Acute Respiratory Distress Syndrome Diagnosis after Coronary Artery Bypass: Comparison between Diagnostic Criteria and Clinical Picture

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Abstract- Acute Respiratory Distress Syndrome (ARDS) is a potential complication of cardiac surgery, given that patients undergoing CABG frequently have hypoxemia and pulmonary dysfunction during initial hours after surgery. Thus, ARDS criteria in these patients are more likely to be positive while these criteria may not match the patient`s clinical picture. We aimed to investigate frequency of rapid onset hypoxemia in Pressure of Arterial Oxygen to Fractional Inspired Oxygen Concentration (PaO2/FiO2) less than 200 and diffuse pulmonary infiltrates as two diagnostic criteria forwards and compared these criteria with the clinical picture of the patients after Coronary Artery Bypass Graft (CABG) in this study. The study was prospective case series which carried out in about six months. All patients admitted to intensive care unit of Tehran Heart Center, who had undergone CABG on cardiopulmonary pump (CPB) recruited in the study. After considering inclusion criteria, age, sex, duration of intubation, arterial blood gas and chest radiography, on 24 hours and 48 hours after admission to the ICU were recorded. Then, patients with rapid onset of hypoxemia (PaO2/FiO2≤200mmHg) and diffuse pulmonary infiltrates and without sign or symptoms of obvious heart failure (probable positive ARDS cases) criteria were recorded and comparison between these probable positive cases with clinician`s clinical diagnosis (blinded to the study) was performed. In this study, a total of 300 patients after on-pump coronary artery bypass surgery were included. Postoperatively, 2 (0.66 %) in the 24 hours and 4 (1.33%) patients in 48 hours after surgery were positive for the two ARDS criteria according to the checklists, but; nobody had saved persistently ARDS criteria persistently during 48 hours after surgery. At the same time, clinician did not report any case of ARDS among 300 patients. In this study patients with ARDS criteria had no significant differences in age (*P*.value=0.937) and sex (*P*.value=0.533). Duration of intubation in patients with ARDS (14.26 ± 4.25 hours) in the first 48 hours was higher but not statistically different from the group without ARDS (11.60 ± 5.45 hours) (*P*.value=0.236). ARDS diagnosis based on rapid onset of hypoxemia (PaO2/FiO2≤200 mmHg) and diffuse pulmonary infiltrates and without signs or symptoms of obvious heart failure criteria in patients undergoing CABG could lead to overdiagnosis or misdiagnosis in less than 24 hours follow up. We recommend following patients for more than 24 hours and revise the current ARDS criteria for CABG patients.

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Keywords: Acute Respiratory Distress Syndrome; Coronary Artery Bypass Graft; cardiopulmonary pump (CPB)

Introduction

Acute Respiratory Distress Syndrome (ARDS) is a common clinical disorder that damages the epithelial and endothelial barriers of alveoli "causing inflammation, acute pulmonary edema, and acute respiratory failure. This syndrome is an important cause of morbidity and mortality in patients in intensive care in the world (1). Since Ashbaugh *et al.,* first described the pathogenesis and pathophysiology of this syndrome. Efforts to provide practical and reliable diagnostic descriptions of this syndrome that can be used in the clinical and research is performed (1). Symptoms of this syndrome as tachypnea, hypoxemia resistant to oxygen within a few hours after it

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starts to cause clinical disorders. Early radiographic findings consist of patchy infiltration indistinguishable from pulmonary edema, worsening progress in the absence of signs of left heart failure. After several decades that the syndrome is characterized by Ashbaugh, many professionals seek to better understand and ultimately tried to describe this syndrome with 3 criteria , sudden onset of hypoxemia with a ratio of arterial oxygen pressure to the fraction of breathing oxygen less/equal than 200 and diffuse pulmonary infiltrates on chest radiograph as essential criteria for this syndrome. To rule out pulmonary edema left ventricular function should be evaluated (2). The incidence of this ARDS is 15-18% of all patients is connected to a ventilator and is associated with a mortality rate of over 50% (3). Coronary heart disease is the most common surgery performed in the world. Some respiratory complications including respiratory distress syndrome occur after Coronary Artery Bypass Graft (CABG) which can cause problems in extubation of the patient who is connected to a ventilator (4).

Several factors are involved in the pathogenesis of respiratory failure after CABG. Inflammatory and anti-inflammatory cytokines release was triggered in major postoperative complications and cause hypoxemia and a longer time to connect to the device. The most common causes of hypoxemia are respiratory distress syndrome and pulmonary edema (4). Due to the prevalence of 0.5% -1.7% of this syndrome after cardiopulmonary bypass and its significant effect on the outcome because of the high mortality rate (50-91.6%) (5) and also with regard to medical costs in the most serious complications after coronary surgery carries (4) and prolonging stay in the Intensive Care Unit (ICU) (6). Since the period after operation is a particularly vulnerable time for the patient, any signs or symptoms of airway or ventilation problems that can cause hypoxia should be noted (7). Clinical evaluation of the patient's physical examination, invasive and non-invasive measurement of gas exchange and chest radiograph should be done. In order to assess the level of hypoxemia, respiratory failure symptoms of Pressure of Arterial Oxygen to Fractional Inspired Oxygen Concentration (PaO_2/FiO_2) should be measured (8).

Given that patients undergoing CABG have frequently impaired respiratory gases and acute pulmonary involvement in the first hours after surgery, criteria for ARDS in these patients are more likely to be positive while he may not comply with these criteria.

According to the clinical picture and Para clinical evaluation of patients after CABG in Tehran Heart Care Center, we aimed to evaluate the frequency of ARDS diagnostic criteria, as well as acute respiratory distress syndrome and compare positive ARDS diagnostic criteria with clinician`s diagnosis based on the clinical picture of patients.

Materials and Methods

The present study was designed as prospective case series study which was carried out in about six-month and approved by the Tehran University Medical Sciences, and organized to encompass 300 patients after CABG on cardiopulmonary pump (CPB), who had signed a consent form to use their information in the study in 2012. Inclusion criteria were: coronary artery disease with no other valvular (severe or need surgical correction) or congenital disease, intubation in the operating room, no preoperative inotropic therapy and/or hemodynamic impairment and/or aortic balloon pump preoperatively or during first three hours of entrance to the ICU, lack of preoperative infection, creatinine level less than 2 mg/dl , leak of respiratory distress or respiratory problems evident before surgery, Carbon dioxide pressure (CO_2) < 45 mmHg and Pressure of Arterial Oxygen (PaO_2) >60 mmHg, Forced Expiratory Volume in first second (FiO_2) >60%, Ejection Fraction (EF) >30% and Body Mass Index (BMI) < 40 $kg.m^{-2}$. In first hours after entrance to the ICU, all patients were evaluated regarding the inclusion criteria, to be included in the study.

Exclusion criteria were: death, surgical intervention heart valves, Postoperative hemodynamic impairment or aortic balloon pump use, reoperation after extubation, any documented loss in ejection fraction (defined as necessitate to inotropic postoperatively and/or intra-aortic balloon pump and/or a decrease in EF to ≤ 30 and/or significant abnormalities in cardiac diastolic function and/or clinical or para-clinical signs or symptoms of heart failure) and any adverse neurological disorder or impairment of consciousness during the first 48 hours postoperatively. Other variables included: age, height, weight, EF before surgery, Arterial Blood Gas (ABG), duration of intubation, chest radiography findings and mortality in the hospital. All patients were under evaluation of postoperative respiratory complications by trained staff in the ICU to collect the most relevant information.

Of all the patients who had no left side heart failure signs and/or symptoms, at the first and second 24 hours ABG, chest radiograph was made, then patient`s graphies were reported by the radiologist who was blinded to the study. In the case of a positive report based on diffuse involvement of pulmonary as it may be similar to pulmonary edema, echocardiography was performed by a cardiologist who was unaware of the study and EF were recorded. If; EF ≤ 30 and/or significant abnormalities in cardiac diastolic function, patients were excluded from the study. After recording the data in case of a positive report of every three criteria (sudden onset hypoxemia as decrease in ratio of PaO2/FiO2≤200 in few hours, and chest radiograph showing a diffuse lung infiltration), patients separately were followed and examined by clinician in the ICU who was completely unaware of the checklist and his diagnosis was based on clinical symptoms and signs. Then a comparison between cases with probable positive ARDS criteria and clinician`s clinical diagnosis was performed.

Statistical analysis

For data analysis, the collected data were organized by SPSS software version 19. Samples were tested for a normal distribution using the Kolmogorov-Smirnov test.

Results

In this study, 300 patients admitted to the ICU of Tehran Heart Center during a six months period were studied, all patients participated in the study and no one was excluded from the study by the exclusion criteria. During first 48 hours after surgery, nobody needed inotropic use or re-operation after extubation, and/or had severe neurological impairment, and overall none of patients had died.

In this study, 215 patients were male (75%), and 75 (25%) were women in the mean age of 61.97(±9.62) with the range of 40-89 years. The mean duration of admission in ICU was 1.58 (± 0.84) days with the range of 1-2 days. The mean duration of intubation of patients was 11.65 (± 5.44) hours (Table 1).

PaO2/FiO2≤ 200 deductible on arrival at the ICU in 207 patients (69%), at the 24 hours in 41 patients (13.66 %) and at the 48 hours postoperatively in 75 patients (25%) was positive. Diffuse pulmonary infiltration on chest radiography in four quadrants were detected in 10 patients (3.33%).

After data analysis patients were divided into two groups with and without upper mentioned ARDS criteria. In positive ARDS group there were 2 (0.66 %) in the 24 hours and 4 (1.33%) cases in the 48 hours after surgery who had ARDS only based on criteria listed in the text , but clinician who was totally unaware of the Checklist of the 300 patients did not report any case of clinically proved ARDS case. In this study, 5 from 6 patients who had ARDS criteria were male.

There was no difference between two groups regarding, age (*P*.value =937), sex (*P*.value =0.533), ICU stay duration (*P*.value=0.469), intubation (*P*.value=0.326), PaO2 in ICU entry duration (*P*.value=0.727), FiO2 at ICU entry (*P*.value =0.658), PaO2 in 24 h after ICU entry (*P*.value =0.540), FiO2 in 24 h after ICU entry (*P*.value =0.593), FiO2 in 48 h after ICU entry (*P*.value =0.439), PaO2/FiO2 entry ICU (*P*.value =0.397) and PaO2/FiO2 after 48 h after ICU entry (*P*.value =0.046). But, PaO2 in 48 h after ICU entry (*P*.value =0.048) and PaO2/FiO2 after 24 h after ICU entry (*P*.value =0.465) were different between two groups (Table 1).

Table 1. Comparison age, ICU stay duration, duration of intubation, ARDS respiratory parameters between two groups

	ARDS in 24 or 48 h after ICU			*P*. value
	Mean(±SD)			
	No	Yes	Total	
Age	61.98 (±9.66)	61.67(±8.16)	61.97(±9.62)	0.937
ICU stay duration (days)	1.59(±0.84)	1.33(±0.51)	1.58(±0.84)	0.469
Intubation duration (minutes)	11.60(±4.54)	14.26(±4.25)	11.65(±5.44)	0.236
PaO2 at ICU entry	132.29(±56.10)	107.00(±26.29)	131.78(±55.57)	0.272
FiO2 at ICU entry	76.94(±10.63)	75.00(±8.36)	76.90(±10.58)	0.658
PaO2 at 24 h after Entry ICU entry	94.48(±25.97)	88.00(±20.15)	94.35(±25.86)	0.544
FiO2 at 24 h after Entry ICU entry	34.90(±6.53)	36.33(±3.67)	34.93(±6.49)	0.539
PaO2 at 48 h after ICU entry	78.19(±22.19)	60.17(±5.34)	77.83(±22.12)	0.048
FiO2 at 48 h after ICU entry	33.52(±6.46)	35.33(±3.61)	33.55(±6.41)	0.439
PaO2/FiO2 in ICU entry	176.59(±85.02)	145.83(±46.68)	175.92(±84.49)	0.397
PaO2/FiO2 24 h after ICU entry	283.37(±130.26)	244.31(±57.14)	282.59(±129.28)	0.465
PaO2/FiO2 48 h after ICU entry	239.81(±81.87)	175.55(±28.12)	238.46(±81.68)	0.046

ARDS; Acute Respiratory Distress Syndrome, ABG; Arterial Blood Gas, PaO2; Pressure of Arterial Oxygen, FiO2, Fractional Inspired Oxygen Concentration, h; hours

Regarding ARDS diagnosis based on a onset hypoxemia as decrease in ratio of PaO2/FiO2≤200 in few hours, and chest radiograph showing a diffuse lung infiltration, there were 2 (0.66 %) in the 24 hours and 4 (1.33%) cases in the 48 hours. Nobody had a continued diagnosis during first 48 hours after surgery (Table 2).

Table 2. Frequency of ARDS criteria and their contribution among the patients with or without ARDS in different time scales

	n (%)			*P*.value
	No	Yes	Total	
	ARDS patients in 24 h after ICU entry			
Diffuse infiltration 24 hours after ICU entry	8 (2.7%)	2 (100%)	10 (3.3%)	0.001
PaO2/FiO2 ≤200 (24 h after ICU entry)	39 (13.1%)	2 (100%)	41 (13.7%)	0.018
	ARDS patients in 48 h after ICU entry			
Diffuse infiltration 48 hours after ICU entry	2 (0.7%)	4 (100%)	6 (2%)	≤0.001
PaO2/FiO2 ≤200 (48 h after ICU entry)	71 (24%)	4 (100%)	75 (25%)	0.004
	ARDS patients in 24 or 48 h after ICU entry			
Diffuse infiltration in 24 or 48 h after ICU	6 (2%)	6 (100%)	12 (4%)	≤0.001
PaO2/FiO2 ≤200 (in 24 or 48 h after ICU)	86 (29.3%)	6 (100%)	92 (30.7%)	0.001
	ARDS patients in 24 and 48 h after ICU entry			
Diffuse infiltration in 24 and 48 h after ICU	4 (1.3%)	0 (0%)	4 (1.3%)	-
PaO2/FiO2 ≤200 (in 24 and 48 h after ICU)	24 (8%)	0 (0%)	24 (8%)	-

ARDS; Acute Respiratory Distress Syndrome, ABG; Arterial Blood Gas, PaO2; Pressure of Arterial Oxygen, FiO2, Fractional Inspired Oxygen Concentration, h; hours

Discussion

In this study, we have analyzed probably ARDS criteria in 300 otherwise healthy on cardiopulmonary pump CABG patients. This is the first study to provide quantitative and statistical evidence of diagnostic criteria for acute respiratory distress syndrome and comparison of the positive ARDS Para-clinical diagnostic criteria with clinician`s clinical diagnosis in patients undergoing CABG in Iran. In this study, the criteria for ARDS in 2 cases (0.66 %) in the 24 hours and 4 cases (1.33%) in the 48 hours after ICU entrance were positive but, nobody had a continued diagnosis during first 48 hours after surgery (Table 2). At same time, clinician did not report clinical ARDS. It means that in CABG patients, one should follow patients for confirming the clinical diagnosis of ARDS for more than 24 hours even in the presence of all criteria for many hours.

However, regarding the overall good prognosis of the patient - such as extubation time and leak of mortality-, it seems that the judgment of expert clinician is more accurate. These results are very important and need to be assessed in a more definite manner by application of cardiac output monitoring and in the normal group CABG patients. However, when we try to extend this results to all cardiac surgery patients, it could mean the necessity to adjust this criteria developing, or ARDS after cardiac surgery is rare, but is associated with very high mortality. Postoperative low cardiac output can cause hypoperfusion leading to respiratory distress syndrome after cardiac surgery.

In a study (11) of 3278 patients undergoing cardiac surgery and CPB between January 1995 and December 1998, 13 patients had postoperative ARDS; multivariate regression analysis showed that previous heart surgery, shock, and blood products are independent predictor factors for ARDS.

In another study (12) conducted in 3444 coronary artery bypass surgeries, incidence of ARDS was 1.0% (38 cases out of 3848), and the overall mortality was 68.4% (26 patients). Multiple regression analysis showed high blood pressure, current smoking, emergency surgery, (NYHA) class three and four, low cardiac output, postoperative left ventricular ejection fraction less than 40% as significant independent predictors of respiratory distress syndrome.

Comparison current results with previous studies in other countries indicate that the incidence of probable ARDS (1%) in this study is like other studies. Restricted inclusion criteria such as; CABG surgery with no other surgery, intubation in the operating room, no preoperative inotropic therapy and/or hemodynamic impairment and/or aortic balloon pump preoperatively, no other cardiac pathologies including a valve disorder which required surgical intervention, or congenital heart disease, lack of preoperative infection, creatinine level less than 2mg/dl, leak of respiratory distress or respiratory problems evident before surgery , Carbon dioxide pressure (CO2) < 45 mmHg and Pressure of Arterial Oxygen (PaO2) >60 mmHg, Forced Expiratory Volume in first second (FiO2) >60%, Ejection Fraction (EF) >30% and Body Mass Index (BMI) < 40 kg.m-2;

results in entrance of partially healthy patients of current study. Meanwhile, many of the above factors under previous studies are the risk factors for acute respiratory distress syndrome (13-17). Although, considering the stringent inclusion criteria the overall incidence of ARDS should be higher in on-pump CABG patients, the lack of a price way to assess low cardiac output situations (e.i.; due to transient stunning after cardiac surgery or due to electrolyte abnormalities) and rule out pulmonary edema definitely could lead to probable over-diagnosis. So, the frequencies of the ARDS criteria belong to this selected group of patients not represent an overall view of cardiac surgery patients.

The mean duration of intubation in patients with ARDS criteria (acute onset of hypoxemia (PaO2/FiO2 ≤ 200 mmHg) and diffuse pulmonary infiltration with four quadrants' lung involvement in the chest radiography) in 48 hours of ICU admission was not significantly different from patients without these criteria. It is not an expected consequence for a group of patients with lower PaO2/FiO2 or ARDS.

Diffuse pulmonary infiltration in four quadrants on chest radiography was positive in 10 patients (3.33%) in 24 hours after entering to the ICU and in 6 patients (2%) at 48 hours after arrival in the ICU (all of these patients in postoperative echocardiography had 30%≤ Ejection Fraction with no abnormalities in cardiac diastolic function). The results showed that it is important that the diagnostic criteria of ARDS is not accurate for patients after CABG surgery due to the high frequency of acute onset of hypoxemia (PaO2/FiO2 ≤ 200 mmHg) (in our study, this rate was 69% at the admission time to the ICU, 13.66% in the 24 hours and 25% in the 48 hours after ICU entry), using these criteria in CABG patients could lose its value as a diagnostic criteria of ARDS.

The results of our study for patients based on diagnostic criteria, ARDS was diagnosed in 2 cases (0.66 %) in the first 24 hours and 4 (1.33%) in the second 24 hours, meanwhile they were discharged from the hospital without any trouble at the track. Probably, according to the low sample size of the present study, low incidence of ARDS and also restricted inclusion criteria, we have low detection rate compared to other studies. More research is needed with a greater sample size and longer follow-up time. Due to the aggressiveness of directly measurement of pulmonary capillary wedge pressure and cardiac output by Swan-Ganz Catheter (which is the gold standard and the most accurate diagnostic mean)), in this study we used echocardiography as a simple and non-invasive method which has the less accuracy to rule out low cardiac output stat and its resultant pulmonary edema was used. Therefore, invasive process may be necessary to be performed to obtain more accurate and more distinct results and confirm the clinician`s diagnosis.

So given the difficulties and complications, high mortality in the Acute Respiratory Distress Syndrome, and overdiagnosis or misdiagnosis based on rapid onset of hypoxemia (PaO2/FiO2 ≤ 200 mmHg) and diffuse pulmonary infiltrates in patients without sign or symptoms of obvious heart failure, we recommend to follow patients more than 24 hours to confirm diagnosis and revise or adjust the ARDS criteria to special group of patients including CABG and cardiac surgery.

Despite unique ideas presented in this study; there are some deficiencies and limitations in this study. The most important items include leak of a accurate mean to assess cardiac output and pulmonary edema (i.e; Swan-Ganz Catheter) and resultant necessary use restricted inclusion criteria (therefore, impossibility to develop results to all cardiac surgery patients), low sample size, short duration of observation and monitoring.

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