CHEST Online Supplement

ICU Admission Muscle and Fat Mass, Survival, and Disability at Discharge

A Prospective Cohort Study

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e-Appendix 1.

Further details on the methods: To correct for variations of body size that could lead to differences in PMA, we calculated the ideal body weight based on the patients' height, gender and age using the Devine formula[1]. We chose not to calculate the body mass index as it entails weight's determination, which is easily confounded by the aggressive fluid administration often provided during the first hours of critical illness. To account for gender differences in muscle mass, we used an accepted adjustment factor of 1.67 multiplied by females' muscle area to compare with male muscle mass[2,3]. Determination of subcutaneous adipose tissue (SAT) was done using in-house software by a radiologist (CD) who was blinded to patient identifiers and clinical information as follows: the reader identified the axial image at the level of T7-8 intervertebral disc space. The SAT was manually determined on each patient and defined as the region of interest between the thoracic cavity/chest wall muscles (labeled with blue line in e-Figure 2) and the skin surface on the axial slice (labeled with green line in e-Figure 2). The area between the two lines was calculated as the aggregated SAT for each patient. All imaging findings were confirmed by a single board-certified cardiothoracic radiologist (JF).

The following baseline patient characteristics were evaluated: age, gender, preadmission morbidities known to be associated with muscle wasting: chronic pulmonary disease requiring any treatment including supplemental oxygen; cancer; diabetes mellitus (DM); congestive heart failure of a NYHA class II, III or IV; end stage renal disease; and corticosteroids use of an equivalent dose of prednisone of more than 15 mg daily for longer than 2 weeks prior to the date of enrollment[4,5]. That information was collected from the patients or patients' surrogates and confirmed with medical documentation in the electronic medical recording of Albany Medical Center. If images or other pertinent documents were not available for confirmation of a diagnosis that required them, efforts were made to obtain actual files via electronic transfer (push-through processing) or mailing in CDs with the images that were loaded in our system for review. If that procedure was not possible, we accepted English-written information signed by a credentialed physician in a scanned report, which was also incorporated to our medical records for further verification. Admission albumin values were collected and their univariable (e-Table 11) and multivariable (e-Tables 3, 6-8) associations with outcomes were determined. Severity of illness at ICU admission was measured by the Acute Physiology and Chronic Health Evaluation (APACHE) II and the Sequential Organ Failure Assessment (SOFA). Preadmission exercise limitation was determined in every patient using the Modified Medical Research Council (mMRC) scale[6] (e-Table 12). Out the total 401 patients, 232 (57%) were able to furnish a response to the mMRC, and 170 (42%) were unable to do so. In that case, the score was obtained via a surrogate familiar with patients' daily life. Out

of this last group, 65 (38%) patients recovered communication capacity to report an mMRC score, which then replaced the surrogate's. Consistency between surrogates-reported and patients-reported scores was found to be higher 90% (e-Table 13).

Measured in-hospital outcomes were days of ICU admission and hospital survival. Post discharge outcome was attainment of independent living at discharge and six months survival. Attainment of independent living was defined as discharge to the patient's home with no need of assisted living. Patients discharged to hospice, long term acute care facilities, a nursing home, or transferred to another hospital were considered not having attained independent living.

Determination of nutritional status was made via the ICU nutritional service, that evaluates every patient at admission and on following days and documents that evaluation in electronic medical recording. Nutritional service provides tailored calories, fluids, proteins and other contents based on the specific patients' pathologies. If a patient is initially deemed to be at a low nutritional risk as reflected by standard scores (nutritional risk screening [NRS 2002], NUTRIC score)[7] and given his/her ability to intake target daily calories and protein content, the diet is not supplemented. Target nutritional goals are defined as an observed intake of more than 75% of meals' trays content. If the patient is considered at nutritional risk, the diet is supplemented via nutritional boosts, tube feeds/enteral tube or TPN, with the goal of reaching 100% of predicted nutritional needs. Information regarding nutritional supplementation in our cohort is presented in e-Table 14, and the association between calories and protein supplementation and outcomes is presented in e-Table 15.

References:

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6 Mahler, D. A. & Wells, C. K. Evaluation of clinical methods for rating dyspnea. *Chest* **93**, 580-586 (1988).

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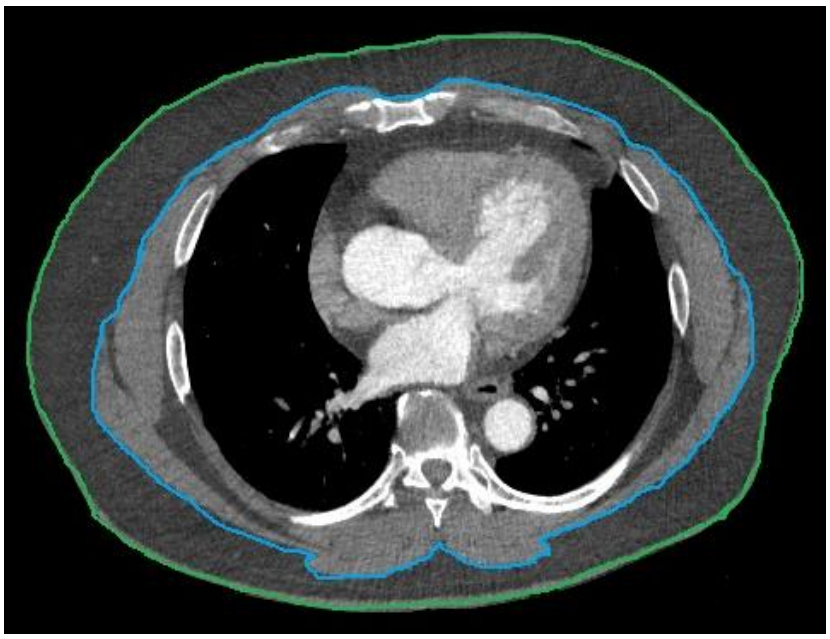
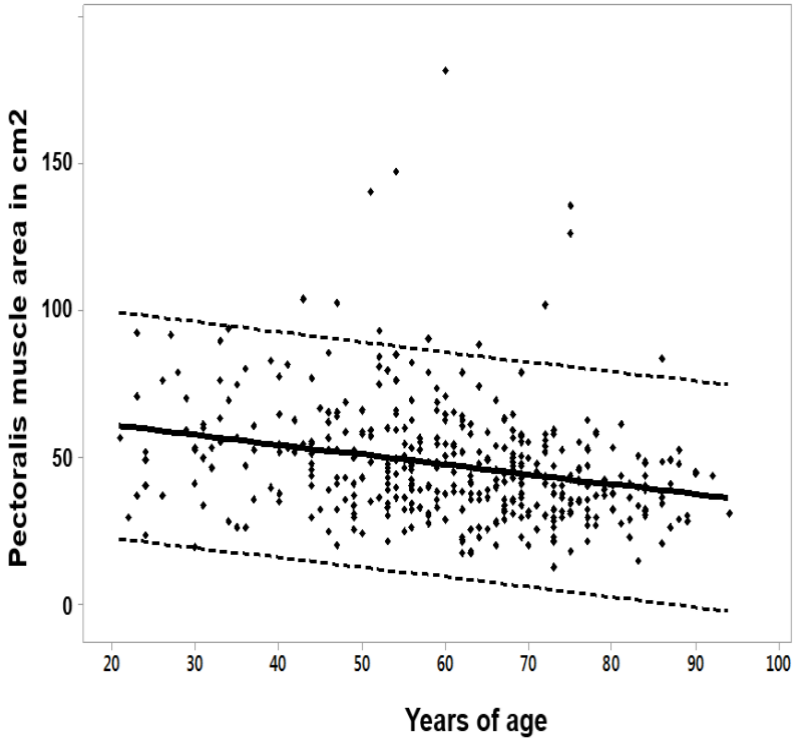
e-Figure 1: Sample computed tomography (CT) scans used to determine subcutaneous adipose tissue (SAT) in our cohort. SAT is defined as the area between the thoracic cavity/chest wall muscles (labeled with blue line) and the skin surface on the axial slice (labeled with green line); at the level of T7-T8.



e-Figure 2: Pectoralis muscle area (PMA) depending on age (p<0.001; r^2=0.069). Dotted lines are 95% prediction interval.



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e-Table 1: Intra observer PMA variability

e-Table 1: Intraobserver PMA variability

	First measurement				Second measurement				Results 1	Results 1	Difference
Pt #	LPMaj	RPMaj	LPMin	RPMin	LPMaj2	RPMaj2	LPMin2	RPMin2	Aggreg #1	Aggreg #2	Dif #1-#2
5	1107	1048	498	477	1084	1038	493	475	31.3	30.9	0.4
10	1941	1579	553	422	1937	1562	550	408	44.95	44.57	0.38
62	1633	1729	357	586	1597	1732	360	578	43.05	42.67	0.38
85	2195	1904	709	1089	2210	1892	697	1105	58.97	59.04	-0.07
96	1859	1734	503	502	1850	1740	499	503	45.98	45.92	0.06
99	1886	1823	452	747	1902	1854	440	758	49.08	49.54	-0.46
108	2524	1608	475	639	2548	1600	483	630	52.46	52.61	-0.15
117	1274	1356	652	479	1268	1369	666	490	37.61	37.93	-0.32
130	1576	1975	446	571	1568	1960	436	588	45.68	45.52	0.16
134	1456	1405	963	798	1432	1428	952	807	46.22	46.19	0.03
138	1123	1534	747	487	1130	1527	756	502	38.91	39.15	-0.24
143	951	998	479	438	968	1012	498	444	28.66	29.22	-0.56
158	887	981	270	472	899	967	289	489	26.1	26.44	-0.34
163	1288	1159	610	519	1303	1167	630	523	35.76	36.23	-0.47
201	1299	1720	316	740	1278	1734	323	748	40.75	40.83	-0.08
240	677	870	260	323	694	888	245	330	21.3	21.57	-0.27
273	831	883	254	326	845	890	253	320	22.94	23.08	-0.14
340	2069	2371	466	553	2078	2365	460	544	54.59	54.47	0.12
352	1836	1945	650	732	1850	1940	670	722	51.63	51.82	-0.19
384	1367	1234	606	653	1370	1256	599	634	38.6	38.59	0.01
									Total #1	Total #2	Difference
				Bias=-0.0875 cm^2 (±0.54)					814.54	816.29	1.75

e-Table 2: Primary indication of CT chest in our cohort: Although 403 patients/CT scans were enrolled, only 401 were analyzed in the end (see figure 2 in the main paper). We report here the indications of all the CTs.

e-Table 2: Primary indications for CT chest (total 403)*

Indication	Number	%
Suspected pulmonary embolism	131	32
Respiratory distress	60	15
Suspected pneumonia or atelectasis	57	14
Suspected or documented trauma	44	11
Suspected cavitary lesion or effusion	30	7
Suspected metastasis or mediastinal mass	29	7
Suspect vascular abnormality	15	3.7
Hemoptysis	12	3
Unspecified chest X ray abnormality	10	2.5
Unspecified chest pain	10	2.5
Suspected pneumomediastinum /pneumothorax	5	1

*Although 403 patients/CT scans were enrolled, only 401 were analyzed in the end (see figure 2 in the main paper). We report here the indications of all the CTs.

e-Table 3: Primary indications of ICU admission, including patients requiring and not requiring CT chest within 24 hours of admission.

e-Table 3: Primary indications for ICU admission, including and excluding CT chest done at ICU admission

	Including patients who got CT chest at admission# (n=1856)		Excluding patients who got CT chest at admission& (n=1368)		*p*=
Indication	**Number**	**%**	**Number**	**%**	
Non-respiratory sepsis	593	32	442	32	0.82
Respiratory failure	402	21	271	20	0.2
Metabolic cause including DKA	222	12	166	12	0.88
Hemorrhagic shock	143	7.7	115	8	0.46
Stroke/seizure/altered mental status	123	6.6	97	7	0.6
Cardiovascular decompensation	106	5.7	86	6	0.49
Pulmonary embolism	91	5	80	6	0.23
Trauma	33	1.7	21	1.5	0.59
Other causes	143	8	90	6.5	0.22

That includes all the patients admitted to the ICU during the enrollment period.
& That includes all the patients admitted to the ICU during the enrollment period, except the ones that got CT chest done within 24 hours of admission and thus considered for enrollment (488 patients), see figure 2 of the main paper.

e-Table 4: Primary indication of ICU admission in our cohort versus general census during the enrolling period.

e-Table 4: Primary indications for ICU admission in our cohort versus general census					
	Overall population (n=1856)		Our cohort (n=401)		*p*=
Indication	**Number**	**%**	**Number**	**%**	
Non-respiratory sepsis	593	32	71	17	**<0.001**
Respiratory failure	402	21	171	42	**<0.001**
Metabolic cause including DKA	222	12	13	3.2	**<0.001**
Hemorrhagic shock	143	7.7	22	5.4	**0.006**
Stroke/seizure/altered mental status	123	6.6	21	5.1	**0.03**
Cardiovascular decompensation	106	5.7	15	3.7	**0.01**
Pulmonary embolism	91	5	66	16	**<0.001**
Trauma	33	1.7	11	2.7	0.58
Other causes	143	8	11	2.7	**<0.001**

e-Table 5: Primary indication of ICU admission in our cohort versus patients not performed CT chest at the time of ICU admission.

e-Table 5: Primary indications for ICU admission in our cohort versus patients with no CT chest performed at admission					
	Patients with no CT at admission (n=1368)		Our cohort (n=401)		*p*=
Indication	**Number**	**%**	**Number**	**%**	
Non-respiratory sepsis	442	32	71	17	**<0.001**
Respiratory failure	271	20	171	42	**<0.001**
Metabolic cause including DKA	166	12	13	3.2	**<0.001**
Hemorrhagic shock	115	8	22	5.4	0.098
Stroke/seizure/altered mental status	97	7	21	5.1	0.29
Cardiovascular decompensation	86	6	15	3.7	0.089
Pulmonary embolism	80	6	66	16	**<0.001**
Trauma	21	1.5	11	2.7	0.076
Other causes	90	6.5	11	2.7	**0.0069**

e-Table 6: Multivariable analysis: risk factors of hospital mortality: Females PMA was multiplied by 1.67 in this analysis.

e-Table 6: Multivariable analysis: Risk factors of hospital mortality			
Variable	**Odds Ratio**	**95% CI**	***p* value**
PMA (Muscle area, per cm^2)	0.96	0.94-0.984	**<0.001**
SOFA score	1.25	1.14-1.36	**<0.001**
Albumin	0.55	0.35-0.85	**0.021**
mMRC	1.1845	0.95-1.465	0.07
Age	0.988	0.968-1.0096	0.62
SAT (adipose tissue)	0.694	0.37-1.304	0.102

e-Table 7: Multivariable analysis of associations with ICU-free days to day 28: Females PMA was multiplied by 1.67 in this analysis.

e-Table 7: Multivariable analysis of ICU-free days to day 28			
Variable	**Slope**	**95% CI**	***p* value**
PMA (Muscle area, per cm^2)	0.056 +/- 0.002	0.01-0.09	**0.007**
SOFA score	-0.67 +/- 0.104	-0.88-0.47	**<0.001**
Albumin	1.351 +/- 0.529	0.31-2.38	**0.011**
mMRC	-1.28 +/- 1.07	3.3-1.19	0.584
Age	0.0481 +/- 0.024	-0.00012-0.096	0.052
SAT (adipose tissue)	-0.005 +/- 0.003	-0.0012-0.0016	0.137

e-Table 8: Multivariable analysis: risk factors of disability at hospital discharge: Females PMA was multiplied by 1.67 in this analysis.

e-Table 8: Multivariable analysis of disability at hospital discharge			
Variable	**OR**	**95% CI**	***p* value**
PMA (Muscle area, per cm^2)	1.00	0.99-1.01	0.937
SOFA score	1.12	1.03-1.22	**0.007**
Albumin	0.59	0.40-0.87	**0.007**
mMRC	4	1.88-8.51	**<0.001**
Age	1.04	1.02-1.06	**<0.001**
SAT (adipose tissue)	1.00	1.00-1.00	0.794

e-Table 9: Outcomes' raw values by genders

e-Table 9: Outcomes raw values by gender				
	Overall n (%)	**Males n (%)**	**Females n (%)**	***p* value**
Died during hospitalization	58 (14.4)	30 (13.8)	28 (15.7)	0.56
Independent at hospital discharge	228 (56.8)	133 (61)	96 (53)	0.1

e-Table 10: Correction of females' muscle sizes by ideal body weight and adjustment factor 1.67[2,3].

e-Table 10: *p* values of PMA over outcomes: Unadjusted/raw value; by IBW; or by gender (1.67 X PMA in females)				
	ICU-free days at day 28	**Hospital mortality**	**Disability at discharge**	**6-months survival**
Raw PMA	*p*=0.037	*p*=0.003	*p*=0.51	*p*<0.001
PMA/IBW	*p*=0.032	*p*<0.001	*p*=0.41	*p*<0.001
PMA X 1.67	*p*=0.021	*p*<0.001	*p*=0.56	*p*<0.001

IBW: Ideal body weight; PMA: Pectoralis muscle area; 1.67 correction factor used for female gender[1,2]

e-Table 11: Association between admission serum albumin and outcomes

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6-months survival	Alive 6 months	Not alive at 6 months	
	3.4 (3.1-3.9)	2.9 (2.5-3.4)	***p*=<0.001**
Hospital survival	Alive at discharge	Not alive at hospital discharge	
	3.3 (2.9-3.8)	2.88 (2.4-3.3)	***p*=<0.001**
Disability at discharge	Independent at discharge	Not independent at discharge	
	3.46 (3-3.9)	3.1 (2.8-3.7)	***p*=<0.001**
Correlation between serum albumin and ICU free days: ***r*2=0.48, p<0.001**			

e-Table 12: Modified Medical Research Council (mMRC)

e-Table 12: mMRC dyspnea score
1: Dyspnea when strenuous exercise **2:** Dyspnea when hurrying on the level or walking up a slight hill **3:** Walks slower than most people on the level, or stops after a mile or so, or stops after 15 min walking at own pace **4:** Stops for breath after walking 100 yards (91m), or after few minutes on level ground **5:** Too dyspneic to leave the house or breathless when dressing

e-Table 13: mMRC determination in our cohort

e-Table 13: mMRC determination	**Total**	**Percentage**
Patients responding to mMRC at the time of consent:	232	57%
Patient's surrogate responding to mMRC at the time of consent:	170	42%
Out of the surrogates' responding group:		
Patients who never regained capacity to provide mMRC score:	105	62% (105/170)
Patients who regained capacity to provide mMRC score	65	38% (65/170)
Patients who provided mMRC score similar from initially obtained:	60	92% (60/65)
Patients who provided mMRC score different from initially obtained:	5	8% (5/65)

e-Table 14: Nutritional supplementation summary in our cohort

e-Table 14: Nutritional supplementation summary			
		Number (%)	**PMA cm2 (IQR)**
Total patients with no nutritional support (low nutritional risk)		**184 (45%)**	**40.4 (26.26-51.25)**
Total patients with nutritional support (high nutritional risk)		**218 (55%)**	**37.5 (25.8-45.8)**
			***p*=0.11**
Type of nutritional support			
Enteral G-tube feeding	188 (86%)		
PO boosts with no G-tube involved	22 (10%)		
Total parenteral nutrition (TPN)	8 (4%)		

e-Table 15: Calories supplementation and outcomes; Protein supplementation and outcomes

e-Table 15.			
Calories supplementation and outcomes			
Outcome	**Kcal/IBW/d (IQR)**	**Kcal/IBW/d (IQR)**	***p*=**
6-months survival	**Survivors**	**Non-survivors**	
	32.1 (28.1-35.6)	32.3 (29.5-35.2)	0.45
Hospital survival	**Survivors**	**Non-survivors**	
	32.1 (28.1-35.6)	32.6 (30.5-35-5)	0.11
Disability at discharge	**Non-disabled**	**Disabled**	
	32.8 (29.1-35.8)	31.1 (27.8-34.5)	0.22
Protein supplementation and outcomes			
Outcome	**Proteins/IBW/d (IQR)**	**Proteins/IBW/d (IQR)**	***p*=**
6-months survival	**Survivors**	**Non-survivors**	
	1.44 (1.2-1.65)	1.47 (1.25-1.65)	0.67
Hospital survival	**Survivors**	**Non-survivors**	
	1.44 (1.23-1.64)	1.48 (1.31-1.69)	0.47
Disability at discharge	**Non-disabled**	**Disabled**	
	1.46 (1.24-1.67)	1.43 (1.21-1.64)	0.57

e-Table References

1 Fuchs, G. *et al.* Lumbar skeletal muscle index derived from routine computed tomography exams predict adverse post-extubation outcomes in critically ill patients. *J Crit Care* 44, 117-123, doi:10.1016/j.jcrc.2017.10.033 (2018).

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