

Supplementary file 2. Summary of outcomes

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A. Mortality

Study	Mortality [% (n)]															
	ICU		Hospital		28-day		30-day		42-day		60-day		90-day		6-month	
	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg
Allingstrup (2012)	16(6)	25.3(19)														
Allingstrup (2017)					20(20)	21(21)							30(30)	32(32)	37(37)	34(34)
Badjatia													0(0)	0(0)		
Buckley			80.0(4)	65.0(11)												
Carteron					20.0(20)	22.0(21)					23(23)	24(23)				
Chapple	20.7(12)	17.2(10)			21.4(12)	24.6(14)							25.5(14)	26.8(15)		
De Azevedo (2019)	38.6(22)	44.4(28)	45.6(26)	46.0(29)												
De Azevedo (2021)	26.4(23)	43.6(41)	31.2(25)	53.4(47)											33.3(29)	54.2(51)
Dresen	38.1(8)	33.3(7)			9.5(2)	19.0(4)										
Fetterplace					13.3(4)	16.7(5)					13.3(4)	16.7(5)				
Franzosi	47.0(35)	28.3(15)	44.6(41)	52.9(18)												
Kim			5.7(2)	20.7(29)												
Lin					23.0(29)	13.6(281)										
Looijaard											18.7(20)	25.2(159)			29.0(31)	31.6(200)
Nakamura					10(6)	10.5(6)										
Nakano			10.7(6)	13.3(6)												
Salciute-Simene	46(23)	21.7(5)														
Song	14.7(5)	42.9(76)	23.5(8)	52.5(93)							20.6(7)	48.0(85)				
Suzuki					1.5(1)	13.6(9)							3.0(2)	19.7(13)		
Van Zanten	4.5(1)	9.1(2)	9.1(2)	13.6(3)	9.1(2)	13.6(3)			13.6(3)	13.6(3)						
Weijs (2012)	21.9(59)	19.8(122)	37.9(102)	33.1(204)	14.5(39)	20.1(124)										
Weijs (2014)	20.8(64)	20.3(109)	36.5(112)	35.6(191)												
Yeh (2017)			19.3(23)	16.0(15)			18.5(22)	7.4(7)								
Yeh (2020)			5(1)	12(2)												
Zhang	20.0(4)	28.6(6)														

B. Length of ICU- and hospital and stay, duration of mechanical ventilation

Study	Length of stay (days)				Duration of mechanical ventilation (days)	
	ICU		Hospital			
	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg
Allingstrup (2012)	10[7-15]	10[6-14] 5[3-9]				
Allingstrup (2017) ^a	7[5-22]	7[4-11]	30[12-53]	34[14-53]		
Badjatia	18±7	20±8				
Buckley	38±42	17±12	38±42	20±13	35±43	16±13
Carteron	14[8-21]	15[10-23]			10[6-16]	11[6-17]
Chapple	13±13	14±18	24±21	26±32		
De Azevedo 2019	21[13-33]	18[10-35]			9[5-14]	9[5-14]
De Azevedo 2021	18[12-36]	23[16-36]	38[18-70]	40[21-60]	10[5-19]	12[7-21]
Dresen	68±34	62±48			1372±642 ^d	1350±1170
Fetterplace	7.8[5.9-13.4]	7.5[4.9-12.7]	22[9.9-43]	15[9.9-25]	6.2[4.5-10.8]	5.1[3.6-8.5]
Franzosi			15[11-21]	15[12-21]		
Kim	4.0[3.0-11.0]	13.0[7.0-22.0]	19.0[12.0-29.0]	28.0[18.25-49.5]		
Looijaard ^b	14[6-23] 12[7-21]	13[7-22] 13[8-22]	41[25-57] 45[30-69]	33[20-50] 34[22-57]	10[5-17] 9[5-18]	10[5-18] 9[6-17]
Matsushima	6.5[3.0-18.0]	6.5[3.0-21.0]	32.0[13.0-102.0]	27.0[13.0-123.0]	7.0[3.8-9.3]	5.5[5.0-9.0]
Nakamura	7[5-12]	9[6-13]	26.5[18-58]	45.5[18.25-75.75]	5[2-6.5]	5.5[3-9]
Nakano	6.0[4.0-9.0]	5.0[4.0-8.0]	29.0[14.0-63.0]	23.0[16.0-35.0]	3.0[1.0-5.0]	2.0[1.0-5.0]
Rugeles	9.5±5.5	10.4±5.0			8.5±4.6	9.7±4.9
Salciute-Simene	17[10-26]	13[8-26]	22[12-42]	23[15-52]	10[6-19]	8[5-12]
Song ^c	14[10-23]	12[9-20] 12[9-17]	32[18-54]	45[21-72] 26[19-50]	11[7-19]	10[8-14] 9[7-16]
Suzuki	12.5±6.8	12.2±6.4				
Van Zanten	18.4±13.4	18.3±12.7	28.5±13.3	28.2±13.2	10.0±8.7	7.4±5.4
Weijs (2012)	31.7±19.6	28.0±18.3 18.8±18.0	65.7±58.4	49.9±38.9 40.1±35.0	28.3±17.0	25.4±17.9 16.4±16.6
Weijs (2014)	19[12-31]	20[12-31] 22[14-34]	37[22-59]	35[21-59] 32[21-55]	16[10-28]	17[10-28] 18[12-29]
Yeh (2017)	10[7-17]	15[9-26]	21[14-32]	30[20-42]		
Yeh (2020)	12.0[6.0-41.7]	12.5[10.6-15.9]	21.4[14.9-60.0] ^c	16.6[13.9-21.1]		
Zhang ^b	27.9±11.44	28.4±11.78			22.59±9.99	23.29±11.81

Values expressed as Mean±SD and Mdn[IQR]. ^avalues for 6-month survivors only, ^bvalues for ICU survivors only, ^cvalues for survivors only, ^dduration expressed in hours

C. Feeding intolerance, pneumonia and overall infections

Feeding intolerance							Pneumonia		Overall infections	
Study	Vomiting		Diarrhea		Gastric residual volume					
	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg
Allingstrup (2017)							4(4)	4(4)	19(19)	12(12)
ApSimon					5(1) ^f	40(8)				
Badjatia							0(0)	15(2)	25(3)	43(6)
Carteron	0	0	16(16) ^a	8(8)	18(18) ^g	12(11)	47(47)	43(41)		
Chapple	17(10)	16(9)	52(30) ^b	45(26)	179±22 ^h	216±212				
Dresen							90(19)	81(17)	52(11) ⁱ	52(11)
Fetterplace			53(16) ^c	53(16)	30(9) ⁱ	27(8)				
Lin									22.2(28)	20.2(416)
Nakamura	6.7(4)	10.5(6)	23.3(14) ^d	33.3(19)	0[0-7.5] ^h	5[0-28.5]	35.6(21)	50.9(29)		
Van Zanten	22.7(5)	27.3(6)	36.4(8) ^e	50(11)	18.2(4)	22.7(5)				
Xiong									18.5(5)	50(13)
Yeh (2017)									1[0-2] ^k	1[0-2]
Yeh (2020)	32(6)	12(2)								

Values expressed as %(n), Mean±SD, Mdn[IQR] and Mdn(range). Values defined as ^a≥3 unusually watery stools per day for 2 consecutive days, ^b≥3 loose bowel motions per day, ^c>3 bowel actions or >300 mL of stool output in a 24-hour period on at least 1 occasion, ^dBristol Stool Scale >5, ^eDaily Defecation Score >15 for at least 1 day or Daily Defecation Score between 6 and 15 for >2 consecutive days, ^f>0.2L, ^g>0.5L, ^hamount, ⁱ>0.3L, ^jwound infection, ^kpneumonia, urinary tract infection, bloodstream infection and surgical site infection.

D. Nitrogen balance

Nitrogen balance		
Study	≥1.2 g/kg	<1.2 g/kg
Allingstrup (2012) ^a	-0.20±0.58	-0.35±0.41 -0.59±0.48
Badjatia		
Post bleed day 2-4	0.7[-2.4-7.1]	-6.9[-10.1-2.5]
Post bleed day 7-9	-0.6[-4.4-3.4]	-6.7[-11.6- -3.1]
Post bleed day 12-14	2.5[-2.9-6.5]	-2.9[-4.9-2.3]
Buckley ^b	5.3±7.0	-15.7±7.6
Kim	3.23±3.76	-9.8±6.4
Nakano ^c	-27.8±44.8	-42.1±57.1

Values expressed as Mean±SD and Mdn[IQR]. ^aprotein equivalents; g/kg/day, ^bmeasured on day 7±4, ^ccumulative

E. Changes in muscle mass

Changes in muscle mass		
Study	≥1.2 g/kg	<1.2 g/kg
Badjatia		
	Thighs (%)	
	-6.5±4.1	-12.5±6.4
Dresen		
	Daily QMLT (mm)	
	-0.15±0.08	-0.28±0.08
Fetterplace		
	Mid upper arm (cm)	
	-1.7±1.5	-2.0±1.2
Nakamura		
	Femoral (%)	
	-12.9±8.5	-16.9±7.0
Nakano		
	Femoral (%)	
	-11.6±5.9	-14.5±7.6
Zhang		
	Diaphragm volume (%)	
	-5.33±14.15	-21.0±0.82

Values expressed as Mean±SD. Abbreviations: QMLT = quadriceps muscle layer thickness

F. Destination at hospital discharge

Study	Home		Rehab facility		Other hospital		Chronic care facility/ nursing home		Other	
	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg
Badjatia	42(5)	38(5)	58(7)	54(7)					0(0)	8(1)
Chapple	41(18)	52(23)	39(17)	30(13)	16(7)	18(8)	0(0.0)	2.3(1)	2.3(1)	0(0.0)
Fetterplace			40(12)	43(13)						
Looijaard	43(13)	38(87)	17(5)	14(31)	13(4)	22(49)	20(6)	18(42)	7(2)	8(19)
	45(25)	33(80)	11(6)	10(25)	19(11)	28(68)	25(14)	21(53)	0(0)	8(20)
Matsushima	63.2(12)	52.9(9)								
Yeh (2017)	17.6(21)	12.8(12)	46.2(55)	64.9(61)	21.0(25)	21.0(25)	15.1(18)	5.3(5)		

Values expressed as %(n).

G. Physical performance and psychological health

	Handgrip strength (kg)		Physical performance		Psychological health	
Study	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg	≥1.2 g/kg	<1.2 g/kg
Allingstrup (2017)			PCS after 6 months 22.9±21.8 23.0±22.3		MCS of SF-36 23.6±24.5 26.8±25.0	
Badjatia			mRS after 14 days 4[2-4] 4[3-5]		MOCA after 14 days 15[3-27] 16[2-24]	
			mRS after 90 days 1[0-2] 2[1-3]		MOCA after 90 days 29[24-29] 26[23-29]	
			SPPB after 14 days 2[0.7-8] 1[0-5]		Fatigue 29±15 41±28	
			SPPB after 90 days 12[10-12] 9[4-12]		Cognitive 35±5 31±12	
			Lower extremity mobility 90±8 73±27			
Chapple					EQ5DAL VAS after 90 days 60±32 53±32	
De Azevedo (2019)	Male (n=29) 18[15-25] 23.5[13.7-32]		PCS after 3 months 93.6±126.1 85.2±110.6			
	Female (n=21) 8.0[2-17] 14[7.0-22.5]		PCS after 6 months 92.0±133.4 90.0±120.6			
De Azevedo (2021)			PCS after 3 months 24.4[0-49.1] 0.0[0.0-37.0]			
			PCS after 6 months 33.6[0-71.6] 0.0[0-55.1]			
Fetterplace	20±6.1 21±9.3	PFIT-s 6.8±3.8 7.9±3.4				
		MRC sum score 55±5.9 52±9.6				
Kim			Patients with mRS 0-3 65.7(23) 33.6(47)			
Matsushima	13[9.8-20.5]	6[4.0-10.4]	MRC sum score 52[48-54.5] 48[33-49.5]			
Nakamura			FSS-ICU 15.5[3-30.75] 18[2.5-35]		EQ5DL 8[5-14.5] 8[5-14]	
			Barthel Index 62.5[0-91.25] 12.5[0-93.75]			
			PIICS [% (n)] 11.7(7) 26.3(15)			
Nakano	14.1[0-20.1] 15.0[0-24.0]	FSS-ICU 9.0[3.0-19.0] 9.5[1.0-19.5]				
		Barthel Index 52.5[5-93.8] 70.0[0-100.0]				
		Days till IMS 1 1.0[1.0-2.0] 1.0[1.0-2.0]				
		Days till IMS 3 3[2.0-5.0] 5.0[3.0-5.8]				
		Days till IMS 4 3.0[2.0-6.0] 5.0[4.0-7.0]				
		MRC sum score 49.5 55.0 [23.0-58.0] [37.0-60.0]				

Values expressed as %(n), Mean±SD and Mdn[IQR]. EQ5DL = EuroQol Dimension 5 Level, FSS-ICU = functional status score for the ICU, IMS = ICU mobility score, MCS = mental component score, MoCA = montreal cognitive assessment, MRC = medical research council, mRS = modified rankin score, PCS = physical component summary, PFIT-s = physical function in ICU test, QMLT = quadriceps muscle layer thickness, SPPB = short physical performance battery, VAS = visual analogue scale.