

Respiratory Critical Care in the Elderly

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Key Points

- The incidence of acute respiratory distress syndrome rises with age and is likely related to the increased incidence of sepsis with increasing age.
- Age-related changes in pulmonary function include a decrease in forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁), and arterial partial pressure of oxygen (PaO₂) and an increase in the oxygen arterial-alveolar (A-a) gradient.
- Both the incidence of pulmonary embolism and the mortality from pulmonary embolism increase with age.
- There are no specific guidelines related to optimal ventilator modalities for older patients.
- For older patients with ventilator-associated pneumonia, aspiration or microaspiration often is a contributing factor.
- Local hospital antibiograms should be used when treating patients with ventilator-associated pneumonia.

Introduction

Respiratory diseases in older patients are a major reason for admission to the intensive care unit (ICU), and critical complications related to underlying respiratory disease have a major impact on patient outcomes. The incidence of acute respiratory failure increases dramatically with age [1]. Older adults (defined as age > 65 years) comprise nearly 50 percent of ICU admissions in the United States [2,3]. Among all ICU patients who receive mechanical ventilation, 125,000 survive to discharge. Half of these survivors are ultimately readmitted to the hospital, and 30 to 60 percent die within 6 months. Interestingly, there is also evidence that older adults are receiving more intense care in critical care unit settings, and this may be the cause of decreased mortality [2]. Therefore, understanding the issues related to older adults with respiratory problems is essential to delivering appropriate medical care and providing accurate prognostication for this population [4,5].

Background: Respiratory Physiology and Age

The respiratory system undergoes many changes with aging that reduce reserve and have substantial impact on an individual's capacity to tolerate the stresses of critical illness.

Table 4.1 Respiratory System Age-Related Changes

Decreased vital capacity (VC)
Decreased forced expiratory volume in 1 second (FEV ₁)
Increased functional residual capacity (FRC)
Increased residual volume (RV)
Reduced elastic recoil of the lung
Reduced arterial partial pressure of oxygen (PaO ₂)
Increased O ₂ arterial-alveolar (A-a) gradient
Increased chest wall stiffness, kyphoscoliosis
Decreased respiratory muscle strength
Decreased respiratory center sensitivity to hypoxia and hypercarbia

Table 4.1 lists some of the age-related changes in respiratory physiology. Age-related changes in respiratory function are defined by decreased strength of the respiratory muscles, a decrease in the elastic recoil of the lung, and a decrease in chest wall compliance [6]. Ventilatory reserve decreases substantially with age as a result of multiple interrelated physiologic changes: osteoporosis, kyphosis, and decreased mobility of joints (e.g., rib-vertebral articulation). Together these changes lead to decreases in lung volume and combined lung and chest wall compliance [7]. Elastance decreases, leading to increased lung compliance, as a result of changes in elastin structure and elastin-collagen ratios [8,9]. The combination of increased lung compliance and decreased chest wall compliance leaves total lung capacity unchanged, but the resulting increase in residual volume means that the vital capacity is reduced, along with a concomitant reduction in expiratory flow rates, as measured by forced expiratory volume in 1 second (FEV₁) [8]. There is also an age-related decrease in FEV₁ of 10 to 30 ml per year and a concomitant decrease in diffusing capacity after the age of 40 [10,11] (Figure 4.1). These limitations mean that the requirement for increased minute ventilation during exercise or illness is met in large part by increases in respiratory rate. Additionally, because age-related decreased chest wall compliance is proportionally larger than the increased lung compliance, the net compliance of the respiratory system is decreased, and therefore, resting work of breathing is increased and the diaphragm and abdominal muscles contribute proportionally *more* to the work of breathing than the thoracic muscles when compared with younger patients [12].

Respiratory muscle performance is impaired by age-related changes in muscle and bone relationships and increased FRC from decreased elastic recoil of the lung [12]. Respiratory muscle status is related to nutritional status and lean body mass; therefore, malnutrition reduces muscle strength and maximal ventilation [13]. Age is significantly correlated with reduced respiratory muscle function and walking capacity [14]. There is a progressive decline in diaphragmatic strength (25 percent) in healthy elderly persons. An investigation into the response of the respiratory muscles to graded exercise demonstrated greater participation of diaphragmatic motion together with rapid shallow breathing during lower-graded exercise in the elderly compared with the young [15]. With regards to gas exchange, an increase in dead space and shunt fraction and a reduction in diffusing capacity have been associated with increasing age [16]. It is estimated that the arterial partial

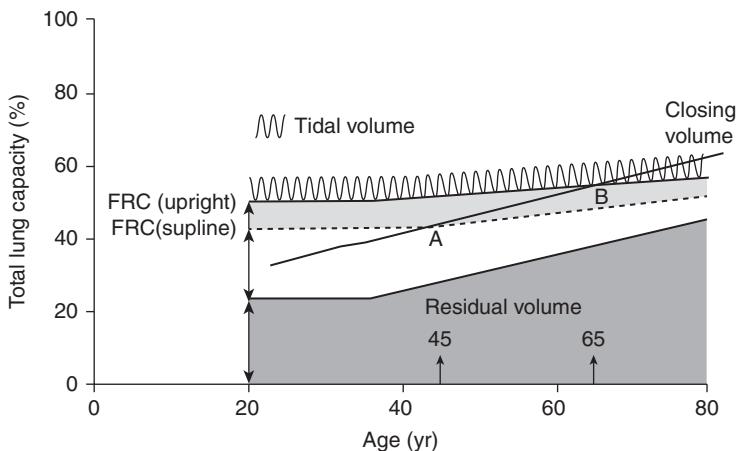


Figure 4.1 Changes in lung volumes and capacities with aging. Residual volume and functional residual capacity (FRC) increase with age, whereas total lung capacity remains the same. Closing volume increases with age and exceeds FRC in the supine position at about age 45 and exceeds FRC in the upright position at about age 65. (Source: Adapted from Corcoran TB, Hillyard S. Cardiopulmonary aspects of anaesthesia for the elderly. *Best Pract Res Clin Anaesthesiol* 2011; 25:329–54. Used with permission.)

pressure of oxygen (PaO_2) decreases by an average rate of 0.35 mmHg per year. Mean arterial oxygen tension on room air decreases from 95 mmHg at age 20 to less than 70 mmHg at age 80. These changes are caused by an increased degree of ventilation/perfusion (V/Q) mismatching and, to a lesser extent, pulmonary shunting. These changes would be expected to impair carbon dioxide elimination and oxygenation in the setting of a significant respiratory insult (e.g., acute respiratory distress syndrome [ARDS]). A study of airspace size relative to age found airspace enlargement in older subjects [17]. In addition to the physiologic changes in lung function, the neural sensing and modulating responses by the central nervous system (CNS) of the respiratory system also change with age. Older subjects have a significantly lower ventilatory response to both hypoxia and hypercapnia, and occlusion-pressure response to both hypercapnia and hypoxemia is reduced by a similar magnitude. The alteration in CNS efferent control is thought to be secondary to the lower augmentation of respiratory drive in older adults [18].

Older adults are more likely to have concomitant illnesses that have an impact on their respiratory system. Congestive heart failure has a significant negative effect on respiratory muscle strength and tension-time index, which is important given that cardiac disease and respiratory disease are commonly coincident [19]. In one study, the prevalence of inspiratory muscle weakness was as high as 76 percent in patients who were hospitalized because of acute heart failure [20]. Hypertension, lower extremity edema, and diabetes are independently associated with a lower level of lung function [21]. It is clear that concomitant diseases associated with aging taken together have a substantial impact on respiratory function.

Risk Factors for Respiratory Failure in Older Adults

Acute respiratory failure is a common complication of critical illness in older adults and is due in large part to the increase in prevalence of chronic illnesses, major organ dysfunction, and an increased risk of acquired causes of respiratory failure [22,23]. The incidences of

pulmonary embolism, chronic obstructive pulmonary disease (COPD), congestive heart failure, and community-acquired pneumonia all rise with age [22,24]. Furthermore, as many as 47 percent of patients over age 65 who have acute respiratory failure have two diagnoses as the etiology of their respiratory decompensation. This is in large part due to the high incidence of congestive heart failure and COPD in this population. The increased incidence of major organ dysfunction combined with decreased pulmonary reserve is likely responsible for the exponential increase in respiratory failure from the third through the ninth decades of life [1,25,26]. Specifically, in the surgical population, an investigation regarding risk factors for postoperative intubation demonstrated that smoking status, presence of COPD, emergent intervention, and age were important determinants of risk [27]. A separate investigation had similar findings, confirming the role of age as a risk factor for unplanned postoperative intubations, and noted an 18-fold increase in mortality risk associated with unexpected requirement for mechanical ventilation [28]. In a review of surgical ICU admissions, it was noted that 48 percent of the readmissions were due to respiratory complications and that readmitted patients were older [29].

Acute Pulmonary Embolism

The occurrence of pulmonary embolism (PE) increases with age, and elderly patients have the highest risk of venous thromboembolic disease (VTE), with an incidence greater than 1 percent per year [30]. With regard to the clinical presentation of PE, older adults report less pleuritic chest pain and are more likely to present with syncope [31]. In an evaluation of older patients, it was noted that only 5 percent of those older than 80 years age have a negative D-dimer test compared with 50 percent of patients younger than 50 years of age [32]. A multicenter prospective management outcome study of patients with suspected PE demonstrated that an age-adjusted D-dimer cutoff was associated with a larger number of patients in whom PE could be ruled out [33].

Elderly patients with a PE have a high (>20 percent) 3-year mortality predominantly due to the high frequency of cancer and other comorbidities [34]. Risk assessment is generally performed based on echocardiography and measurement of circulating biomarkers associated with right ventricular strain. While echocardiographic evidence of right ventricular dysfunction is often used clinically to stratify risk, the extent of right ventricular dysfunction does not appear to be associated with mortality in older adults [35]. Cardiac biomarkers are more useful for identifying low-risk individuals with nonmassive PEs than echocardiography data, and these findings have been replicated in older adult populations [36,37].

New interventions for both massive and submassive PEs include ultrasound-assisted catheter-directed low-dose thrombolysis, which is still under investigation, but early studies have shown efficacy with possibly a lower risk of hemorrhage, although those studies may not be adequately powered to detect this complication [38,39]. Meta-analyses of prior investigations of thrombolysis for massive PEs have suggested that bleeding complications, including intracranial hemorrhage, are higher in those with advanced age, but whether it is age or simply the concomitant risk factors, including malignancy, that increase risk is unknown [40,41]. While there are no specific independent guidelines for elderly adults who are critically ill with massive PEs, the current literature suggests that they be treated similar to the general population, but with recognition of the potential for increased risk of complications due to age and burden of comorbidities.

Pneumonia in Older Adults

Several studies have demonstrated that older patients have an increased incidence of pneumonia and greater mortality after pneumonia compared with younger patients. The physiologic changes discussed earlier and a reduced ability to expectorate and clear bacteria and decreased physiologic reserve are factors that increase this risk. In addition, oropharyngeal bacterial colonization with *Staphylococcus aureus*, *Klebsiella pneumonia*, and *Escherichia coli* are more common in elderly patients and serve as harbingers of subsequent pneumonia. Patients with severe community-acquired pneumonia who are older than 65 years of age have many preexisting diseases, including COPD (48 percent), heart disease (16 percent), diabetes (18 percent), and malignancy (12 percent) [42]. Elderly patients are more at risk for aspiration, including silent aspiration [43]. Factors supporting this include alterations in the swallowing mechanism that occur with age, cognitive impairment, medication use, malnutrition, poor oral health, and Parkinson's disease [44].

Frail older patients may not present with the typical fever, cough, and shortness of breath that characterize pneumonia in younger patients. Many older patients with pneumonia present with nonproductive cough, delirium, anorexia, falls and dizziness, or signs of sepsis. Older patients who present with hypothermia and sepsis from pneumonia have significant in-hospital mortality [45].

While older patients frequently have bacterial pneumonia and sepsis precipitating an ICU admission, they also are frequently critically ill secondary to viral respiratory infections. Patients older than 65 years have higher rates of hospitalization for laboratory-confirmed influenza. In the United States during the 2014–15 influenza season, the rates of hospitalization for patients older than 65 years was 258 per 100,000 population compared with 41 per 100,000 population for younger patients [46].

A recent systematic review examined current evidence on antibiotic treatment of older adults with community-acquired pneumonia (CAP), healthcare-associated pneumonia (HCAP), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP). This study demonstrated that patients older than age 65 are often excluded from clinical trials of bacterial pneumonia, and no data were found on the comparative efficacy of antibiotic treatment in elderly adults compared with younger patients [47]. What the study did note was increased treatment failure rates in participants who were aged 65 years and older.

Ventilator-associated pneumonia is a complication for older patients in the ICU who are mechanically ventilated. There are no studies examining the recognition or treatment of VAP in older patients, and general guidelines should be followed. The 2016 Infectious Disease Society of America guidelines on HCAP and VAP make recommendations regarding treatment, including using hospital-specific antibiograms to guide empirical antibiotic choices. There are no recommendations based on patient age [48]. One study using a molecular microbiology study of 44 patients age 60 years and older demonstrated that gastro-pulmonary aspiration is an important mechanism in the development of VAP, especially late-onset VAP [49]. Risk for aspiration should be recognized and evaluated in all older patients on mechanical ventilation and after extubation.

Acute Respiratory Distress Syndrome in Older Adults

Acute respiratory distress syndrome (ARDS) is a disease resulting in acute hypoxic respiratory failure most commonly due to sepsis, pneumonia, aspiration, trauma,

Table 4.2 Acute Respiratory Distress Syndrome: The Berlin Definition

- Onset within 1 week of a known clinical insult or new/worsening respiratory symptoms.
- Chest imaging with bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules.
- Respiratory failure not fully explained by cardiac failure or fluid overload; objective assessment needed, such as echocardiography.
- Oxygenation:
 - Mild: $200 \text{ mmHg} < \text{PaO}_2/\text{FIO}_2 \leq 300 \text{ mmHg}$ with PEEP or CPAP $\geq 5 \text{ cmH}_2\text{O}$
 - Moderate: $100 \text{ mmHg} < \text{PaO}_2/\text{FIO}_2 \leq 200 \text{ mmHg}$ with PEEP or CPAP $\geq 5 \text{ cmH}_2\text{O}$
 - Severe: $\text{PaO}_2/\text{FIO}_2 \leq 100 \text{ mmHg}$ with PEEP $\geq 5 \text{ cmH}_2\text{O}$

Abbreviations: PaO_2 = partial pressure of arterial oxygen; FIO_2 = fraction of inspired oxygen; PEEP = positive end-expiratory pressure; CPAP = continuous positive airway pressure.

(Source: From Ranier et al. [50].)

pancreatitis, and transfusion of allogeneic blood products. The injury of ARDS involves the alveolar epithelium and the lung capillary endothelium. The definition of ARDS was revised (Berlin definition) in 2012 and demonstrates better predictive validity for mortality compared with the 1994 American-European Consensus Conference definition. Table 4.2 lists the Berlin definition of ARDS [50]. The significantly increased incidence of ARDS associated with older age is partly due to the higher incidence of sepsis with aging, the primary risk factor for ARDS in adults [51,52]. An investigation of ARDS in the trauma population showed that the incidence of ARDS increases with age but plateaus in the 60- to 69-year-old population [53]. In a global incidence study, 10.4 percent patients with ICU admissions and 23.4 percent of patients requiring mechanical ventilation had ARDS. These results are similar to those of prior investigations, where clinical recognition of ARDS was only 51.3 percent for mild ARDS but increased to 78.5 percent for severe disease [54].

The first large randomized, controlled trial to evaluate a therapy for ARDS was published in 2000 and demonstrated that the ARDSnet approach to low-tidal-volume ventilation results in a substantial reduction in mortality [55]. The original ARDSnet investigation was notable for a young mean age and excluded patients with significant chronic lung disease, leaving open the question of whether this study is generalizable to the large population of older adults who develop sepsis and ARDS. Furthermore, because the low-tidal-volume strategy used tidal volumes and plateau pressures and older adults are known to have increased lung compliance and decreased chest wall compliance, it remains unknown whether the ARDSnet strategy would have the same effect in older adults with different pulmonary responses to similar volumes and pressures. A reanalysis of prior studies in ARDS found that while overall survival was high, older adults were twice as likely to die of acute lung injury and had greater difficulty achieving liberation from mechanical ventilation and being discharged from the ICU than younger adults [56]. In addition to low-tidal-volume ventilation, investigators have examined several other therapies for ARDS. A follow-up study by the ARDSnet investigators examined the role of corticosteroids as adjunctive therapy and showed that pulmonary parameters improved but that the increased rate of muscle weakness led to an increase in reintubations, and this would be of even greater concern in an older adult population [57]. Prone positioning has been investigated several

times over the past decade, and the most definitive study of prone positioning for ARDS demonstrated improved outcomes, and importantly, the average age was approximately 60 years, but with large standard deviations consistent with the fact that a fair number of these patients were older adults. This trial showed significant reductions in mortality and ICU length of stay, and this approach has been adopted as a component of standard care for those with ARDS [58].

Additional supportive therapies that have received great attention in the past decade include a resurgent interest in the use of extracorporeal membrane oxygenation (ECMO). Most institutions and protocols have generally excluded the use of ECMO in older patients (age greater than 60 or 65 years). The authors of the CESAR trial recommended transferring patients with severe but potentially reversible hypoxic respiratory failure, based on Murray score, to an ECMO center to improve survival without disability. The study itself started with 766 patients, of which 586 were excluded, and of those excluded, 10 percent of those referred for enrollment were excluded due to age (>65 or <18 years). These age-based exclusions are fairly standard for ECMO, and thus the implications of ECMO for older adults are unclear [59]. In a retrospective review of the Extracorporeal Life Support Organization (ELSO) registry from 1990 to 2013 for adults of age greater than 65 years, survival for older adults was 41 percent versus 55 percent for the entire population. Nonsurvivors were more likely to have hemorrhagic complications (cannulation site, pulmonary hemorrhage, disseminated intravascular coagulation, excessive hemolysis while on ECMO support). Death from withdrawal of life support occurred in 11 percent of patients. While the mortality rate in this review was certainly higher for older adults, the survival rate was still in a range that many clinicians would consider acceptable for a lethal disease when there are limited alternative options [60].

Mechanical Ventilation in Older Adults

There are no data to suggest that one mode of mechanical ventilation is better than any other mode of ventilation in older patients. As noted earlier in relation to ARDS, the study population used in the landmark study of low-tidal-volume ventilation did not include many older patients, and it also excluded many patients based on comorbidities, which are common in the elderly. Interestingly, a recent study using Medicare data demonstrated that among hospitalized nursing home residents with advanced dementia, there was an increase in the use of mechanical ventilation over time without substantial improvement in survival [61]. The use of mechanical ventilation increased from 39 per 1,000 hospitalizations in 2000 to 78 per 1,000 hospitalizations in 2013 [61]. As the number of ICU beds in a hospital increased over time, patients with advanced dementia were more likely to receive mechanical ventilation.

Discontinuation of Mechanical Ventilation and Prolonged Mechanical Ventilation

Expertise in liberation from mechanical ventilation has evolved over the past 20 years, yet it remains unclear specifically how the current knowledge applies to older adults. Because at baseline older adults have a respiratory exertional response that is similar to rapid shallow breathing, using this measure may be a less accurate marker of ongoing respiratory failure during weaning in the elderly [7,62]. Thus, physiologically, a patient may be judged to have

failed a spontaneous breathing trial (SBT) when they have not. Yet this observation is further complicated by the fact that older adults also have a diminished response to hypoxia and hypercapnia, and therefore an older adult patient on a SBT may be more likely to appear comfortable despite having developed significant hypoxia or hypercapnia [18]. The most direct evidence regarding older adults and extubation comes from a study by Ely et al., who investigated outcomes of older patients in a large multicenter trial of ARDS [56]. Although older patients achieved physiologic recovery from acute lung injury in equal proportions to younger patients, their ICU length of stay and duration of mechanical ventilation were increased because of higher reintubation rates. In a medical ICU population, El Solh et al. observed that patients older than age 70, compared with a younger matched cohort, were more likely to fail extubation because of an inability to handle secretions [63]. While liberation from mechanical ventilation in older adults remains an area in which there are limited data, it is clear from an understanding of physiology and our limited data that the intensivist should carefully consider the impact of aging on respiratory function when making decisions on liberation from ventilation.

Prolonged mechanical ventilation (PMV) is defined as requiring mechanical ventilator support for longer than 21 days. Approximately 300,000 individuals annually in the United States require mechanical ventilation in the acute setting for more than 4 days [64]. Among these individuals, 3 to 7 percent will survive and remain ventilator dependent after 21 days [65]. Tracheostomy use in those requiring mechanical ventilation rose substantially from 1993 to 2008 (from 6.9 percent in 1993 to 9.8 percent) but then began a slow decline. This increase in the tracheostomy rate was driven primarily by patients in the surgical population and was associated with a decreased length of hospital stay [66]. A study of 437 admissions to a long-term acute care hospital (LTACH) for PMV between 2001 and 2006 investigated the impact of age on survival and discontinuation of mechanical ventilation. Increasing age was associated with more physiologic abnormalities and comorbidities, but after adjustment for these factors, the authors did not find an independent effect of age on ability to wean [67]. In the postacute settings, elderly adults were most likely to have successful discontinuation of mechanical ventilation if they had fewer comorbidities and less respiratory impairment, and interestingly, these factors were more important than physical function prior to the acute care hospitalization [68]. While the authors do not comment on this specifically, their data show that regardless of age, fewer than 10 percent of adults who failed to wean are alive at 24 months. While age alone was not associated with survival per se, for adults older than 84 years of age with PMV, those who were able to be weaned had a survival rate of only 20 percent at 24 months [68].

Conclusion

The respiratory system changes substantially with aging such that older adults have diminished ventilatory and oxygenation reserve and are at higher risk than younger adults of developing most common respiratory ailments, including pneumonia, ARDS, and respiratory failure. While much is known about these common respiratory ailments and there have been many controlled trials, age-specific knowledge is much more limited. Despite this, the evidence does suggest that while age increases the risk of developing certain adverse outcomes, it is important to keep in mind that it often the concomitant illness and comorbidities that drive the response to therapy and outcome more than simply the chronologic age.

References

1. Behrendt CE. Acute respiratory failure in the United States: incidence and 31-day survival. *Chest* 2000; **118**(4):1100–5.
2. Lerolle N, Trinquet L, Bornstain C, et al. Increased intensity of treatment and decreased mortality in elderly patients in an intensive care unit over a decade. *Crit Care Med* 2010; **38**(1):59–64.
3. Angus DC, Shorr AF, White A, et al. Critical care delivery in the United States: distribution of services and compliance with Leapfrog recommendations. *Crit Care Med* 2006; **34**(4):1016–24.
4. Wunsch H, Guerra C, Barnato AE, et al. Three-year outcomes for Medicare beneficiaries who survive intensive care. *JAMA* 2010; **303**(9):849–56.
5. Kahn JM, Benson NM, Appleby D, Carson SS, Iwashyna TJ. Long-term acute care hospital utilization after critical illness. *JAMA* 2010; **303**(22):2253–59.
6. Janssens JP. Aging of the respiratory system: impact on pulmonary function tests and adaptation to exertion. *Clin Chest Med* 2005; **26**(3):469–84, vi–vii.
7. Sprung J, Gajic O, Warner DO. Review article: age related alterations in respiratory function – anesthetic considerations. *Can J Anaesth* 2006; **53**(12):1244–57.
8. Knudson RJ, Burrows B, Lebowitz MD. The maximal expiratory flow-volume curve: its use in the detection of ventilatory abnormalities in a population study. *Am Rev Respir Dis* 1976; **114**(5):871–79.
9. Zeleznik J. Normative aging of the respiratory system. *Clin Geriatr Med* 2003; **19**(1):1–18.
10. Janssens JP, Pache JC, Nicod LP. Physiological changes in respiratory function associated with ageing. *Eur Respir J* 1999; **13**(1):197–205.
11. Knudson RJ, Kaltenborn WT, Knudson DE, Burrows B. The single-breath carbon monoxide diffusing capacity: reference equations derived from a healthy nonsmoking population and effects of hematocrit. *Am Rev Respir Dis* 1987; **135**(4):805–11.
12. Turner JM, Mead J, Wohl ME. Elasticity of human lungs in relation to age. *J Appl Physiol* 1968; **25**(6):664–71.
13. Arora NS, Rochester DF. Respiratory muscle strength and maximal voluntary ventilation in undernourished patients. *Am Rev Respir Dis* 1982; **126**(1):5–8.
14. Watsford ML, Murphy AJ, Pine MJ. The effects of ageing on respiratory muscle function and performance in older adults. *J Sci Med Sport* 2007; **10**(1):36–44.
15. Teramoto S, Fukuchi Y, Nagase T, Matsuse T, Orimo H. A comparison of ventilation components in young and elderly men during exercise. *J Gerontol A Biol Sci Med Sci* 1995; **50A**(1):B34–39.
16. Stam H, Hrachovina V, Stijnen T, Versprille A. Diffusing capacity dependent on lung volume and age in normal subjects. *J Appl Physiol* 1994; **76**(6):2356–63.
17. Gillooly M, Lamb D. Airspace size in lungs of lifelong non-smokers: effect of age and sex. *Thorax* 1993; **48**(1):39–43.
18. Peterson DD, Pack AI, Silage DA, Fishman AP. Effects of aging on ventilatory and occlusion pressure responses to hypoxia and hypercapnia. *Am Rev Respir Dis* 1981; **124**(4):387–91.
19. Mancini DM, Henson D, LaManca J, Levine S. Respiratory muscle function and dyspnea in patients with chronic congestive heart failure. *Circulation* 1992; **86**(3):909–18.
20. Verissimo P, Casalaspo TJ, Gonçalves LH, et al. High prevalence of respiratory muscle weakness in hospitalized acute heart failure elderly patients. *PLoS One* 2015; **10**(2):e0118218.
21. Enright PL, Kronmal RA, Higgins M, Schenker M, Haponik EF. Spirometry reference values for women and men 65 to 85 years of age: cardiovascular health study. *Am Rev Respir Dis* 1993; **147**(1):125–33.
22. Marrie TJ, Lau CY, Wheeler SL, Wong CJ, Feagan BG. Predictors of symptom resolution in patients with community-acquired pneumonia. *Clin Infect Dis* 2000; **31**(6):1362–67.

23. Ray P, Birolleau S, Lefort Y, et al. Acute respiratory failure in the elderly: etiology, emergency diagnosis and prognosis. *Crit Care* 2006; **10**(3):R82.
24. Rich MW. Heart failure in the 21st century: a cardiogeriatric syndrome. *J Gerontol A Biol Sci Med Sci* 2001; **56**(2):M88–96.
25. Siner JM, Pisani MA. Mechanical ventilation and acute respiratory distress syndrome in older patients. *Clin Chest Med* 2007; **28**(4):783–91, vii.
26. El Solh AA, Ramadan FH. Overview of respiratory failure in older adults. *J Intensive Care Med* 2006; **21**(6):345–51.
27. Alvarez MP, Samayoa-Mendez AX, Naglak MC, Yuschak JV, Murayama KM. Risk factors for postoperative unplanned intubation: analysis of a national database. *Am Surg* 2015; **81**(8):820–25.
28. Nafiu OO, Ramachandran SK, Ackwerh R, et al. Factors associated with and consequences of unplanned post-operative intubation in elderly vascular and general surgery patients. *Eur J Anaesthesiol* 2011; **28**(3):220–24.
29. Timmers TK, Verhofstad MH, Moons KG, Leenen LP. Patients' characteristics associated with readmission to a surgical intensive care unit. *Am J Crit Care* 2012; **21**(6):e120–28.
30. Oger E. Incidence of venous thromboembolism: a community-based study in western France. EPI-GETBP Study Group. Groupe d'Etude de la Thrombose de Bretagne Occidentale. *Thromb Haemost* 2000; **83**(5):657–60.
31. Schouten HJ, Geersing GJ, Oudega R, et al. Accuracy of the Wells clinical prediction rule for pulmonary embolism in older ambulatory adults. *J Am Geriatr Soc* 2014; **62**(11):2136–41.
32. Righini M, Le Gal G, Bounameaux H. Venous thromboembolism diagnosis: unresolved issues. *Thromb Haemost* 2015; **113**(6):1184–92.
33. Righini M, Van Es J, Den Exter PL, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. *JAMA* 2014; **311**(11):1117–24.
34. Faller N, Limacher A, Méan M, et al. Predictors and causes of long-term mortality in elderly patients with acute venous thromboembolism: a prospective cohort study. *Am J Med* 2016.
35. Hofmann E, Limacher A, Méan M, et al. Echocardiography does not predict mortality in hemodynamically stable elderly patients with acute pulmonary embolism. *Thromb Res* 2016; **145**:67–71.
36. Konstantinides S, Goldhaber SZ. Pulmonary embolism: risk assessment and management. *Eur Heart J* 2012; **33**(24):3014–22.
37. Vuilleumier N, Simona A, Méan M, et al. Comparison of cardiac and non-cardiac biomarkers for risk stratification in elderly patients with non-massive pulmonary embolism. *PLoS One* 2016; **11**(5):e0155973.
38. Kucher N, Boekstegers P, Müller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. *Circulation* 2014; **129**(4):479–86.
39. Kuo WT, Banerjee A, Kim PS, et al. Pulmonary embolism response to fragmentation, embolectomy, and catheter thrombolysis (PERFECT): initial results from a prospective multicenter registry. *Chest* 2015; **148**(3):667–73.
40. Chatterjee S, Chakraborty A, Weinberg I, et al. Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding, and intracranial hemorrhage: a meta-analysis. *JAMA* 2014; **311**(23):2414–21.
41. Fiumara K, Kucher N, Fanikos J, Goldhaber SZ. Predictors of major hemorrhage following fibrinolysis for acute pulmonary embolism. *Am J Cardiol* 2006; **97**(1):127–29.
42. Rello J, Rodriguez R, Jubert P, Alvarez B. Severe community-acquired pneumonia in the elderly: epidemiology and prognosis. Study Group for Severe Community-Acquired Pneumonia. *Clin Infect Dis* 1996; **23**(4):723–28.
43. Kikuchi R, Watabe N, Konno T, et al. High incidence of silent aspiration in elderly

- patients with community-acquired pneumonia. *Am J Respir Crit Care Med* 1994; **150**(1):251–53.
44. van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Risk factors for aspiration pneumonia in frail older people: a systematic literature review. *J Am Med Dir Assoc* 2011; **12**(5): 344–54.
 45. Tiruvoipati R, Ong K, Gangopadhyay H, et al. Hypothermia predicts mortality in critically ill elderly patients with sepsis. *BMC Geriatr* 2010; **10**:70.
 46. D'Mello T, Brammer L, Blanton L, et al. Update: influenza activity – United States, September 28, 2014–February 21, 2015. *MMWR Morb Mortal Wkly Rep* 2015; **64** (8):206–12.
 47. Avni T, Shiver-Ofer S, Leibovici L, et al. Participation of elderly adults in randomized controlled trials addressing antibiotic treatment of pneumonia. *J Am Geriatr Soc* 2015; **63**(2):233–43.
 48. Kalil AC, Metersky ML, Klompaas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016; **63**(5):e61–111.
 49. Liu QH, Zhang J, Lin DJ, et al. Gastropulmonary route of infection and the prevalence of microaspiration in the elderly patients with ventilator-associated pneumonia verified by molecular microbiology-GM-PFGE. *Cell Biochem Biophys* 2015; **71**(3):1457–62.
 50. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA* 2012; **307**(23):2526–33.
 51. Angus DC, Linde-Zwirble WT, Lidicker J, et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med* 2001; **29**(7):1303–10.
 52. Manzano F, Yuste E, Colmenero M, et al. Incidence of acute respiratory distress syndrome and its relation to age. *J Crit Care* 2005; **20**(3):274–80.
 53. Hudson LD, Milberg JA, Anardi D, Maudner RJ. Clinical risks for development of the acute respiratory distress syndrome. *Am J Respir Crit Care Med* 1995; **151**(2 Pt 1):293–301.
 54. Bellani G, Laffey JG, Pham T, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA* 2016; **315** (8):788–800.
 55. Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; **342**(18):1301–8.
 56. Ely EW, Wheeler AP, Thompson BT, et al. Recovery rate and prognosis in older persons who develop acute lung injury and the acute respiratory distress syndrome. *Ann Intern Med* 2002; **136**(1):25–36.
 57. Steinberg KP, Hudson LD, Goodman RB, et al. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. *N Engl J Med* 2006; **354**(16): 1671–84.
 58. Guérin C, Reignier J, Richard JC. Prone positioning in the acute respiratory distress syndrome. *N Engl J Med* 2013; **369**(10): 980–81.
 59. Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet* 2009; **374**(9698):1351–63.
 60. Mendiratta P, Tang X, Collins RT, et al. Extracorporeal membrane oxygenation for respiratory failure in the elderly: a review of the Extracorporeal Life Support Organization registry. *ASAIO J* 2014; **60**(4): 385–90.
 61. Teno JM, Gozalo P, Khandelwal N, et al. Association of increasing use of mechanical ventilation among nursing home residents with advanced dementia

- and intensive care unit beds. *JAMA Intern Med* 2016.
62. Zaugg M, Lucchinetti E. Respiratory function in the elderly. *Anesthesiol Clin North Am* 2000; **18**(1):47–58, vi.
 63. El Solh AA, Bhat A, Gunen H, Berbary E. Extubation failure in the elderly. *Respir Med* 2004; **98**(7):661–68.
 64. Zilberman MD, Luippold RS, Sulsky S, Shorr AF. Prolonged acute mechanical ventilation, hospital resource utilization, and mortality in the United States. *Crit Care Med* 2008; **36**(3):724–30.
 65. MacIntyre NR, Epstein SK, Carson S, et al. Management of patients requiring prolonged mechanical ventilation: report of a NAMDRC consensus conference. *Chest* 2005; **128**(6):3937–54.
 66. Mehta AB, Syeda SN, Bajpayee L, et al. Trends in tracheostomy for mechanically ventilated patients in the United States, 1993–2012. *Am J Respir Crit Care Med* 2015; **192**(4):446–54.
 67. Sansone GR, Frengley JD, Vecchione JJ, Manogaram MG, Kaner RJ. Relationship of the duration of ventilator support to successful weaning and other clinical outcomes in 437 prolonged mechanical ventilation patients. *J Intensive Care Med* 2016.
 68. Dermot Frengley J, Sansone GR, Shakya K, Kaner RJ. Prolonged mechanical ventilation in 540 seriously ill older adults: effects of increasing age on clinical outcomes and survival. *J Am Geriatr Soc* 2014; **62**(1):1–9.