

AIM OF THE WORK

The aim of the work was to evaluate the prognostic value of venous to arterial carbon dioxide difference in post cardiac surgery patient.

PATIENTS & METHODS

Patients

The study was carried out on 70 patients, who were admitted to the open-heart intensive care unit in Shark El Madina hospital after performing elective cardiac surgery under cardiopulmonary bypass.

Sample size was calculated using G-power statistical maneuver for assessment of sample size. Sample size depending on effect size [r], α error probability of 0.05 and power of 0.8. The total sample size was calculated to be at least 64 patients with a degree of freedom 62 and critical T of 1.6698.

Approval of the medical ethics committee of Alexandria Faculty of medicine and an informed consent was taken from the next of keen before conducting the study.

Inclusion criteria

1. Patient undergoing elective cardiac surgery coronary artery bypass graft (CABG) or valve replacement under cardiopulmonary bypass.
2. Age >18 years

Exclusion criteria

1. Age <18, > 60 years.
2. BMI >35.
3. Emergency surgery.
4. Coagulopathy, sepsis, systemic inflammatory response syndrome.
5. Pregnancy.
6. Significant hepatic or renal failure.

Methods

All the patients included in the study were subjected to the following:

1. Complete history taking including demographic data, age, sex and past medical history.
2. Complete clinical examination and vital signs including blood pressure, heart rate, respiratory rate and temperature.
3. Routine laboratory investigations including: complete blood count, serum creatinine, blood urea and random blood sugar and bleeding profile were performed on admission and every other day for correction of any changes in their values.
4. Electrocardiogram (ECG) on admission and daily.
5. Chest x-ray on admission and when needed.

6. A central venous catheter was inserted in all patients.
 - a. Site: Right internal jugular vein.
 - b. Timing: just pre-operative.
 - c. Confirmation of the site of the catheter using x-ray chest was done.

Measurements

7. Arterial blood gases and central venous blood gases simultaneously were recorded at 3, 6 and 12 hours post operative.
8. Serum lactate level was recorded at 3, 6, and 12 hours post operative.

All patients were followed up for:

1. Primary outcome: In hospital complications including: cardiac, haematological, pulmonary, neurological, renal complications.
2. Secondary outcome: 28-day mortality.

Statistical analysis of the data⁽¹⁾

Data were fed to the computer and analyzed using IBM *SPSS software package version 20.0*.⁽²⁾ Qualitative data were described using number and percent. Quantitative data were described using Range (minimum and maximum), mean, standard deviation and median. Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Fisher's Exact test or Monte Carlo correction. The distributions of quantitative variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agostino test, also Histogram and QQ plot were used for vision test. If it reveals normal data distribution, parametric tests was applied. If the data were abnormally distributed, non-parametric tests were used. For normally distributed data, comparison between two independent population were done using independent t-test, also paired t-test is used to analyse two paired data. Agreement of the different predictives with the outcome was used and was expressed in sensitivity, specificity, positive predictive value, negative predictive value and accuracy. Receiver operating characteristic curve (ROC) was plotted to analyse a recommended cutoff, the area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. Significance of the obtained results was judged at the 5% level.

1. Kotz S, Balakrishnan N, Read CB, Vidakovic B. Encyclopedia of statistical sciences. 2nd ed. Hoboken, N.J.: Wiley-Interscience; 2006.
2. Kirkpatrick LA, Feeney BC. A simple guide to IBM SPSS statistics for version 20.0. Student ed. Belmont, Calif.: Wadsworth, Cengage Learning; 2013.

RESULTS

Demographic data

Gender

Most of this study population were males (44 patients) (62.9 %) while 37.1% were females, (Table 1, Figure 1).

Table (1): Distribution of the studied cases according to demographic data (n = 70)

	No.	%
Age		
18 – 30	2	2.9
30 – 40	7	10.0
41 – 50	23	32.9
50 – 60	38	54.3
Min. – Max.	22.0 – 60.0	
Mean ± SD.	49.91 ± 8.75	
Median	51.0	
Gender		
Male	44	62.9
Female	26	37.1

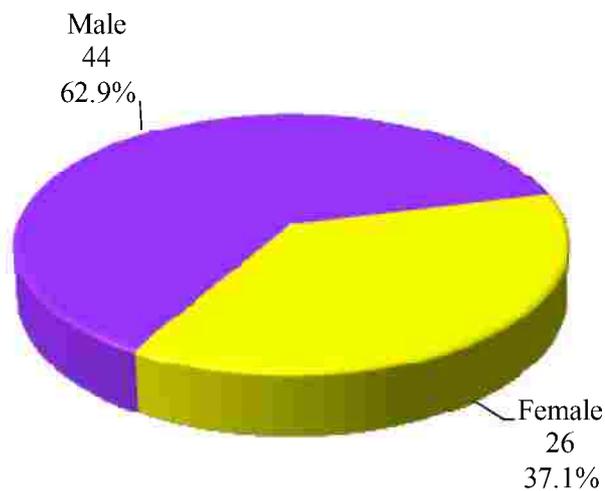


Figure (1): Distribution of the studied cases according to gender

Age

The age of the patients in the study ranges between 18 and 60 years with a mean of 49.91 ± 8.75 , (Table 1, Figure 2).

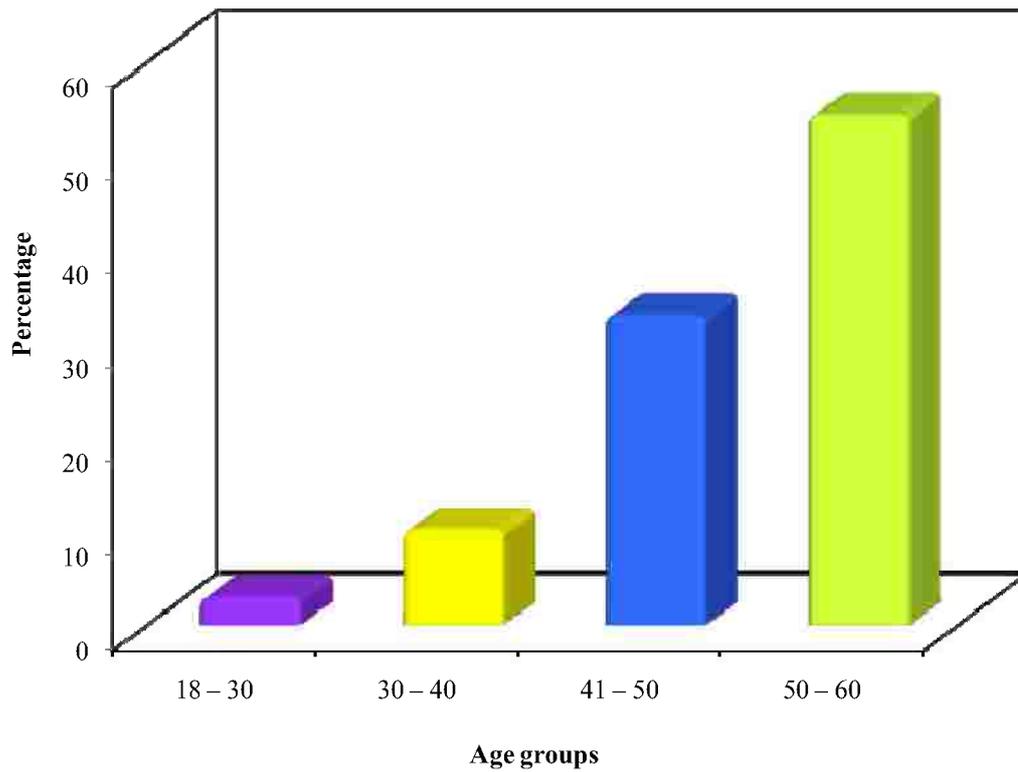


Figure (2): Distribution of the studied cases according to age

Type of operation

Table (2): Distribution of the studied cases according to the type of operation (n = 70)

	No.	%
CABG	45	64.3
Valve	25	35.7

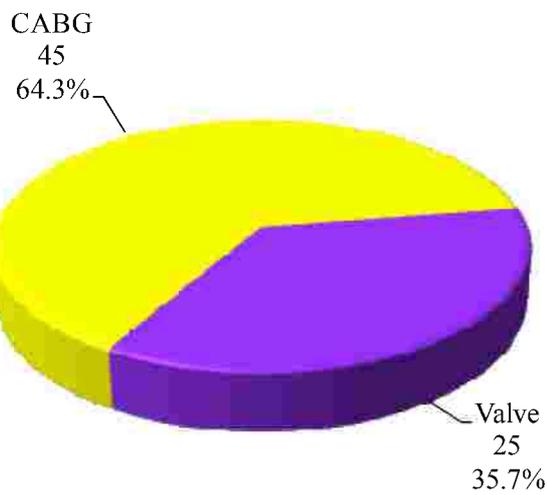


Figure (3): Distribution of the studied cases according to type of operation

Table (3), figure (4): demonstrate that Δ PCO₂ at T3 was ranging between 4 and 12 mmHg with a mean of 7.13 ± 2.04 , while at T6 it was ranging between 2 and 13 mmHg with a mean of 5.7 ± 2.71 and at T12 Δ PCO₂ was ranging between 2.0 and 15.0 mmHg with a mean of 5.59 ± 2.62 (and a median 5 mmHg).

At T3 the number of patients in whom Δ PCO₂ was ≤ 6 mmHg was 29 patients representing 41.4% and patients with Δ PCO₂ > 6 were 41 patients representing 58.6 %, while at T6 patients with Δ PCO₂ ≤ 6 mmHg were 43 patient representing 61.4 % and Δ PCO₂ > 6 in 27 patients representing 38.6 % and at T12 patients with Δ PCO₂ ≤ 6 were 45 patients representing 64.3 % and patients with Δ PCO₂ > 6 were 25 patients representing 35.7 %.

Table (3): Distribution of the studied cases according to Δ PCO₂ (n = 70)

	Δ PCO ₂					
	T3		T6		T12	
	No.	%	No.	%	No.	%
Δ PCO₂ (mmHg)						
≤ 6	29	41.4	43	61.4	45	64.3
> 6	41	58.6	27	38.6	25	35.7
Min. – Max.	4.0 – 12.0		2.0 – 13.0		2.0 – 15.0	
Mean \pm SD.	7.13 ± 2.04		5.71 ± 2.71		5.59 ± 2.62	
Median	7.0		5.0		5.0	

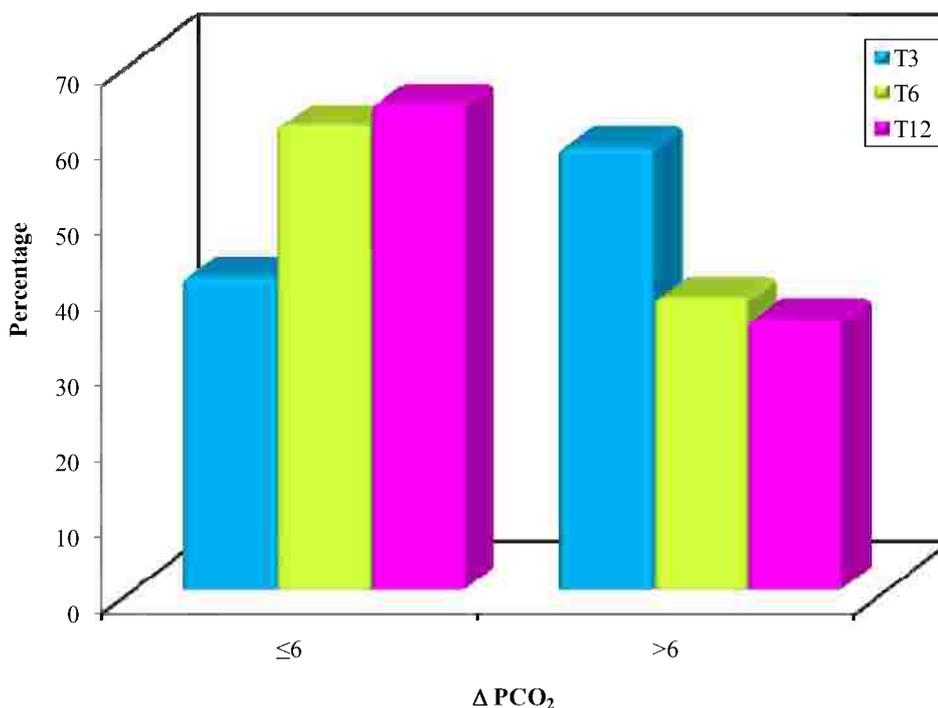


Figure (4): Distribution of the studied cases according to Δ PCO₂ (mmHg)

Table (4), figure (5): demonstrate that the level of lactate at T3 was ranging between 1.10 and 6.10 with a mean of 2.58 ± 0.91 and median 2.35.

While at T6 lactate level ranges between 0.8 and 4.70 with a mean 1.8 ± 0.88 and median 1.55 and at T12 lactate level was ranging between 0.9 and 3.0 with a mean 1.50 ± 0.57 and median 1.30.

Table (4): Distribution of the studied cases according to Lactate level (n = 70)

	Lactate in mmol/L		
	T3	T6	T12
Lactate (mmol/L)			
Min. – Max.	1.10 – 6.10	0.80 – 4.70	0.90 – 3.0
Mean \pm SD.	2.58 ± 0.91	1.80 ± 0.88	1.50 ± 0.57
Median	2.35	1.55	1.30

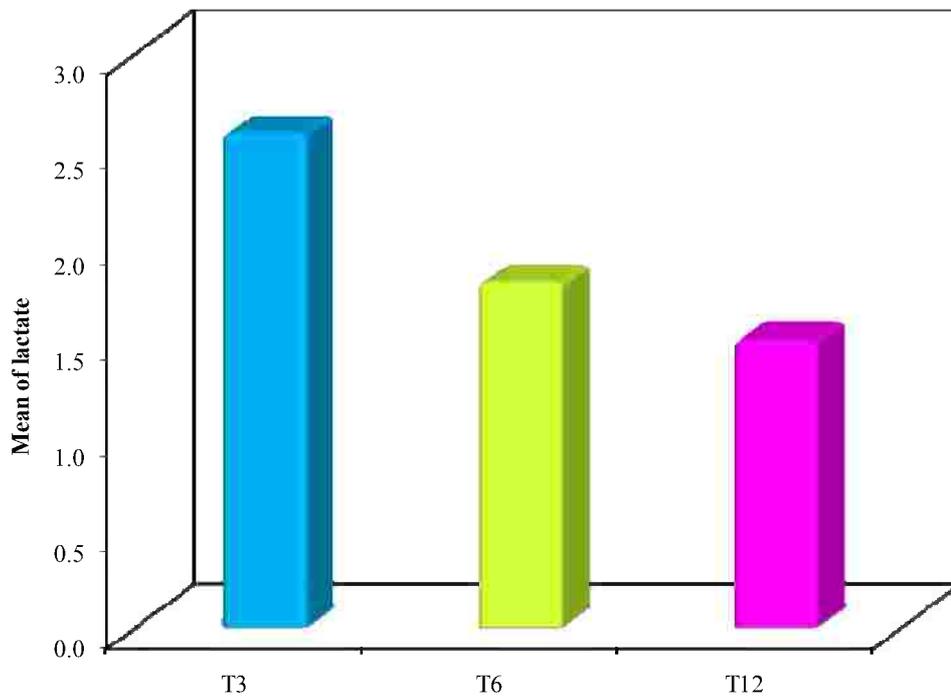


Figure (5): Distribution of the studied cases according to Lactate level (mmol/L)

Results

Table (5), figure (6): show the relationship between serum lactate level at T3, T6 and T12 and ΔPCO_2 in those patients who had $\Delta\text{PCO}_2 > 6$ and $\Delta\text{PCO}_2 \leq 6$.

It shows that in the patients with $\Delta\text{PCO}_2 \leq 6$ mmHg the serum lactate level at T3 was ranging between 1.10 and 5 mmol/L with mean of 2.06 ± 0.61 and median 2.0, at T6 lactate ranges between 0.8 and 2.0 mmol/L with mean of 1.28 ± 0.34 and median 1.2, at T12 lactate was ranging between 0.9 and 1.9 mmol/L with a mean of 1.16 ± 0.25 and median 1.10. but in patients with $\Delta\text{PCO}_2 > 6$ mmHg lactate level at T3 was ranging between 1.7 and 6.10 mmol/L with a mean of 2.96 ± 0.91 and median 2.90, and at T6 lactate was ranging between 1.4 and 4.7 with a mean of 2.63 ± 0.85 and median 2.5, at T12 lactate level ranges between 1.2 and 3. mmol/L with a mean of 2.12 ± 0.46 and median 2.0

There was statistically significant difference in lactate levels at T3, T6 and T12 between patients with $\Delta\text{PCO}_2 \leq 6$ mmHg and patients with $\Delta\text{PCO}_2 > 6$ mmHg.($p < 0.05$).

Table (5): Relation between ΔPCO_2 with Lactate level (n = 70)

	Lactate in mmol/L		
	T3	T6	T12
$\Delta\text{PCO}_2 \leq 6$ (mmHg)			
Min. – Max.	1.10 – 5.0	0.80 – 2.0	0.90 – 1.90
Mean \pm SD.	2.06 ± 0.61	1.28 ± 0.34	1.16 ± 0.25
Median	2.0	1.20	1.10
$\Delta\text{PCO}_2 > 6$ (mmHg)			
Min. – Max.	1.70 – 6.10	1.40 – 4.70	1.20 – 3.0
Mean \pm SD.	2.96 ± 0.91	2.63 ± 0.85	2.12 ± 0.46
Median	2.90	2.50	2.0
T	4.627*	7.857*	9.635*
P	<0.001*	<0.001*	<0.001*

t: Student t-test

*: Statistically significant at $p \leq 0.05$

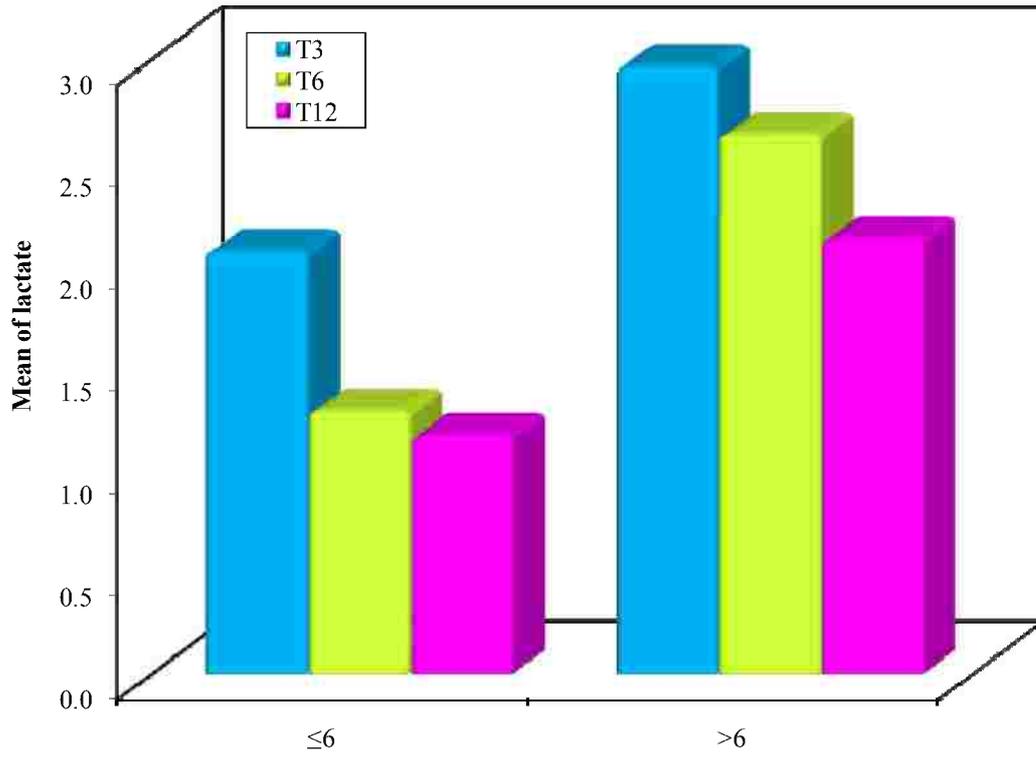


Figure (6): Relation between ΔPCO_2 (mmHg) with Lactate level (mmol/L)

Table (6), figure (7): show the relationship between lactate level and the change in ΔPCO_2 from T3 to T6 among 16 patients in whom ΔPCO_2 was normalized from T3 to T6, the lactate level at T3 was ranging between 1.7 and 3.8 mmol/L with a mean of 2.34 ± 0.61 and median 2.2 while at T6 lactate was ranging between 0.8 and 2.0 mmol/L with a mean of 1.35 ± 0.33 and median 1.3.

There was statistically significant decrease in serum lactate level with normalization of ΔPCO_2 from T3 to T6, ($p < 0.05$)

Table (6): Relation between change in ΔPCO_2 from T3 to T6 with change in Lactate level

	Normalized ΔPCO_2 From T3 to T6	
	T3 (n = 16)	T6 (n = 16)
Lactate (mmol/L)		
Min. – Max.	1.70 – 3.80	0.80 – 2.0
Mean \pm SD.	2.34 ± 0.61	1.35 ± 0.33
Median	2.20	1.3
P	$<0.001^*$	

p: p value for Paired t-test for comparing between T3 and T6

*: Statistically significant at $p \leq 0.05$

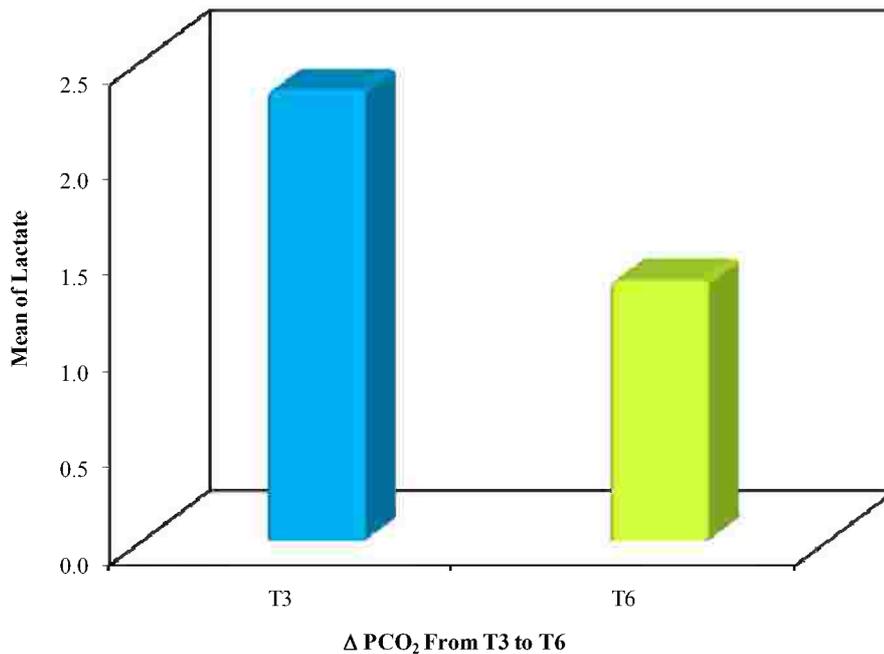


Figure (7): Relation between changes in ΔPCO_2 from T3 to T6 with change in Lactate level (mmol/L)

Results

Table (7), figure (8): show the relationship between lactate level and the change in Δ PCO₂ from T3 to T12

Among 18 patients in whom Δ PCO₂ was normalized from T3 to T12, the lactate level at T3 was ranging between 1.7 and 4.2 mmol with a mean of 2.48 ± 0.73 and median 2.35 while at T12 lactate was ranging between 0.9 and 1.90 mmol with a mean of 1.22 ± 0.28 and median 1.1.

There was statistically significant decrease in the serum lactate between T3 and T12 with the normalization of Δ PCO₂ from T3 to T12 ($p < 0.05$)

Table (7): Relation between change in Δ PCO₂ from T3 to T12 with change in Lactate level in mmol/L

	Normalized Δ PCO ₂ From T3 to T12	
	T3 (n = 18)	T12 (n = 18)
Lactate (mmol/L)		
Min. – Max.	1.70 – 4.20	0.90 – 1.90
Mean \pm SD.	2.48 ± 0.73	1.22 ± 0.28
Median	2.35	1.10
P	<0.001*	

p: p value for Paired t-test for comparing between T3 and T12

*: Statistically significant at $p \leq 0.05$

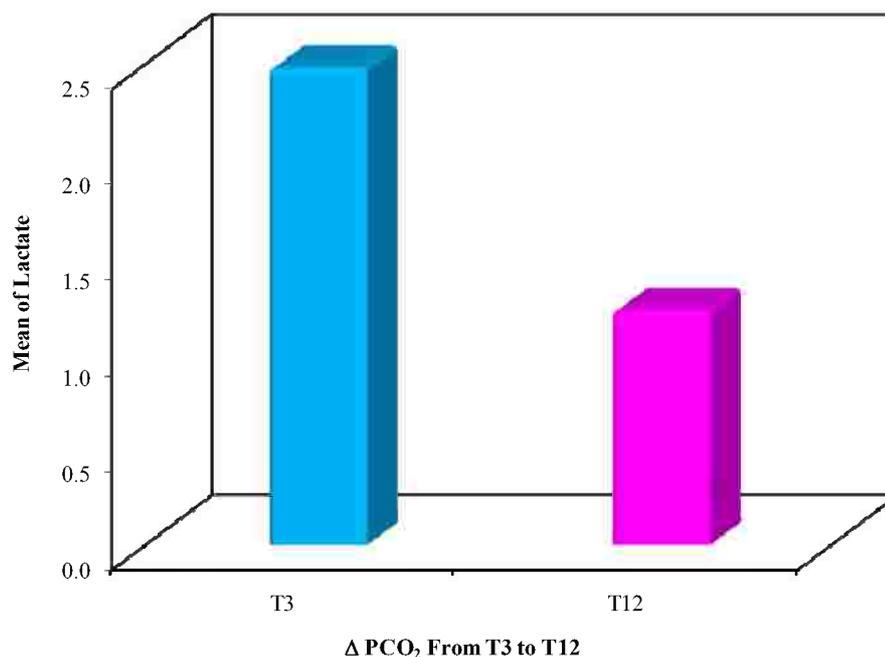


Figure (8): Relation between change in Δ PCO₂ from T3 to T12 with change in Lactate level (mmol/L)

Results

Table (8), figure (9): show the relationship between lactate level and the change in ΔPCO_2 from T6 to T12.

Among 2 patients in whom ΔPCO_2 was normalized from T6 to T12, the lactate at T6 was ranging between 2.1 and 2.2 mmol with a mean of 2.15 ± 0.07 and median 2.15 while at T12 lactate was ranging between 1.6 and 1.9 mmol with a mean of 1.75 ± 0.21 and median 1.75.

There was no significant change in lactate level between T6 and T12 with the normalization of ΔPCO_2 from T6 to T12. ($P=0.156$)

Table (8): Relation between changes in ΔPCO_2 from T6 to T12 with change in Lactate level in mmol/L

	Normalized ΔPCO_2 From T6 to T12	
	T6 (n = 2)	T12 (n = 2)
Lactate (mmol/L)		
Min. – Max.	2.10 – 2.20	1.60 – 1.90
Mean \pm SD.	2.15 ± 0.07	1.75 ± 0.21
Median	2.15	1.75
P	0.156	

p: p value for Paired t-test for comparing between T6 and T12

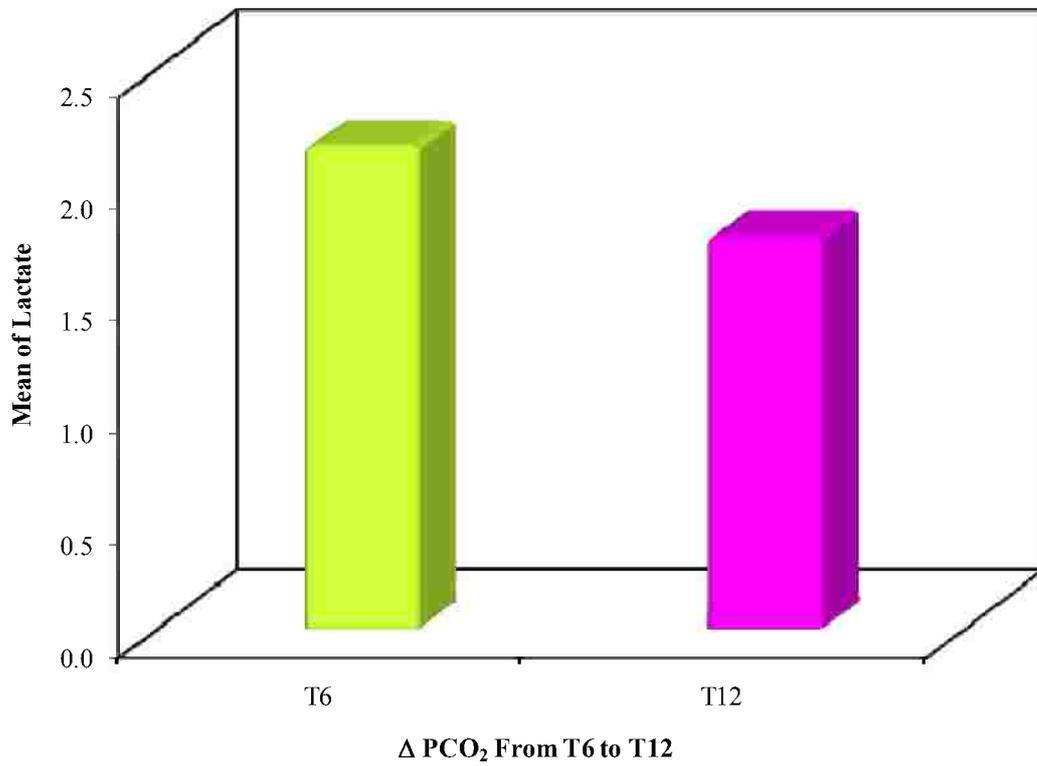


Figure (9): Relation between changes in Δ PCO₂ from T6 to T12 with change in Lactate level (mmol/L)

Table (9), figure (10): demonstrate the frequency and percentage of different complications in the studied cases

Arrhythmia is the most common complication that can occur in patients undergoing cardiac surgery on cardiopulmonary bypass accounting 22.9 % (16 patients). This was followed by delayed recovery amounting 17.1 % (12 patients). Other complications included heart failure (poor inotropy) amounting 10 % (7 patients), delirium amounting 11.4 % (8 patients), acute renal failure amounting 8.6 % (6 patients), bleeding, liver dysfunction amounting 4.3 % (3 patients). Sepsis, seizures and tamponade amounting 2.9 % (2 patients) for each.

Table (9): Distribution of the studied cases according to complications (n = 70)

	No.	%
Complications		
Delayed recovery	12	17.1
Cardiac arrest	0	0.0
Poor inotropy (HF)	7	10.0
Bleeding	3	4.3
Arrhythmias	16	22.9
Acute renal failure	6	8.6
Pneumonia	2	2.9
Stroke	1	1.4
Seizures	2	2.9
Delirium	8	11.4
Sepsis	2	2.9
Liver dysfunction	3	4.3
Tamponade	2	2.9
Prosthetic valve dysfunction	0	0.0
SAM (systolic anterior motion)	0	0.0
Diaphragmatic palsy	0	0.0

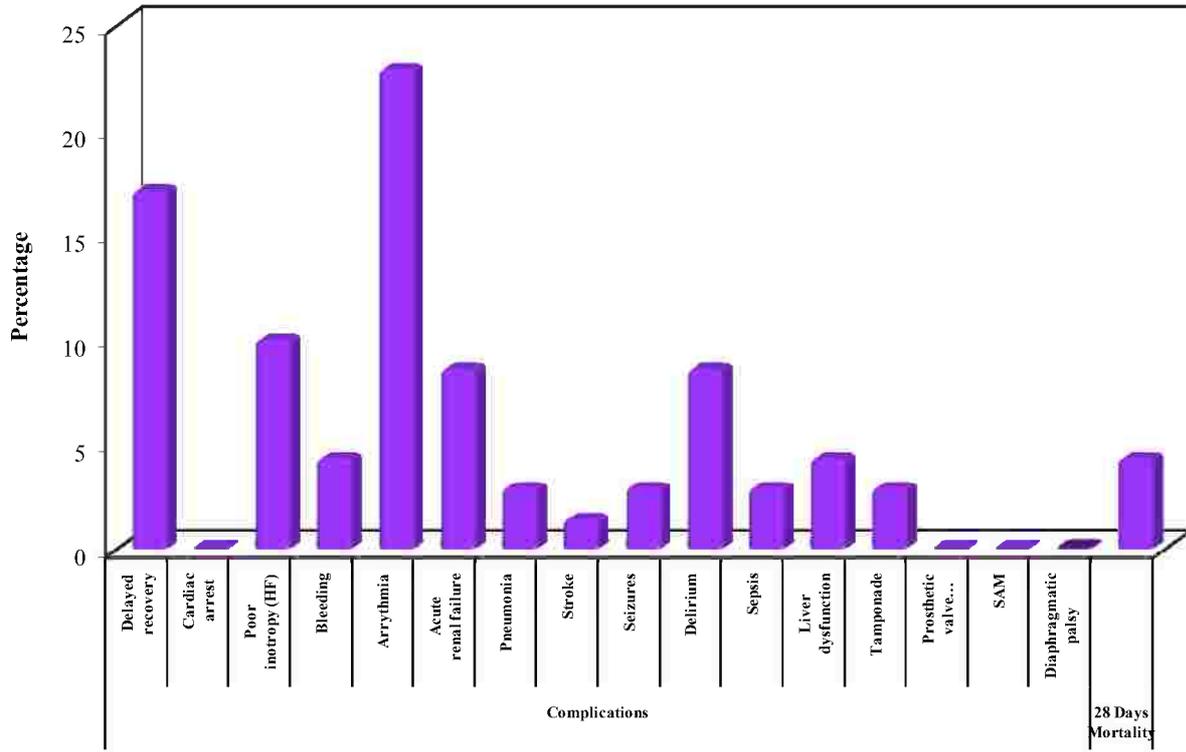


Figure (10): Distribution of the studied cases according to complications

Results

Table (10) Demonstrate that 28-days mortality among studied cases was 4.3 %.

Table (10): Distribution of the studied cases according to Mortality (n = 70)

	No.	%
28 Days Mortality	3	4.3

Table (11), figure (11) demonstrate the frequency and percentages of different complications and mortality in the studied cases according to the type of operation.

There was no significant difference in the incidence of complications between CABG patients and valve replacement patients.

Table (11): Distribution of the studied cases according to complications (n = 70)

	CABG (n = 45)		Valve (n = 25)		χ^2	p
	No.	%	No.	%		
Delayed recovery	8	17.8	4	16.0	0.036	^{FE} p=1.000
Cardiac arrest	0	0.0	0	0.0	-	-
Poor inotropy (HF)	2	4.4	5	20.0	4.321	^{FE} p=0.089
Bleeding	2	4.4	1	4.0	0.008	^{FE} p=1.000
Arrythmia	7	15.6	9	36.0	3.810	0.051
Acute renal failure	2	4.4	4	16.0	2.738	0.177
Pneumonia	1	2.2	1	4.0	0.183	^{FE} p=1.000
Stroke	1	2.2	0	0.	0.564	^{FE} p=1.000
Seizures	1	2.2	1	4.0	0.183	^{FE} p=1.000
Delirium	5	11.1	3	12	0.016	^{FE} p=1.000
Sepsis	2	4.4	0	0.0	1.144	^{FE} p=0.534
Liver dysfunction	3	6.7	0	0.0	1.741	^{FE} p=0.548
Tamponade	0	0.0	2	8.0	3.706	^{FE} p=0.124
Prosthetic valve dysfunction	0	0.0	0	0.0	-	-
SAM	0	0.0	0	0.0	-	-
Diaphragmatic palsy	0	0.0	0	0.0	-	-
28 Days Mortality	2	4.4	1	4.0	0.008	^{FE} p=1.000

χ^2 : Chi square test

FE: Fisher Exact test

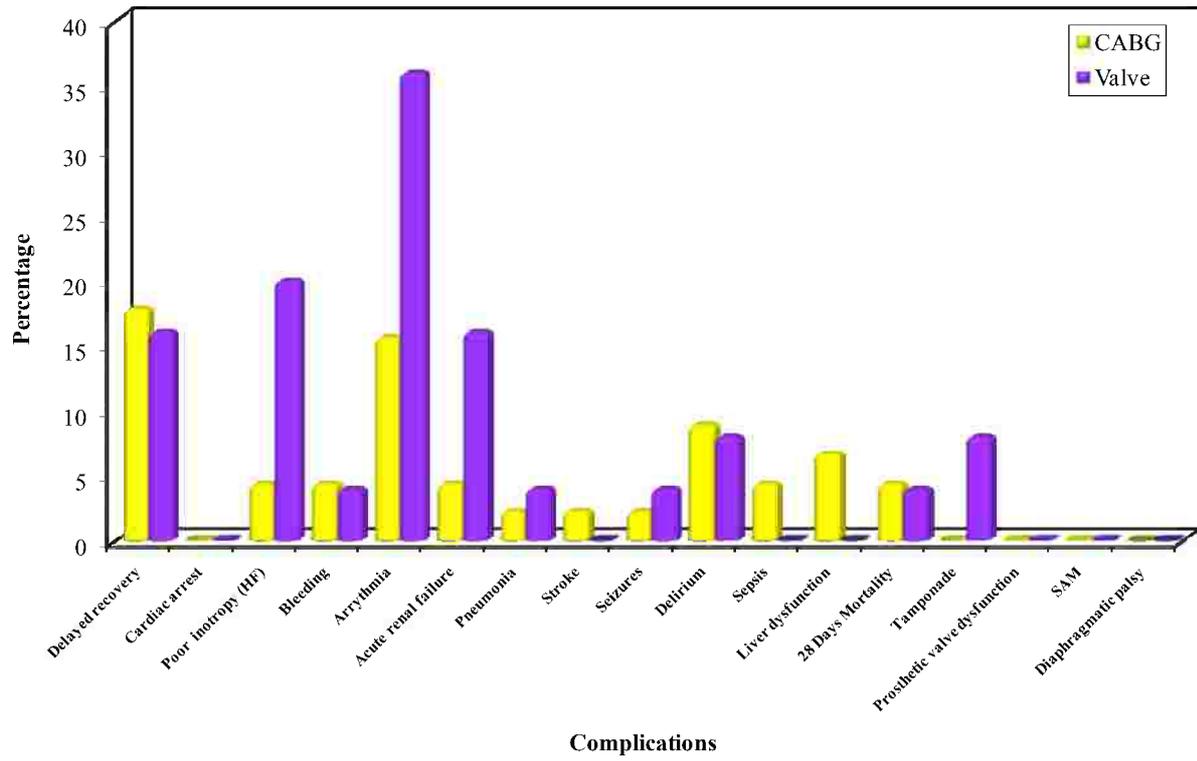


Figure (11): Distribution of the studied cases according to complications

Results

Table (12), figure (12): show the relationship between ΔPCO_2 at T3 and the incidence of complications. It shows that among 29 patients with $\Delta\text{PCO}_2 \leq 6$ mmHg only 6 patients representing 20.7 % developed one or more complication while in 41 patients with $\Delta\text{PCO}_2 > 6$ mmHg at T3 20 patients representing 48.8 % developed one or more complication.

There was statistically significant difference in the incidence of complications at T3 between patients with $\Delta\text{PCO}_2 > 6$ and patients with $\Delta\text{PCO}_2 \leq 6$ mmHg.

Table (12): Relation between ΔPCO_2 at T3 and Complications

	ΔPCO_2 at T3				χ^2	P
	≤ 6 (n = 29)		> 6 (n = 41)			
	No.	%	No.	%		
Complications						
No	23	79.3	21	51.2	5.741*	0.017*
Yes	6	20.7	20	48.8		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

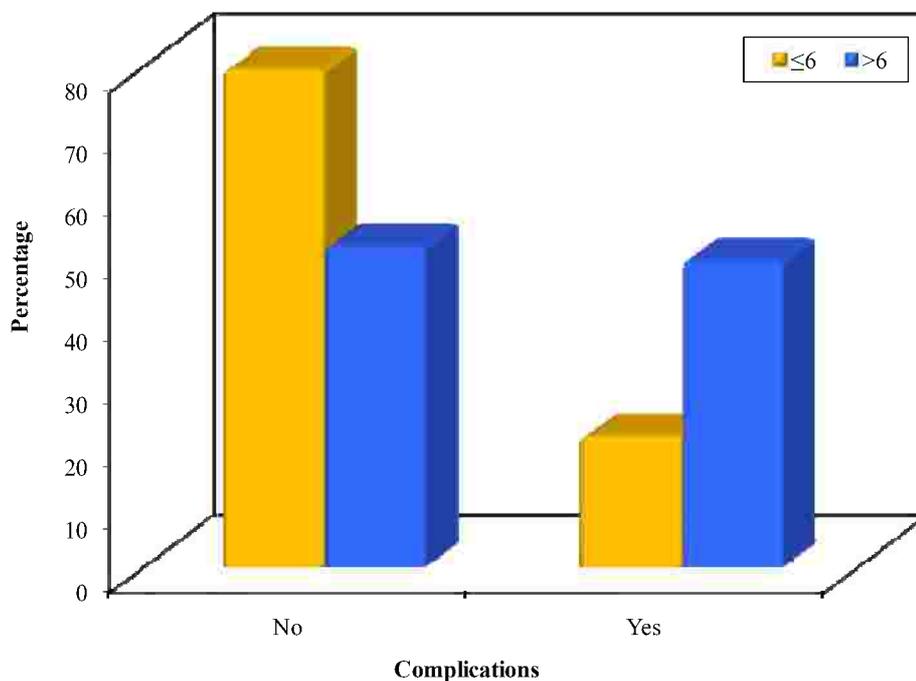


Figure (12): Relation between ΔPCO_2 at T3 and Complications

Results

Table (13), figure (13): show the relationship between ΔPCO_2 at T6 and the incidence of complications. As shown that among 43 patients with $\Delta\text{PCO}_2 \leq 6$ only 7 patients representing 16.3 % developed one or more complication while in 27 patient with $\Delta\text{PCO}_2 > 6$ mmHg at T6, 19 patients representing 70.4 %.

There was statistically significant relationship between ΔPCO_2 at T6 and the incidence of complications, ($p \leq 0.05$).

Table (13): Relation between ΔPCO_2 at T6 and complications

	ΔPCO_2 at T6				χ^2	p
	≤ 6 (n = 43)		> 6 (n = 27)			
	No.	%	No.	%		
Complications						
No	36	83.7	8	29.6	20.785*	<0.001*
Yes	7	16.3	19	70.4		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

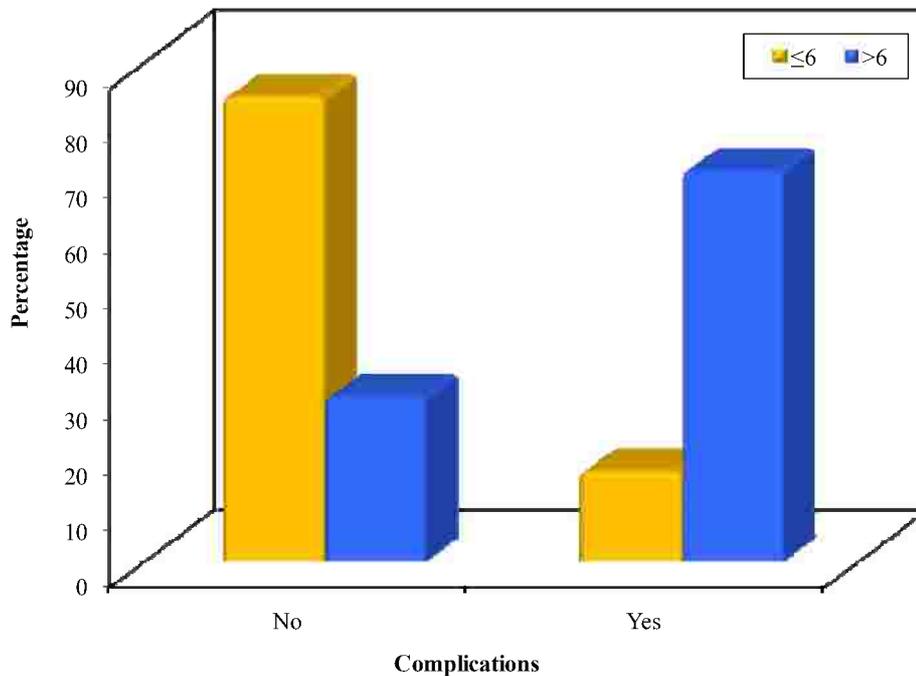


Figure (13): Relation between ΔPCO_2 at T6 and complications

Results

Table (14), figure (14): show the relationship between ΔPCO_2 at T12 and the incidence of complications. They show that among 45 patients with $\Delta\text{PCO}_2 \leq 6$ mmHg only 7 patients representing 15.6 % developed one or more complication while in 25 patients with $\Delta\text{PCO}_2 > 6$ mmHg at T12, 19 patients representing 76.0 % developed one or more complications.

There was statistically significant relationship between ΔPCO_2 at T12 and the incidence of complications ($p \leq 0.05$)

Table (14): Relation between ΔPCO_2 at T12 and complications

	ΔPCO_2 at T12				χ^2	P
	≤ 6 (n = 45)		> 6 (n = 25)			
	No.	%	No.	%		
Complications						
No	38	84.4	6	24.0	25.150*	<0.001*
Yes	7	15.6	19	76.0		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

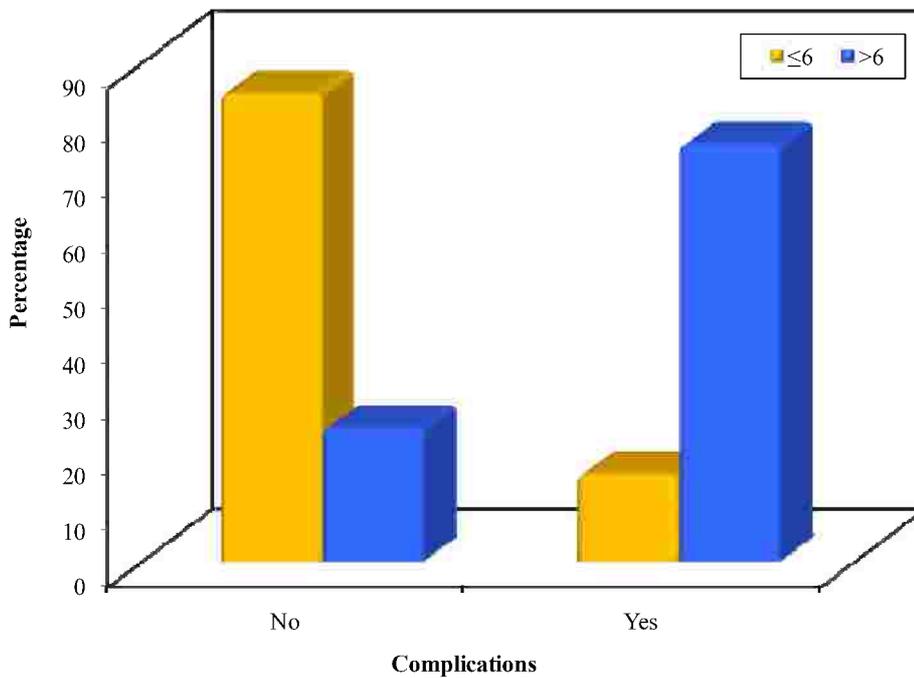


Figure (14): Relation between ΔPCO_2 at T12 and complications

Results

Table (15) shows the relationship between 28-day mortality and ΔPCO_2 at T3, T6 and T12 postoperatively. It shows that all 28-day mortality cases were having $\Delta\text{PCO}_2 >6$ mmHg at T3, T6 and T12.

Table (15): Relation between 28 Day mortality and ΔPCO_2 at T3, T6 and T12

	ΔPCO_2 at T3				ΔPCO_2 at T6				ΔPCO_2 at T12			
	≤ 6 (n = 29)		> 6 (n = 41)		≤ 6 (n = 43)		> 6 (n = 27)		≤ 6 (n = 45)		> 6 (n = 25)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
28 Day mortality	0	0.0	3	7.3	0	0.0	3	11.11	0	0.0	3	12.0

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

ROC curve: figure (15), table (16):

At T3 ROC curve shows an area under the receiver operating curve of 0.739 with a ΔPCO_2 cutoff value 8 mmHg predicting development of complications with 46.15 % sensitivity and 90.0 % specificity.

At T6 it shows an area under the receiver operating curve of 0.806 with a ΔPCO_2 at T6 cutoff value 6 mmHg predicting development of complication with 73.08 % sensitivity and 81.82 % specificity.

At T12 it shows an area under the receiver operating curve of 0.831 with a ΔPCO_2 at T12 cutoff value 6 mmHg predicting development of complications with 73.08 % sensitivity and 86.36 % specificity.

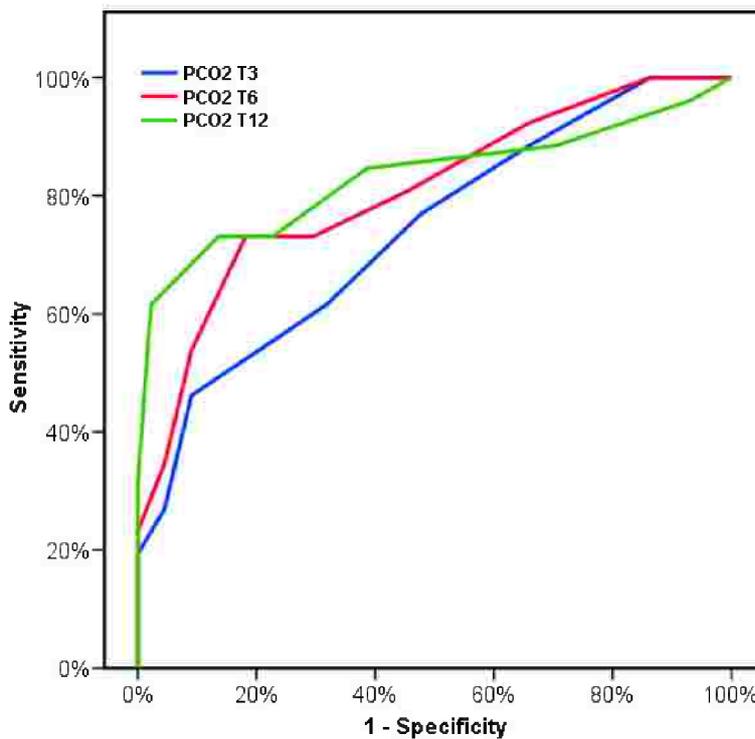


Figure (15): ROC curve for ΔPCO_2 T3, T6 and T12 to diagnose patients with Complications

Table (16): Agreement (sensitivity, specificity and accuracy) for ΔPCO_2 T3, T6 and T12 with Complications

ΔPCO_2		No Complications	Complications	Sensitivity	Specificity	PPV	NPV	Accuracy
T3	≤ 8	40	14	46.15	90.91	75.0	74.07	74.29
	> 8	4	12					
T6	≤ 6	36	7	73.08	81.82	70.37	83.72	78.57
	> 6	8	19					
T12	≤ 6	37	7	73.08	86.36	76.0	84.44	81.43
	> 6	6	19					