00 (0.99–1.00)	0.62	1.00 (0.99–1.00)	0.09	1.00 (1.00–1.01)	0.04
PCT	1.01 (1.00–1.02)	0.31	0.99 (0.96–1.02)	0.61	1.01 (0.99–1.02)	0.31	1.02 (0.98–1.56)	0.31
PT	1.00 (0.99–1.01)	0.86	1.23 (1.03–1.45)	0.02	1.00 (0.99–1.01)	0.97	1.04 (0.93–1.17)	0.31
CRP	1.00 (1.00–1.01)	0.83	1.00 (0.99–1.00)	0.81	1.00 (0.99–1.00)	0.89	1.00 (0.99–1.00)	0.91

Multivariate cox regression analysis was used to explore the association between possible risk factors and overall survival in different corticosteroid dose groups. HR, hazard ratio; CI, confidence interval; PaO_2, partial pressure of oxygen; FiO_2, fraction of inspired oxygen; ARDS, acute respiratory distress syndrome; PLT, platelet count; PCT, procalcitonin; PT, prothrombin time; CRP, C-reactive protein.

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