EUR. J. ONCOL.; Vol. 23, n. 1, pp. 30-40, 2018

Acute Respiratory Distress Syndrome in cancer patients: epidemiology, risk factors and outcomes

Eduardo Mantovani Cardoso[1], Aniele Tomadon[2], Keli Lovison[2], Raysa Cristina Schmidt[2], Thais Tsing Chung[2], Péricles A.D. Duarte[2]

[1] Universidade Estadual do Oeste do Paraná–Cascavel/PR- Brazil; [2] General ICU–Hospital do Câncer/UOPECCAN–Cascavel/PR- Brazil

Summary. *Purpose:* This study aimed to evaluate the incidence and outcomes of Acute Respiratory Distress Syndrome (ARDS) in adult oncological patients in the ICU of a dedicated cancer hospital, as well as analyse the risk and protective factors associated with mortality in this population. *Methods:* A prospective cohort study evaluating all adult cancer patients admitted to the ICU, from January 2012 to December 2013. *Results:* The incidence of ARDS (n=87) was 11.9% of cancer patients in the ICU, and 17.8% among those in mechanical ventilation. ARDS was more common in onco-hematological patients. Patients with ARDS had longer ICU length of stay, more complications (mainly acute kidney injury [AKI]) and mortality than non-ARDS patients. Among patients with ARDS, those with a later ARDS onset (>48 h hospitalised) and with a more positive Fluid Balance (FB) had a higher mortality incidence. No differences were found in the ventilatory parameters, although the patients who died presented reduced pulmonary static compliance. *Conclusions:* The incidence and morbimortality of ARDS were high (particularly in onco-hematological patients). Later onset ARDS and highly positive FB presented a trend to a higher mortality.

Key words: Respiratory Distress Syndrome, adult, cancer, Intensive Care Unit, mortality

List of abbreviations

AKI	Acute Kidney Injury
APACHE:	Acute Physiology and Chronic Health Evaluation score
ARDS:	Acute Respiratory Distress Syndrome
COPD:	Chronic Obstructive Pulmonary Disease
Cstat	Pulmonary Static Complacency
FiO2	Fraction of inspired oxygen
ICU:	Intensive Care Unit
MV	Mechanical Ventilation
PaO2	Partial pressure of Oxygen
PEEP	Positive end-expiratory Pressure
PRBC	Packed Red Blood Cells
SD:	Standard deviation
TRALI	Transfusion-related Acute Lung Injury
VAP	Ventilation-associated Pneumonia

Introduction

Cancer remains one of the leading causes of death and hospital costs worldwide, particularly in developing countries (1, 2). The increase in survival rates, due to new screening and treatment strategies (3), also led to an increase in the incidence of admissions of cancer patients in the ICU (4). Oncological patients occupy up to 15% of all ICU beds with important medical, social and economic impacts (5-10).

Mortality caused by ARDS in cancer patients, particularly in onco-hematological malignancies, is superior to that of other ICU populations (11, 12) due to factors such as immunosuppression and infections, comorbidities, chemotherapeutic agents, radiation therapy, or the involvement of neoplastic tissue in the lung (13, 14).

*Objective***s**

This study aimed to evaluate the incidence and outcomes of ARDS in adult oncological patients in the ICU of a dedicated cancer hospital, as well as analyse the protective and risk factors associated with the mortality of this population.

Methods

Prospective cohort study. All patients admitted to the adult ICU from a dedicated cancer centre in southern Brazil from January 2012 to December 2013 were evaluated for ARDS. The ICU has eight beds and admits an almost exclusively oncologic population.

Inclusion criteria were: adult patients admitted to the ICU during the study period with cancer (solid or hematological) and who developed ARDS.

Exclusion criteria: Patients who were <18 years and those who stayed in the ICU for only <2 h (therefore, patients between 2 and 24 h were included) were excluded from the analysis.

Criteria and definitions:

- ARDS: Berlin Consensus Definition (15);
- Acute Kidney Injury (AKI): Any serum creatinine level higher than or equal to 1.5 times the baseline serum level, excluding patients with known prior renal disease (16);
- Sepsis: By the ACCP/SSCM Criteria (17), in use at the time of data collection;
- Vasoactive drug use: Any dose of norepinephrine, dopamine or vasopressin;
- Previous diseases (e.g. Chronic Obstructive Pulmonary Disease, Heart Failure, Chronic Kidney Disease): clinically defined by the healthcare team;

Clinical management (e.g. sedation, antibiotics, tracheostomy, glycemic control, vasoactive drugs, etc.), as well as the ventilatory strategy, were defined by the assistant ICU team (physician and respiratory therapist).

Descriptive statistical analysis was performed and percentages were expressed as frequency, mean and standard deviation. The analysis of baseline and epidemiological data and outcome were conducted using the Student's t-test, analysis of variance and Tukey's test, applying a significance level of $p<0.05$.

Multivariate analysis by logistic regression was performed to identify variables related to higher mortality.

The study was conducted in accordance with the recommendations in Resolution 466/2012 of the Brazilian National Council of Health. This study was approved by the Research Ethics Committee of the Universidade Estadual do Oeste do Paraná-UNIOESTE.

Results

During the study period, 729 adult oncological patients were admitted to the ICU. Of those, 489 required mechanical ventilation (MV). ARDS incidence (n=87) among cancer patients was 11.9% of the admissions and 17.8% in the subgroup that received MV.

Comparison between mechanically ventilated patients with and without ARDS showed that the first ones were more critically ill at ICU admission (higher APACHE II score), younger, had more hematological malignancies (mostly leukemias and lymphomas), higher rates of smoking and lower incidence of elective surgery as etiology. ICU length of stay, MV duration and mortality were significantly higher. Data on MV patients (ARDS or not) are shown in Table 1.

Among ARDS patients, 67.8% were admitted to the ICU due to medical causes; most common etiology was Pneumonia (57%), followed by extra-pulmonary sepsis (19%). Prevalence of previous radiation therapy or chemotherapy was 17% and 31%, respectively (even though only 4% had neutropenia). The most common administered antibiotics were Cefepime, Meropenem, Amikacin, Vancomycin and Teicoplanin. The most frequent complications during ICU stay were Acute Kidney Injury (AKI) (68.9%) and Ventilation-Associated Pneumonia (VAP) (64.4%).

Data analysis of the oncological patients that developed ARDS revealed that some factors were associated with higher mortality, including later-onset ARDS and a more positive fluid balance (supplemental archives [Table S-1], and Figures 2 and 3). However, logistic regression showed that only smoking and alcoholism were associated with higher mortality.

Table 1. Comparison of mechanically ventilated patients with and without ARDS

	MV, no ARDS	MV, ARDS	p-value
n	489	87	- - -
Male sex, %	65.5%	57.5%	0.189
Mean age (years) ± SD	60.9 ± 13.90	55.1 ± 17.18	< 0.001
Mean APACHE II at admission ± SD	24.4 ± 8.64	27.9 ± 8.94	< 0.001
Type of neoplasm, %	- - -	- - -	< 0.001
Solid	87.1%	65.5%	
Gastrointestinal (including liver)	41.1%	36.8%	
Urologycal	8.6%	8.0%	
Head and Neck (including thyroid)	17.5%	4.6%	
Oncohematologycal	12.9%	34.5%	
Lymphoma	3.1%	11.5%	
Leukemia	6.7%	17.2%	
Other previous comorbidities, %	- - -	- - -	0.357
None	34.4%	40.2%	
COPD	16.5%	10.3%	
Heart Failure	11.0%	10.3%	
Other neoplasia (in remission or not)	6.2%	4.6%	
Obesity (moderate or severe)	7.2%	5.7%	
Social habits, %	- - -	- - -	- - -
Tobacco smoking	27.8%	47.1%	< 0.001
Alcoholism	15.6%	17.2%	0.828
Cause of admission, %	- - -	- - -	< 0.001
Medical	46.2%	66.7%	
Elective Surgery	45.4%	23.0%	
Urgent Surgery	8.4%	10.3%	
Total MV duration, days, mean ± SD	3.4 ± 5.28	6.9 ± 6.41	< 0.001
ICU Length of stay, days, mean ± SD	5.9 ± 6.94	10.6 ± 10.16	< 0.001
ICU Mortality, %	55.3%	93.1%	< 0.001
Hospital Mortality, %	58.9%	96.6%	< 0.001

SD: Standard Deviation; MV: Mechanical Ventilation; ARDS: Acute Respiratory Distress Syndrome; ICU: Intensive Care Unit; COPD: Chronic Obstructive Pulmonary Disease; APACHE: Acute Physiology and Chronic Health Evaluation.

Supplemental File 1 - Table S-1. - Clinical and demographic data of patients with ARDS. n = 87

	Discharged alive (ICU)	Death ICU)	p-value
n	6	81	
Male sex, %	33.3%	59.2%	0.418
Age, years, mean ± SD	54.0 ± 18.67	55.3 ± 16.59	0.855
< 40	33.3%	14.8%	
41–60	50%	43.2%	
> 60	16.7%	42.0%	
APACHE II admission, mean ± SD	26.0 ± 7.13	28.0 ± 9.08	0.600
0–10	0	1.2%	
11–20	16.7%	28.4%	
21–25	33.3%	14.8%	
>25	50.0%	55.6%	
Type of neoplasm, %	- - -	- - -	- - -
Solid	66.7%	65.4%	0.701
Gastrointestinal (including liver)	50.0%	35.8%	0.797
Urologycal	0	8.6%	0.978
Oncohematologycal	33.3%	34.6%	0.701
Myeloma	0	3.7%	0.496
Lymphoma	0	12.3%	0.802
Leukemia	33.3%	16.0%	0.602
Recent chemotherapy, %	33.3%	32.1%	0.696
Recent radiation therapy, %	0	1.2%	0.860
Other previous comorbidities, %	- - -	- - -	- - -
None	50.0%)	39.5%	0.940
COPD	0	11.1%	0.867
Heart Failure	16.6%	9.2%	0.902
Hypertension	16.6%	33.3%	0.695
Other neoplasm (in remission or not)	16.6%	3.7%	0.656
Obesity (moderate or severe)	0	6.2%	0.778
Social habits, %	- - -	- - -	- - -
Tobacco smoking	50.0%	46.9%	0.781
Alcoholism	16.7%	17.3%	0.602
Cause of admission, %	- - -	- - -	- - -
Medical	66.7%	66.7%	0.654
Elective surgery	0	24.7%	0.377

(continued)

Supplemental File 1 - Table S-1. - Clinical and demographic data of patients with ARDS. n = 87

Urgent surgery	33.3%	8.6%	0.222
ARDS cause, %	- - -	- - -	- - -
Pulmonary	50.0%	80.3%	0.222
Pneumonia	50.0%	76.5%	
Broncoaspiration	0	1.2%	
Extra-pulmonary	50.0%	19.7%	0.223
Sepsis	50.0%	16.0%	
TRALI	0	1.2%	
Other	0	2.5%	
Time (days) from hospital admission to ARDS, mean ± SD	4.2 ± 10.57	9.0 ± 9.61	0.239
Time (days) from ICU admission to ARDS, mean ± SD	0.3 ± 0.51	2.7 ± 3.28	0.086
0	66.7%	34.6%	
1–2	33.3%	27.2%	
3–7	0	27.2%	
>7	0	11.0%	
Time (hours) of MV before ARDS, mean ± SD	0.2 ± 0.40	1.0 ± 1.60	0.227
0	83.3%	55.5%	0.368
1–24	16.7%	18.5%	0.663
25–72	0	21.0%	0.473
>72	0	5.0%	0.658
Fluid balance 1st day of ARDS, mean ± SD	1557.2 ± 1872.06	2956.1 ± 2481.61	0.181
< (−1.000)	16.7%	2.46%	
(−999) to (−300)	0	4.9%	
(−299) to (+300)	0	4.9%	
(+301) to (+1.200)	33.3%	12.3%	
> (+1.201)	50.0%	72.8%	
Units of PRBCs before ARDS, mean ± SD	1.7 ± 3.20	1.6 ± 2.99	0.937
0 (none)	66.6%	60.6%	
1–2	16.7%	19.7%	
>2	16.7%	19.7%	

MV: Mechanical Ventilation; ARDS: Acute Respiratory Distress Syndrome; ICU: Intensive Care Unit; COPD: Chronic Obstructive Pulmonary Disease; APACHE: Acute Physiology and Chronic Health Evaluation; PRBCs: Packed Red Blood Cells

Supplemental File 2 - Table S-2. Ventilatory parameters and outcomes of patients with ARDS. n = 87

	Discharged alive (ICU)	Death (ICU)	p-value
n	6	81	
Lowest PaO_2/FiO_2, mean ± SD	158.5 ± 96.41	147.9 ± 55.93	0.675
≤100	33.3%	20.5%	
101–200	50.0%	59.0%	
201–300	16.7%	20.5%	
Highest PEEP, cmH_2O, mean ± SD	14.2 ± 4.44	12.2 ± 4.06	0.272
≤5	0	0	
6–9	16.7%	28.4%	
10–14	33.3%	34.6%	
15–18	33.3%	23.4%	
>18	16.7%	13.6%	
Worst (lowest) Cstat, mean ± SD	33.0 ± 8.41	28.9 ± 8.33	0.116
<30	16.7%	53.8%	
31–50	83.3%	44.8%	
>50	0	1.4%	
Total MV duration, days, mean ± SD	8.2 ± 1.72	6.7 ± 6.63	0.224
1	0	1,2%	
2–5	16.7%	43.2%	
6–10	83.3%	19.8%	
>10	0	35.8%	
Vasoactive drugs, hours, %	- - -	- - -	- - -
0 (none)	0	2.5%	0.305
1–24	0	17.3%	
25–48	16.7%	18.5%	
>48	83.3%	58.0%	
ICU complications (others), %	- - -	- - -	- - -
AKI	16.7%	72.8%	0.016
Dialysis	0	22.2%	0.439
Pneumonia	33.3%	66.7%	0.229
Other infections	33.3%	18.5%	0.726
Lung biopsy	0	7.4%	0.885
ICU length of stay, days, mean ± SD	15.7 ± 7.65	10.2 ± 10.26	0.203
1	0	9.9%	
2–5	0	33.3%	
6–10	33.3%	19.8%	
>10	66.7%	37.0%	
Hospital Length of stay, days, mean ± SD	23.8 ± 7.30	19.4 ± 19.42	0.584

MV: Mechanical Ventilation; ARDS: Acute Respiratory Distress Syndrome; ICU: Intensive Care Unit; COPD: Chronic Obstructive Pulmonary Disease; AKI: Acute Kidney Injury; PEEP: Positive End Expiratory Pressure; Cstat: Static Compliance; APACHE: Acute Physiology and Chronic Health Evaluation.SD: Standard Deviation.

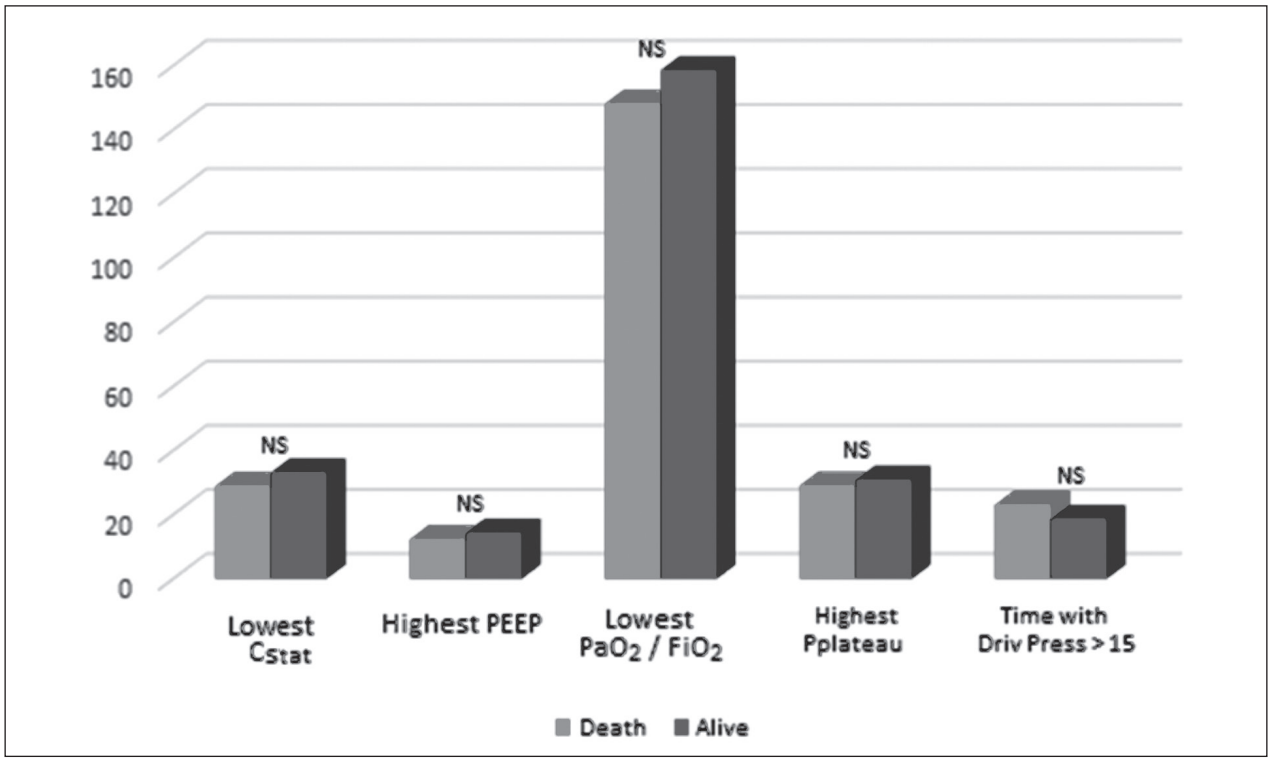

Figure 1. Ventilatory parameters of cancer patients with ARDS (n = 87)
Cstat = Static Complacency (in mL/cmH_2O); PEEP: Positive end-expiratory Pressure (in cmH_2O); PaO_2: Partial pressure of arterial oxygen; FiO_2: Fraction of inspired oxygen; Pplateau: Inspiratory plateau pressure (in cmH_2O); DrivPress: Driving Pressure (cmH_2O); NS: Non-significant.

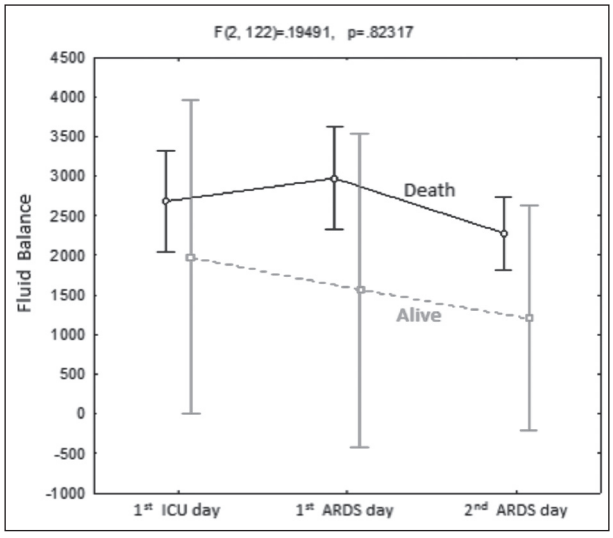

Figure 2. Fluid Balance in 1st ICU day, 1st ARDS day, 2nd ARDS day (n = 87)
Fluid Balance in mL/24h. ICU: Intensive Care Unit; ARDS: Acute Respiratory Distress Syndrome.

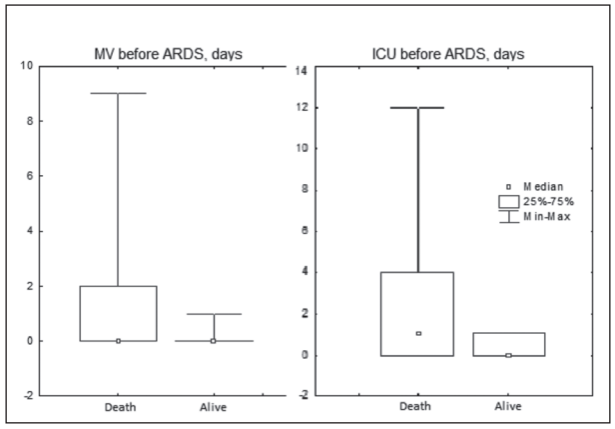

Figure 3. MV and ICU time (before ARDS) x Mortality (n = 87).
MV: Mechanical ventilation; ICU: Intensive Care Unit; ARDS: Acute Respiratory Distress Syndrome.

MV parameters were not significantly different when survivors and non-survivors were compared, although deceased patients had a higher incidence of pulmonary static compliance (Cstat) <30 mL/cmH_2O (supplement archives [Table S-2] and Figure 1).

Discussion

On this study, 11% of cancer patients admitted to the ICU developed ARDS, a similar percentage to that previously reported (11). The APACHE score was significantly higher in our ARDS patients than non-ARDS. Illness severity scores and acute physiologic alterations have been shown to predict mortality in ICU for both oncological and non-oncological patients (18-20). Besides, these scores are usually higher in oncological subjects (13).

Among ARDS patients, the prevalence of hematological cancer (mostly Leukemia and Lymphoma) was higher than non-ARDS, where the vast majority had solid tumours. Up to 11% of patients with hematological malignancies hospitalised will require ICU admission (21), and they are, in general, more severely ill, have higher rates of ARDS (22, 23) and mortality (24) than solid tumours patients. However, at least some of this result (higher mortality in onco-hematological patients) could be explained by the fact that most of the patients with solid tumours were admitted to the ICU for post-operative care after elective surgeries that have lower severity and risk of ARDS (25). When solid tumour and onco-hematological patients are compared, considering both being admitted to the ICU due to medical causes, such as acute respiratory failure or sepsis, ARDS incidence and mortality are similar (13).

ARDS patients' mortality in our study was exceptionally high, even when compared to other studies of oncological patients in the ICU (12). Although ARDS lethality went down recently, due to improving MV management and ICU care in general, the mortality remains high (26). Cancer-associated ARDS makes treatment more difficult due to poorly responsive infections related to immunosuppression, chemotherapy, radiation therapy and the involvement of lung tissue by neoplastic infiltrates (14, 15); for those reasons, mortality in cancer patients with ARDS is higher than non-cancer. We theorise that this particularly high mortality in our research could have been attributed to the fact that many patients that were included in this study ended up receiving exclusively palliative care, with therapeutical limitations, or other patients that rapidly died in a few hours (excluded from most similar studies). Besides, some studies of ARDS in oncological patients, even though retrospective or epidemiological, included mostly patients that were in randomised clinical trials (RCTs); consequently, they were highly selected patients, with usually strict inclusion criteria (12, 13). Thus, our study contributes and differentiates itself because we analysed 'real life' patients (without the effect of participation on RCTs). On the other hand, we should take into account the quality and intensity of care on ICU outcomes: sepsis mortality, e.g. has been shown to be higher in developing countries than in developed ones (27), and, at least in Brazil, it is higher in public hospital's ICUs than in private ones (28). Therefore, this work may provide thoughtful insight into the reality of ARDS in cancer patients, specially from developing countries, which may be different from optimistic results recently reported, that showed a reasonably similar mortality from ARDS in oncological and non-oncological patients (11, 12).

The main factors associated with higher disease severity and mortality in ARDS patients were the duration of MV and ICU stay prior to ARDS development (later onset of ARDS resulting in higher mortality), excessively positive fluid balance before ARDS development and the presence of clinical complications, particularly AKI. Patients with a positive fluid balance are more prone to pulmonary edema with worsening of pulmonary compliance interfering with gas exchange, unfavorable clinical outcomes (e.g. AKI) and higher mortality (29). However, the effects of positive fluid balance before or during ARDS are still controverse (30).

Duration of either ICU stay or time of MV before ARDS might point to different pathophysiologies and influence prognosis, including mortality and illness severity (31). Complications, such as nosocomial infections and AKI, have been described as factors of worse prognosis in ARDS, especially in oncological patients (12, 13, 32,33).

In our study, ventilatory parameters from ARDS patients that did not survive were usually worse than in the survivors: worse (lower) lung compliance, lower PaO_2/FiO_2 and higher driving pressure. On the other hand, PEEP was higher in the surviving patients (although lower mean PaO_2/FiO_2). MV strategies with lower tidal volume, plateau pressure, driving pressure and, possibly, higher PEEP have been shown to reduced mortality in ARDS in many different studies (26, 34-37), although 'very high' PEEP and alveolar recruitment strategies did not show any benefit (38). A previous study that analysed the impact of MV over mortality on oncological ARDS patients did not find prognostic association (13). Nevertheless, it is possible that because of the characteristics of that studied population (ARDSnet study subgroups), some variables might have been artificially different than those of daily practice (e.g. the median of the highest PEEP on this study was 8 cmH_2O, significantly inferior to our results and to those published by most epidemiological studies) (26, 39). Regardless of that, it has been found that in patients with hematological malignancies, those with lower PaO_2/FiO_2 and higher $PaCO_2$ had higher mortality rates (33). Lung compliance and gas exchange were found to be worse in oncological versus non-oncological ARDS patients, reflecting a possibly higher degree of lung involvement (14, 15, 19).

This study has several limitations (some of which are inherent to its nature), which may compromise the interpretation of the data. This was an observational study of a single centre (a specialised cancer hospital in Southern Brazil). This might not reflect the reality of most ICUs in our country or in the world, especially considering differences in outcomes regarding low/medium income versus high-income countries. In addition, the number of patients may not be large enough to answer questions about specific groups, such as the difference between solid cancer and onco-hematological patients. However, it was still comparable to many studies of the oncological patient in the ICU (24). Likewise, we did not have a control group of non-oncological patients developing ARDS. Due to being an observational study, the impact of evaluation and management strategies was not specifically studied, once the clinical decision was left to the medical and multi-professional team, according to local protocols and routines. However, the objective of the study was to evaluate the 'real life' situation of adult oncological patients who developed ARDS in the ICU of a dedicated cancer hospital in a developing country, and therefore, the design of the study was set up for this purpose.

Due to the study design, patients were only monitored until ICU discharge. For this reason, the late outcomes (including quality of life) were not evaluated in the present study.

Conclusions

In a population of oncological patients in a Brazilian ICU, the incidence of ARDS was high, particularly on medical and onco-hematological patients, with high mortality and complication rates. Patients with late-onset ARDS (after >24-48 h of ICU stay), more positive fluid balance on the 1st day of ARDS and lower lung compliance tended to have higher mortality rates.

Ethical approval and Consent to Participate

The study was conducted in accordance with the recommendations in Resolution 466/2012 of the Brazilian National Council of Health. This study was approved by the Research Ethics Committee of the Universidade Estadual do Oeste do Paraná-UNIOESTE. Accordingly, post-informed consent was waived, since this current study only describes the results of a population already previously treated.

Author's Contributions

PADD designed the study, analysed the data, wrote the manuscript; EMC, AT, KL collected the data, analysed the data, wrote the manuscript; RCS, TTC analysed the data, wrote and revised the manuscript. All the authors read and approved the final manuscript.

Acknowledgements

The authors would like to thank the physicians, health professionals and residents, working at the General ICU at the Cancer Hospital/UOPECCAN, Cascavel, Brazil.

References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013.
2. Bray F, Soerjomataram I. The Changing Global Burden of Cancer: Transitions in human development and implications for Cancer prevention and control. In: Gelband H, Jha P, Sankaranarayanan R, et al., editors. Cancer: Disease control priorities, Third Edition (Volume 3). Washington (DC): The International Bank for Reconstruction and Development/The World Bank; 2015. Chapter 2. Available from: https://www.ncbi.nlm.nih.gov/books/NBK343643/ doi: 10.1596/978-1-4648-0349-9_ch2
3. Brenner H. Long-term survival rates of cancer patients achieved by the end of the 20th century: a period analysis. Lancet 2002; 360(9340): 1131-5.
4. Angus DC, Barnato AE, Linde-Zwirble WT, Weissfeld LA, Watson RS, Rickert Tet al. Use of intensive care at the end of life in the United States: an epidemiologic study. Crit Care Med 2004; 32(3): 638-43.
5. Vincent JL, Moreno R, Takala J, Willatts S, de Mendonça A, Bruining H, Reinhart CK, Suter PM, Thijs LG. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intens Care Med 1996; 22(7): 707-10.
6. Vincent JL, Sakr Y, Sprung C, Ranieri V, Reinhart K, Gerlach H et al. Sepsis in European intensive care units: Results of the SOAP study. Crit Care Med 2006; 34(2): 344-53.
7. Taccone F, Artigas A, Sprung C, Moreno R, Sakr Y, Vincent J. Characteristics and outcomes of cancer patients in European ICUs. Crit Care 2009; 13(1): R15.
8. Soares M, Salluh JI, Torres VB, Leal JV, Spector N. Short- and long-term outcomes of critically ill patients with cancer and prolonged ICU length of stay. Chest 2008; 134(3): 520-6.
9. Schellongowski P, Sperr WR, Wohlfarth P, et al. Critically ill patients with cancer: chances and limitations of intensive care medicine—a narrative review. ESMO Open 2016; 1(5): e000018.
10. Cooper LM, Linde-Zwirble WT. Medicare intensive care unit use: Analysis of incidence, cost, and payment. Crit Care Med 2004; 32(11): 2247-53.
11. Azoulay E, Lemiale V, Mokart D, Pène F, Kouatchet A, Perez P, et al. Acute respiratory distress syndrome in patients with malignancies. Intens Care Med 2014; 40(8): 1106-14.
12. Soubani A, Shehada E, Chen W, Smith D. The outcome of cancer patients with acute respiratory distress syndrome. J Crit Care 2014; 29(1): 183.e7-.e12.
13. Burghi G, Lemiale V, Seguin A, Lambert J, Lacroix C, Canet E et al. Outcomes of mechanically ventilated hematology patients with invasive pulmonary aspergillosis. Intens Care Med 2011; 37(10): 1605-12.
14. Afessa B, Azoulay E. Critical care of the hematopoietic stem cell transplant recipient. Crit Care Clin 2010; 26(1): 133-50.
15. The ARDS Definition Task Force. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camporota L, Slutsky AS. Acute respiratory distress syndrome: the Berlin definition. JAMA 2012; 307(23): 2526-33.
16. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8(4): R204-12.
17. Bone R, Balk R, Cerra F, Dellinger R, Fein A, Knaus W et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest 1992; 101(6): 1644-55.
18. Xia R, Wang D. Intensive care unit prognostic factors in critically ill patients with advanced solid tumors: a 3-year retrospective study. BMC Cancer 2016; 16:188.
19. Agarwal R, Aggarwal AN, Gupta D, Behera D, Jindal SK.Etiology and outcomes of pulmonary and extrapulmonary acute lung injury/ARDS in a respiratory ICU in North India. Chest 2006; 130(3): 724-9.
20. Brun-Buisson C, Meshaka P, Pinton P, Vallet B. EPISEPSIS: a reappraisal of the epidemiology and outcome of severe sepsis in French intensive care units. Intens Care Med 2004; 30(4): 580-8.
21. Wallace DJ, Seymour CW, Kahn JM. Hospital-level changes in adult ICU bed supply in the United States. Crit Care Med 2017; 45(1): e67-76.
22. Azoulay E, Mokart D, Pène F, Lambert J, Kouatchet A, Mayaux J, et al. Outcomes of critically ill patients with haematologic malignancies: prospective multicenter data from France and Belgium-a groupe de recherché respiratoire en reanimation onco-hematologique study. J Clin Oncol 2013; 31(22): 2810-8.
24. Puxty K, Mcloone P, Quasim T, Kinsella J, Morrison D. Survival in solid cancer patients following intensive care unit admission. Intens Care Med 2014; 40(10): 1409-28.
23. Geerse DA, Span LF, Pinto-Sietsma SJ, van Mook WN. Prognosis of patients with haematological malignancies admitted to the intensive care unit: Sequential Organ Failure Assessment (SOFA) trend is a powerful predictor of mortality. Eur J Intern Med 2011; 22(1): 57-61.
25. Bos MMEM, Keizer NFD, Meynaar IA, Bakhshi-Raiez F, Jonge ED. Outcomes of cancer patients after unplanned admission to general intensive care units. Acta Oncol 2012; 51(7): 897-905.
26. Bellani G, Laffey J, Pham T, Fan E, Brochard L, Esteban A 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.
27. Schultz MJ, Dunser MW, Dondorp AM, Adhikari NKJ,

Iyer S, Kwizera A, et al. Current challenges in the management of sepsis in ICUs in resource-poor settings and suggestions for the future. Intens Care Med 2017; 43(5): 612-24.
28. Conde KAP, Silva E, Silva CO, Ferreira E, Freitas FGR, Castro I, et al. Differences in Sepsis treatment and outcomes between public and private hospitals in Brazil: A multicenter observational study. PLoS One 2013; 8(6): e64790.
29. Grams ME, Estrella MM, Coresh J, Brower RG, Liu KD. Fluid balance, diuretic use and mortality in cute kidney injury. Clin J Am SocNephrol 2011; 6(5): 966-73.
30. Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, deBoisblanc B, et al. The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006; 354(24): 2564-75.
31. Vincent JL, Sakr Y, Groeneveld J, Zandstra DF, Hoste E, Malledant Y, Lei K, Sprung CL. ARDS of early or late onset: Does it make a difference? Chest 2010; 137(1): 81-7.
32. Türkoglu M, Erdem GU, Suyani E, Sancar ME, Yalcin MM, Aygencel G, et al. Acute Respiratory Distress Syndrome in patients with hematological malignancies. Hematology 2013; 18(3): 123-30.
33. Mokart D, Craenenbroeck T, Lambert J, Textoris J, Brun JP, Sannini A, et al. Prognosis of acute respiratory distress syndrome in neutropenic cancer patients. Eur Respir J 2012; 40(1): 169-76.
34. Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. 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.
35. Gattinoni L, Caironi P, Cressoni M, Chiumello D, Ranieri VM, Quintel M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. N Engl J Med 2006; 354(17): 1775-86.
36. Briel M, Meade M, Mercat A, Brower RG, Talmor D, Walter SD, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. JAMA 2010; 303(9): 865-73.
37. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the Acute Respiratory Distress Syndrome. N Engl J Med 2015; 372(8): 747-55.
38. Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators. Effect of lung recruitment and titrated Positive End-Expiratory Pressure (PEEP) vs low PEEP on mortality in patients with Acute Respiratory Distress Syndrome. A randomized clinical Trial. JAMA 2017; 318(14): 1335-45.
39. Esteban A, Ferguson ND, Meade MO, Frutos-Vivar F, Apezteguia C, Brochard L, et al. Evolution of mechanical ventilation in response to clinical research. Am J Respir Crit Care Med 2008; 177(2): 170-7.

Correspondence:
Péricles A.D. Duarte
General ICU-Hospital do Câncer/UOPECCAN
Brazil
E-mail: pericles.duarte@uol.com.br