

Application of the Sequential Organ Failure Assessment (SOFA) Score in Comparison to Acute Physiology and Chronic Health Evaluation (APACHE III) Score to Patients with Cancer Admitted to the Intensive Care Department: An Egyptian Experience

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Abstract: Introduction: Prognostic models, such as Sequential Organ Failure Assessment (SOFA) Score, and the Acute Physiology and Chronic Health Evaluation (APACHE) III were developed to quantify the severity of illness and the likelihood of hospital survival for a general intensive care unit (ICU) population. Little is known about the performance of these models in specific populations, such as patients with cancer. Objective: The aim of present study was to describe the utility of the Sequential Organ Failure Assessment score in assessing the severity of organ dysfunction compared to Acute Physiology and Chronic Health Evaluation (APACHE III) in patients with cancer patient admitted to the intensive care unit. Methods Design: Prospective cohort study. Setting: Eighty patients (in Critical Care Department, Cairo University, Egypt) included in eight month (October 2009 to May 2010) for an acute medical complication. They were divided into two groups. Group (1) included 50 patients having malignancy and group (2) included 30 patients with no malignancy. All had eligibility criteria of multiorgan failure. Interventions: None. Measurements: the worst variables included in the APACHE III and SOFA scores were collected during date of admission and follow up in the first 24 hrs of the ICU stay. Discrimination was determined by computing the area under the receiver-operating characteristic curve (AUC). Calibration was calculated using the Hosmer-Lemeshow goodness-of-fit test. **Results:** In group (1); the main reasons for ICU admission were hepatic coma (28%), respiratory failure (18%), postoperative care (18%), and other (36%). The ICU mortality rates was 54% , that increased into 81.8% when mechanical ventilation was required. ICU length of stay (LOS) 4.56 ± 2.21 , 5.33 ± 3.71 days in survivors and nonsurvivors, respectively. While in group (2); the main reasons for ICU admission were shock (26.7%), renal (20%) ,respiratory failure (16.7%), hepatic coma (16.7%), and other (19.3%). The ICU mortality rates was 26.7%, that increased into 61.5%. when mechanical ventilation was required. ICU length of stay (LOS) 12.04 ± 10.82 , 9.62 ± 7.38 days in survivors and nonsurvivors, respectively. Discrimination was superior for APACHE III on 24hr (AROC = 0.95, 0.83). Calibration was better using APACHE III on 24hr, , showed good calibration as indicated by hosmer –lemeshow (chi 5.275, 14.25 at df 7, 8 , p: 0.626, 0.075), in group (1) & (2) respectively. **Conclusion:** The Acute Physiology and Chronic Health Evaluation (APACHE III) reported to have better discrimination ability than SOFA-based model at 24hour of admission and a better accuracy to predict ICU mortality in oncological and non oncological patients.

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1. Introduction

Advances in oncological and supportive care have led to improved prognosis and extension of survival time in cancer patients. However, such advances have often been achieved through aggressive therapies and support, at high expense. Some of these patients require admission to the intensive care unit (ICU) for acute concurrent illness, postoperative care, or complications of their cancer or its therapy. The outcomes in these patients have improved and the described short-term survival rates are similar to that observed in patients without cancer [1- 2]. Efforts have been made to identify parameters that are associated with poor prognosis and to develop scoring models for predicting hospital mortality at ICU admission of

cancer patients. Different prognostic systems, such as Sequential Organ Failure Assessment (SOFA) Score [3] and the Acute Physiology and Chronic Health Evaluation (APACHE) III [4] have been developed to predict the outcome of critically ill patients admitted to the ICU. Although these models perform well in predicting the mortality of the general ICU patient population, they may well under- or overestimate mortality in selected patient subpopulations that were not well represented in the original cohort on which the model was developed. Specific oncological scoring systems have been assessed with variable success. [5,6]

The aim of this study is to describe the utility of the Sequential Organ Failure Assessment score in assessing the severity of organ dysfunction and

compared to Acute Physiology and Chronic Health Evaluation (APACHE III) in cancer patients requiring admission to the ICU.

Patients and Methods

Design and Setting:

This prospective observational cohort study was conducted at Critical Care Department, Cairo University (Egypt) on 80 patients during the period from October 2009 to May 2010. They were divided into two groups. Group (1) included 50 patients had malignancy and group (2) included 30 patients had no malignancy. All had eligibility criteria of multiorgan failure. The study was observational and descriptive, and the need for informed consent was waived.

Selection of patient, data collection, and analysis:

During the study period, all patients aged >16 years with cancer requiring ICU admissions because of life-threatening complications were evaluated, except those patients who stayed in the ICU for <48 hours or after uncomplicated surgery. The following variables were collected: age, gender, duration of mechanical ventilation, length of stay in the ICU, and the ICU survival. The presence of 6 organ dysfunctions (cardiovascular, neurological, respiratory, renal, hepatic, and coagulation) was assessed using the SOFA. [3, 7]The presence of each organ dysfunction was defined when degree of dysfunction was equal to 1 and more. The most abnormal value for each clinical and laboratory parameters included in the SOFA system and APACHE III were recorded on admission and follow up after 24 hours. Patients were classified into two tumor groups: solid tumor and non solid tumor (leukemia, lymphoma/ myeloma).

Data Presentation and Statistical Analysis:

Data were collected and verified prior to analysis. Statistical analyses were performed using SPSS software for windows, version 12.0 (SPSS Inc., Chicago IL, USA). Continuous data are presented as mean + standard deviation (SD). The t-test has been used to compare two groups when normally distributed, and when the mean values were violated Mann-whitney test has been used. While analysis of variance (ANOVA) test has been used to compare more than two groups when normally distributed, and when the mean values were violated kruskal-wills tests was performed. Categorical Variables were reported as absolute numbers (frequency percentages), and analyzed using Chi-square test. Stepwise forward multiple

logistic regressions has been performed using the two scoring systems as independent predictors of outcome. Validation of the prognostic scores was performed using standard tests to measure discrimination and calibration of predictive models. Although several measures exist for evaluating the performance of prognostic models, all identified studies used receiver operating characteristic (ROC) curves and the area under the curve (AUC) [8] to evaluate discrimination and the Hosmer- Lemeshow goodness-of-fit H- or -statistics [9] to evaluate the calibration of the prognostic models. 'Discrimination' refers to a model's ability to distinguish survivors from non-survivors. The AUC represents the probability that a patient who died had a higher predicted probability of dying than a patient who survived. An AUC of 0.5 indicates that the model does not predict better than chance. The discrimination of a prognostic model is considered perfect if AUC = 1, good if AUC >0.8, moderate if AUC is 0.6 to 0.8, and poor if AUC <0.6 [10].

3. Results

During the period under study, in group (1) 50 patients were included in the study. Their mean age was 54.62± 16.94 years, 29 (58%) were men and 21(42%) were females. The main reasons for ICU admission were hepatic failure (28%), respiratory failure (18%), postoperative care (18%), neurological complications (10%), cardiovascular complications (10%), post CPR (8%), renal/metabolic complications (4%) and coagulopathy (4%). In the categorization of patients by specific malignancy were 80% solid tumors, 10% leukemia, and 10% lymphoma/ myeloma. Thirty three (66%) patients required mechanical ventilation (MV), with ICU mortality of 81.8%. The independent predictors of poor ICU outcome were: the need for MV. While in group (2); their mean age was 53.40± 18.99 years, 19 (63.3%) were men and 11(36.7%) were females. The main reasons for ICU admission were shock (26.7%), renal (20%), respiratory failure (16.7%), hepatic coma (16.7%), neurological complications (9.3%), post CPR (6.7%) and coagulopathy (3.3%).The ICU mortality rates was 26.7% , that increased into 61.5%. when mechanical ventilation was required. ICU length of stay (LOS) 12.04 ± 10.82, 9.62± 7.38 days in survivors and nonsurvivors, respectively, see tables (1&2). There were 89.5% of the patients who had 2 or more organ dysfunctions before or on the day of admission to ICU. The incidence of organ dysfunction was noted more frequently for hepatic, respiratory, and cardiovascular.

Table (1): Comparison between survivors & nonsurvivors in group (1) cancer patients (50 pts) regarding demographic data, length of stay, type of tumor, reason of admission, and mechanical ventilation (duration & reasons of MV) , using chi-square and t-test

	Total n=50 N (%)	Survivors n=23 N (%)	Nonsurvivors n=27 N (%)	p-value
Age (years)		50.26 ±17.01	58.07 ± 15.165	0.098
Male	29 (58)	10 (34.5)	19 (70.4)	0.055
Female	21 (42)	13 (56.5)	8 (29.6)	
ICU length of stay		4.56 ±2.21	5.33± 3.71*	0.389
Type of tumor				
Solid	40 (80)	19 (82.6)	21 (77.8)	0.657
Nonsolid	10 (20)	4 (17.4)	6 (22.2)	
Reasons of admission				
Hepatic	14 (28.0)	4 (17.4)	10 (37.0)	0.048
Respiratory	9 (18.0)	3 (13)	6 (22.2)	
Post operation	9 (18.0)	8 (34.4)	1 (3.7)	
Cardiovascular	5 (10.0)	3 (13.0)	2 (7.4)	
Neurological	5 (10.0)	2 (8.7)	3 (11.1)	
Post CPR	4(8)	1(4.3)	3 (11.1)	
Renal	2(4)	2(8.7)	None	
Coagulopathy	2(4)	None	2 (7.4)	
Mechanical ventilation	33 (66)	6 (26 %)	27(100%)	0.0001
Duration (in day)		1.17±1.69*	4.00±2.52*	0.001
Reason of M.V				
Coma	14(42.4)	None	14 (51.8)	0.0001
Shock	7 (21.2)	3 (50.0)	4 (14.8)	
Respiratory failure	8 (24.2)	2 (33.3)	6 (22.2)	
Post CPR	4 (12.1)	1 (16.7)	3 (11.1)	

Table(2):Comparison between survivors & nonsurvivors in group (2) nonmalignant patient (30 pts) in demographic data, length of stay, reasons for admission and mechanical ventilation(duration & reason for MV), using chi-square and t-test.

	Total n=30 N (%)	Survivors n=22 N (%)	Nonsurvivors n=8 N (%)	p-value
Age (years)	54.62±16.94	53.40 ± 18.99	58.87 ± 14.22	.466
Male	19 (63.3)	13 (59.1)	6 (75)	0.424
Female	11 (36.7)	9 (40.9)	2 (25)	
ICU length of stay		12.04 ± 10.82*	9.62 ± 7.38*	0.565
Reason of admission				
Cardiovascular	7 (26.7)	6 (27.3)	1 (12.5)	0.174
Renal	6 (20.0)	6 (27.3)	None	
Respiratory	5(16.7)	4 (18.2)	1 (12.5)	
Hepatic	5 (16.7)	3 (13.6)	2 (25.0)	
Neurological	4 (9.3)	1 (4.5)	3 (37.5)	
Post CPR	2(6.7)	1 (4.5)	1 (12.5)	
Coagulopathy	1(3.3)	1(4.5)	None	
Mechanical ventilation	13 (100)	5 (22.7%)	8(100%)	
Duration (in day)		1.63±3.56*	7.75±7.49*	0.005
Reason of M.V				
Coma	7(53.8)	2 (40)	5 (62.5)	0.001
Respiratory failure	4 (30.8)	3 (60)	1 (12.5)	
Shock	1 (7.7)	None	1 (12.5)	
Post CPR	1 (7.7)	None	1 (12.5)	

The SOFA& APACHE III score of group(1) patients having survived the ICU stay were 4.30 ± 3.03, 50.08±24.35 on admission and 3.47± 2.33 , 38.60±18.54 on 24hr, respectively, and of the patients not surviving the ICU stay were 9.81±3.89, 96.07± 28.95 on admission , and 10.25±3.89,

92.37±30.57 on 24 hr respectively. While SOFA& APACHE III score of group (2) patients having survived the ICU stay were 4.90 ± 2.38, 50.86±17.14 on admission and 4.04± 2.29 , 39.04±15.86 on 24hr, respectively, and of the patients not surviving the ICU stay were 7.75±2.60,

71.12± 17.14 on admission , and 62.37±17.31 on 24 hr, respectively. Nonsurvivors had significantly higher values of all scores

compared to survivor in both groups; see table (3, 4) and figures (1-4).

Table(3)Comparison between survivors & non survivors regarding SOFA & APACHE III scoring system (Mean + SD) on admission , 24 hour in group (1) .

	Survivors (n=23)	Non survivors (n=27)	p-Value
SOFA on admission	4.30 + 3.03*	9.81 + 3.89	0.0001
SOFA on 24hr	3.47 + 3.47*	10.25 +4.15	0.0001
APACHE III on adm	50.08 + 24.35	96.03 +28.95	0.0001
APACHE III on 2	38.60 + 18.54	92.37 +30.57	0.0001

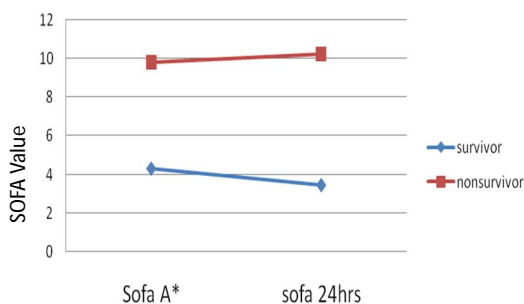


Figure (1): SOFA score follow in cancer patients

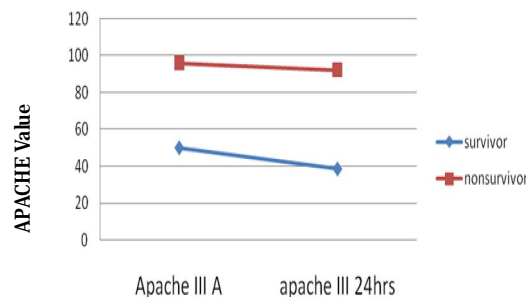


Figure (2): APACHE III score follow up in cancer patients

A *=score in admission

Table (4) Comparison between survivors & non survivors regarding SOFA & APACHE III scoring system (Mean ± SD) on admission& 24 hour in group (2).

	Survivors	Non survivors	p-Value
SOFA on admission	4.90 ±2.38	7.75 ±2.60	0.009
SOFA on 24hr	4.04 ±2.29	7.50 ±3.25	0.003
APACHE III on admission	50.86 ±17.14	71.12 ±17.24	0.008
APACHE III on 24hr	39.04 ±15.86	62.37 ±17.31	0.002

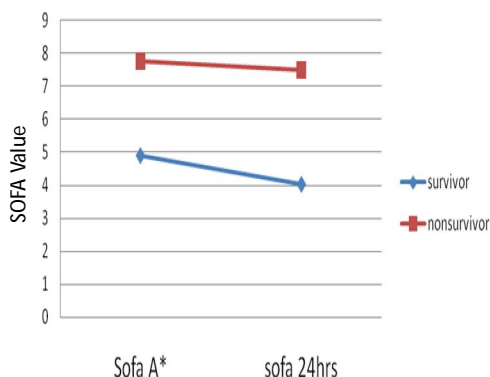


Figure (3): SOFA score follow in non cancer patients

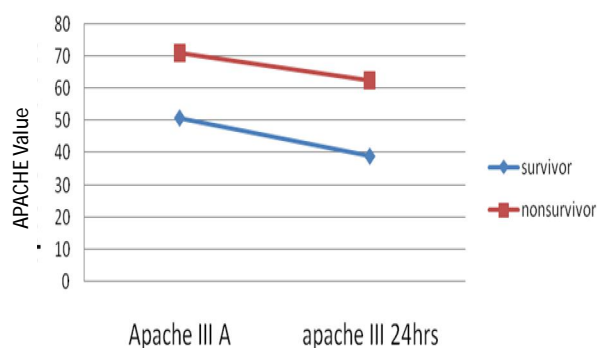


Figure (4): APACHE III score follow up in non cancer patients

A *=score in admission

To assess the performance of SOFA and APACHE III on cancer and patients, forward stepwise logistic regression has been performed ,utilizing both scores on admission and on 24 hrs against outcome as an end point yielding APACHE III on 24 hrs as best predictor. For both groups, the four scoring has been used as independent predictor for the ICU outcome. Assessing the calibration of the APACHE III on 24 hrs in group

(1)&(2); showed good calibration as indicated by hosmer–lemoshow (chi 5.275 at df 7, p: 0.626) (chi 14.25 at df 8, p: 0.075), respectively. To assess the discrimination of APACHE III on 24 hrs in group (1)&(2); , ROC curve analysis has been performed ,AUC 0.95,0.83, sensitivity 85%,75%, specificity 83%,82% respectively, see tables (5-7) &figures(5)&(6).

Table (5): Best predictor in group (1)& group (2)

	Variable	wald	P value	Exp (B)	95%CI	
					LOWER	Upper
Group(1)	APACHE III in 24 hr	13.008	0.0001	1.084	1.038	1.133
Group(2)	APACHE III in 24 hr	6.04	0.014	1.089	1.017	1.166

Table (5): Classification table of APACHE III in

observed(n)	Predicted (n)		
	survival	Non-survival	%
Survival (23)	19	4	82.6
Nonsurvival (27)	5	22	81.5
Overall percentage			82.0

Table(6): Classification table of APACHE III in 24hr

observed(n)	Predicted (n)		
	survival	Non-survival	%
Survival (22)	20	2	90.9
Nonsurvival (8)	4	4	50.0
Overall percentage			80.0

24hr in group (1)

group (2)

Table(7): calibration& Discriminationin both group

	score	Calibration			Discrimination:		
		chi	df	p-value	AUC	sensitivity	specificity
Group(1)	APACHE III on 24 hrs	5.275	7	0.626	0.95	85%	83%
Group(1)	APACHE III on 24 hrs	14.25	8	0.075	0.83	75%	82%

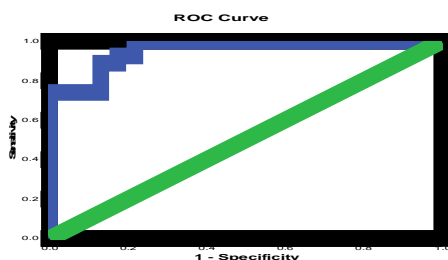


Figure (5): AUC APACHE III in 24 hr for group(1) patient was 0.95 with a standard error (SE) 0.022. When using the cutoff point at APACHE III of 42.0 to predict patient outcome , the sensitivity 85% and specificity 83%

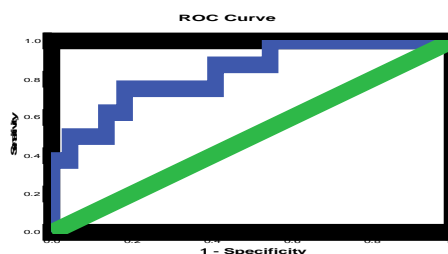


Figure (6); AUC APACHE III in 24 hr for group (2) patient was 0.83 with a standard error (SE) 0.035. When using the cutoff point at APACHE III of 32.0 to predict patient outcome , the sensitivity 75% and specificity 82%

4. Discussion

Increasing numbers of cancer patients require critical care, and the present of one in five patients admitted to ICUs have malignancies [1, 2]. In addition, the outcomes in these patients have improved and the described short-term survival rates are similar to that observed in patients without cancer [11–12]. Prognostic models have been traditionally accepted as surrogate markers of severity of acute illness. However they must be validated prior to being used in a specific setting. This is particularly important in case of a specific subgroup of patients, such as patients with cancer. General prognostic models uniformly underestimate likelihood of hospital mortality in oncological patients [13, 14]. Nonetheless, data are still insufficient, as most of the available studies were single centered and conducted in specialized ICUs [15,16]. In the present study, the database from cohort study performed in Egypt was used to simultaneously validate two prognostic scoring systems in patients with cancer admitted to general ICUs. The selection of scores to be evaluated was made attempting to take into account one traditional general score (APACHE III) and organ dysfunction score (SOFA).

The results of the current study showed that the changes in the severity of organ dysfunction were important in the outcome of the patients with cancer admitted to ICU. Some degree of organ dysfunction necessitating treatment is frequently present in a majority of critically ill patients. The assessment of organ dysfunction scores is often used to determine the baseline severity of illness. The SOFA score was designed to describe the sequence of complications in critically ill patients.[7] The score is intended to objectively quantify the degree of organ dysfunction over time to evaluate the time course of the severity of the disease. Additionally, it allows evaluation of the function of each of 6 organs separately. A further objective of the system is the simplicity of the collection of the variables needed and ease of calculation of the score. Initially, the score was not intended to be predictive of risk of mortality. Nevertheless, it was directly observed that a greater SOFA score for each organ was associated with an increasing mortality rate.[7] Since its proposal, other studies reported on the good prognostic performance of the model and of its derived scores.[3,16-19] The results of our study confirmed that the SOFA score is a good tool for assessing the impact of organ dysfunction in patients with cancer. Ferreira et al [19] when initial SOFA >11 predicted a mortality of 95%. Soares et al [20] reported that the SOFA at ICU admission was not associated with a worse outcome in critically ill patients with cancer and prolonged ICU length of stay. Because many biases were found

in the use of SOFA score system. First, organ dysfunction failure is a dynamic process and the degree of dysfunction may vary with time and treatment [21] and that a score should result from severe dysfunction from one organ system or from very mild dysfunction organ systems. Second, serial or repetitive assessment of organ dysfunction scores allow for a more effective representation of an outcome prediction than does a single measurement. [22, 23]Third, the data collected on the day of admission or during the ICU stay may not completely reflect the unforeseen events that may be major determinants of outcome. [22] Fourth, the co-morbidity condition [24] is not taken into account sufficiently in this scoring system. So although the SOFA score is useful in analyzing the number and the severity of acute organ failures related to ICU mortality but not validated to predict outcomes in the ICU.

Our study showed the APACHE III score, in 24 hour in comparison to SOFA score, was best predictor of outcome in cancer patients. The mean APACHE III in 24 hour was 38.60 ± 18.54 , 39.04 ± 15.86 in survivors and 92.37 ± 30.57 , 62.37 ± 17.13 in non-survivors (p-value 0.0001, 0.002) in group (1) & (2), respectively. Assessing the calibration of the APACHE III on 24 hrs in group (1)&(2); showed good calibration as indicated by Hosmer–Lemeshow (chi 5.275 at df 7, p: 0.626) (chi 14.25 at df 8, p: 0.075), respectively. Assess the discrimination of APACHE III on 24 hrs in group (1)&(2); , ROC curve analysis has been performed ,AUC 0.95,0.83, sensitivity 85%,75%, specificity 83%,82% respectively. Discrimination of all APACHE III models was excellent ROC curve area (> 0.9) [25] as in cancer patients. The performance of the APACHE III system was excellent with AUC of 0.9 and correct classification rate of 88.2% in a database of 17440 admissions (4). Staudinger et al [26] study of 414 cancer patients, APACHE III scores were higher in non survivors than in survivors (AUC=0.75) and when the cut-off probability of mortality in APACHE III score 79 the observed mortality 100 % . In a study of Afessa et al. [10] of 112 recipients of hematopoietic stem cells, APACHE III scores had moderate discriminative power (AUC= 0.70) and good calibration for predicting hospital mortality. Soares et al. [27] studied 542 cancer patients, and reported the APACHE III was good discrimination (AUC= 0.81) González et al. [28] study, in 250 cancer patients, represented APACHE III as best predictor over SOFA score, Adam and Soubani [29] study, of 139 lung cancer patients, they reported that APACHE III demonstrated significant differences between survivors and nonsurvivors (mean APACHE III: survivors 54.3+21.4,

nonsurvivors 85.8+28.5, p, 0.0001).

The development of acute respiratory failure remains one of the fore most reasons for ICU admission of cancer patients [26, 30, 31, 32]. In the current study, the need for mechanical ventilation had a profound and sustained adverse effect on outcome.

This study has several limitations. First, the small sample size is the most important limitation of the study since it may influence the evaluation of calibration and discrimination of the scores. Second, a selection bias is likely, because not all critically ill patients with cancer were admitted to the medical ICU. Besides, the decision to transfer a critically ill patient with cancer to the ICU is generally based on the bed availabilities and agreement among patients and their relatives, oncologists, and intensivists. Third, the performance status, the long-term survival and quality of life are not investigated in this study. Fourth, in this study, a majority of the cancer patients presented with solid tumors rather than hematologic malignancies and HCC was the major type of cancer. In this study, the results may not be generalizable, that we had no specific information about the characteristics of the cancer, including type, stage, histological findings, anticancer treatments or performance status. The defined groups of 'solid' and 'hematological' cancers encompass different diseases with different biological behaviors and severities, thus we could not correlate mortality to these characteristics. Finally, decisions to limit therapy, and particularly 'do not resuscitate' orders, were not recorded.

Conclusion

The ICU outcome of cancer patient with a medical complication requiring critical care is mainly related to the acute physiological changes due to the complication and not to the characteristics of the underlying neoplastic disease. So the Acute Physiology and Chronic Health Evaluation (APACHE III) reported to have better discrimination ability than SOFA-based models at 24hour of admission and a better accuracy to predict ICU mortality in oncologic patients. However The SOFA can provide the clinician with important information relating to the degree and progression of organ dysfunction in cancer patients

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