pulmonary hypertension, or a mixture of these conditions. The work of George et al[13] shows that the bulk of pulmonary hypertension evaluated and treated by community providers is likely not addressed by the PAH-directed guidelines published in this issue.

The articles by George et al[13] and Taichman et al[7] in this issue reveal the best of our accomplishments in PAH and the ongoing challenges that face patients with pulmonary hypertension and their providers. In PAH, advancing mechanistic insight, therapies directed specifically at the right ventricle, new trial designs and end points, and the hope of personalized medicine will shape future guidelines from CHEST and other organizations. In all other forms of pulmonary hypertension, we are just beginning a journey. It is hoped that improved understanding of pathobiology will drive new treatments and will allow inclusion of groups 2 to 5 pulmonary hypertension in future recommendations. Science is like an endurance sport, with major accomplishments in the past 2 decades in PAH in particular, but a long and hilly road still lies ahead to effectively treat all forms of pulmonary hypertension.

References

1. Barst RJ, Rubin LJ, Long WA, et al; Primary Pulmonary Hypertension Study Group. A comparison of continuous intravenous epoprostenol (prostacyclin) with conventional therapy for primary pulmonary hypertension. *N Engl J Med*. 1996;334(5):296-301.
2. Galiè N, Rubin LJ, Hoeper M, et al. Treatment of patients with mildly symptomatic pulmonary arterial hypertension with bosentan (EARLY study): a double-blind, randomised controlled trial. *Lancet*. 2008;371(9630):2093-2100.
3. Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013; 62(suppl 25):D34-D41.
4. King TE Jr, Brown KK, Raghu G, et al. BUILD-3: a randomized, controlled trial of bosentan in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2011;184(1):92-99.
5. Zisman DA, Schwarz M, Anstrom KJ, Collard HR, Flaherty KR, Hunninghake GW; Idiopathic Pulmonary Fibrosis Clinical Research Network. A controlled trial of sildenafil in advanced idiopathic pulmonary fibrosis. *N Engl J Med*. 2010;363(7):620-628.
6. Ghofrani HA, D'Armini AM, Grimminger F, et al; CHEST-1 Study Group. Riociguat for the treatment of chronic thromboembolic pulmonary hypertension. *N Engl J Med*. 2013;369(4):319-329.
7. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults: CHEST guideline and expert panel report. *Chest*. 2014;146(2):449-475.
8. Califf RM, Adams KF, McKenna WJ, et al. A randomized controlled trial of epoprostenol therapy for severe congestive heart failure: the Flolan International Randomized Survival Trial (FIRST). *Am Heart J*. 1997;134(1):44-54.
9. Sitbon O, Humbert M, Jaïs X, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation*. 2005;111(23):3105-3111.
10. Barst RJ, Gibbs JS, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol*. 2009;54(suppl 1):S78-S84.
11. McLaughlin VV, Archer SL, Badesch DB, et al; American College of Cardiology Foundation Task Force on Expert Consensus Documents; American Heart Association; American College of Chest Physicians; American Thoracic Society, Inc; Pulmonary Hypertension Association. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
12. Tonelli AR, Arelli V, Minai OA, et al. Causes and circumstances of death in pulmonary arterial hypertension. *Am J Respir Crit Care Med*. 2013;188(3):365-369.
13. George MG, Schieb LJ, Ayala C, Talwalkar A, Levant S. Pulmonary hypertension surveillance: United States, 2001 to 2010. *Chest*. 2014; 146(2):476-495.
14. Pugh ME, Sivarajan L, Wang L, Robbins IM, Newman JH, Hemnes AR. Causes of pulmonary hypertension in the elderly. *Chest*. 146(1): 159-166.

A New Standard of Care for Critically Ill Patients With Cancer

Elie Azoulay, MD, PhD
Paris, France
on behalf of the Groupe de Recherche en Réanimation Onco-Hématologique (Grrr-OH)

Several million patients worldwide live with cancer.[1,2] Possible outcomes are complete cancer eradication; cancer control using chemotherapy, targeted therapies, or both; and palliative treatments that may both prolong life and increase quality of life.[3] All patients with cancer are at a high risk for pulmonary disease due to infections, infiltration by malignant cells, or treatment toxicities.[4] Severe respiratory episodes, usually with acute respiratory failure, affect up to 40% of patients with cancer.[5]

Mechanical ventilation (MV), whether invasive or noninvasive ventilation (NIV), must be considered the standard of care for consenting patients who are not bedridden and who are receiving curative or palliative chemotherapy. This statement indicates a major change

AFFILIATIONS: From the AP-HP, Hôpital Saint-Louis, Université Paris-Diderot, Sorbonne Paris-Cité.

FINANCIAL/NONFINANCIAL DISCLOSURES: The author has reported to *CHEST* the following conflicts: Dr Azoulay has received research grants from Pfizer, Inc and fees for lecturing from Gilead and MSD and is on the on board of Gilead.

CORRESPONDENCE TO: Elie Azoulay, MD, PhD, AP-HP, Hôpital Saint-Louis, Medical ICU, Université Paris-Diderot, Sorbonne Paris-Cité, Faculté de medicine, 1 avenue Claude Vellefaux, 75010 Paris, France; e-mail: elie.azoulay@sls.aphp.fr

DOI: 10.1378/chest.14-0620

in the care of critically ill patients with cancer. It is based on substantial improvements achieved over the past decade in the survival of patients with cancer requiring MV.[6,7] Previous survival rates, in contrast, were so low that MV was considered futile in this population.[8,9] The improved survival is ascribable to advances in both cancer and ICU management[8-10] as well as to better patient selection for ICU admission. Patients with cancer are increasingly admitted to the ICU,[11,12] with a current hospital mortality rate of 40%. Full-code treatment is used for the first few days, and the response is then assessed to determine the best subsequent course of action.[13]

In this issue of *CHEST* (see page 257), Azevedo et al[14] provide valuable information on survival in patients with cancer requiring mechanical ventilation. Their prospective multicenter study was performed in 28 ICUs in Brazil. Most of the patients had solid tumors, and 67% were admitted for medical reasons. The results should help to further erode the view still held by many intensivists that MV is not beneficial in patients with cancer. The ICU and hospital survival rates were 46% and 33%, respectively. Although lower than those in patients without cancer receiving MV,[15] these survival rates are far higher than those reported in patients with cancer 2 decades ago.[16] This study, together with more recently published data,[7] argue for a broad policy of ICU admission of patients with cancer. It indicates a clear need for defining a standard of care (Table 1): At ICU admission, patients with cancer should not be deprived from potentially lifesaving interventions such as MV, renal replacement therapy, and vasopressor therapy.[8] Moreover, survival is particularly high in patients requiring chemotherapy initiation in the ICU for newly diagnosed malignancies with specific organ dysfunctions, such as leukemic pulmonary infiltration, leukostasis, tumor lysis syndrome, or macrophage activation syndrome.[17]

This large prospective multicenter study of patients who received MV has several major strengths. Although the investigators are experts in the field, not all the study ICUs admitted large numbers of patients with cancer. The data collection method allows comparisons with previous studies. The results provide large-scale confirmation of earlier evidence that NIV failure and MV in patients with tumoral obstruction are associated with high mortality rates.[18,19] Several caveats are in order, however. First, hematology patients accounted for only 14% of the population. Second, long-term outcomes were not available, and disease control 6 months after ICU discharge was not assessed. Similarly, quality-of-life data were not obtained, casting doubt on whether ICU management increased survival or merely prolonged the dying process. Third, as ICU mortality was probably very low in patients successfully managed with NIV, the 40% hospital mortality rate in these patients raises concerns about the goals of care after ICU discharge. Also, important information not provided in the article is how the treatment-limitation decisions taken for

TABLE 1] Features of the Standard of Care for Critically Ill Patients With Cancer

Feature
Early assessment of physiologic disturbances (tachypnea, tachycardia, transient hypotension, marbling, oliguria, oxygen saturation, impairment of consciousness)
Early admission to the ICU. Establish with the patient her/his appropriate goals of care and communicate about them with all people involved (relatives, nurses, medical team, consultants).
Noninvasive diagnostic strategy based on a careful risk assessment tailored to each individual patient
Early appropriate antimicrobial therapy. Consider subsequent de-escalation.
NIV (unless patients have criteria for ARDS) and/or intubation according to patient status and response to NIV. Consider palliative NIV or palliative vasoactive therapy.
Avoid delaying life support (fluid challenge, vasoactive drugs, airway protection if coma, renal replacement therapy, and so forth).
Check that surgery or catheter withdrawal is not needed.
Appropriate transfusion policies
Urgent chemotherapy (malignancies at the earliest stage with specific organ dysfunction, hemophagocytic lymphohistiocytosis, or tumor lysis syndrome)
Work closely with the hematologists/oncologists to inform patients and relatives, to make decisions about performing minimally invasive (or invasive) diagnostic tests, to initiate or intensify chemotherapy, and to diagnose drug-related organ toxicity.

NIV = noninvasive ventilation.

21% of patients were made[20] and the proportion of patients who received palliative NIV.[21] Last, although this study supports recent findings encouraging the use of MV in patients with cancer, it also identifies a subset of patients who seem unlikely to benefit from MV (patients with poor performance status, extensive and uncontrolled disease, or nonpulmonary organ dysfunctions).

The study by Azevedo et al[14] offers three major opportunities to further improve outcomes in this high-risk population (Fig 1). First, although the difference was not statistically significant, patients who died spent more time in wards before ICU admission than patients who survived (2 median [0–8 interquartile range] vs 4 [0–13] days, $P = .11$). Similarly, earlier studies showed that delayed ICU admission was associated with higher mortality.[7,22-24] Interventional studies on optimal ICU admission timing are warranted, not only in the overall population of patients with cancer but also in patients receiving chemotherapy and having a single mild organ dysfunction. Better delineation of the criteria that should prompt oncologists and hematologists to consider ICU admission, and intensivists to admit patients with cancer, is urgently needed. The second opportunity for improvement identified in the study by Azevedo et al[14] pertains to the high mortality after NIV failure. NIV was recommended for first-line ventilatory support in immunocompromised patients at a time when MV was associated with 90% mortality.[25] However, since then, the marked decrease in mortality and the concerns raised about NIV in hypoxemic patients have challenged the wisdom of this approach.[18,26] We believe that NIV should not be used in patients with ARDS. In immunocompromised patients with acute respiratory failure but no criteria for ARDS, the evidence has to be confirmed. Thus, a trial of NIV is warranted to appraise the findings that were reported 15 years ago. Last, the study by Azevedo et al[14] suggests a need for clearly defining the standard of care for critically ill patients with cancer. For instance, the finding that only one-third of patients with cancer admitted to the participating ICUs received MV and that among patients given MV only one-third received vasopressors and only 7% renal replacement therapy casts doubt on whether appropriate intensity of care was provided. Along this line, all the deaths occurred after treatment-limitation decisions. The use of intensive care must change in patients with cancer. Studies must provide survival rates separately for patients who receive full-code management, an ICU trial, or palliative ICU management. In addition to hospital mortality, these studies must provide data on long-term overall survival, event-free and disease-free survival, quality of life, and other markers of post-ICU burden.

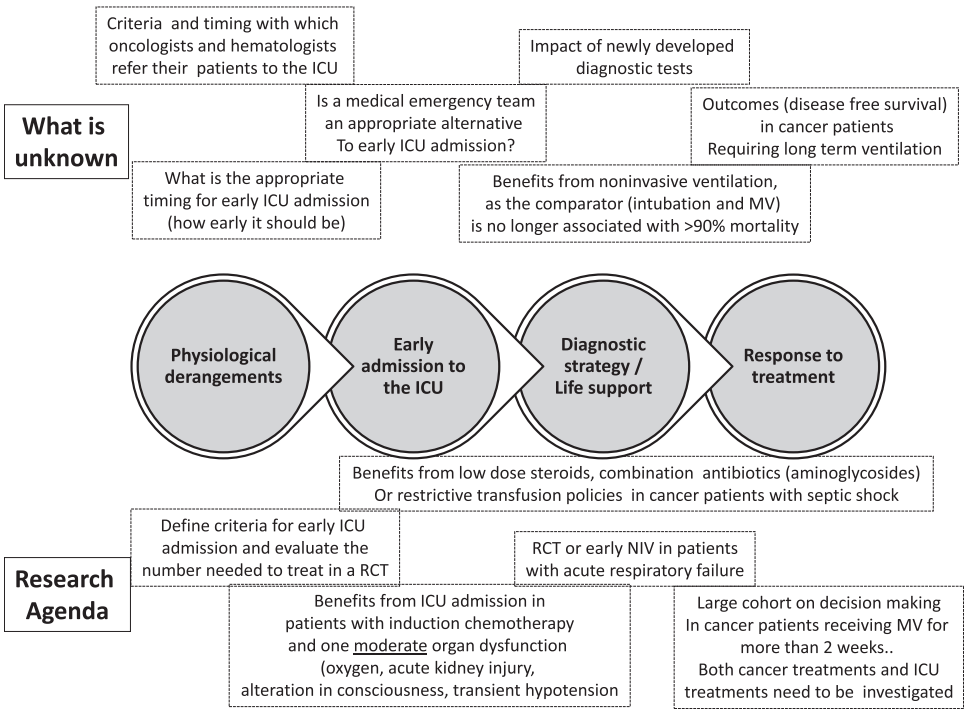

Figure 1 – *Remaining questions and research agenda. MV = mechanical ventilation; NIV = noninvasive ventilation; RCT = randomized controlled trial.*

References

1. Verdecchia A, Francisci S, Brenner H, et al; EUROCARE-4 Working Group. Recent cancer survival in Europe: a 2000-02 period analysis of EUROCARE-4 data. *Lancet Oncol*. 2007;8(9):784-796.
2. Vogelzang NJ, Benowitz SI, Adams S, et al. Clinical cancer advances 2011: annual report on progress against cancer from the American Society of Clinical Oncology. *J Clin Oncol*. 2012;30(1):88-109.
3. Smith TJ, Temin S, Alesi ER, et al. American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. *J Clin Oncol*. 2012;30(8):880-887.
4. Azoulay E, Schlemmer B. Diagnostic strategy in cancer patients with acute respiratory failure. *Intensive Care Med*. 2006;32(6):808-822.
5. Rabbat A, Chaoui D, Montani D, et al. Prognosis of patients with acute myeloid leukaemia admitted to intensive care. *Br J Haematol*. 2005;129(3):350-357.
6. Groeger JS, White P Jr, Nierman DM, et al. Outcome for cancer patients requiring mechanical ventilation. *J Clin Oncol*. 1999;17(3):991-997.
7. Azoulay E, Mokart D, Pène F, et al. Outcomes of critically ill patients with hematologic malignancies: prospective multicenter data from France and Belgium—a groupe de recherche respiratoire en réanimation onco-hématologique study. *J Clin Oncol*. 2013;31(22):2810-2818.
8. Azoulay E, Afessa B. The intensive care support of patients with malignancy: do everything that can be done. *Intensive Care Med*. 2006;32(1):3-5.
9. Azoulay E, Soares M, Darmon M, Benoit D, Pastores S, Afessa B. Intensive care of the cancer patient: recent achievements and remaining challenges. *Ann Intensive Care*. 2011;1(1):5.
10. Dellinger RP, Levy MM, Rhodes A, et al; Surviving Sepsis Campaign Guidelines Committee including The Pediatric Subgroup. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*. 2013;39(2):165-228.
11. Peigne V, Rusinová K, Karlin L, et al. Continued survival gains in recent years among critically ill myeloma patients. *Intensive Care Med*. 2009;35(3):512-518.
12. Khassawneh BY, White P Jr, Anaissie EJ, Barlogie B, Hiller FC. Outcome from mechanical ventilation after autologous peripheral blood stem cell transplantation. *Chest*. 2002;121(1):185-188.
13. Lecuyer L, Chevret S, Thiery G, Darmon M, Schlemmer B, Azoulay E. The ICU trial: a new admission policy for cancer patients requiring mechanical ventilation. *Crit Care Med*. 2007;35(3):808-814.
14. Azevedo LCP, Caruso P, Silva UVA, et al. Outcomes for patients with cancer admitted to the ICU requiring ventilatory support: results from a prospective multicenter study. *Chest*. 2014;146(2):257-266.
15. Esteban A, Frutos-Vivar F, Muriel A, et al. Evolution of mortality over time in patients receiving mechanical ventilation. *Am J Respir Crit Care Med*. 2013;188(2):220-230.
16. Groeger JS, Lemeshow S, Price K, et al. Multicenter outcome study of cancer patients admitted to the intensive care unit: a probability of mortality model. *J Clin Oncol*. 1998;16(2):761-770.
17. Benoit DD, Depuydt PO, Vandewoude KH, et al. Outcome in severely ill patients with hematological malignancies who received intravenous chemotherapy in the intensive care unit. *Intensive Care Med*. 2006;32(1):93-99.
18. Depuydt PO, Benoit DD, Vandewoude KH, Decruyenaere JM, Colardyn FA. Outcome in noninvasively and invasively ventilated hematologic patients with acute respiratory failure. *Chest*. 2004;126(4):1299-1306.
19. Soares M, Darmon M, Salluh JI, et al. Prognosis of lung cancer patients with life-threatening complications. *Chest*. 2007;131(3):840-846.
20. Azoulay E, Garrouste M, Goldgran-Toledano D, et al. Increased nonbeneficial care in patients spending their birthday in the ICU. *Intensive Care Med*. 2012;38(7):1169-1176.
21. Azoulay E, Kouatchet A, Jaber S, et al. Noninvasive mechanical ventilation in patients having declined tracheal intubation. *Intensive Care Med*. 2013;39(2):292-301.
22. de Montmollin E, Tandjaoui-Lambiotte Y, Legrand M, et al. Outcomes in critically ill cancer patients with septic shock of pulmonary origin. *Shock*. 2013;39(3):250-254.
23. Mokart D, Lambert J, Schnell D, et al. Delayed intensive care unit admission is associated with increased mortality in patients with cancer with acute respiratory failure. *Leuk Lymphoma*. 2013;54(8):1724-1729.
24. Lengliné E, Raffoux E, Lemiale V, et al. Intensive care unit management of patients with newly diagnosed acute myeloid leukemia with no organ failure. *Leuk Lymphoma*. 2012;53(7):1352-1359.
25. Organized jointly by the American Thoracic Society, the European Respiratory Society, the European Society of Intensive Care Medicine, and the Société de Réanimation de Langue Française, and approved by ATS Board of Directors, December 2000. International Consensus Conferences in Intensive Care Medicine: noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med*. 2001;163(1):283-291.
26. Azoulay E, Lemiale V. Non-invasive mechanical ventilation in hematology patients with hypoxemic acute respiratory failure: a false belief? *Bone Marrow Transplant*. 2012;47(4):469-472.

Embrace Simplicity When Treating Lady Windermere

Julie Jarand, MD
Stephen K. Field, MD, FCCP
Calgary, AB, Canada

The early reports of *Mycobacterium avium* complex (MAC) lung disease described a difficult-to-treat, primarily upper-lobe, fibrocavitary lung condition with radiologic features similar to those of pulmonary TB. The majority of affected patients were men with preexisting lung disease, usually COPD; previously treated TB; or an immunodeficiency.[1] Prince and colleagues[2] recognized that fibronodular bronchiectasis (FNB) was not an uncommon manifestation of MAC lung disease seen mostly in elderly, thin women who often were lifetime nonsmokers without preexisting lung disease.

AFFILIATIONS: From the Division of Respirology, Department of Medicine, University of Calgary; and Tuberculosis Services, Calgary Zone, Alberta Health Services.

FINANCIAL/NONFINANCIAL DISCLOSURES: The authors have reported to *CHEST* that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

CORRESPONDENCE TO: Stephen K. Field, MD, FCCP, Division of Respirology, Department of Medicine, University of Calgary and Alberta Health Services, Room 1437, Health Science Centre, 3330 Hospital Dr NW, Calgary, AB, T2N 4N1, Canada; e-mail: sfield@ucalgary.ca

DOI: 10.1378/chest.14-0046

CHEST™

Outcomes for Patients With Cancer Admitted to the ICU Requiring Ventilatory Support

Results From a Prospective Multicenter Study

Luciano C. P. Azevedo, MD, PhD; Pedro Caruso, MD, PhD; Ulysses V. A. Silva, MD; André P. Torelly, MD; Eliézer Silva, MD, PhD; Ederlon Rezende, MD; José J. Netto, MD; Claudio Piras, MD, PhD; Suzana M. A. Lobo, MD, PhD; Marcos F. Knibel, MD; José M. Teles, MD; Ricardo. A. Lima, MD, PhD; Bruno S. Ferreira, MD; Gilberto Friedman, MD, PhD; Alvaro Rea-Neto, MD, PhD, FCCP; Felipe Dal-Pizzol, MD, PhD; Fernando A. Bozza, MD, PhD; Jorge I. F. Salluh, MD, PhD; and Márcio Soares, MD, PhD; on behalf of the Brazilian Research in Intensive Care Network (BRICNet)

BACKGROUND: This study was undertaken to evaluate the clinical characteristics and outcomes of patients with cancer requiring nonpalliative ventilatory support.

METHODS: This was a secondary analysis of a prospective cohort study conducted in 28 Brazilian ICUs evaluating adult patients with cancer requiring invasive mechanical ventilation (MV) or noninvasive ventilation (NIV) during the first 48 h of their ICU stay. We used logistic regression to identify the variables associated with hospital mortality.

RESULTS: Of 717 patients, 263 (37%) (solid tumors = 227; hematologic malignancies = 36) received ventilatory support. NIV was initially used in 85 patients (32%), and 178 (68%) received MV. Additionally, NIV followed by MV occurred in 45 patients (53%). Hospital mortality rates were 67% in all patients, 40% in patients receiving NIV only, 69% when NIV was followed by MV, and 73% in patients receiving MV only ($P < .001$). Adjusting for the type of admission, newly diagnosed malignancy (OR, 3.59; 95% CI, 1.28-10.10), recurrent or progressive malignancy (OR, 3.67; 95% CI, 1.25-10.81), tumoral airway involvement (OR, 4.04; 95% CI, 1.30-12.56), performance status (PS) 2 to 4 (OR, 2.39; 95% CI, 1.24-4.59), NIV followed by MV (OR, 3.00; 95% CI, 1.09-8.18), MV as initial ventilatory strategy (OR, 3.53; 95% CI, 1.45-8.60), and Sequential Organ Failure Assessment score (each point except the respiratory domain) (OR, 1.15; 95% CI, 1.03-1.29) were associated with hospital mortality. Hospital survival in patients with good PS and nonprogressive malignancy and without tumoral airway involvement was 53%. Conversely, patients with poor functional capacity and cancer progression had unfavorable outcomes.

CONCLUSIONS: Patients with cancer with good PS and nonprogressive disease requiring ventilatory support should receive full intensive care, because one-half of these patients survive. On the other hand, provision of palliative care should be considered the main goal for patients with poor PS and progressive underlying malignancy. CHEST 2014; 146(2):257-266

Manuscript received August 10, 2013; revision accepted January 7, 2014; originally published Online First January 30, 2014.

ABBREVIATIONS: ARF = acute respiratory failure; MV = mechanical ventilation; NIV = noninvasive ventilation; PS = performance status; SAPS 3 = Simplified Acute Physiology Score (third version); SOFA = Sequential Organ Failure Assessment

AFFILIATIONS: From the ICU (Dr Azevedo), Hospital Sirio-Libanes; ICU (Dr Caruso), Hospital A. C. Camargo; ICU (Dr E. Silva), Hospital Israelita Albert Einstein; and ICU (Dr Rezende), Hospital do Servidor Público Estadual, São Paulo; Programa de Pós-Graduação em Oncologia (Drs Azevedo, Salluh, and Soares) and ICU (Dr Netto), Instituto Nacional de Câncer, Hospital do Câncer II; ICU (Dr Lima), Hospital

Acute respiratory failure (ARF) with the need for ventilatory support is a frequent complication and a significant reason for admission to ICUs.[1] During the course of critical illness, up to 65% of all patients will need invasive mechanical ventilation (MV) or noninvasive ventilation (NIV).[2,3] Moreover, ventilatory support is the major organ supportive therapy carried out in critically ill patients with cancer.[4-8] The main common causes of respiratory failure in patients with malignancies are infections, direct tumoral involvement of the respiratory system, cancer-related medical disorders, and anticancer drug-induced respiratory distress.[9] As a consequence of the underlying disease or complications, ARF in patients with cancer in the ICU has been considered for many years to be poorly responsive to supportive care and to be associated with high mortality.[10,11] Nevertheless, advances in critical care and oncology, as well as a more appropriate selection of patients, have improved these outcomes substantially. However, information on the prognosis of patients with malignancies who are mechanically ventilated usually comes from single-center studies carried out in specialized ICUs. Additionally, studies using databases of patients in the general ICU[12,13] usually have limited information regarding cancer and its treatment-related aspects.[14] The identification of factors associated with outcomes in this setting may aid physicians, patients, and families in deciding goals and treatment directives. Thus, the aim of the current study was to describe the clinical outcomes and prognostic factors in critically ill patients with cancer requiring ventilatory support early in the course of their ICU stay.

FOR EDITORIAL COMMENT SEE PAGE 241

Materials and Methods

Design, Setting, and Eligibility Criteria

This study was a secondary analysis of a multicenter prospective cohort study conducted in 28 Brazilian ICUs (e-Appendix 1) between August 1 and September 30, 2007.[15] The study was strictly observational, and every clinical decision (including the decision to start, change the modality, or cease the ventilatory support) was at the discretion of attending physicians. The Comitê de Ética em Pesquisa of Instituto Nacional de Câncer (No. 013/07) approved the study, as did local institutional review boards at all the other participating sites and the Brazilian National Ethics Committee. Informed consent was waived because of the observational character of the trial.

In the current study, all adult patients ($\geq$ 18 years old) with a definite diagnosis of cancer and who required ventilatory support (invasive MV or NIV) for $\geq$ 24 h during the first 48 h of ICU admission to the participating ICUs were evaluated. Patients in complete cancer remission for $>$ 5 years and readmissions were not considered.

Samaritano; ICU (Dr Knibel), Hospital São Lucas; Hospital Pasteur (Dr Ferreira); and D'Or Institute for Research and Education (Drs Bozza, Salluh, and Soares), Rio de Janeiro; ICU (Dr U. V. A. Silva), Fundação Pio XII, Hospital do Câncer de Barretos, Barretos; ICU (Dr Torelly), Santa Casa de Misericórdia de Porto Alegre; and ICU (Dr Friedman), Universidade Federal do Rio Grande do Sul, Porto Alegre; ICU (Dr Piras), Vitória Apart Hospital, Vitória; the Division of Critical Care Medicine (Dr Lobo), Department of Internal Medicine, Medical School and Hospital de Base, São José do Rio Preto; ICU (Dr Teles), Hospital Português, Salvador; ICU (Dr Rea-Neto), Hospital de Clínicas da Universidade Federal do Paraná, Curitiba; and Laboratório de Fisiopatologia Experimental (Dr Dal-Pizzol), Programa de Pós-Graduação Ciências da Saúde, Unidade Acadêmica de Ciências da Saúde, Universidade do Extremo Sul Catarinense, Criciúma, Brazil.

FUNDING/SUPPORT: This article was supported by the Instituto Nacional de Câncer, the National Council for Scientific and Technological Development of Brazil (CNPq), and Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

CORRESPONDENCE TO: Márcio Soares, MD, PhD, D'Or Institute for Research and Education, Rua Diniz Cordeiro, 30, Botafogo, Rio de Janeiro, Brazil, 22281-100; e-mail:marciosoaresms@gmail.com.

DOI: 10.1378/chest.13-1870

Data Collection and Processing

We used a specific and standardized case report form to collect the study data. Demographic, clinical, and laboratory data included age, sex, hospital location before ICU admission, main reasons for ICU admission and for the need for ventilatory support, comorbidities, performance status (PS) (Eastern Cooperative Oncology Group scale),[16] results determined by the Simplified Acute Physiology Score (third version) (SAPS 3),[17] the Sequential Organ Failure Assessment (SOFA) score,[18] and cancer- and treatment-related information. The Adult Comorbidity Evaluation-27 was used to evaluate comorbid diseases and conditions according to the severity of organ decompensation and prognostic impact.[19] An overall comorbidity score (none, mild, moderate, or severe) was attributed based on the highest-ranked single ailment. Patients with hematologic malignancies were categorized as low grade or high grade.[20] Neutropenia was defined as a neutrophil count $<$ 500/mm^3. For the purposes of the current study, we classified patients according to the used ventilatory strategy into three groups: NIV only (patients exclusively ventilated with NIV), MV only (patients who were initially intubated for MV), and NIV followed by MV (when MV was used in those who initially received NIV, regardless of the indication). Sepsis and ARDS were diagnosed according to the current definitions during the study period.[21,22] Cancer was considered to be a direct reason for MV in the case of bilateral metastatic nodules, carcinomatous lymphangitis, or tumoral masses resulting in airway obstruction, lung compression, or atelectasis. Vital status at hospital discharge was the main outcome of interest.

Statistical Analysis

We used standard descriptive statistics to describe the study population. Continuous variables were reported as mean $\pm$ SD or median (25%-75% interquartile range) as appropriate. We performed univariate and multivariate logistic regression to identify factors associated with hospital mortality.[23] Linearity between each continuous variable and the dependent variable was demonstrated using locally weighted scatterplot smoothing.[23] In the case of nonlinearity, the variable was stratified according to the inflection points and clinical significance. For categorical variables with multiple levels, the reference level was attributed to the one with the lowest probability of the dependent variable. Variables yielding P values $<$ .2 by univariate analysis and those considered clinically relevant were entered into the multivariate analysis to estimate the independent association of each covariate with the dependent variable. To control for biases regarding the probability of NIV use as an initial modality of ventilatory support, we fitted a propensity score that included cancer status, SOFA score, admission to an exclusive oncologic ICU, respiratory rate, and cardiogenic pulmonary edema as a reason for

NIV.[24] The results of the multivariate analysis were summarized as ORs and respective 95% CIs. Possible interactions were tested. The model's calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test.[23] With this test, P values $> .05$ indicate a good fit for the model. For all other analyses, two-tailed P values $< .05$ were considered statistically significant.

Results

Characteristics of the Study Population

Of the 717 patients admitted to the 28 participating ICUs, 263 (37%) fulfilled the eligibility criteria, and these constituted the study population (Fig 1). The median patient inclusion from each center was six (25%-75%, 4-13; range, 1-33). Two hundred twenty-seven patients (86%) had solid tumors, and 36 patients (14%) had hematologic malignancies. Ventilatory support was required more frequently by patients with hematologic malignancies (36 of 50 patients [72%]) than by patients with solid tumors (227 of 667 patients [34%]) (OR, 4.98; 95% CI, 2.54-9.92; $P < .001$).

The patients' main characteristics are depicted in Table 1. The most frequent types of cancer were lower GI (n = 33 [13%]), lung (n = 31 [12%]), breast (n = 23 [9%]), upper GI (n = 23 [9%]), urogenital (n = 22 [8%]), head and neck (n = 20 [8%]), pancreas/liver/biliary tract (n = 20 [8%]), brain (n = 15 [6%]), lymphomas (n = 14 [6%]), leukemias (n = 11 [4%]), gynecologic (n = 9 [3%]), multiple myeloma (n = 8 [3%]), and others (n = 34 [13%]). Nine patients (3%) underwent bone marrow transplant (autologous = 7; allogenic = 2).

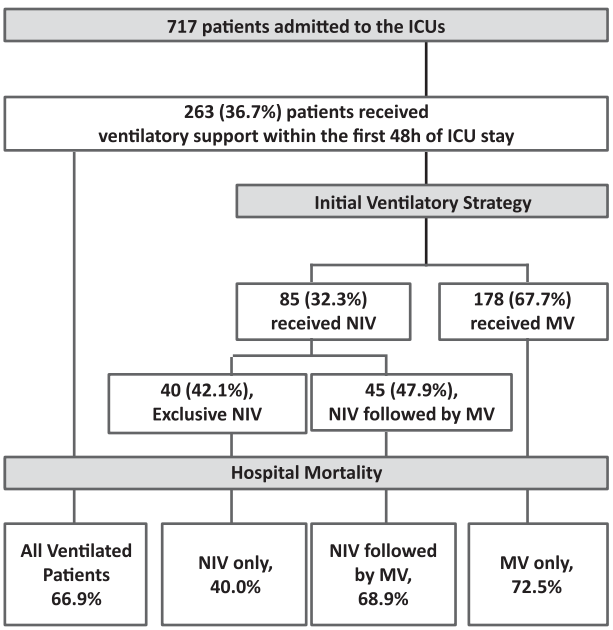

Figure 1 – *Study flowchart. MV = mechanical ventilation; NIV = noninvasive ventilation.*

Patients were admitted to the ICU after a median of 3 (0-11) days following hospital admission. There were 175 medical admissions (67%); 48 patients (18%) and 40 patients (15%) had undergone scheduled and emergency surgical procedures, respectively. The main sources of admission were the ward/floor (133 [44%]), operating/recovery rooms (n = 81 [31%]), ED (n = 49 [19%]), and step-down units (n = 18 [7%]).

Ventilatory Support

Invasive MV was initially used in 178 patients (68%), and 85 (32%) received NIV as ventilatory support. Table 2 depicts the main reasons for ventilatory support in the patients. The presence of sepsis, ARDS, and tumoral involvement were the main causes of ventilatory support and were also significant risk factors for hospital mortality in the univariate analysis. Table 3 summarizes the patients' characteristics according to the initial ventilatory strategy. As expected, patients undergoing initial invasive MV had increased disease severity (higher SAPS 3 and SOFA scores, greater use of dialysis and vasopressors, and higher lactate concentrations), longer ventilatory support requirements, and increased ICU and hospital mortality.

Invasive MV was used subsequently in 45 patients (53%) initially ventilated with NIV. The use of MV was more frequent in patients with septic shock ($P < .001$), ARDS ($P = .013$), and a respiratory rate ≥ 35 breaths/min ($P = .017$) during the first day of NIV (e-Table 1).

Outcome Analysis

Hospital mortality rates were 67% in all patients, 40% in NIV-only group patients, 69% when NIV was followed by MV, and 73% in MV-only group patients ($P < .001$). End-of-life decisions were taken in 21% of the patients.

Table 1 depicts the factors associated with hospital mortality in the univariate analysis of the entire population. Male sex, admission due to a medical condition, disease severity (SAPS 3 and SOFA scores and use of vasopressors), metastatic solid tumor, high-grade hematologic disease, cancer active or in progression, PS 2 to 4, presence of comorbidities, low Pao_2/Fio_2 ratios, and only use of MV, as well as the need for MV after an NIV trial were associated with hospital mortality.

TABLE 1] Patients' Characteristics and Univariate Analysis of Predictors of Hospital Mortality

Variables	All Patients (N = 263)	Survivors (n = 87 [33%])	Nonsurvivors (n = 176 [67%])	OR (95% CI)	*P* Value
Age, y	62.0 ± 15.7	62.9 ± 17.8	61.6 ± 14.5	0.99 (0.98-1.01)	.520
Male sex	125 (48)	32 (37)	93 (53)	1.92 (1.14-3.26)	.020
Hospital stay before ICU admission, d	3 (0-11)	2 (0-8)	4 (0-13)	1.01 (0.99-1.03)	.114
Medical admission	175 (67)	43 (49)	132 (74)	3.07 (1.79-5.28)	< .001
SAPS 3 score, points	64.4 ± 17.4	55.9 ± 15.6	68.6 ± 16.8	1.05 (1.03-1.07)	< .001
SOFA on the first day of ICU, points	10 (8-14)	9 (7-11)	11 (8-14)	1.19 (1.10-1.29)	< .001
SOFA on the first day of ICU, excluding respiratory points	8 (6-10)	7 (5-9)	9 (7-12)	1.22 (1.11-1.33)	< .001
Type of cancer					
Locoregional solid tumor	144 (55)	62 (71)	82 (47)	1.00	.001
Metastatic solid tumor	83 (32)	16 (18)	67 (38)	3.17 (1.67-5.99)	…
Low-grade hematologic malignancy	13 (5)	6 (7)	7 (4)	0.88 (0.28-2.76)	…
High-grade hematologic malignancy	23 (9)	3 (3)	20 (11)	5.04 (1.43-7.04)	…
Cancer status					
Controlled/remission	29 (11)	14 (16)	15 (9)	1.00	.029
Active: newly diagnosed	138 (52)	50 (57)	88 (50)	1.64 (0.73-3.68)	…
Active: recurrence/progression	96 (37)	23 (26)	73 (41)	2.96 (1.25-7.04)	…
Performance status					
0-1	100 (38)	48 (55)	52 (30)	1.00	< .001
2-4	163 (62)	39 (45)	124 (70)	2.94 (1.72-5.00)	…
Neutropenia	27 (10)	5 (6)	22 (13)	2.35 (0.86-6.42)	.129
COPD	40 (15)	15 (17)	25 (14)	0.80 (0.40-1.60)	.644
Comorbidity score, ACE-27					
None/mild	120 (46)	48 (55)	52 (30)	1.00	< .001
Moderate/severe	143 (54)	39 (45)	124 (70)	2.94 (1.72-5.00)	…
Dialysis	19 (7)	4 (5)	15 (9)	1.93 (0.62-6.01)	.317
Vasopressors	98 (37)	23 (26)	75 (43)	2.07 (1.18-3.63)	.016
Ventilatory strategy category					
NIV only	40 (15)	24 (28)	16 (9)	1.00	.001
NIV followed by MV	45 (17)	10 (11)	31 (18)	3.32 (1.36-8.12)	…
MV only	178 (68)	49 (56)	129 (73)	3.95 (1.94-8.06)	…

(Continued)

TABLE 1 *(continued)*

Variables	All Patients (N = 263)	Survivors (n = 87 [33%])	Nonsurvivors (n = 176 [67%])	OR (95% CI)	*P* Value
Blood gas analysis					
Pao_2/Fio_2	236 (138-324)	256 (188-326)	212 (130-323)	0.98 (0.96-1.00)	.044
$Paco_2$, mm Hg	38 (31-46)	38 (31-46)	38 (31-47)	0.99 (0.97-1.01)	.81
Hco_3, mmol/L	20.1 (16.6-23.5)	20.7 (18.0-23.6)	20.0 (15.6-23.6)	0.98 (0.94-1.02)	.254
Lactate, mmol/L	2.1 (1.3-3.5)	2.5 (1.3-3.3)	2.0 (1.3-3.7)	1.05 (0.96-1.14)	.609
Outcome data					
ICU LOS, d	7 (4-16)	7 (4-16)	7 (5-12)	...	.344
Hospital LOS, d	19 (10-36)	19 (10-36)	20 (14-35)	...	.1532
Duration of ventilatory support, d	5 (2-12)	3 (1-7)	6 (3-13)	...	< .001
End-of-life decisions	55 (21)	0	55 (31)	...	< .001
ICU mortality	142 (54)	...	...	...	...
Hospital mortality	176 (67)	...	...	...	...

Data are presented as mean ± SD, median (25%-75% interquartile range), or No. (%). ACE-27 = Adult Comorbidity Evaluation; LOS = length of stay; MV = mechanical ventilation; NIV = noninvasive ventilation; SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment.

Table 4 shows the multivariate logistic regression of variables related to hospital death. Medical admission, active underlying malignancy newly diagnosed, underlying malignancy in recurrence or progression, tumor as reason for ventilatory support, poor PS, NIV followed by MV, use of invasive MV only, and higher SOFA scores (each point except the respiratory domain, which was removed from the calculation of the score to avoid collinearity with other respiratory variables in the statistical analysis.) were independently associated with hospital mortality.

To evaluate the mortality in different and frequent clinical scenarios, Fig 2 further explores the combination of the factors associated with death in multivariate analysis. Of note, hospital survival in patients with good PS and without cancer recurrence or tumoral airway involvement was 53%.

Discussion

In the current study, we demonstrated that patients with cancer requiring ventilatory support who were admitted to ICUs may have reasonable mortality rates, especially when they have good PS and nonprogressive disease. Moreover, we determined important independent predictors of mortality in these patients, which can assist physicians in decisions relating to patients' management and the counseling of patients and families. ICU refusal of patients merely because of a cancer diagnosis is no longer supported. Previous studies have demonstrated that mortality rates in critically ill patients with cancer are not substantially different from those of other patients in the ICU with similar disease severity and other comorbidities such as heart failure, liver cirrhosis, or other severe chronic diseases.[5,25]

The variables associated with hospital mortality in the multivariate analysis may be grouped into characteristics related to cancer, PS, and severity of organ failure. In the first group, as reported previously,[10,26,27] patients with recurrent or progressive disease and direct involvement of the respiratory tract by tumor had increased mortality (Fig 2). Moreover, the occurrence of tumor-caused ARF is relatively infrequent (8%-11% in other series[4] and 12% in the patients in this study) and may be caused by neck or mediastinal bulky neoplastic disease leading to airway compression or by disseminated parenchymal disease, or lymphangitis. Either way, it is usually associated with increased mortality, except when caused by tumors highly responsive to chemotherapy.[4]

The severity of acute physiologic alterations and organ dysfunctions are other major determinants of short-term mortality,[28-30] as demonstrated in our study by the

TABLE 2] Main Reasons for the Need for Ventilatory Support

Variables	All Patients (N = 263)	Survivors (n = 87 [33%])	Nonsurvivors (n = 176 [67%])	OR (95% CI)	*P* Value
Severe sepsis/septic shock	169 (64)	47 (54)	122 (69)	1.92 (1.13-3.27)	.022
ARDS	80 (30)	17 (20)	63 (36)	2.30 (1.24-4.24)	.011
Tumor	32 (12)	5 (6)	27 (15)	2.97 (1.10-8.01)	.032
Coma	27 (10)	9 (10)	18 (10)	0.99 (0.42-2.23)	.999
Cardiogenic pulmonary edema	11 (4)	8 (9)	3 (2)	0.17 (0.04-0.66)	.007
Cardiopulmonary arrest	10 (4)	2 (2)	8 (5)	2.02 (0.42-9.74)	.505
Pulmonary embolism	9 (3)	0	9 (5)	…	.032
Hemoptysis/alveolar hemorrhage	4 (2)	1 (1)	3 (2)	1.49 (0.15-14.55)	.999
COPD exacerbation	4 (2)	1 (1)	3 (2)	1.49 (0.15-14.55)	.999
Other/Unknown	27 (10)	16 (18)	11 (6)	0.30 (0.13-0.70)	.004

Data are presented as No. (%).

SOFA score (excluding respiratory domain) on the first day of ICU stay. Other studies have also demonstrated that changes in the number of organ failures over the first few ICU days are closely correlated with survival.[31] Taccone et al[32] reported that the mortality rate is comparable between patients with solid cancer and general patients (27%) in the ICU. However, taking into consideration only patients presenting with more than three organ failures, mortality was higher in patients with cancer. In our study, when combined with poor disease control and compromised PS, the presence of extrarespiratory organ failures is clearly associated with mortality rates (Fig 2). In this particular high-risk group of patients, early recognition before the onset or the worsening of organ failures and provision of close monitoring and support (including early ICU referral) are essential.[6,33] It is also worth emphasizing that all the clinical predictors identified in our study as independently associated with hospital mortality are easily available and may help health personnel identify patients who may benefit from intensive care and protect others from the inappropriate use of aggressive therapies.

The nonpalliative use of NIV in patients in the ICU with cancer was assessed in our study. We observed that 53% of patients who initially received NIV were later intubated and submitted to invasive MV. Mortality rates in these patients were substantially higher in comparison with those who were ventilated with NIV only (69% vs 40%), and a subsequent need for MV after an NIV trial was independently associated with worse outcomes. Such findings are comparable to those of previous reports.[14,28] Moreover, in our study, patients with sepsis, ARDS, and a respiratory rate $\geq$ 35 breaths/min at baseline were more prone to be subsequently intubated after an initial trial of NIV, which suggests that the decision to offer NIV in these cases should be more judicious.

The use of NIV has been increasing significantly in patients with cancer, and its use had a protective effect in most,[13,14,31,34] but not all,[29,35] studies. It is possible that delayed intubation in this severely ill subgroup of patients may have accounted for their grim prognosis, because it is recognized as an independent risk factor for the use of MV after NIV.[9,36] However, very few studies adjusted the association of NIV as initial ventilatory support according to disease severity,[13,31,35] as we did in the current study using a propensity score. When corrected for disease severity and baseline characteristics, the use of NIV is commonly reported to be beneficial.[16,28] Nonetheless, our study was not specifically designed to evaluate the clinical scenarios of NIV use and risk factors for NIV failure. The need for invasive MV after an NIV trial in patients with cancer is a complex phenomenon that incorporates the variables relating to the underlying malignancy, the acute complication leading to the need for ventilatory support, and the patient's evolution during the first days of NIV support. In addition, the decision to start, cease, or change the ventilatory strategy was left to the discretion of the attending team. Therefore, the results of the current study preclude us from drawing definite recommendations to choose the most appropriate ventilatory strategy for patients with cancer and respiratory failure.

TABLE 3] Patients' Characteristics and Outcomes According to the Initial Ventilatory Strategy

Variables	Invasive MV (n = 178 [68%])	NIV (n = 85 [32%])	*P* Value
Age, y	62.0 ± 14.7	62.0 ± 17.2	.994
Male sex	83 (47)	42 (49)	.771
Hospital stay before ICU admission, d	3 (0-11)	3 (0-10)	.701
Medical admission	109 (61)	66 (78)	.012
SAPS 3 score, points	64.9 ± 17.5	63.3 ± 17.4	.507
SOFA on the first day of ICU, points	11 (8-14)	9 (7-11)	< .001
SOFA on the first day of ICU, excluding respiratory points	9 (7-12)	7 (5-9)	< .001
Type of cancer			
Locoregional solid tumor	111 (62)	33 (39)	.001
Metastatic solid tumor	47 (26)	36 (42)	…
Low-grade hematologic malignancy	5 (3)	8 (9)	…
High-grade hematologic malignancy	15 (8)	8 (9)	…
Cancer status			
Controlled/remission	20 (11)	9 (11)	.387
Active: newly diagnosed	98(55)	40 (47)	…
Active: recurrence/progression	60 (34)	36 (42)	…
Performance status			
0-1	66 (37)	34 (40)	.748
2-4	112 (63)	51 (60)	…
Neutropenia	19 (11)	14 (17)	.259
Comorbidity score (ACE-27)			
None/mild	82 (46)	38 (45)	.940
Moderate/severe	96 (54)	47 (55)	…
COPD	26 (15)	14 (17)	…
Dialysis	43 (24)	9 (11)	.016
Vasopressors	142 (75)	36 (42)	< .001
Reasons for ventilatory support			
Severe sepsis/septic shock	116 (65)	53 (62)	.758
ARDS	64 (36)	16 (18)	.007
Tumor	18 (10)	14 (16)	.203
Pulmonary embolism	6 (3)	3 (4)	.999
Cardiogenic pulmonary edema	2 (1)	9 (11)	.001
Blood gas analysis			
Pao_2/Fio_2	232 (127-327)	241 (180-315)	.147
$Paco_2$, mm Hg	39 (31-47)	36 (30-45)	.296
Hco_3, mmol/L	19.5 (15.9-23.0)	21.0 (18.4-24.0)	.030
Lactate, mmol/L	2.4 (1.4-4.1)	1.9 (1.3-2.8)	.045
Outcome data			
ICU LOS, d	9 (5-19)	6 (3-12)	.001
Hospital LOS, d	20 (10-37)	19 (11-34)	.655
Duration of ventilatory support, d	6 (3-13)	3 (1-6)	< .001
End-of-life decisions	33 (19)	22 (26)	.227
ICU mortality	110 (62)	32 (38)	< .001
Hospital mortality	129 (73)	47 (55)	.009

Data are presented as mean ± SD, median (25%-75% interquartile range), or No. (%). See Table 1 for expansion of abbreviations.

TABLE 4] Multivariate Analysis of Predictors of Hospital Mortality in all Patients in Need of Ventilatory Support (N = 263)

Variables	Coefficients	OR (95% CI)	*P* Value
Medical admission			
No	…	1.00	…
Yes	1.534	4.64 (2.22-9.71)	< .001
Cancer status			
Controlled/remission	…	1.00	…
Active: newly diagnosed	1.279	3.59 (1.28-10.10)	.015
Active: recurrence/progression	1.301	3.67 (1.25-10.81)	.018
Tumor as a reason for ventilatory support	1.395	4.04 (1.30-12.56)	.016
Performance status			
0-1	…	1.00	…
2-4	0.870	2.39 (1.24-4.59)	.009
Ventilatory strategy category			
NIV only	…	1.00	…
NIV followed by MV	1.091	3.00 (1.09-8.18)	.034
MV only	1.260	3.53 (1.45-8.60)	.006
Pa_{O_2}/F_{IO_2}			
≥ 300	…	1.00	…
150 to < 300	−0.073	0.93 (0.46-1.88)	.839
< 150	0.462	1.59 (0.67-3.79)	.297
SOFA on the first day of ICU, excluding respiratory points	0.145	1.15 (1.03-1.29)	.015
Propensity score for the use of NIV	−0.014	0.99 (0.97-1.01)	.203
Constant	−3.842	…	…

Hosmer-Lemeshow goodness-of-fit ($\chi^2 = 7.169$; $P = .519$). See Table 1 for expansion of abbreviations.

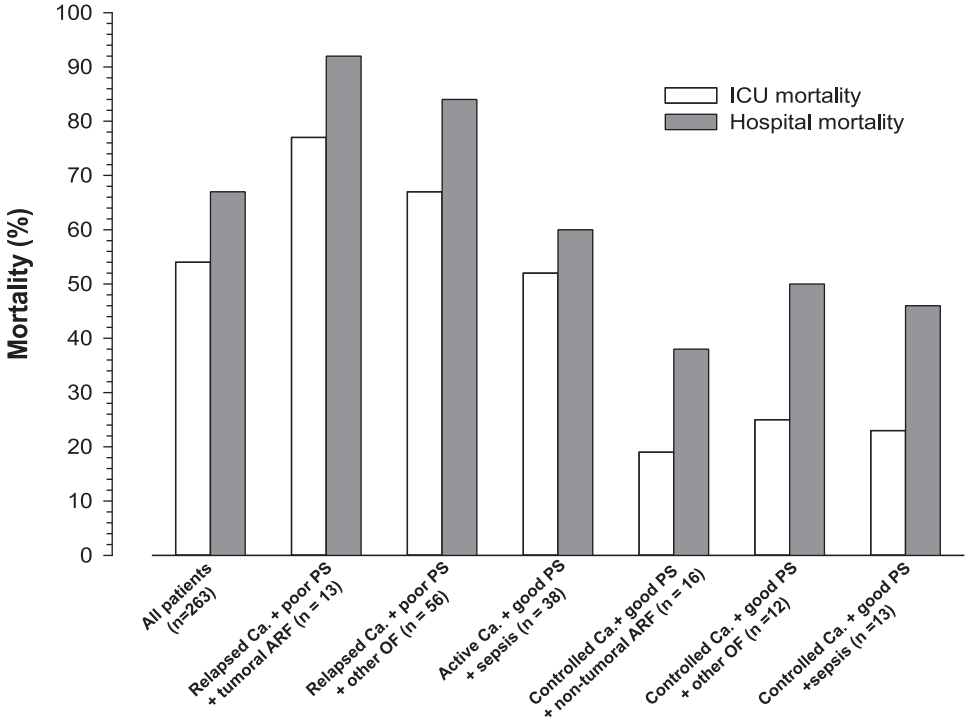

Figure 2 – *ICU and hospital mortality rates for the different subgroups of patients with cancer and need for ventilatory support. ARF = acute respiratory failure; Ca = cancer; OF = organ failure; PS = performance status.*

As a secondary analysis, the current study has some inherent additional limitations. Patients with hematologic malignancies and those who have undergone a bone marrow transplant were underrepresented. Therefore, caution is needed when extrapolating our results to these subgroups of patients. On the other hand, because most of the included patients were admitted to general ICUs, the external validity of our results may be more significant compared with studies carried out in oncology-specialized ICUs.

Conclusions

In conclusion, mortality rates in critically ill patients with cancer requiring ventilatory support remain relatively high. Patients with good PS and nonprogressive disease requiring ventilatory support should receive full intensive care, because one-half of these patients survive. On the other hand, the provision of palliative care should be considered the main goal for patients with poor PS and progressive underlying malignancy.

Acknowledgments

Author contributions: M. S. had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the analysis. L. C. P. A., J. I. F. S., and M. S contributed to the study conception, data acquisition, analysis, and interpretation, drafting of the manuscript, revision of the manuscript for important intellectual content, and approval of the final copy; P. C. contributed to the study conception, data acquisition, revision of the manuscript for important intellectual content, and approval of the final copy; U. V. A. S., A. P. T., E. S., E. R., J. J. N., C. P., S. M. A. L., M. F. K., J. M. T., R. A. L., B. S. F., G. F., A. R.-N., F. D.-P., and F. A. B. contributed to the data acquisition, revision of the manuscript for important intellectual content, and approval of the final copy.

Financial/nonfinancial disclosures: The authors have reported to *CHEST* that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Role of sponsors: The sponsors had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

Other contributions: The authors are indebted to the Instituto Nacional de Câncer, especially the Department of Clinical Research, FAPERJ, and CNPq, for all their support.

Additional information: The e-Appendix and e-Table can be found in the Supplemental Materials section of the online article.

References

1. Azevedo LC, Park M, Salluh JI, et al; The ERICC (Epidemiology of Respiratory Insufficiency in Critical Care) investigators. Clinical outcomes of patients requiring ventilatory support in Brazilian intensive care units: a multicenter, prospective, cohort study. *Crit Care*. 2013;17(2):R63.
2. Roupie E, Lepage E, Wysocki M, et al. Prevalence, etiologies and outcome of the acute respiratory distress syndrome among hypoxemic ventilated patients. SRLF Collaborative Group on Mechanical Ventilation. Société de Réanimation de Langue Française. *Intensive Care Med*. 1999;25(9):920-929.
3. Demoule A, Girou E, Richard JC, Taillé S, Brochard L. Increased use of noninvasive ventilation in French intensive care units. *Intensive Care Med*. 2006;32(11):1747-1755.
4. Soares M, Depuydt PO, Salluh JI. Mechanical ventilation in cancer patients: clinical characteristics and outcomes. *Crit Care Clin*. 2010;26(1):41-58.
5. Azoulay E, Soares M, Darmon M, Benoit D, Pastores S, Afessa B. Intensive care of the cancer patient: recent achievements and remaining challenges. *Ann Intensive Care*. 2011;1(1):5.
6. Azoulay E, Mokart D, Pène F, et al. Outcomes of critically ill patients with hematologic malignancies: prospective multicenter data from France and Belgium—a groupe de recherche respiratoire en réanimation onco-hématologique study. *J Clin Oncol*. 2013;31(22):2810-2818.
7. Soares M, Salluh JI, Ferreira CG, Luiz RR, Spector N, Rocco JR. Impact of two different comorbidity measures on the 6-month mortality of critically ill cancer patients. *Intensive Care Med*. 2005;31(3):408-415.
8. Staudinger T, Stoiser B, Müllner M, et al. Outcome and prognostic factors in critically ill cancer patients admitted to the intensive care unit. *Crit Care Med*. 2000;28(5):1322-1328.
9. Azoulay E, Schlemmer B. Diagnostic strategy in cancer patients with acute respiratory failure. *Intensive Care Med*. 2006;32(6):808-822.
10. Soares M, Salluh JI, Spector N, Rocco JR. Characteristics and outcomes of cancer patients requiring mechanical ventilatory support for >24 hrs. *Crit Care Med*. 2005;33(3):520-526.
11. Groeger JS, White P Jr, Nierman DM, et al. Outcome for cancer patients requiring mechanical ventilation. *J Clin Oncol*. 1999;17(3):991-997.
12. Lecuyer L, Chevret S, Guidet B, et al. Case volume and mortality in haematological patients with acute respiratory failure. *Eur Respir J*. 2008;32(3):748-754.
13. Gristina GR, Antonelli M, Conti G, et al; GiViTI (Italian Group for the Evaluation of Interventions in Intensive Care Medicine). Noninvasive versus invasive ventilation for acute respiratory failure in patients with hematologic malignancies: a 5-year multicenter observational survey. *Crit Care Med*. 2011;39(10):2232-2239.
14. Adda M, Coquet I, Darmon M, Thiery G, Schlemmer B, Azoulay E. Predictors of noninvasive ventilation failure in patients with hematologic malignancy and acute respiratory failure. *Crit Care Med*. 2008;36(10):2766-2772.
15. Soares M, Caruso P, Silva E, et al; Brazilian Research in Intensive Care Network (BRICNet). Characteristics and outcomes of patients with cancer requiring admission to intensive care units: a prospective multicenter study. *Crit Care Med*. 2010;38(1):9-15.
16. Zubrod CG, Schneiderman M, Frei E III, et al. Appraisal of methods for the study of chemotherapy of cancer in man: comparative therapeutic trial of nitrogen mustard and triethylene thiophosphoramide. *J Chronic Dis*. 1960;11(1):7-33.
17. Moreno RP, Metnitz PG, Almeida E, et al; SAPS 3 Investigators. SAPS 3—From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. *Intensive Care Med*. 2005;31(10):1345-1355.
18. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med*. 1996;22(7):707-710.
19. Kallogjeri D, Piccirillo JF, Spitznagel EL Jr, Steyerberg EW. Comparison of scoring methods for ACE-27: simpler is better. *J Geriatr Oncol*. 2012;3(3):238-245.
20. Benoit DD, Vandewoude KH, Decruyenaere JM, Hoste EA, Colardyn FA. Outcome and early prognostic

indicators in patients with a hematologic malignancy admitted to the intensive care unit for a life-threatening complication. *Crit Care Med*. 2003;31(1):104-112.

21. Levy MM, Fink MP, Marshall JC, et al; SCCM/ESICM/ACCP/ATS/SIS. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med*. 2003;31(4):1250-1256.
22. Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994;149(3 pt 1):818-824.
23. Hosmer DW, Lemershow S. *Applied Logistic Regression*. 2nd ed. New York, NY: Wiley-Interscience; 2000.
24. Gayat E, Pirracchio R, Resche-Rigon M, Mebazaa A, Mary JY, Porcher R. Propensity scores in intensive care and anaesthesiology literature: a systematic review. *Intensive Care Med*. 2010;36(12):1993-2003.
25. Tanvetyanon T, Leighton JC. Life-sustaining treatments in patients who died of chronic congestive heart failure compared with metastatic cancer. *Crit Care Med*. 2003;31(1):60-64.
26. Soares M, Darmon M, Salluh JI, et al. Prognosis of lung cancer patients with life-threatening complications. *Chest*. 2007;131(3):840-846.
27. Soares M, Carvalho MS, Salluh JI, et al. Effect of age on survival of critically ill patients with cancer. *Crit Care Med*. 2006;34(3):715-721.
28. Azoulay E, Alberti C, Bornstain C, et al. Improved survival in cancer patients requiring mechanical ventilatory support: impact of noninvasive mechanical ventilatory support. *Crit Care Med*. 2001;29(3):519-525.
29. Depuydt PO, Benoit DD, Vandewoude KH, Decruyenaere JM, Colardyn FA. Outcome in noninvasively and invasively ventilated hematologic patients with acute respiratory failure. *Chest*. 2004;126(4):1299-1306.
30. Rosolem MM, Rabello LS, Lisboa T, et al. Critically ill patients with cancer and sepsis: clinical course and prognostic factors. *J Crit Care*. 2012;27(3):301-307.
31. Azoulay E, Thiéry G, Chevret S, et al. The prognosis of acute respiratory failure in critically ill cancer patients. *Medicine (Baltimore)*. 2004;83(6):360-370.
32. Taccone FS, Artigas AA, Sprung CL, Moreno R, Sakr Y, Vincent JL. Characteristics and outcomes of cancer patients in European ICUs. *Crit Care*. 2009;13(1):R15.
33. Song JU, Suh GY, Park HY, et al. Early intervention on the outcomes in critically ill cancer patients admitted to intensive care units. *Intensive Care Med*. 2012;38(9):1505-1513.
34. Molina R, Bernal T, Borges M, et al; the EMEHU study investigators. Ventilatory support in critically ill hematology patients with respiratory failure. *Crit Care*. 2012;16(4):R133.
35. Depuydt PO, Benoit DD, Roosens CD, Offner FC, Noens LA, Decruyenaere JM. The impact of the initial ventilatory strategy on survival in hematological patients with acute hypoxemic respiratory failure. *J Crit Care*. 2010;25(1):30-36.
36. Carrillo A, Gonzalez-Diaz G, Ferrer M, et al. Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure. *Intensive Care Med*. 2012;38(3):458-466.