Acute Organ Failure and Risk of Admission to Intensive Medical Care in Cancer Patients, A Single Centre Inception Cohort Study

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Abstract

Background: Risk of acute organ failure (AOF) in cancer patients on systemic antineoplastic treatment is unknown. However, up to 5% of non-hematologic and 15% of hematologic cancer patients will need to be admitted to an intensive care unit (ICU). IPOPSCI-2017/01 is a prospective cohort study designed to ascertain the cumulative incidence of AOF and ICU admission in adult cancer patients.

Methods: Single centre prospective cohort study with consecutive sampling of adult cancer patients admitted for unscheduled inpatient care while on, or up to 8 weeks after, systemic cancer treatment. Primary endpoints were cumulative risk of developing AOF and of ICU admission. Six months accrual expected an accrual of 400 patients to infer a population risk of ICU admission with a precision error of 2% and type 1 error of 5%.

Results: Between August 2018 and February 2019, 10392 patients were on systemic anti-neoplastic treatment, 358 had unscheduled inpatient care and were eligible for inclusion and 285 were included. Mean age was 60.9 years-old, 50.9% were male, 52.3% had adjusted Charlson Comorbidity Index ≥3 and hematologic cancers accounted for 17.9% of patients. The cumulative risk of AOF on hospital admission was 29.5% (95%CI: 26-33) and during hospital stay was 39.6% (95%CI: 35-44). Cumulative risk of ICU admission of the patients with AOF was 15.0% (95%CI: 12-18) and if artificial life support criteria and AOF, cumulative risk of ICU admission was 31.5% (95%CI:CI: 23-40). On admission, 62.1% of patients were considered not eligible for artificial organ replacement therapy (no-AORT) and 34.3% of patients who developed AOF while in-hospital were judged no-AORT. Overall, 17 (15%) patients with AOF were admitted to ICU, 31.5% for AORT. Median follow up was 9.5 months. Inpatient mortality was 17.5%, with ICU mortality rate of 58.8%, with median cohort survival 134 days (95%CI: 106-162). On multivariate analysis, AOF was an independent poor prognostic factor (HR 1.6; 95%CI: 1.2-2.2).

Conclusions: Risk of AOF in cancer patients admitted for unscheduled inpatient care while on systemic treatment is 39.6%, and risk of ICU admission is 15.0%. AOF in cancer patients was an independent poor prognostic factor for inpatient hospital stay and 6-months survival.

Background

The incidence of cancer is estimated to be more than 3 million cases *per* year, in Europe, with approximately 1.5 million cancer related-deaths. (1) With the improvement of diagnostic tests and treatments for cancer there has been a steady decrease in cancer-related mortality. (2) The increasing number of patients receiving cancer-treatment results in more frequent adverse drug reactions, some of which associated with acute organ failure and thus increasing the number of cancer-patients who may require admission to Intensive Care Units (ICU). (3), (4), (5)

Incidence of acute organ failure (AOF) in patients on anti-neoplastic systemic treatment is unknown. It is estimated that 5% of patients with solid tumors and 15% with hematological cancer will need admission to an ICU in the early stages of their disease. (5), (6), (7) Patients with advanced cancer may benefit from

ICU admission. (8), (9), (10),(11)The two most common causes of ICU admission in patients with cancer are acute respiratory failure and sepsis. Although survival rates for cancer patients admitted for ICU care are lower than the ones of patients without comorbidities, their mortality rates are similar to those with other comorbidities, namely chronic heart failure. Early identification of organ failure and timely admission in ICU are critical for the short-term prognosis of these patients. However, long-term outcome depends on the characteristics of the malignant disease and its prognosis, not on the severity of the acute event. (12)

This study was designed to estimate the incidence of acute organ failure (AOF) in cancer patients on systemic anti-neoplastic treatment, to estimate the incidence of ICU admission and prognosis of these patients in the setting of the largest Portuguese comprehensive cancer center.

Methods

Study design

This was a prospective cohort study with consecutively sampled cancer patients admitted for in hospital care due to a medical complication of cancer treatment at Instituto Português de Oncologia Francisco Gentil do Porto from August 2018 to February 2019.

Key inclusion criteria were a subject age of 18 years-old or more, a histological or cytological diagnose of malignancy, active antineoplastic treatment – defined as the administration of at least one systemic antineoplastic agent in the 8 weeks prior to hospital admission – and an unscheduled hospital admission for inpatient care with eligibility assessed within the first 60 hours of inpatient care. All patients provided written informed consent prior to study inclusion. Patients were excluded if they had undergone surgical treatment within 4 weeks of admission. Unscheduled hospital admission was defined as hospital admission which cannot be planned in advance by the health professional due to an acute health event, with need of urgent medical care that cannot be delivered in an ambulatory schedule.

The primary study endpoints were the cumulative incidence of organ failure defined as the occurrence of any of the following according to quick SOFA (Sequential Organ Failure Assessment) criteria: respiratory rate of 22/min or greater, altered mental status, systolic blood pressure of 100 mmHg or less, or clinical deterioration that is cause for clinical concern of the attending medical oncologist or hematologist and, cumulative risk of admission to intensive medical care. Secondary endpoints were the probability of resuming antineoplastic treatment after discharge and the survival of cancer patients who developed an AOF while undergoing systemic antineoplastic treatment.

All included patients were treated according to institutional guidelines and local best practices. Data collection for this study was performed after each patient's hospital discharge through a standardized case report form. All patients were followed until the end of June 2019.

A sample size of 400 subjects was estimated to allow the computation of the risk of admission to intensive medical care with a precision error of 2% and type 1 error of 5%. (13)

This study was approved by the hospital administration and ethics committee number CES/IPO: 204/018.

Statistical analysis

Baseline characteristics of included subjects at inpatient care admission were described using descriptive statistics as indicated. Two main subgroups were considered, those that had AOF at admission or during the inpatient hospital stay and those without AOF. An exploratory analysis of the baseline characteristics between these subgroups was performed using parametric and non-parametric tests as appropriate.

Cumulative risk of AOF was calculated as the proportion of patients with AOF at admission or during inpatient stay from those that were included in the study. Cumulative risk of admission to intensive care unit (ICU) was calculated as the proportion of patients admitted to ICU from those that were included in the study.

The outcome of cancer patients who develop AOF while undergoing systemic antineoplastic treatment was evaluated by inpatient hospital mortality and median survival was calculated using the Kaplan-Meier method. The outcome data for subjects admitted to the ICU were the mortality rate during ICU stay and 30-days after discharge from the unit, and the median survival was calculated by Kaplan-Meier method.

Exploratory analysis of these outcome measures based on the admission assessment for prior eligibility for intensive medical treatment was evaluated by log rank method. Furthermore, exploratory analysis of the impact of other baseline characteristics was explored with the use of univariate and multivariate cox proportional hazard model. No correction for multiple hypothesis testing was established as this analysis was exploratory and hypothesis generating. All data was analyzed using the SPSS Statistics v25.0.

Results

Patient and disease characteristics

From August 2018 to February 2019, 10.392 patients were on systemic anti-neoplastic treatment, 358 had unscheduled inpatient care and were eligible for inclusion and 285 were included (Fig. 1). Cohort's median follow-up time was 9.5 months (minimum 6 – maximum 12).

Baseline characteristics at the time of acute inpatient admission are described in Table 1. Mean age was 60.9 years-old ± 11.8, with 50.9% (n = 145) male subjects. The majority (52.3%, n = 149) of patients presented significant comorbidities as assessed by adjusted Charlson Comorbidity Index, and 35.1% (n = 100) were taking 5 or more drugs daily. Hematologic cancer was present in 51 patients (17.9%) and non-

hematologic in 82.1% (n = 234). The most frequent hematologic cancers were non-follicular lymphoma (37.3%, n = 19), multiple myeloma or malignant plasma cell neoplasms (27.5%, n = 14) and lymphoid leukaemia (13.7% n = 7). Regarding the non-hematologic cancers, the most frequent topography of the primary tumor was the digestive tract or glands in 26.5% (n = 62), lungs and respiratory tract in 19.2% (n = 45) and breast in 17.5% (n = 41).

Table 1
Baselines Characteristics of patients at the time of acute inpatient admission

Characteristic	**N (%)**
Total N = 285	
Age – years *(mean ± SD)*	60.9 ± 11.8
Male Gender	145 (50.9)
Adjusted Charlson Comorbidity Index	
0	31 (10.9)
1	52 (18.2)
2	53 (18.6)
≥ 3	149 (52.3)
Number of daily drugs in current use	
0	30 (10.5)
1–5	155 (54.4)
≥ 5	100 (35.1)
Neoplasia, type	
Non-Hematologic	234 (82.1)
Hematologic	51 (17.9)
Primary topography of Non-Hematologic tumors	
Digestive tract and digestive glands	62 (26.5)
Lungs and respiratory tract	45 (19.2)
Breast	41 (17.5)
Head and Neck	14 (6.0)
Gynecologic	14 (6.0)
Others[†]	58 (24.8)
Type of hematologic tumors	
Non-Follicular lymphoma	19 (37.3)
Multiple myeloma or malignant plasma cell neoplasms	14 (27.5)
Lymphoid leukemia	7 (13.7)
Myeloid leukemia	6 (11.8)

Characteristic Total N = 285	N (%)
Others*	5 (9.7)
Time since diagnosis – months *(median [range])*	15 [0-253]
Current antineoplastic treatment	
Curative intent	76 (26.7)
Time since last treatment – days *(median [range])*	13 [0–56]
> 1 previous treatment lines	160 (56.1)
Inpatient admission cause	
Infection	116 (40.7)
Febrile neutropenia	49 (17.2)
Severe sepsis/Septic shock	35 (12.3)
Uncontrolled pain	31(11.2)
Respiratory insufficiency (not infectious)	17 (6.0)
Neurologic dysfunction (not infectious)	15 (5.3)
General status degradation	15 (5.3)
Other causes‡	108 (37.9)

SD, standard deviation; CCI, Charlson Comorbidity Index

†Others: malignant neoplasms of mesothelial or soft tissue, malignant neoplasms of male genital organs, malignant neoplasms of urinary tract, malignant neoplasms of skin, malignant neoplasms of thyroid or other endocrine glands, malignant neoplasms of bone and articular cartilage, malignant neoplasms of ill-defined, secondary and unspecified sites, Malignant neoplasms of independent (primary) multiple sites.

**Others: follicular lymphoma, mature T/NK-cell lymphoma, others and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue*

‡ Other causes: Gastrointestinal disturbances, hemorrhage, hepatic failure, kidney failure, electrolytic disturbances, pancytopenia, cardiac failure or other cardiac causes, cord compression syndrome, mucositis, superior vena cava syndrome, anemia.

*†, *, ‡frequency less than 5%.*

Median time since diagnosis of neoplasia and the inpatient admission was 15 months (range 0-253) and median time since the last administration of antineoplastic treatment was 13 days (range 0–56). Antineoplastic treatment was prescribed with curative intent in 76 patients (26.7%). The most frequent causes for acute inpatient admission were infections (40.7%, n = 116), followed by uncontrolled pain (11.2%, n = 31) and respiratory insufficiency not attributable to infectious causes (6.0%, n = 17). Of the

116 patients admitted with fever, 56.9% (n = 66) had no infection focus identified at admission. Most frequent sites of infection where respiratory (20.7%, n = 24), gastrointestinal (7.8%, n = 9), cutaneous (6.0%, n = 7) and other sites (8.6%, n = 10). At inpatient hospital admission, 62.1% (n = 177) of patients were considered not eligible for artificial organ replacement therapy.

Risk of acute organ failure and intensive care unit admission

Cumulative risk of AOF at admission for inpatient care was 29.5% (95%CI: 26–33) and cumulative risk of AOF (at admission or during inpatient care) was 39.6% (95%CI: 35–44). For those patients with artificial life support criteria indication at admission, the cumulative risk of AOF was 50.0% (95%CI: 41–59).

Cumulative risk of intensive care unit admission of the patients with AOF was 15.0% (95%CI: 12–18). For those patients with artificial life support criteria, cumulative risk of intensive care unit admission of the patients with AOF was 31.5% (95%CI: 23–40).

Characteristics and comparisons between patients undergoing systemic antineoplastic treatment who presented an AOF and those who did not present AOF are described in Table 2. Patients with AOF were 3.3 years older ($p = 0.03$), with a higher proportion of patients with ≥ 3 adjusted CCI score (62.5% vs 45.3%, $p = 0.04$) and with a higher prevalence of hematologic malignancies (25.7% vs 12.8%, $p = 0.007$). Most patients with AOF were in first line of antineoplastic treatment (53.1% vs 37.8%, $p = 0.015$), and there were no differences between both groups and the intent of treatment (curative or palliative). Most frequent inpatient admission cause of AOF was infection (54.9% vs 31.4%, $p < 0.001$). Of those patients who developed AOF 34.3% were considered to not benefit from artificial organ replacement therapy.

Table 2
Baseline characteristics according to the occurrence of AOF.

Characteristic	**No AOF**	**AOF**	***p***
N (%)	**N = 172**	**N = 113**	
Age – years *(mean ± SD)*	59.6 ± 11.8	62.9 ± 11.6	0.03
Male Gender	84 (48.8)	61 (54.0)	0.40
Adjusted CCI			0.04
0	22 (12.8)	9 (8.0)	
1	37 (21.5)	15 (13.4)	
2	35 (20.3)	18 (16.1)	
≥ 3	78 (45.3)	70 (62.5)	
Number of daily drugs in current use			
0	19 (11.0)	11 (9.8)	0.82
1–5	95 (55.2)	60 (52.7)	
≥ 5	58 (33.7)	42 (37.5)	
Neoplasia, type			0.007
Non-Hematologic	150 (87.2)	84 (74.3)	
Hematologic	22 (12.8)	29 (25.7)	
Primary topography of Non-Hematologic tumors			
Digestive tract and digestive glands	45 (30.0)	17 (20.2)	0.26
Lungs and respiratory tract	22 (14.7)	23 (27.4)	
Breast	27 (18.0)	14 (16.6)	
Head and Neck	9 (6.0)	5 (6.0)	
Gynecologic	9 (6.0)	5 (6.0)	
Others[†]	38 (25.3)	20 (23.8)	
Previous antineoplastic treatment			0.08
Curative intent	39 (22.7)	37 (32.7)	
Palliative intent	133 (77.3)	76 (67.3)	
Time since last treatment – days *(median [range])*	16 [0–56]	17 [0–56]	0.88
> 1 previous treatment lines	107 (62.2)	53 (46.9)	0.015

Characteristic N (%)	No AOF N = 172	AOF N = 113	*p*
Time since diagnosis – months *(median [range])*	18,5 [0-178]	11 [0-253]	0.03
Inpatient admission cause			
Infection	54 (31.4)	62 (54.9)	< 0.001
Febrile neutropenia	23 (13.4)	26 (23)	
Severe sepsis/Septic shock	NA	35 (31)	
Uncontrolled pain	26 (15.1)	6 (5.3)	
Respiratory insufficient (not infectious)	5 (2.9)	12 (10.6)	
Neurologic dysfunction (not infectious)	6 (3.5)	9 (8.0)	
General status degradation	12 (7.0)	3 (2.7)	
Other causes‡	69 (40.1)	21 (18.6)	
Artificial organ replacement therapy			
Withheld	113 (65.7)	59 (34.3)	0.12

SD, standard deviation; CCI, Charlson Comorbidity Index; NA, Not applicable.

† Others: mesothelial or soft tissue, male genital organs, urinary tract, skin, thyroid or other endocrine glands, bone and articular cartilage, ill-defined, secondary and unspecified sites, neoplasms of independent (primary) multiple sites.‡ Other causes: Gastrointestinal disturbances, hemorrhage, hepatic failure, kidney failure, electrolytic disturbances, pancytopenia, cardiac failure or other cardiac causes, cord compression syndrome, mucositis, superior vena cava syndrome, anemia.†, ‡ frequency less than 5%.

Characteristics of ICU admitted patients

Of the 17 patients admitted in the ICU, 23.5% (n = 4) had hematologic cancers, 17.6% (n = 3) digestive tract cancer, 17.6% (n = 3) breast cancer, 17.6% (n = 3) male genital cancer, 11.8% (n = 2) lung cancer, 5.9% (n = 1) hypopharynx cancer, 5.9% (n = 1) small intestine neuroendocrine cancer. Antineoplastic systemic treatment was considered with curative intent in 8 patients (47.1%). AOF was present at hospital admission in 13 patients (76.5%). The main diagnosis on ICU admission was infection (58.9%; n = 10), febrile neutropenia (29.4%; n = 5), severe sepsis or septic shock (41.2%; n = 7), non-infectious respiratory insufficiency (11.8%; n = 2) and neurologic dysfunction, cardiac insufficiency, acute renal failure, carcinoid syndrome and perforated hollow viscus with 1 case each.

Patient outcomes

Overall, in hospital mortality was 17.5% and for those patients admitted in the ICU in hospital mortality was 58.8%. Of those patients discharged home, 63.8% resumed antineoplastic treatment. For patients

who required ICU care, 57.1% resumed antineoplastic treatment. On univariate analysis, the probability of resuming systemic therapy was higher for those patients being treated with curative intent for their cancer, for those who had improved health status at the time of the discharge and those with hematologic cancers (Table 3). Median survival was 134 days (95%CI: 106–162), with an overall mortality of 65.6% (n = 187) (Fig. 2). Median survival for ICU admitted patients was 73 days (95%CI: 0-163).

Table 3
Baseline characteristics between patients who resumed systemic treatment and those who did not.

Characteristic **N (%)**	**No systemic treatment resumed** **N = 85**	**Resumed systemic treatment** **N = 150**	***p***
Age – years *(mean ± SD)*	61.7 ± 10.5	59.8 ± 11.7	0.20
Gender			0.28
Male	46 (40.0)	69 (60.0)	
Adjusted CCI			0.49
0	7 (28.0)	18 (72.0)	
1	19 (43.2)	25 (56.8)	
2	15 (30.6)	34 (69.4)	
≥ 3	44 (37.6)	73 (62.4)	
Number of daily drugs in current use			0.75
0	11 (42.3)	15 (57.7)	
1–5	47 (36.4)	82 (63.6)	
≥ 5	27 (34.2)	52 (65.8)	
Neoplasia, type			0.03
Non-Hematologic	76 (39.4)	117 (60.6)	
Primary topography of Non-Hematologic tumors			0.18
Digestive tract and digestive glands	30 (54.5)	25 (45.5)	
Lungs and respiratory tract	10 (31.3)	22 (68.8)	
Breast	12 (32.4)	25 (67.6)	
Head and Neck	6 (50.0)	6 (50.0)	
Ginecologic	2 (18.2)	9 (81.8)	
Others[†]	16 (34.8)	30 (65.2)	
Previous antineoplastic treatment			
Curative intent	15 (21.7)	54 (78.3)	0.004
Paliative intent	70 (42.2)	96 (57.8)	

Characteristic N (%)	No systemic treatment resumed N = 85	Resumed systemic treatment N = 150	*p*
Time since last treatment – days *(median [range])*	13.0 [0–56]	12.0 [0–56]	0.34
> 1 previous treatment lines	53 (40.8)	77 (59.2)	0.13
Time since diagnosis – months *(median [range])*	18.0 [0-150]	14.5 [0-215]	0.47
Inpatient admission cause			0.07
Infection	26 (26.0)	74 (74.0)	
Uncontrolled pain	11 (40.7)	16 (59.3)	
Respiratory insufficient (not infectious)	7 (53.8)	6 (46.2)	
Neurologic disfunction (not infectious)	2 (25.0)	6 (75.0)	
General status degradation	4 (50.0)	4 (50.0)	
Other causes‡	35 (44.3)	44 (55.7)	
AOF	29 (37.7)	48 (62.3)	0.77
Discharge patient health status			0.04
Improved	64 (32.8)	131 (67.2)	
Stable	18 (50.0)	18 (50.0)	
Worsen	3 (75.0)	1 (25.0)	

AOF, Acute organ failure; SD, standard deviation; CCI, Charlson Comorbidity Index; NA, Not applicable;

† Others: malignant neoplasms of mesothelial or soft tissue, malignant neoplasms of male genital organs, malignant neoplasms of urinary tract, malignant neoplasms of skin, malignant neoplasms of thyroid or other endocrine glands, malignant neoplasms of bone and articular cartilage, malignant neoplasms of ill-defined, secondary and unspecified sites, Malignant neoplasms of independent (primary) multiple sites.

‡ Other causes: Gastrointestinal disturbances, hemorrhage, hepatic failure, kidney failure, electrolytic disturbances, pancytopenia, cardiac failure or other cardiac causes, cord compression syndrome, mucositis, superior vena cava syndrome, anemia.

Patients who developed AOF had a median survival was 87 days (95%CI: 41–133), which was significantly lower than that of patients with no-AOF (median 149 days [95%CI: 110–188], p = 0.028) (Fig. 3). AOF was associated with both an increased risk of in hospital mortality, HR 3.4 (95%CI: 1.8–6.5; p < 0.0001) and increased post-discharge mortality HR 1.6 (95%CI 1.2–2.2, p = 0.002) after adjustment for the following covariates: age ≥ 60 years-old, adjusted CCI ≥ 3, hematologic or non-hematologic

malignancy, treatment intent curative or palliative, first or more than 1 line of anti-neoplastic treatment and admission cause.

Discussion

We have conducted a prospective cohort study that included cancer patients treated with systemic anti-neoplastic therapies in the largest Portuguese comprehensive cancer center, during a six-month period to assess the cumulative risk of acute organ failure and the cumulative incidence of ICU admission while on treatment. We estimate the risk of AOF on hospital admission in patients undergoing systemic anti-cancer treatment at 29.5% and the risk of ICU admission at 15%. To our knowledge, this is the first published study addressing the risk of developing AOF in cancer patients while on ambulatory anti-neoplastic systemic treatment. The determination of the incidence of AOF in cancer patients is of particular interest since it may impact short-term survival and lead to higher medical resource use due to the referral of patients for ICU care. (7),(8)

Most studies addressing acutely ill cancer patients are focused on patients admitted for intensive medical care and their short-term outcomes (e.g., in-hospital mortality, 28-days mortality) (7), (8), (14). These studies are commonly retrospective and with heterogeneous patient samples, different case mix of medical and surgical patients, or hematologic and solid cancer patients and bone marrow transplant recipients. Our sample included cancer patients on systemic antineoplastic treatment with an unscheduled hospital admission while on-treatment, with the main purpose of evaluating the incidence of AOF on these patients. We cannot rule out selection bias resulting in possible underestimation of these risk, as the accrual of patients was based on a single center recruitment and some patients whose treatment had been prescribed at our centre may have been admitted for acute care treatment at other hospitals or died at home due to AOF. Moreover, some patients that were clinically unstable to consent or were discharged or died before being able to sign the consent form for study participation were not included, however the impact of these on our estimates is uncertain.

In this our study, patients with older age, adjusted CCI $\geq$ 3 and hematological diseases were more likely to have AOF when admitted for unscheduled inpatient care after systemic cancer therapy. This was more frequent during a first line systemic treatment and in patients with shorter time interval from the diagnosis of cancer, which is probably related with the aggressiveness of first treatment lines in patients whose baseline biological reserve is yet unknown. (15) Infection was the primary reason for unscheduled hospitalization, and of these, 17.2% presented with febrile neutropenia and 12.3% with sepsis or septic shock, thus contributing to the high prevalence AOF.

The choice of quick SOFA as the outcome measure for defining AOF was due to its ease of applicability and because it is a validated measure for in-hospital mortality in non-ICU setting in patients with confirmed or suspected infection. (16), (17), (18) Additionally, in the non-infectious context, it has been

prospectively studied for assessment of acute organ failure with 2-day and 30-day mortality prognostic accuracy of 79.9% and 76.2%. (19) Quick SOFA has also been prospectively compared against systemic inflammatory response syndrome (SIRS) score in predicting ICU and hospital mortality in critically ill cancer patients with better prognostic accuracy compared with SIRS for both parameters. (19) Therefore we believe that the outcome measurement and adjudication method does not bias the estimated risk of AOF in these patients.

When considering the entire hospitalization period cumulative risk of AOF increased to 39.6%. The reported a risk for severe sepsis of 12.3% compares with prior estimates that range from 4.9% and of 46% in ICU admitted cancer patients. (20),(21). When considering AORT, 1 in 3 patients that developed AOF were admitted for ICU care, 75% of which on the first day of hospital stay and half of these patients were undergoing treatment with curative intention. Infection was the primary diagnosis at ICU admission and ICU admitted patients had an inhospital mortality in excess of 50%. These estimates are consistent with previous findings, particularly when considering the studies that included hematological cancer patients. For instance, one study found the incidence of ICU mortality in solid cancer patients to be 31% and of hospital mortality of patients' ICU admitted, 38%, with outcomes depending on cancer topography, type of admission (planned or emergency) and specialty. (22) Other study, found the incidence of ICU and hospital mortality rates for hematological cancer patients to be 54.1% and 67.8%, respectively. (23)

Overall, in-hospital mortality was 17.5% and survival for these patients was poor, with median survival of 4.5 months overall and 2.5 months for those admitted for ICU care. The occurrence of AOF was associated with a 3-fold increase in mortality and also associated with a 2-fold increase in mortality after hospital discharge even after adjustment for age and comorbidity. This higher mortality for patients who developed AOF is probably not directly related to the acute event, but inherent to the patient's condition or subsequent treatment decisions. Patients with a previous episode of AOF while on treatment may be at increased risk of subsequent hospitalizations with higher likelihood of a serious adverse event and death. On the other hand, the occurrence of AOF may lead to changes in the patient's therapeutic plan, with dose reductions, changes or suspension of treatment which by itself may be associated with decreased survival. Despite the worse prognosis of patients who develop AOF while on systemic medical treatment, patients undergoing potentially curative therapy and those with advanced cancer with predictable long-term survival may benefit from ICU admission. (5) For patients with advanced cancer an ICU trial can be valuable as it can potentially prolong survival with good quality of life. (8) Though ICU admission recommendations for critically ill cancer patients have been proposed by an international expert consensus, there are no established criteria for ICU admission of oncologic patients. (4) In the future we intend to design and study the applicability of a protocol with pre-established admission criteria for the critically ill cancer patient in ICU.

Conclusions

In this single center prospective cohort study, cancer patients who required unscheduled inpatient medical care had a cumulative risk of acute organ failure was 39.6% and 15% risk for intensive medical care

treatment. Acute organ failure was associated with increased mortality both during hospital stay and after discharge. To our knowledge, this is the first published study examining the risk of acute organ failure in cancer patients on systemic anti-cancer therapy.

Abbreviations

AOF: Acute Organ Failure

AORT: Artificial Organ Replacement Therapy
CCI: Charlson Comorbidity Index

ICU: Intensive Care Unit

NA: Not applicable

SD: Standard deviation

Quick SOFA: Quick Sequential Organ Failure Assessment

SIRS: Systemic Inflammatory Response Syndrome

Declarations

Ethics approval and consent to participate

This study was approved by the hospital administration and ethics committee number CES/IPO: 204/018.

All patients consent to participate in this study with signed written consent form.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to Union European General Data Protection Regulation but are available from the corresponding author on reasonable request after approval by the institution ethics committee and by the local responsible for assessing the impact of data protection.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Study conception and design: SC, BP, FC, AM, NS, FF

Data acquisition: SC, TR, IP, DD, AA, IV, SP

Data analysis and interpretation: SC, TR, NS, FF

Manuscript elaboration: SC, NS

Manuscript revision: SC, TR, IP, DD, AA, IV, SP, BP, FC, AM, NS, FF

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Agreement to be accountable for integrity of the study: SC, TR, IP, DD, AA, IV, SP, BP, FC, AM, NS, FF

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Not applicable.

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Figures

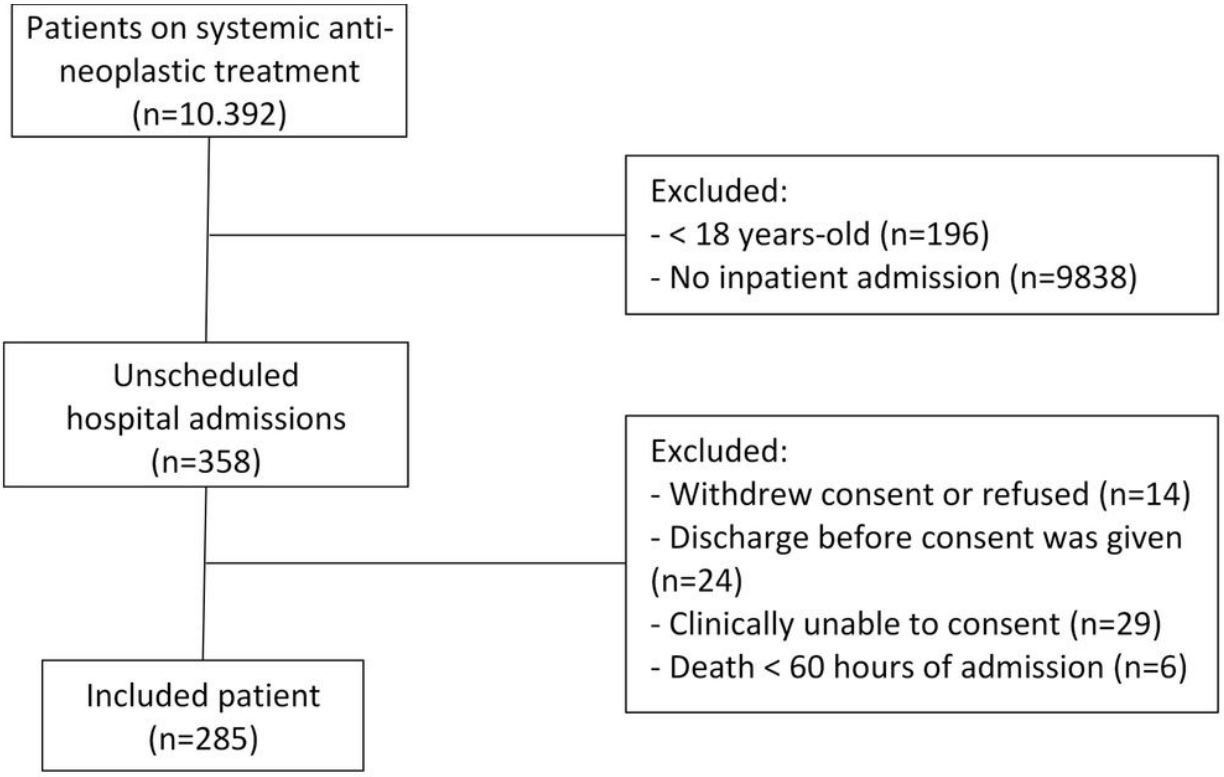

Figure 1

Overview of patients on anti-neoplastic systemic treatment, unscheduled admitted and included in the study

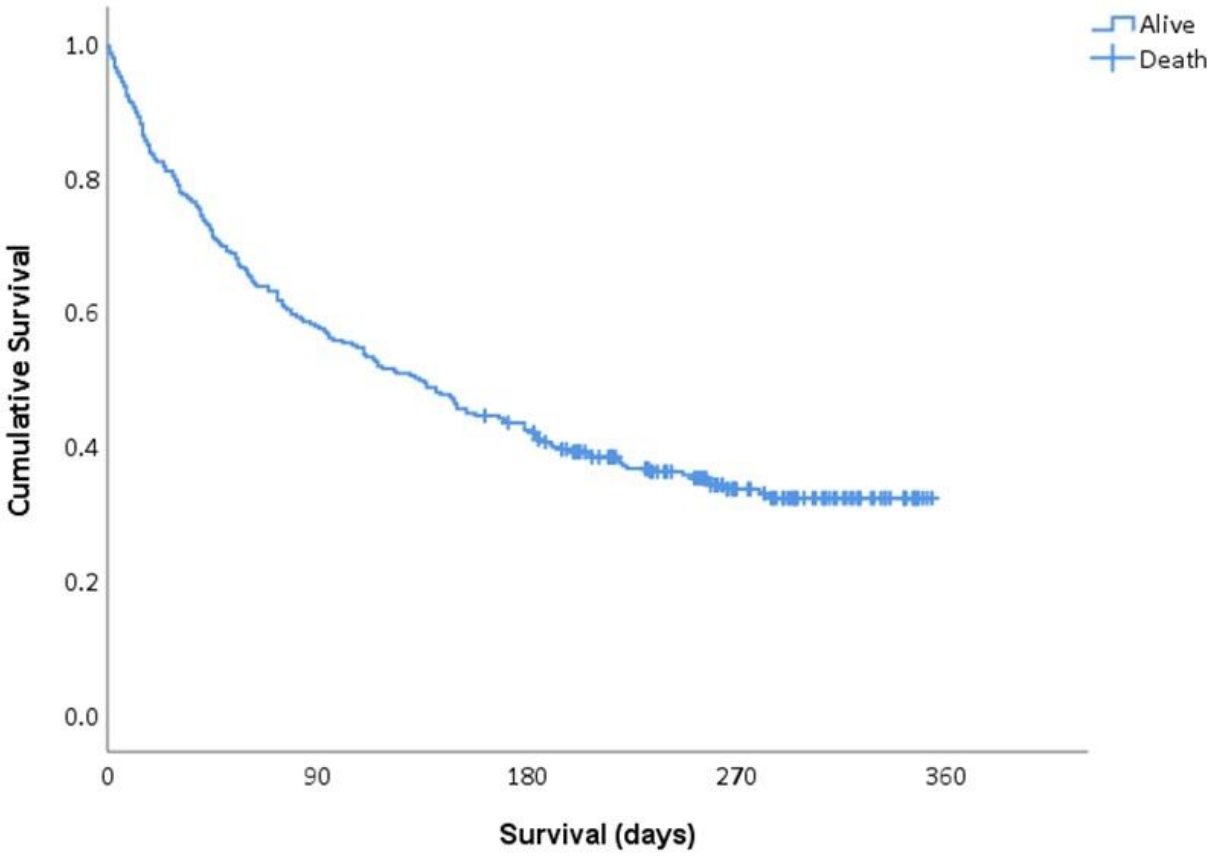

Figure 2

Median survival of patients with an unscheduled hospital admission.

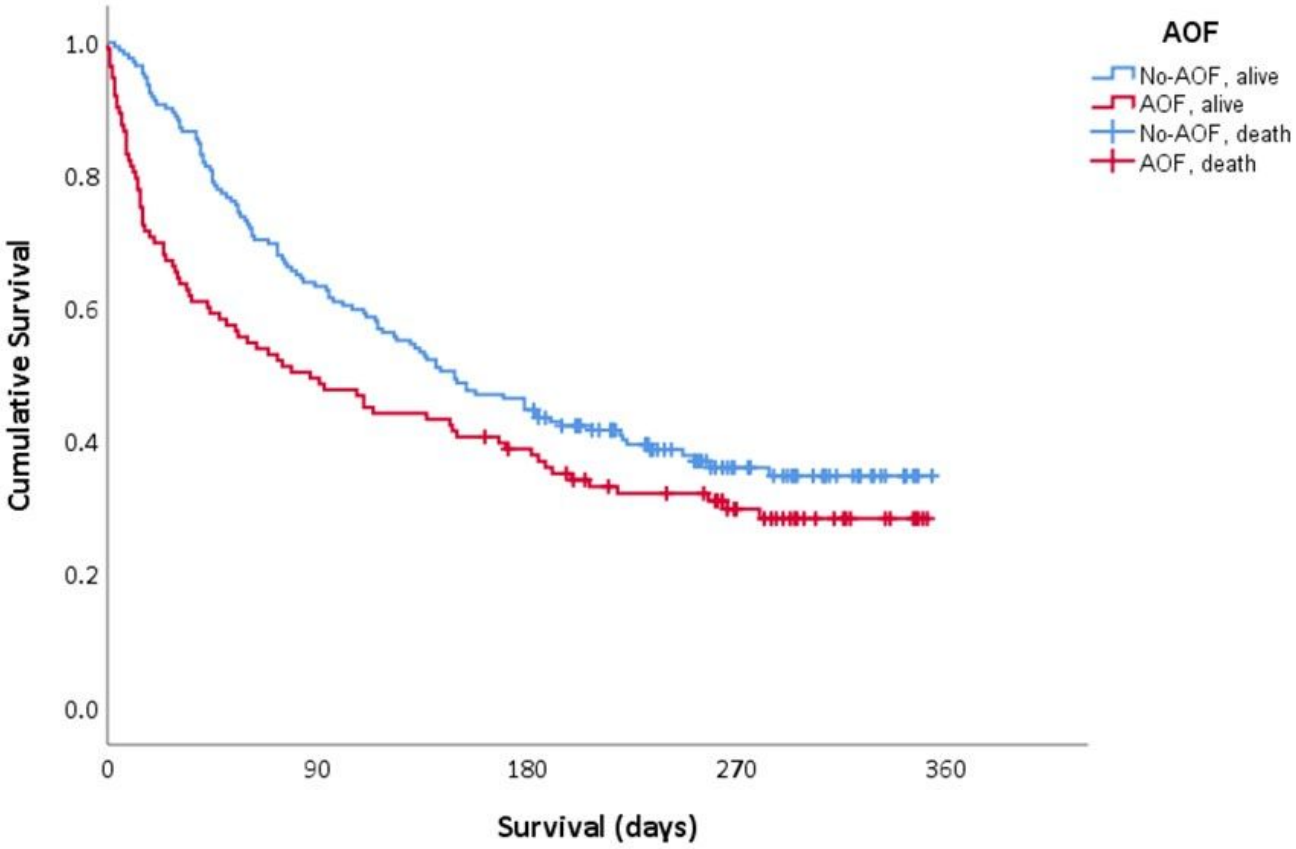

Figure 3

Median survival of patients according the occurrence of AOF.

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