ANESTHESIOLOGY

# Atrophy of Diaphragm and Pectoral Muscles in Critically Ill Patients

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*ANESTHESIOLOGY 2019; 131:569–79*

## ABSTRACT

**Background:** Muscle atrophy occurs early during critical illnesses. Although diffuse, this atrophy may specifically affect the diaphragm under artificial inactivity accompanying invasive mechanical ventilation. The primary objective of this study was to highlight diaphragm atrophy during the first 5 days of critical illness. Monitoring of pectoral thickness (a nonpostural muscle with mainly phasic function) served as a control.

**Methods:** Diaphragm and pectoral thicknesses were measured by ultrasound within the first 24 h of admission in 97 critically ill patients, including 62 on mechanical ventilation. Thirty-five patients were reexamined at day 5.

**Results:** Baseline median (interquartile) values of diaphragm and pectoral thicknesses at day 1 were 2.4 (2.0, 2.9) and 5.9 (4.7, 7.2) mm, respectively (n = 97). Higher values of diaphragm thickness at baseline were positively associated with male sex, chronic obstructive pulmonary disease, and diabetes. Diaphragm and pectoral atrophies (defined as a decrease of 10% or more between day 1 and day 5) were detected in 48% (17 of 35) and 29% (10 of 34) respectively, and were uncorrelated with each other. Diaphragm atrophy was significantly more frequent in patients with septic shock and in those with mechanical ventilation, as compared with their respective counterparts (71% [10 of 14] *vs.* 33% [7 of 21], $P = 0.027$ and 71% [17 of 28] *vs.* 0% [0 of 7], $P = 0.004$, respectively), whereas pectoral atrophy was more common in patients treated with steroids as compared with their counterparts (58% [7 of 12] *vs.* 14% [3 of 22], $P = 0.006$). A statistically significant association between diaphragm atrophy and outcome was not found. Pectoral atrophy seemed associated with less successful weaning from mechanical ventilation at day 14 (12% [1 of 8] *vs.* 58% [11 of 19], $P = 0.043$).

**Conclusions:** Ultrasound enables identification of specific early diaphragm atrophy that affects the majority of mechanically ventilated patients and septic shock patients. Diaphragm atrophy and pectoral muscle atrophy seem to be two unrelated processes.

(ANESTHESIOLOGY 2019; 131:569–79)

## EDITOR'S PERSPECTIVE

### What We Already Know about This Topic

- Muscle atrophy is common in the critically ill, and diaphragm atrophy occurs during mechanical ventilation. It is not known whether wasting of diaphragm and nondiaphragm muscle is related.

### What This Article Tells Us That Is New

- Ultrasound was used for serial assessment of diaphragm and pectoral muscle in 97 critically ill patients. Diaphragm and pectoral atrophy occurred in 48% and 29%, respectively, and was associated with septic shock (diaphragm) and steroid use (pectoral); atrophy of the two muscle types appears unrelated.

Critical illnesses often lead to early muscle wasting.[1,2] The muscular atrophy that affects respiratory and peripheral muscles can be explained by many physiologic mechanisms including mitochondrial dysfunction, protein catabolism, microvascular alterations, inactivation of sodium channels, alteration in calcium homeostasis, and tensegrity impairment.[3] A more specific involvement of diaphragm fibers may directly be caused by the aggressive action of both sepsis and the mechanical ventilation support,[4–7] leading to ventilator-induced diaphragm dysfunction.[8] The subsequent impairment of diaphragm contractility and the reduction of its muscle mass are associated with prolonged weaning and poor outcome.[8,9] Under normal conditions, the muscle fibers of the diaphragm contract a dozen of times per minute; however, in artificial inactivation of the diaphragm, by sedation or paralysis, such contractions are suddenly arrested, incurring muscular atrophy which could happen earlier than that of peripheral muscles (especially nonpostural muscles with mainly phasic function, which usually contract on demand and have a low inactive tonus).[4]

Several studies[10–12] have demonstrated that ultrasonography is a good tool to visualize and measure the apposition zone of the diaphragm with a good accuracy. We designed the present work to assess diaphragm muscle atrophy during the first days of critical illness, and to describe its determinants. The main objective of the study was to detect a clinically significant decrease in diaphragm thickness assessed by ultrasonography at day 5. To scrutinize the possible role of diaphragm inactivity in the occurrence of its muscle

This article is accompanied by an editorial on p. 462. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). For a downloadable PPT slide containing this article's citation information, please visit https://anesthesiology.pubs.asahq.org/ss/downloadable_slide.aspx. A.M.D. and G.C. contributed equally to this article.

Submitted for publication July 27, 2018. Accepted for publication March 18, 2019. From the Intensive Care Unit (E.V., S.R., C.P.), Commission Innovation Recherche (E.V., F.D.), and Department of Anesthesiology (A.R.), Saint Joseph Saint Luc Hospital, Lyon, France; AP-HP (Greater Public Hospitals in Paris), Henri Mondor University Hospital, DHU A-TVB, Medical Intensive Care, Creteil, France (G.C., A.M.D.); Paris Est Creteil University, Creteil School of Medicine, IMRB, GRC CARMAS, Creteil, France (G.C., A.M.D.); and INSERM, U955 Unit, Creteil, France (G.C., A.M.D.).







<zdoi;10.1097/ALN.0000000000002737>

atrophy, we categorized patients by their need for mechanical ventilation. We also monitored the pectoral muscle, which is a nonpostural muscle, not involved in ventilation, and whose mechanism of atrophy could be independent of active breathing cessation.[4] We hypothesized that diaphragm atrophy would be more pronounced than pectoral atrophy after forced, artificial inactivation of the former.

## Materials and Methods

This observational, prospective, and monocentric study was approved by the French research ethic board Committee for the Protection of Persons Sud-Est II, Edouard Herriot Hospital, Lyon, France. It was conducted between June 2013 and January 2016 in a single intensive care unit (ICU). All included patients (or their relatives) provided written informed consent.

### Study Population and Design

All patients consecutively admitted to the ICU were screened and enrolled in the study if they satisfied the following criteria in total: older than 18 yr of age, covered by the French social security system, nonopposition of the patient or relatives to participation in the trial. Patients were excluded if they had one of the following criteria: tracheostomy, chronic noninvasive or invasive ventilation, known diaphragmatic paralysis or neurologic disease with motor dysfunction, pregnancy, breast-feeding, ventilation longer than 24 h before hospitalization, an expected duration of ICU stay or mechanical ventilation (in ventilated patients) of less than five days, or a do-not-resuscitate order. Screening was only carried out when at least one of the ultrasound operators was present in the ICU. Inclusion in the study did not interfere with the daily clinical management, especially weaning from mechanical ventilation, which was protocolled.[13]

### Ultrasonography Measurements and Reproducibility

Ultrasound images of the right hemidiaphragm zone of apposition and of the right pectoral muscle were recorded for each patient on day 1, and repeated on day 5, when applicable. Follow-up on day 5 was not performed if one of the following events occurred: change of ventilation condition (*i.e.*, intubation or extubation), discharge from ICU, or death. Measurement sites (*i.e.*, diaphragm apposition on axillary line, and pectoral muscle) were marked with a transparent film to repeat the images exactly from the same points. Images were taken with Vivid S6 (General Electric Healthcare, USA) ultrasound machine with a 10-MHz probe. Right diaphragm thickness was measured with the technique described by Wait and Cohn on patients in semi-sitting position.[11,14] The probe was placed on the right anterior axillary line. The diaphragm was identified as the hypoechogenic zone sandwiched between the two hyperechogenic lines: pleural and peritoneal membranes (fig. 1). Diaphragm thickness was measured on time movement and captured as the distance between the two lines at the end of expiration. The right pectoral muscle was observed under the clavicle, with the probe pointing to the coracoid process as described by Grechenig *et al.*[15] (fig. 2). Images were taken by two trained operators (A.R. and E.V., certified for critical care ultrasonography) and analyzed offline by only one (E.V.); three measurements were averaged out for each patient on day 1, and day 5 when applicable. Muscle atrophy was quantified for each patient by dividing the change in thickness (thickness on day 5 minus thickness on day 1)

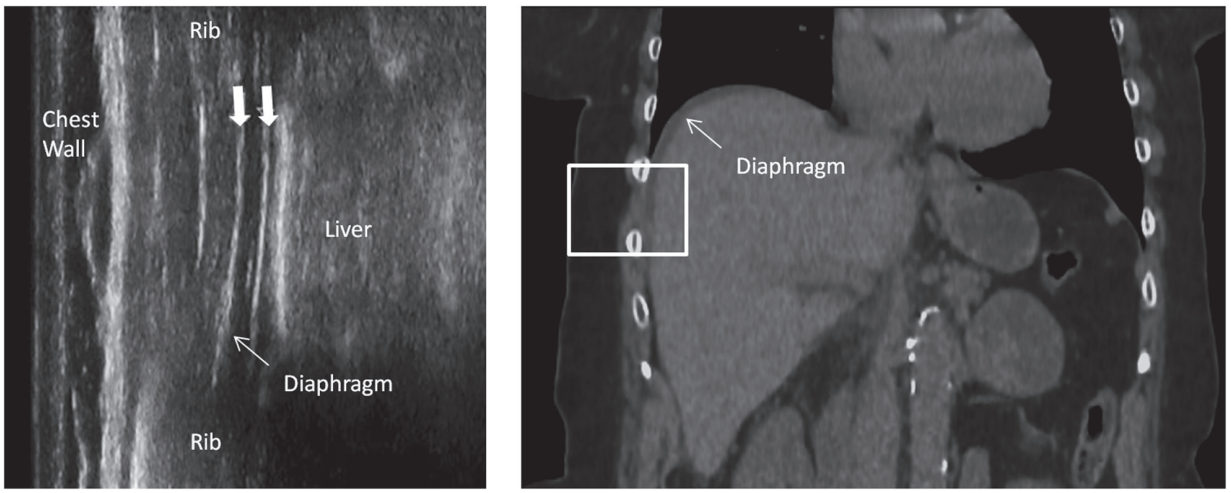


**Fig. 1.** Example of ultrasound visualization of the diaphragm at the zone of apposition (left panel) and comparative computed tomography scan (right panel). The diaphragm could be identified as the hypoechogenic zone bounded by the two hyperechogenic pleural and peritoneal layers (*parallel arrows* in the left panel).

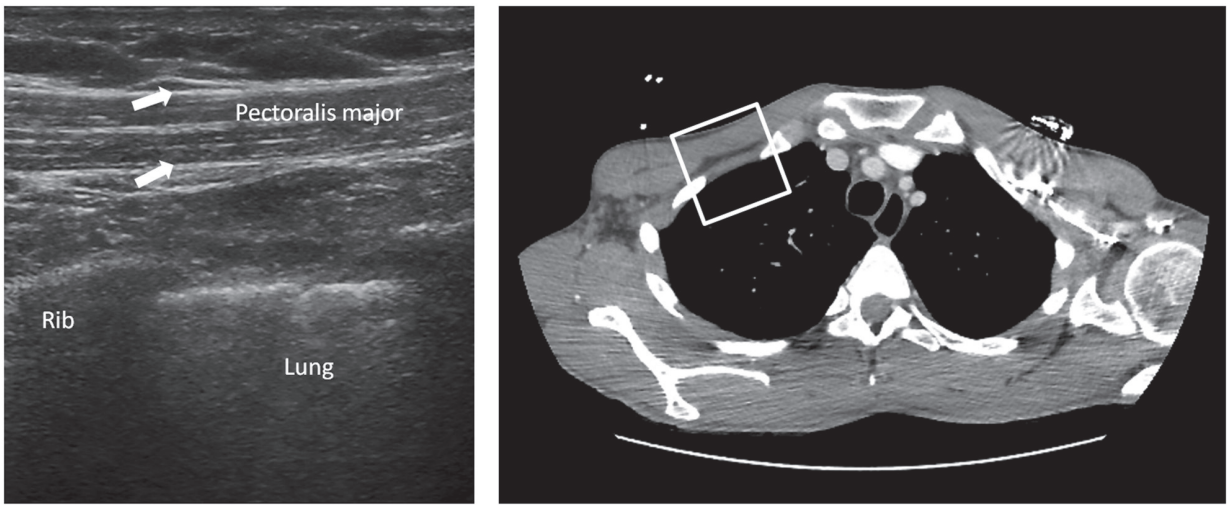


**Fig. 2.** Ultrasound image of the pectoral muscle under the clavicle (left panel), and comparative computed tomography scan (right panel). The pectoralis major is outlined by its two fasciae (*arrows*) and stands out in front of the pectoralis minor (visible on the left).

by the thickness on day 1 and expressing it as a percentage. Diaphragm atrophy was defined as a 10% or more relative decrease in diaphragm thickness between day 1 and day 5.[16] The same definition could be applied for pectoral atrophy.

Agreement between the two observers was assessed in 20 patients from the study. The two ultrasonographers performed separate recordings of diaphragm and pectoral thicknesses for each patient, and these measurements were all analyzed and compared by one of them (E.V.).

## Endpoints and Data Recording

The primary outcome was the change in diaphragm thickness between day 1 and day 5. The secondary endpoints were (1) percentage of pectoral atrophy on day 5, (2) clinical characteristics associated with baseline diaphragm and pectoral thickness, and (3) ICU characteristics and outcomes associated with diaphragm and pectoral atrophy. The following data were assessed at ICU admission: age (considering those of older than 65 yr as elderly patients at risk for sarcopenia),[17] sex, weight, smoking history, comorbidities (including high blood pressure, cardiovascular disease, diabetes, and chronic obstructive pulmonary disease), admission diagnosis, and disease severity (assessed by Sequential Organ Failure Assessment and Simplified Acute Physiology Score II scores, where patient's condition is classified very severe with values greater than 7 and greater than 59, respectively).[18,19] Some relevant ICU clinical characteristics were collected between day 1 and day 5, such as mechanical ventilation, septic shock (assessed by using Sepsis 3 definition),[20] muscle paralysis, use of sedation, and corticosteroid therapy (including low doses to treat septic shock). Successful weaning from mechanical ventilation at day 14 was defined as patient survival with definitive liberation from invasive mechanical ventilation 14 days after inclusion in the study. In-ICU and in-hospital length of stay and mortality were also recorded.

## Statistical Analysis

Based on a preliminary study showing a daily diaphragm thinning of 6% during mechanical ventilation,[21] we hypothetically calculated an overall thinning of 20% from day 1 to day 5. With an estimated diaphragm thickness of 29 ± 3 mm at day 1,[22] an $\alpha$-risk (type I error) of 5%, and a statistical power of 90%, 33 patients requiring mechanical ventilation were deemed necessary to show a 20% reduction in diaphragm thickness between day 1 and day 5. Anticipating that 20% of included patients requiring mechanical ventilation would die or would be extubated before day 5, 40 patients with mechanical ventilation were considered necessary. However, we decided to include a minimum of 80 patients, of whom at least 40 were on mechanical ventilation, and 40 with spontaneous breathing.

Data were analyzed using IBM SPSS Statistics for Windows (Version 19.0, IBM Corp, USA). Results were reported as medians (first, third quartiles) or numbers (percentage). Mann–Whitney *U* test was used to compare continuous variables. Chi-square test or Fisher exact test were used to compare categorical variables, as appropriate. Diaphragm and pectoral muscle thickness changes from day 1 to day 5 were compared by Wilcoxon paired test. Spearman rank correlation coefficient was used for bivariate correlations. Two-sided *P* values less than 0.05 were considered significant. No outliers were detected during the analysis, and the data presented here are exhaustive.

The reproducibility was expressed by the intraclass correlation coefficient[23] and the coefficient of repeatability,[24]

as proposed by Bland and Altman. Intraclass correlation coefficient was determined with consistency and 95% CI. Coefficient of repeatability was calculated using the British Standards Institution repeatability coefficient (twice the SD of the differences in repeated measurements).[24] The coefficient of repeatability is directly related to the 95% limits of agreement. It is expressed in the measurement units and is the smallest significant difference between repeated measurements.

## Results

We herein report the primary and preplanned analysis of these data.

### Patient Population and Follow-up

Ninety-seven patients were included in the study (fig. 3). At the time of inclusion, 62 patients were on mechanical ventilation and 35 were breathing spontaneously. Patient's clinical characteristics at ICU admission (day 1 cases [n = 97]) are listed in Supplemental Digital Content 1 (http://links.lww.com/ALN/B929). Among the 62 patients requiring mechanical ventilation, only 28 could be followed up on day 5; the remaining patients were either extubated (n = 18) or dead (n = 16) before day 5. Of the 35 spontaneously breathing patients, only seven could be followed up on day 5; the remainders were either intubated (n = 8)

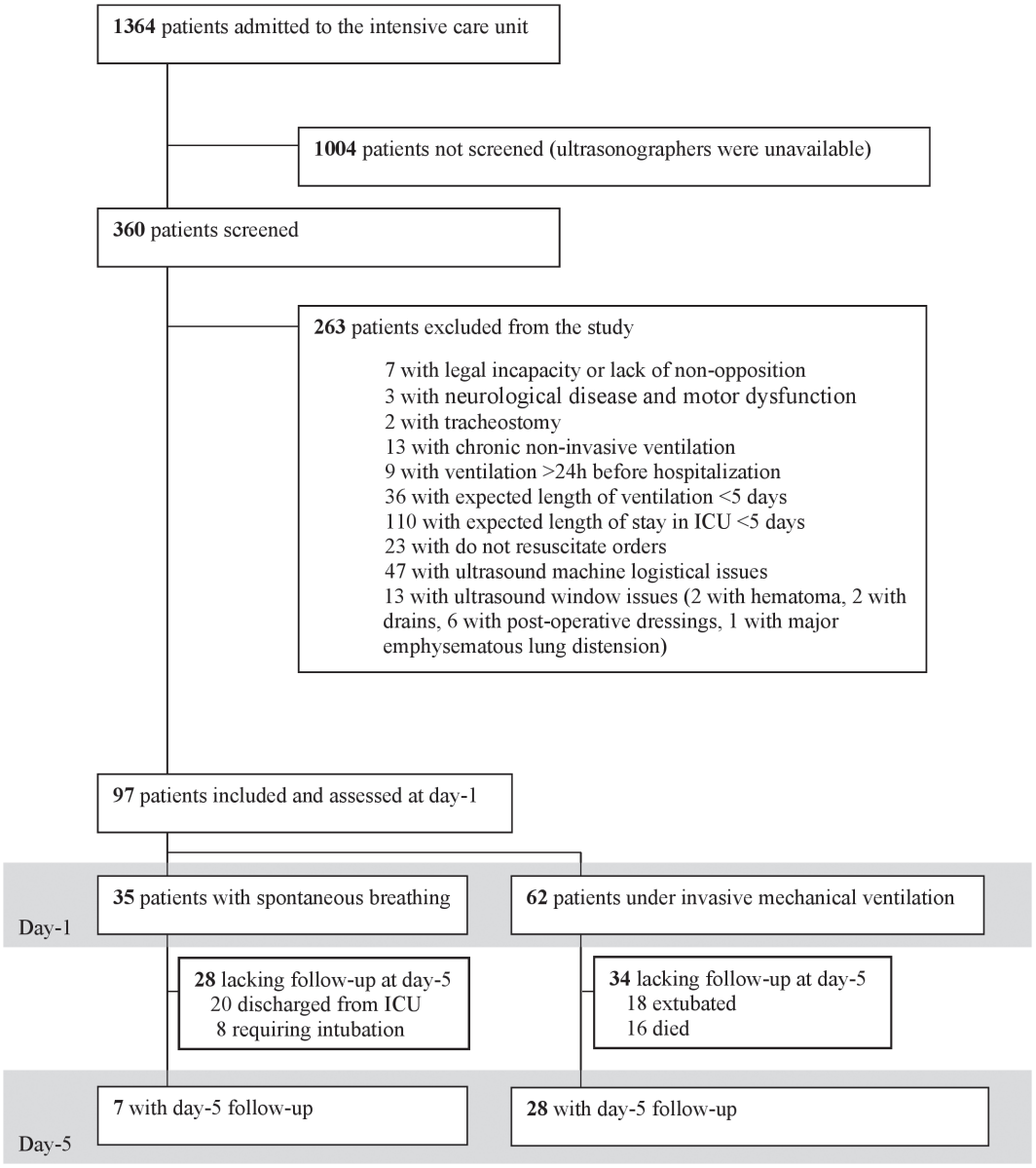


**Fig. 3.** Flow chart of the study population. ICU, intensive care unit.

or discharged from ICU (n = 20) between day 1 and day 5. Characteristics of patients followed up on day 5 (complete cases on day 5 [n = 35]) are reported in Supplemental Digital Content 2 (http://links.lww.com/ALN/B930).

## Diaphragm and Pectoral Thicknesses

Diaphragm thickness was successfully assessed using ultrasound in all patients on day 1 and alike for pectoral thickness, except in one patient. At day 1, the whole population (day 1 cases [n = 97]) had a diaphragm and pectoral median thicknesses of 2.4 (2.0, 2.9) and 5.9 (4.7, 7.2) mm, respectively. At day 1, a higher diaphragm thickness was positively associated with male sex, diabetes, and chronic obstructive pulmonary disease, whereas the pectoral muscle was thicker in overweight (Supplemental Digital Content 3, http://links.lww.com/ALN/B972) and younger patients (table 1). The correlation between diaphragm and pectoral thicknesses at day 1 was not statistically significant (rho = 0.171, $P$ = 0.095; fig. 4). There was no significant association between baseline thicknesses and outcome (data not shown).

## Diaphragm and Pectoral Atrophy

The marks on the chest wall were still present in all patients at day 5, on which the measurements of diaphragm and pectoral thicknesses could be repeated. In the overall population (complete cases on day 5 [n = 35]), a substantial thinning of the diaphragm was observed between day 1 and day 5 (from 2.5 [2.1, 3.0] to 2.1 [1.9, 2.5] mm, with a mean difference of 0.3 mm [95% CI, 0.2–0.5], $P$ < 0.001, fig. 5A), whereas the change in pectoral thickness was not significant (from 5.6 [4.8, 6.9] to 5.9 [4.9, 7.0] mm, with a mean difference of 0.1 mm [95% CI, −0.3 to +0.5], $P$ = 0.308, fig. 5B). The occurrence of diaphragm and pectoral atrophies (as defined by a 10% or more relative decrease in thickness) were 48% (17 of 35) and 29% (10 of 34), respectively. There was no statistically significant correlation between the change in thickness of diaphragm and pectoral (rho = −0.02, $P$ = 0.912; fig. 4B). In *post hoc* subgroup analyses, pectoral atrophy occurred more in patients treated with steroids, whereas diaphragm atrophy occurred more in patients with mechanical ventilation, septic shock (Supplemental Digital Content 4, http://links.lww.com/ALN/B973), or multiple organ failure, as compared with their respective counterparts; other variables did not consistently influence diaphragm or pectoral atrophy (tables 2 and 3). *Post hoc* outcome analyses found that diaphragm atrophy was not associated with patient's outcomes, whereas pectoral atrophy was associated with less successful weaning at day 14 (Supplemental Digital Content 5, http://links.lww.com/ALN/B931).

## Reproducibility

Intraclass correlation coefficient were 0.982 (95% CI, 0.955 to 0.993) and 0.985 (95% CI, 0.963 to 0.994) for diaphragm and pectoral thicknesses, respectively. Coefficients of repeatability were 0.3 and 0.9 mm for diaphragm and pectoral thicknesses, respectively.

# Discussion

Baseline diaphragm and pectoral thicknesses were not homogeneous in the studied population and seemed influenced by different preexisting comorbidities but with no definite conclusion given the limited sample size. In the 35 patients followed from day 1 to day 5, we observed atrophy of diaphragm over the first days of the critical illness, especially in patients with mechanical ventilation, septic shock, or organ

**Table 1.** Diaphragm and Pectoral Thickness According to Patient Baseline Characteristics (n = 97)

| | | Diaphragm Thickness (mm) | | Pectoral Thickness (mm) | |
|---|---|---|---|---|---|
| Sex | Male (n = 68) | 2.6 (2.1–3.0) | $P$ = 0.042 | 5.9 (4.7–7.2) | $P$ = 0.725 |
| | Female | 2.1 (1.8–2.7) | | 5.5 (4.6–7.2) | |
| Elderly | Yes (n = 63) | 2.4 (2.0–3.0) | $P$ = 0.934 | 5.6 (4.6–6.5) | $P$ = 0.016 |
| (Age older than 65 yr) | No | 2.3 (2.1–2.9) | | 6.9 (5.4–8.1) | |
| Overweight | Yes (n = 44) | 2.5 (2.1–3.0) | $P$ = 0.277 | 6.4 (5.4–7.8) | $P$ =0.004 |
| (BMI greater than 25 kg/m$^2$) | No | 2.3 (2.0–2.9) | | 5.4 (4.5–6.6) | |
| Hypertension | Yes (n = 37) | 2.6 (2.1–3.0) | $P$ = 0.078 | 6.1 (5.0–7.3) | $P$ = 0.215 |
| | No | 2.2 (1.9–2.8) | | 5.5 (4.6–7.1) | |
| Diabetes | Yes (n = 28) | 2.8 (2.1–3.2) | $P$ = 0.018 | 6.5 (4.8–8.1) | $P$ = 0.242 |
| | No | 2.3 (1.9–2.8) | | 5.8 (4.6–7.0) | |
| Smoking | Yes (n = 36) | 2.6 (2.0–3.2) | $P$ = 0.394 | 5.8 (4.6–7.9) | $P$ = 0.897 |
| | No | 2.3 (2.0–2.9) | | 6.0 (4.7–7.0) | |
| COPD | Yes (n = 29) | 2.8 (2.0–3.3) | $P$ = 0.019 | 5.9 (4.8–7.7) | $P$ = 0.753 |
| | No | 2.2 (2.0–3.0) | | 5.9 (4.6–7.1) | |
| Heart disease | Yes (n = 41) | 2.3 (2.0–2.8) | $P$ = 0.589 | 5.8 (4.7–6.9) | $P$ = 0.870 |
| | No | 2.4 (2.0–3.1) | | 6.0 (4.6–7.6) | |
| Ventilation | MVS (n = 62) | 2.3 (2.0–2.9) | $P$ = 0.340 | 5.8 (4.7–7.3) | $P$ = 0.961 |
| | SB | 2.7 (2.0–3.0) | | 6.0 (4.6–7.1) | |

Data are median (interquartile range). BMI, body mass index; COPD, chronic obstructive pulmonary disease; MVS, Mechanical ventilation support; SB, spontaneous breathing.

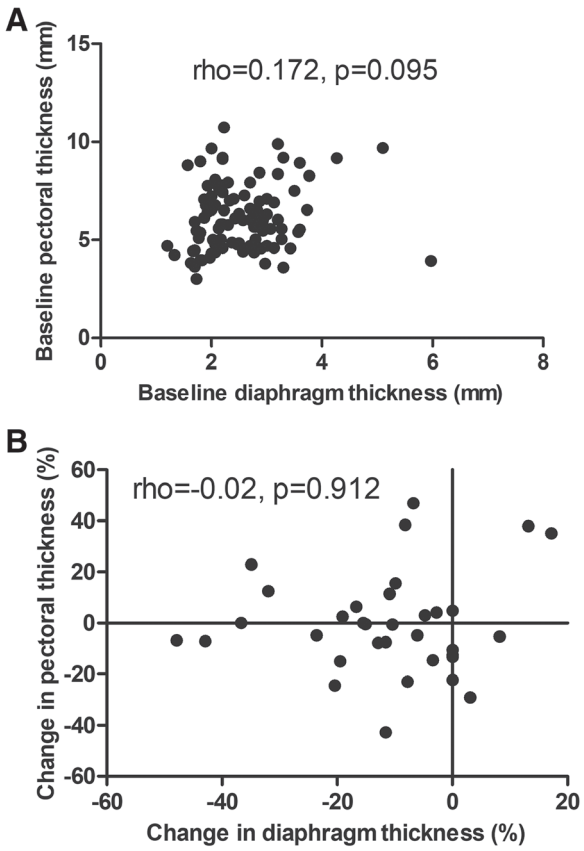


**Fig. 4.** Relationships between diaphragm and pectoral values of thickness in all of day 1 cases (n = 97; *A*) and atrophy in complete cases on day 5 (n = 35; *B*). There was no correlation between diaphragm and pectoral baseline thicknesses at day 1 (*A*), and there was also no correlation between changes in thickness of diaphragm and pectoral from day 1 to day 5 (*B*). Rho denotes Spearman's rank correlation coefficient.

failure. Pectoral atrophy happened more in patients treated with steroids during the first 5 days in ICU, and seemed associated with poor outcomes, unlike diaphragm atrophy.

## Diaphragm and Pectoral Thicknesses

In this series of 97 patients, the diaphragm was thicker in men than in women, confirming previously reported data.[25] We also found a higher baseline diaphragm thickness in patients with chronic obstructive pulmonary disease, which is consistent with previous autopsy data demonstrating an increase of the number and size of diaphragm muscle fibers in emphysematous patients.[26,27] Such muscular hypertrophy has been ascribed to excessive respiratory workload and lower muscular efficiency in chronic obstructive pulmonary disease patients.[28] This observation is also congruent with the greater diaphragm thickening recently reported in chronic obstructive pulmonary disease patients.[29] More surprisingly, diabetic patients also had a thicker diaphragm than their counterparts. Several epidemiologic studies have shown a slight decrease in forced expiratory volume in diabetic patients, suggesting that diaphragm hypertrophy could have been induced by a workload-driven mechanism similar to that occurring in chronic obstructive pulmonary disease.[30,31] On the other hand, other physiologic studies have suggested a decreased respiratory muscle strength in diabetics which could be the underlying mechanism.[32,33] Further studies are essential to scrutinize the effect of diabetes on diaphragm thickness. The two factors associated with pectoral thickness in our series were age and obesity. Age classically generates sarcopenia,[34] whereas for obesity its role in precipitating peripheral trophicity remains controversial (although some studies reported an increase in lean muscles in obese individuals[35,36]).

## Diaphragm Atrophy

Our work corroborates the previous studies findings concerning the use of ultrasound to quantify early diaphragm atrophy in critically ill patients.[16,21,25,37,38] On the contrary, pectoral atrophy was infrequent in our population. This discrepancy is congruent with the results of Levine *et al.*,[4] who found a marked histologic atrophy of the diaphragm but not the pectoral muscles in mechanically ventilated patients. A recent tomographic study also showed a more remarkable atrophy of the diaphragm compared with limb muscles in ICU septic patients.[39] However, another report showed 10% atrophy of the rectus femoris in the early course of critical illness,[2] which may reflect the fact that the rectus femoris is involved in permanent static tone which is abruptly abolished in critical illness. All together, these findings may suggest a major role for inactivity in the pathophysiology of muscle atrophy during critical illness, with a preferential alteration of muscles used for permanent contractions (*e.g.*, diaphragm) or resting tone (*e.g.*, muscles involved in static tone). Interestingly, in our very limited sample (n = 35), the use of steroids was strongly associated with pectoral atrophy. Steroids increase protein catabolism[40,41] and are controversial risk factors for ICU-acquired peripheral weakness.[42] However, some experimental studies have suggested a possible protective role of steroids against ventilator-induced diaphragm dysfunction *via* inhibition of the calpain system.[43,44]

## Muscular Atrophy and Outcome

We have not found any apparent association between diaphragm atrophy and clinical outcomes in complete cases on day 5 (n = 35). However, a significant impact of diaphragm atrophy on mechanical ventilation outcomes has been highlighted in a recent study of much larger sample size.[16] Several factors can explain this discrepancy (*e.g.*, diaphragm thinning or thickening could widely be influenced by the respiratory load endured by the respiratory muscles[16,29]), and the presence of competing pathologic processes may trigger thickening in opposite directions. In our study, diaphragm thickness was

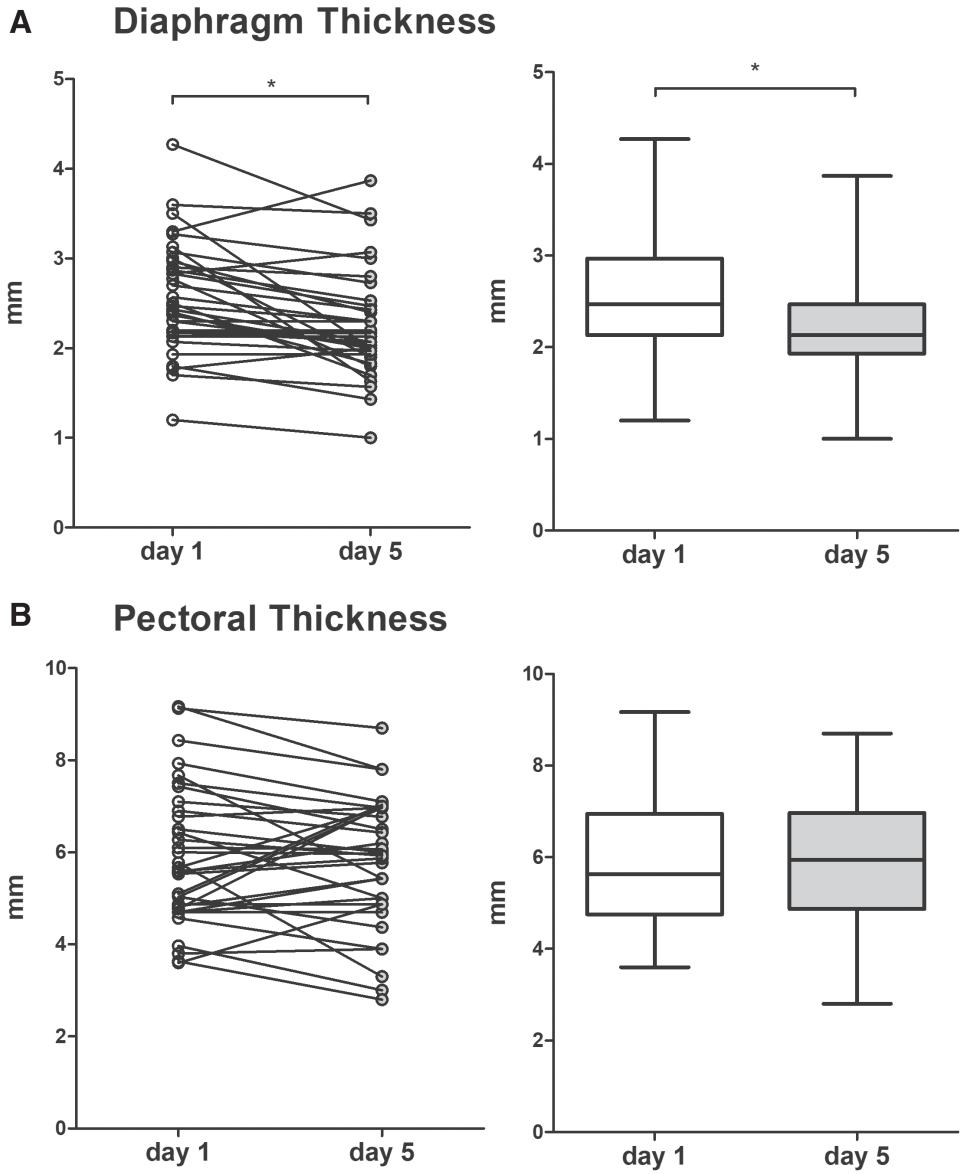


**Fig. 5.** Diaphragm (*A*) and pectoral (*B*) thickness at day 1 and in complete cases on day 5 (n = 35). Individual values (*left*) and box plot representation (*right*) for diaphragm thickness (*A*) and pectoral thickness (*B*) measurement at day 1 and day 5. Overall, a thinning of the diaphragm was observed between day 1 and day 5, whereas change in pectoral thickness was not significant. *$P < 0.001$ for paired Wilcoxon test for difference between diaphragm thickness at day 1 and day 5.

only ascertained on day 1 and day 5, and we may have failed to detect very early atrophy in many patients. Furthermore, our small sample size did not enable us to adjust associations for important confounders. Unlike diaphragm atrophy, pectoral atrophy was associated with prolonged weaning from mechanical ventilation and a trend toward prolonged ICU stay in our study. A similar association with worse outcomes was previously reported with atrophy of the rectus femoris.[2] Further studies with bigger sample sizes are needed to depict the respective impacts of diaphragm and peripheral muscles atrophies on the outcomes of critically ill patients.

## Strengths and Limitations

The strength of our study lies in the parallel and sequential assessment of diaphragm and pectoral thicknesses by trained sonographers. Our study has several limitations. First, the monocentric design and limited sample size, hence the need for an external validation. Second, the lack of functional test precludes direct extrapolation to respiratory or peripheral muscle weakness. Third, the agreement between observers' measurements is almost proportional to the changes in thickness they measured (*i.e.*, the smaller the change, the lower the

**Table 2.** Patients Characteristics According to Diaphragm Atrophy at Day 5

| | All Patients (n = 35) | Diaphragm Atrophy (n = 17) | No Diaphragm Atrophy (n = 18) | *P* Value |
|---|---|---|---|---|
| Age, yr | 73 (60 to 80) | 74 (55 to 80) | 73 (64 to 80) | 0.680 |
| Male sex | 28 (80%) | 12 (71%) | 16 (89%) | 0.176 |
| BMI, kg/m$^2$ | 24 (22 to 28) | 23 (21 to 26) | 26 (22 to 29) | 0.248 |
| Characteristics at inclusion | | | | |
| SAPS II | 57 (43 to 65) | 65 (45 to 80) | 51 (36 to 57) | 0.012 |
| SOFA score | 8 (4 to 9) | 9 (7 to 11) | 6 (2 to 9) | 0.013 |
| Lactate, mmol/l | 1.7 (1.2 to 4.3) | 2.4 (1.4 to 4.7) | 1.3 (1.1 to 2.4) | 0.072 |
| Sepsis | 24 (69%) | 14 (82%) | 10 (56%) | 0.088 |
| Septic shock | 14 (40%) | 10 (59%) | 4 (22%) | 0.027 |
| ICU management | | | | |
| MV | 28 (80%) | 17 (100%) | 11 (61%) | 0.008 |
| Sedation | 26 (74%) | 16 (94%) | 10 (55%) | 0.018 |
| Length of sedation, h | 46 (0 to 78) | 46 (19 to 82) | 24 (0 to 82) | 0.292 |
| Curarization | 11 (31%) | 6 (35%) | 5 (28%) | 0.632 |
| Length of curarization, h | 0 (0 to 24) | 0 (0 to 27) | 0 (0 to 29) | 0.630 |
| Steroids | 13 (37%) | 7 (41%) | 6 (33%) | 0.631 |
| Fluid balance, ml | 1,143 (–3,625 to 2,679) | 2,705 (–3,936 to 6,467) | –423 (–3,498–1,472) | 0.254 |
| Nutritional intake, Kcal | 5,900 (3,500 to 7,260) | 6,900 (5,552 to 7,525) | 4,355 (1,400 to 7,167) | 0.070 |
| Duration of parenteral nutrition, h | 120 (90 to 120) | 120 (75 to 120) | 120 (96 to 120) | 0.974 |
| Duration of enteral nutrition, h | 48 (0 to 96) | 96 (2 to 100) | 36 (0 to 96) | 0.381 |

Data are n (%) or median (interquartile range). BMI, body mass index; ICU, intensive care unit; MV, mechanical ventilation; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment. Patients were classified according to a threshold of diaphragm atrophy of –10%.

**Table 3.** Patients Characteristics According to Pectoral Atrophy at Day 5

| | All Patients (n = 34) | Pectoral Atrophy (n = 10) | No Pectoral Atrophy (n = 24) | *P* Value |
|---|---|---|---|---|
| Age, yr | 73 (60 to 80) | 68 (64 to 74) | 76 (57 to 82) | 0.381 |
| Male sex | 27 (79%) | 9 (90%) | 18 (75%) | 0.324 |
| BMI, kg/m$^2$ | 24 (22 to 28) | 22 (19 to 25) | 26 (23 to 29) | 0.089 |
| Characteristics at inclusion | | | | |
| SAPS II | 55 (43 to 65) | 54 (38 to 64) | 55 (43 to 65) | 0.895 |
| SOFA score | 8 (4 to 9) | 7 (2 to 9) | 8 (4 to 10) | 0.285 |
| Lactate, mmol/l | 1.7 (1.2 to 4.3) | 1.7 (1.2 to 5.3) | 1.7 (1.2 to 4.2) | 0.925 |
| Sepsis | 23 (68%) | 5 (50%) | 18 (75%) | 0.156 |
| Septic shock | 13 (38%) | 3 (30%) | 10 (42%) | 0.524 |
| ICU management | | | | |
| MV | 27 (79%) | 8 (80%) | 19 (79%) | > 0.999 |
| Sedation | 25 (73%) | 6 (60%) | 19 (79%) | 0.248 |
| Length of sedation, h | 45 (0 to 76) | 24 (0 to 96) | 45 (4 to 71) | 0.867 |
| Curarization | 10 (29%) | 3 (30%) | 7 (29%) | 0.961 |
| Length of curarization, h | 0 (0 to 24) | 0 (0 to 54) | 0 (0 to 20) | 0.809 |
| Steroids | 12 (35%) | 7 (70%) | 5 (21%) | 0.006 |
| Fluid balance, ml | 1,143 (–3,625 to 2,579) | –1,422 (–2,705 to 1,324) | 1,461 (–4,445 to 3,079) | 0.603 |
| Nutritional intake, Kcal | 5,900 (3,500 to 7,260) | 4,400 (3,905 to 6,180) | 6,900 (4,400 to 7,330) | 0.179 |
| Duration of parenteral nutrition, h | 120 (90 to 120) | 120 (105 to 120) | 120 (58 to 120) | 0.398 |
| Duration of enteral nutrition, h | 72 (0 to 96) | 72 (24 to 96) | 72 (0 to 108) | 0.905 |

Data are n (%) or median (interquartile range). BMI, body mass index; ICU, intensive care unit; MV, mechanical ventilation; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment. Patients were classified according to a threshold of pectoral atrophy of -10%

agreement), despite our efforts to optimize this reproducibility by using a high-frequency probe and by marking the observation site. Lastly, some factors could theoretically have biased the pectoral thickness measurement, including orientation of the beam, compression of the muscle by the probe, or muscle infiltration with edema.[45] Understanding the primary mechanism of ICU-acquired weakness remains a challenge for the intensivists. Our results may help clarify the distinctive patterns of ventilator-induced diaphragm dysfunction and skeletal muscle weakness, which are two outstanding pathologic

entities linked to critical illness myopathy.[8] Further studies are needed to corroborate these ultrasound results with higher technical accuracy such as computed tomography or magnetic resonance imaging. Gradation and comparative analysis of muscle function and mass could also be of high interest.

## Conclusion

Baseline diaphragm thickness was influenced by sex and comorbidities (including chronic obstructive pulmonary disease and diabetes). The diaphragm displayed clinically significant atrophy during the first 5 days of critical illness, especially in patients with septic shock, organ failure, or invasive mechanical ventilation. Given the small sample size, the study did not detect a link between atrophy of the diaphragm and clinical outcomes. Pectoral atrophy seemed confined to patients treated with steroids, and was associated with a poor outcome.

## Research Support

Support was provided solely from institutional and departmental sources (Intensive Care Unit, Saint Joseph Saint Luc Hospital, Lyon, France).

## Competing Interests

The authors declare no competing interests.

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After surgeons revealed in 1904 that researcher Ernest A. Fourneau (1872 to 1949) had synthesized an alternative local anesthetic to cocaine, his Parisian firm, Poulenc Frères, branded his amylocaine as "Stovaine" for their English-speaking consumers. Over the years, that branding has been viewed quite differently by anesthesia museum curators in the southern and northern hemispheres. In Australia, "Stovaine" was characterized by Drs. C. M. Ball and R. N. Westhorpe as "modestly named with an anglicized version of his own name (Fourneau meaning furnace or stove)." However, in the United States, "Stovaine" was viewed as a pragmatic branding, so that Fourneau's company could avoid peddling the anesthetic with the socially awkward name of "Fourneaucaine." (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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