

Evaluation of Acute Physiology and Chronic Health Evaluation (APACHE) IV Score Warrick Scoring High Resolution CT Chest and Six-Minute Walk Test in Predicting Mortality in Patients with Interstitial Lung Disease

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Abstract

Background: Some clinical parameter and APACHE IV scoring systems allow assessment of severity of the disease in patients with interstitial lung diseases (ILD) and provide an estimate of in-hospital morbidity and mortality.

Aim of Study: This study aimed to detect the ability of clinical parameters and APACHE IV score in predicting the mortality of interstitial lung disease patients in chest department.

Patients and Methods: A prospective observational cohort study was performed at the Chest Department of Bab El-Sha'eria and Al-Hussein Al-Azhar University Hospitals. The study included patients with interstitial lung disease admitted between January 2015 and December 2019. Data were collected from 50 patients (29 female and 21 male) with age range from 24-61 years old (43.6 ± 9.43). During the 1st day of admission, full history taking, HRCT Chest, Warrick score, pulmonary function test, arterial blood gases, APACH IV score, six minute walking test were recorded.

Results: The study revealed that there; 38 (76%) patients with Interstitial Lung Disease survived and 12 (24%) non survived. There was a significant difference between PaO₂, O₂ sat, PaCO₂, Systolic Pulmonary Artery pressure, and 6-minute walking distance, 4-meter walk time/seconds, APACH IV, Warrick score on admission between survived and non-survived subjects.

Conclusion: Six-minute walk test, 4 meter walking time, systolic pulmonary artery pressure APACHE IV score and Warrick scoring high resolution C-T chest can be used as useful test in predicting mortality in interstitial lung disease.

Key Words: *Interstitial lung – Predicting factors – APACH IV.*

Introduction

THE interstitial lung diseases are a clinically challenging characterized by varying degrees of fibrosis and inflammation of the lung parenchyma or interstitium [1]. High-resolution computed tomographic (HRCT) imaging of the chest is the current gold standard for imaging patients with interstitial lung disease [1]. Acute Physiology and Chronic Health Evaluation (APACHE) IV scoring systems designed for making quantitative assessment regarding the severity of a disease, its course and its prognosis [2]. APACHE IV predicts hospital mortality and gives useful marks for evaluating efficiency in ICUs [3]. ILD often generates big problem among respiratory clinicians, especially when need for definitive diagnosis and treatment also when to predict outcome of patients in ward admission and in respiratory intensive care, many studies were done to predict hospital mortality for ild using APACH II,III [4].

Aim of the Work: This study to detect the ability of clinical assessment and APACHE IV score in predicting outcome of patients with interstitial lung disease in chest department and respiratory ICU.

Patients and Methods

A prospective observational cohort study was performed at the Chest Department and respiratory ICU of Bab El-Sha'eria and Al-Hussein University Hospitals. During the period from January 2015 to December 2019 and patients were randomly selected. The study included fifty patients with ILD all patients with interstitial lung disease admitted to chest department and referred to the

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Respiratory Intensive Care Unite (RICU) when there is increasing severity of the patient's illness, need for ICU intervention(s) or monitoring. Diagnosis of ILD were made by multidisciplinary review of clinical, pathological and radiological data in accordance with published guidelines [5]. 35 patients with interstitial lung disease complicated by respiratory failure included in the study and they using long term oxygen therapy and 15 without respiratory failure. All patients were admitted in ward and referred to RICU when needed. All patients identified, numbered, followed through duration of admission, and followed for two years and all patients were subjected to the following:

- 1- Full history taking.
- 2- General and local chest examination.
- 3- 6-Minute walking test, 4-meter walk time, seconds.
- 4- Laboratory investigations (urea, creatinine, Na, K, serum albumin, CBC, ESR, hepatic profile).
- 5- Echocardiography by Philips I. E33 X-Matrex japan.
- 6- Pulmonary function test PFT by Geratherm Respiratory diffustik and one way valve 5710.
- 7- Arterial Blood Gases. GEM premier 3000 arterial blood gases analyzer, USA.
- 8- High resolution CT chest and Warrick score for every patient. Hispeed; GE Medical Systems. Yokogawa, Japan.
- 9- Outcome of patients is survived or non-survived during period of hospital admission and patients complete two years follow-up is considered survived case.
- 10- APACHE IV score for every patient on the first day of admission in Chest Department [3].

Exclusion criteria: Patients who were excluded from the present study include those with age less than 18 years, and cases complicated with pneumothorax, pregnant, malignant diseases, and Patients cannot walk on the ground were excluded from the study, and patients cannot complete pulmonary function test.

Chest HRCT assessment: Pulmonary involvement identified and scored according to a semi quantitative Warrick score, 1991 [6].

Pulmonary function test: Spirometry was performed for all patients, measurement of forced expiratory volume (FEV₁), forced vital capacity (FVC) and FEV₁/FVC.

ABG: Arterial blood samples were withdrawn; the following values were recorded O₂ saturation % (SpO₂%), PaO₂ mmHg, PaCO₂ mmHg, and pH.

Six-minute walk test: Conducted in 30 meter long, flat corridor, and transit-free to avoid turn more often which slows patient's pace. Standardized instructions and encouragement were given, according to ATS guidelines [7]. The test discontinued if the patient had thoracic pain, intolerable dyspnea, cramps, dizziness, staggering, diaphoresis, pallor [7].

Gait Speed Test (4-metre) [8].

The test was performed using the following instructions:

- a- Instruct the patient to walk at their normal pace using an assistive device, if needed.
- b- The patient walk down a hallway through a 1-metre zone for acceleration, a central 4 metre "testing" zone, and a 1-metre zone for deceleration and the patient should not start to slow down before the 4-metre mark.
- c- The timer was started with the first footfall after the 0-metre line.
- d- Stop the timer with the first footfall after the 4-metre line [8]. And calculate time taken to walk 4 meters, and divide 4 meter over the time to give Gait speed in meters per second.

Echocardiography for every patient to assess left ventricular function and right ventricular function and measure pulmonary artery pressure.

Ethical consideration: Ethical approval was taken from Research Ethical Committee at Faculty of Medicine Al-Azhar University, and an informed written consent was taken from all patients participate in the study.

Statistical methods: Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired *t*-test in normally distributed quantitative variables while non-parametric Mann-Whitney test was used for non-normally distributed quantitative variables [9]. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5 [10].

Correlations between quantitative variables were done using Spearman correlation coefficient [11]. *p*-values less than 0.05 were considered as statistically significant.

Results

Fifty patient with interstitial lung disease were included in the study and results reveal, 21 males, 29 females, 38 survived and 12 non survived, 16 patients were smoking 18 using long term oxygen and diagnosed clinically as IPF 36 patients, due to collagen 4 patients, Sarcoidosis 5 patients, Hyper sensitivity pneumonitis 5, degree of Warrick score mild 4, moderate 20, severe 26 patients Table (1).

Table (1): Patients demographic data, history, diagnosis and Co-morbidity.

Patients demographic data	Count	%
<i>Groups:</i>		
Survived	38/50	76.0
Non survived	12/50	24.0
<i>Gender:</i>		
Male	21/50	42.0
Female	29/50	58.0
Smoking	16/50	32.0
Corticosteroid use	27/50	54.0
Respiratory failure	35/50	70.0
Hypertension	18/50	36.0
Diabetes mellitus	19/50	38.0
Ischaemic heart disease	12/50	24.0
<i>Duration of disease since diagnosis/year:</i>		
New	13/50	26.0
1	8/50	16.0
2	19/50	38.0
3	8/50	16.0
4	2/50	4.0
<i>Clinical diagnosis:</i>		
Sarcoidosis	4/50	8.0
Hyper sensitivity pneumonitis	5/50	10
Collagen disease	5/50	10.0
IPF*	36/50	72.0
<i>HRCT chest-degree of Warrick score:</i>		
Mild	4/50	8.0
Moderate	20/50	40.0
Severe	26/50	52.0

*Interstitial pulmonary fibrosis.

Patient age ranged from 29-65 years with mean for age 43.68 years, smoking index 340.63, mean FEV₁ 2.3, FEV₁/FVC 82.2%, PaO₂ 64.38, PaCO₂ 37.58, O₂ Sat 88.98, Systolic pulmonary artery pressure 41.78, 6 minute walking test 295.50, 4-meter walk time 3.66, BMI 27.30, APACH IV 73.52, Warrick score 16.36.

Table (2): Clinical, pulmonary function blood gases, echo findings of the studied group.

	Mean	Standard Deviation
Age	43.68	9.43
Smoking index	340.63	126.94
FEV ₁	2.30	0.32
FVC	2.79	0.36
FEV ₁ /FVC	82.22	4.89
FEF ₂₅₋₇₅	1.50	0.23
PH	7.37	0.05
PaO ₂	64.38	15.74
PaCO ₂	37.58	6.44
O ₂ Sat	88.98	3.21
Ejection Fraction	56.68	7.37
Systolic pulmonary pressure	41.78	11.66
6 minute walking test	295.50	39.58
4-meter walk time/seconds	3.66	0.69
Body Mass Index	27.30	3.11
APACH IV	73.52	35.98
Warrick score	16.36	5.34

FEV1: Forced expiratory volume in 1st second.

FVC : Forced volume capacity.

FEF25-75 : Forced expiratory flow 25-75.

APACH IV: Acute Physiology and Chronic Health Evaluation IV.

In comparison between survived and non-survived group show no statistical significance for sex, smoking, Corticosteroid use, Duration of disease since diagnosis year some co morbidity as diabetes, hypertension, clinical diagnosis and statistical significance in Long term oxygen *p*-value 0.017, ischemic heart disease with *p*-value 0.025 Table (3).

Table (3): Comparison between survived and none survived.

	Groups				<i>p</i> -value
	Survived		Non survived		
	Count	%	Count	%	
<i>Sex:</i>					
M	18/38	47.3	3/12	25.00	0.185
F	20/38	52.6	9/12	75.00	
<i>Smoking</i>					
Corticosteroid use	12/38	31.6	4/12	33.3	1.00
Respiratory failure	18/38	47.4	9/12	75.0	0.094
Hypertension	25/38	66.3	10/12	83.7	0.017
Diabetes mellitus	12/38	31.6	6/12	50.0	0.309
Ischaemic heart disease	12/38	31.6	7/12	58.3	0.171
<i>Duration of disease since diagnosis year:</i>					
New	11/38	28.9	2/12	16.7	0.477
1	6/38	15.8	2/12	16.7	
2	15/38	39.5	4/12	33.3	
3	4/38	10.5	4/12	33.3	
4	2/38	5.3	0/12	0.0	
<i>Clinical diagnosis:</i>					
Sarcoidosis	3/38	7.9	1/12	8.3	1.00
Hyper sensitivity pneumonitis	4/38	10.5	1/12	8.3	
Collagen disease	4/38	10.5	1/12	8.3	
IPF	27/38	71.1	9/12	75	

In comparison between survived and non-survived group show no statistical significance for age, smoking index, FEV₁, FVC, FEV₁/FVC, FEF₂₅₋₇₅. And there is statistically significance in comparison between PaO₂, O₂ sat, PaCO₂, SYST PA pressure, and 6 minute walking test, 4-meter walk time, seconds, APACH IV, Warrick score in survived and non-survived Table (4).

Table (4): Clinical, pulmonary function blood gases, echo findings of the studied group, in survived and non-survived group.

	Groups				P-value
	Survived		Non survived		
	Mean	SD	Mean	SD	
Age	43.95	9.21	42.83	10.47	0.725
Smoking index	315.83	116.19	415.00	145.72	0.185
FEV ₁	2.29	0.30	2.35	0.37	0.578
FVC	2.80	0.35	2.78	0.39	0.896
FEV ₁ /FVC	81.58	4.48	84.23	5.76	0.103
FEF ₂₅₋₇₅	1.47	0.22	1.59	0.23	0.131
PH	7.38	0.05	7.36	0.04	0.112
PaO ₂	68.63	15.51	50.92	5.87	<0.001
PaCO ₂	35.66	4.81	43.67	7.32	<0.001
O ₂ sat	89.84	2.56	86.25	3.62	<0.001
Ejection Fraction	57.58	6.09	53.83	10.28	0.252
Systolic Pulmonary Artery pressure	38.53	8.34	52.08	14.80	<0.001
6MWT D*	303.71	34.03	269.50	45.96	0.008
4-MWT**	3.55	0.65	4.00	0.74	0.049
BMI	27.01	3.07	28.23	3.19	0.243
APACH IV	57.08	16.83	125.58	30.40	<0.001
Warrick score	14.97	4.81	20.75	4.67	0.001

* 6 minute walking test distance/meter.
**4 meter walking time/second.

APACH IV can predict mortality with Sensitivity 91.7%, Specificity 97.4% and cut off 87.5 Table (5).

Table (5): Specificity, Sensitivity for APACH IV in predicting mortality.

Area Under the Curve	p-value	95% Confidence interval		Cut off	Sensitivity %	Specificity %
		Lower bound	Upper bound			
		0.964	<0.001			

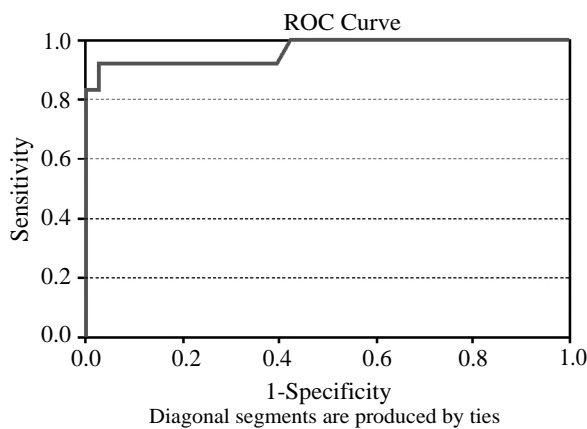


Fig. (1): ROC curve for prediction of mortality using APACH IV.

Warrick scoring high resolution CT findings in predicting mortality with Sensitivity 75%, Specificity 76.3% and cut off 18.5.

Table (6): Specificity, Sensitivity for Warrick scoring high resolution CT findings in predicting mortality.

Area Under the Curve	p-value	95% Confidence interval		Cut off	Sensitivity %	Specificity %
		Lower bound	Upper bound			
		0.799	0.002			

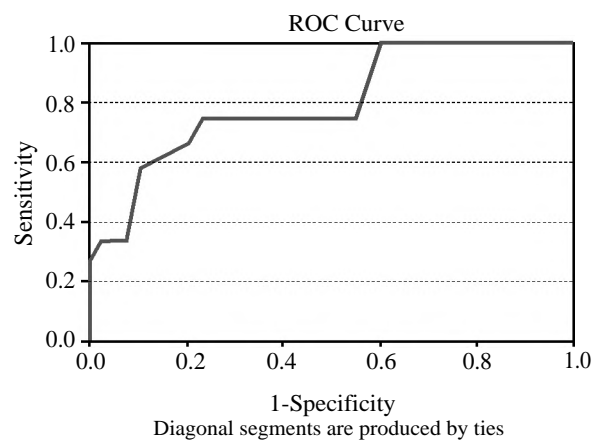


Fig. (2): ROC curve for prediction of mortality using Warrick scoring.

Table (7): Specificity, Sensitivity for six minute walking time test in predicting mortality.

Area Under the Curve	p-value	95% Confidence interval		Cut off	Sensitivity %	Specificity %
		Lower bound	Upper bound			
		0.742	0.012			

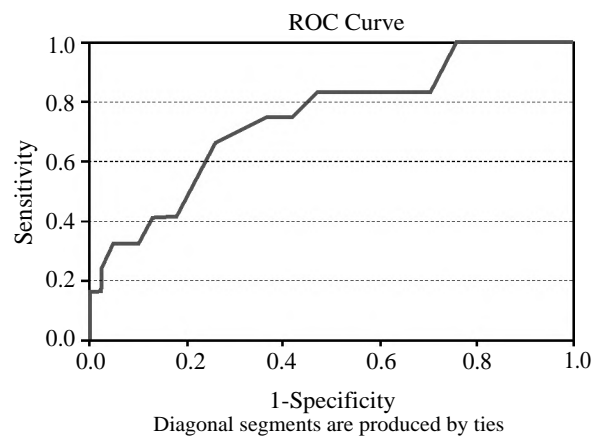


Fig. (3): ROC curve for prediction of mortality using 6m walking test.

Table (8): Specificity, Sensitivity pulmonary artery pressure in predicting mortality.

Area Under the Curve	p-value	95% Confidence interval		Cut off	Sensitivity %	Specificity %
		Lower bound	Upper bound			
0.781	0.004	0.621	0.940	48.5	58.3	81.6

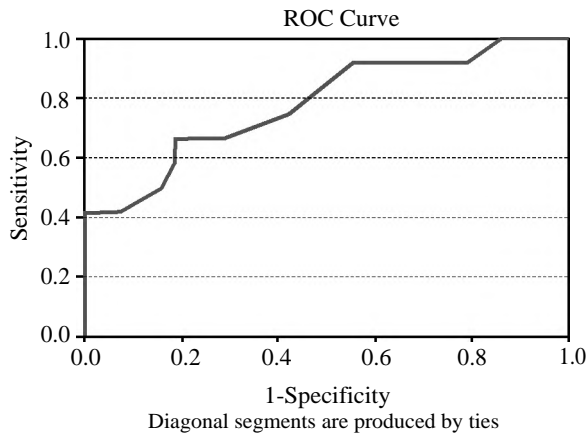


Fig. (4): ROC curve for prediction of mortality using Systolic pulmonary artery pressure in interstitial lung disease patients.

There are many causes for death in studied group include Interstitial lung disease (primary cause) 10 cases, Collagen disease SLE 1 case, Pneumonia 4 cases, renal failure 3 cases, sudden death 2 cases, uncontrolled DM 1 case, and some cases with more than one cause for death Table (8).

Table (9): Causes of death in studied group (non survived 12*patient).

Cause	Number	Total cases
Interstitial lung disease (primary cause)	10	12
Collagen disease SLE	1	Some patients with more than one cause of death
Pneumonia	4	
Ischemic heart disease	3	
Renal failure	3	
Sudden death	2	
Uncontrolled DM (DKA)	1	

*Some patients with more than one cause of death.

Discussion

This study to detect the ability of clinical factors and APACHE IV score in predicting mortality of interstitial lung disease patients in Chest Department. A prospective observational cohort study was performed at the Chest Department of Bab El-Sha'eria and Al-Hussein Al-Azhar University Hos-

pitals. The study includes patient with interstitial lung disease with and without respiratory failure, all patients admitted to the Chest Department between January 2015 and December 2019. Data were collected and results reveal that 50 patients (29 female and 21 male) with age ranged from 29 to 65 years with mean age 43.6 ± 9.43 years, This agree with results reported by Taghreed et al. [12] as they found that the mean \pm SD age among the ILD patients was 48.30 ± 12.60 years. Ryerson et al. [13] they found that the mean \pm SD age among the ILD patients were 63.90 ± 11.60 years, respectively.

Patients were excluded from the present study include patients younger than 18 years of age, patients complicating with pneumothorax, pregnant, Patients cannot walk on the ground were excluded from the study, and patients cannot complete pulmonary function test. In the present study there is calculation of APACH IV score and Warrick score test for high resolution CT chest and evaluation for gait by six minute walking, 4 meter walking test and also evaluation of right ventricle and pulmonary artery pressure for predicted mortality rate during admission, all these factors were evaluated for predicting mortality in patients with interstitial lung disease.

This study demonstrated that females more than male (29 female, 21 male) among the studied ILD patients (58 vs. 42%), Table (2). While in study by Taghreed et al. [12] they found that females were more common than males among the ILD patients (60% vs. 40%, respectively). While Ryerson et al. [13] they found that males were more common than females (56% vs. 44%) respectively.

In the present study there is 16 patient smoking with mean smoking index 340.6 ± 126 and this in agreement to study by Ayman et al. [14] in ILD they found that the smoking index in ILD without depression 300 ± 00 and in the present study the mean FEV1 2.3 ± 0.32 , FEV₁/FVC 82.22 ± 4.89 , PaO₂ 64.38 ± 15.74 , O₂Sat 88.98 ± 3.21 systolic pulmonary artery pressure 41.78 ± 11.66 , 6 minute walking test 295.50 ± 39.58 , 4-meter walk time per seconds 3.66 ± 0.69 Table (2) and this in agreement with study by Hoda et al. [15] they found that the PaO₂ range was 31-96mmHg with a mean \pm SD 68.10 ± 14.19 . The SaO₂ range was 56-99% with a mean \pm SD 90.99 ± 8.10 . The FEV 1 % range was from 19 to 114% with a mean \pm SD of 46.76 ± 17.61 . The FEV₁/FVC ratio range was from 32 to 100 with a mean \pm SD of 82.84 ± 12.29 . The FEF_{25-75%} range was from 11 to 132% with a mean \pm SD of 48.30 ± 26.03 . The 6MWD range was from 40 to 480m

with a mean \pm SD of 249.96 ± 138.84 and pulmonary artery pressure was estimated pulmonary artery systolic pressure ranged from 30 to 95mmHg with a mean \pm SD of 51.2 ± 14.9 .

In the present study comparison between survived and non-survived group show no statistical significance in predicting mortality for sex, smoking, Corticosteroid use, Duration of disease since diagnosis year some co morbidity as diabetes, hypertension and there is statistical significance in predicting mortality for Long term oxygen therapy with p -value 0.017, ischemic heart disease with p -value 0.025 Table (3). And the comparison show no statistical significance for age, smoking index, FEV₁, FVC, FEV₁/FVC, FEF₂₅₋₇₅. And there is statistically significance in comparison between PaO₂, O₂ sat, PaCO₂, Systolic PA pressure, and 6 minute walking test distance, 4-meter walk time/seconds, APACH IV, Warrick score in survived and non-survived Table (4). And this in comparison to other studies as Collard [16] shows marked decrease in FVC by more than 10% whereas others can live for prolonged periods even after a 10% decline in FVC.

And in study by Antonella and Sergio [17] reported that lower rate of decrease in lung function does not necessarily translate into longer survival.

And in study by Lettieri, et al. [18] reported Pulmonary arterial hypertension Pulmonary arterial hypertension (PAH) is a common accompaniment of IPF, may contribute substantially to morbidity and mortality in IPF and has a significant impact on outcomes.

And in study Antonella and Sergio [17] reported that in patients with IPF, especially those with more advanced disease, evaluating for the presence of PAH may be useful in determining prognosis and may have a role in monitoring the disease course.

In study by Flaherty et al. [19] they found that the importance of stratifying patients by the degree of desaturation during a 6-minutes walk test (6-MWT) as a mean to estimate the mortality risk before different interventions such as transplantation.

In the present study the mean value of APACHE IV in survived patients was 57.08 ± 16.83 and in non-survived patients was 125.58 ± 30.40 , there is highly significant difference between survived and non-survived patients regarding values of APACHE IV score p -value <0.001 (Table 4).

And this in agreement to some studies to evaluate APACHE IV score in ICU patients as Moses et al. [20] they found that mean APACHE IV in survived patients was 32.7 ± 11.11 and in non-survived was patients was 76.7 ± 10.75 p -value <0.0001 .

And results by Kamal et al. [21] they reported that mean APACHE IV in survived patients was 78.9 ± 12.6 and in non-survived was patients was 106.4 ± 2.9 p -value=0.000.

And in study to evaluate APACH IV score and SOFA score in predicting outcome of patients in respiratory ICU by Ahmad et al. [22] they found that the mean APACHE IV score in survived and nonsurvived patients was 72.0 ± 13.08 , 105.2 ± 29.9 , respectively with highly significant difference between survived and nonsurvived patients regarding values of APACHE IV score ($p < 0.001$) and they cutoff point of APACHE IV score was more than 81, and area under receiver operating characteristic curve (AUROC) was 0.81.

APACHE IV score can predict mortality with Sensitivity 91.7%, Specificity 97.4% and cut off 87.5 with discrimination between patients Table (5).

And this in agreement with results by Kamal et al. [21] they conducted a study on comparison between APACHE II and APACHE IV scoring systems in predicting outcome in patients with acute lung injury ALI and the adult respiratory distress syndrome ARDS, they found that the cutoff point of APACHE IV score was >90 and gives prediction of high possibility of death with sensitivity 94.73% and specificity 93.74% and the area under ROC curve was 0.92.

In the present study mean Warrick scoring for high resolution CT findings was 14.97 ± 4.81 in survived patients and 20.75 ± 4.67 in non survived patients and with statistical significance in predicting mortality with Sensitivity 75%, Specificity 76.3% and cut off 18.5 Tables (4,6).

In the present study there are many causes for death in studied group include Interstitial lung disease (primary cause) 10 cases, Collagen disease SLE 1 case, Pneumonia 4 cases, renal failure 3 cases, sudden death 2 cases, uncontrolled DM 1 case, and some cases present with more than one cause for death Table (9).

Conclusion: Six-minute walk test, 4meter walking time, systolic pulmonary artery pressure APACHE IV score and Warrick scoring high reso-

lution C-T chest can be used and useful test in predicting mortality in interstitial lung disease.

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تقييم الفسيولوجيا الحادة والصحة المزمنة الرابع (APACHEIV) ومعدل واريك للأشعة المقطعية عالية الدقة للصدر واختبار المشى لمدة ست دقائق في التنبؤ بوفيات المرضى الذين يعانون من أمراض الرئة الخلالية

هدف العمل: تهدف هذه الدراسة إلى الكشف عن قدرة الإختبارات السريرية ودرجة APACHEIV في التنبؤ بوفيات مرضى الرئة الخلالية في قسم الصدر.

المرضى والطرق: تم إجراء دراسة رصدية مستقبلية في قسم الصدر بمستشفى باب الشعرية والحسين بجامعة الأزهر. اشتملت الدراسة على مرضى الرئة الخلالية المقبولين بين يناير ٢٠١٥ وديسمبر ٢٠١٩. تم جمع البيانات من ٥٠ مريضاً (٢٩ أنثى و٢١ ذكر) تتراوح أعمارهم بين ٢٤-٦١ سنة (٤٣.٦ ± ٩.٤٣). في خلال اليوم الأول من القبول، تم تسجيل التاريخ الكامل، درجة Warrick للأشعة المقطعية، اختبارات الوظيفة الرئوية، غازات الدم الشريانية، درجة APACHEIV. واختبار المشى لمدة ست دقائق.

النتائج: كشفت الدراسة أن هناك ٢٨ (٧٦٪) من المرضى المصابين بمرض رئوي خلالي ظلوا على قيد الحياة حتى خرجوا من المستشفى وخلال المتابعة لمدة سنتين و ١٢ (٢٤٪) فارقوا الحياة. كان هناك فرق كبير بين PaO₂، PaCO₂، ضغط الشريان الرئوي الانقباضي، ومسافة المشى ٦ دقائق، وقت المشى ٤ أمتار/ثانية، APACHEIV، درجات ومعدل واريك عند القبول بين الأشخاص الباقين على قيد الحياة وغير الأحياء.

الخلاصة: درجة APACHEIV وسجل واريك عالي الدقة C-T إختبار المشى لمدة ست دقائق، ضغط الشريان الرئوي الانقباضي، يمكن استخدامه كإختبار مفيد في التنبؤ بالوفيات في أمراض الرئة الخلالية.