

Prediction of Post Operative Complication in Patients with Valvular Heart Surgery Based on O₂ Challenge Test and A-A Gradient

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ABSTRACT: Patients with valvular heart diseases may have more physiological lung derangements and therefore at current study we studied correlation of O₂ challenge, A-AG tests and spirometry values of patients who underwent valve surgery on post op respiratory complications. Method: 180 adult patients undergoing non-emergency cardiac valvular surgery were studied. On operating room all patients had arterial blood gas profile (ABG) at room air, 20 minutes after putting on ventilator with 100% O₂, and pump oxygenator. Pulmonary function tests, alveolar Oxygen Pressure, mean Arterial pressure of carbon dioxide and alveolar-arterial gradients measured. Results: FEV₁, FVC and FEV₁/FVC%, pressure of arterial Blood Gasses (O₂ and CO₂) with fraction of inspired oxygen of 100% and air (PO₂-100 and PO₂-air), were significantly different between patients with POPC and patients without POPC (p-value <0.05). Indeed PO₂-100 and PO₂-air were significantly lower in patients with POPC. A-AG100 (p-value: 0.02) and A-AG21 (p-value: 0.02) were significantly higher in patients with POPC in comparison with patients without POPC. The AUC of A-AG100 for predicting POPC was 0.59 (95% confidence interval (CI) 0.51-0.67). The optimal cut point of A-AG100 was 311 and showed evidence of high relatively sensitivity of 80% and a negative predictive value of 61%. Conclusion: Valvular heart surgery still has significant post op complication and mortality. There is significant correlation between A-AG100, A-AG21 percent, PaO₂100, and FEV₁/FVC with post op complications in these patients. We recommend measurement of these values in pre op evaluation of patient who need cardiac surgery.

KEYWORDS: Post op complications, valvular heart diseases, pulmonary function tests, O₂ challenge tests, alveolar arterial gradients

Introduction

Pulmonary function testing (PFT) including spirometry, static lung volumes, diffusion of the lung for Carbon Dioxide (DLCO), oximetry, and arterial blood gases has been used for evaluation of the risk of postoperative complications. However, in many medical centers and hospitals, PFTs are not routinely performed before cardiac surgery [1].

Although postoperative pulmonary complications are frequent and important, the accuracy of preoperative lung volume in the prediction of postoperative pulmonary complications has not been studied sufficiently [2]. Some studies showed that patients with moderate-to-severe airway obstruction combined with hypoxemia had a significant higher risk of Post-operative Complication in comparison to patients with a normal respiratory function. They suggest that if; age, type of operation, and comorbidity, are taken into account a preoperative respiratory functional assessment could be useful in identifying an increased risk of major Post-operative Complication in selected patients [3,4].

A history of chronic obstructive pulmonary disease (COPD) is one of risk stratification's variables in patients undergoing cardiac surgery.

4% to 27% of patients undergoing cardiac surgery have a clinical history of COPD. These patients convey a higher risk of postoperative pulmonary complications [2]. Many of the patients with valve surgery have restrictive obstructive lung diseases that may be due to cardiomegaly, effusion or interstitial and peribronchial or pericapillary lung fibrosis, during long periods of exposure to passive congestion of lung which is somewhat reversible [5,6,7]. It is well defined in patients with mitral stenosis [6-8]. Post-operative pulmonary complications, such as atelectasis or pneumonia may affect from 6% to 10% of subjects without pulmonary disease [6,8]. These complications is higher in patients with coexisting respiratory diseases, and may vary between 25% and 90% according to different reports but, mortality due to respiratory causes is rare after extra-thoracic operations and in thoracic surgeries without resection [6]. Despite presence of inconclusive studies on dynamic and static lung volumes on post-operative pulmonary complication, we could not find any studies that evaluate impact of physiological tests like O₂ challenge test, and Arterial-Alveolar gradient (A-AG) at post op complication.

We put our focus on evaluation of classic pulmonary function tests and these physiological

tests, on post op pulmonary complication and in hospital outcome of patients. Patients with valvular heart diseases may have more physiological lung derangements and therefore at current study we considered O₂ challenge, A-AG tests and also spirometry values of patients who underwent valve surgery. Other kinds of cardiac surgery would be evaluated separately.

Patients and methods

This prospective study was conducted at a tertiary hospital since March to December 2015.

Adult patients (aged >18 years) undergoing non-emergency cardiac valvular surgery was eligible to participate in the study. This study was approved by our local ethical committee according to the Helsinki Declaration of the World Medical Association (2000). All patients were informed and given written consent form.

Demographic data and all patient history of comorbid diseases like diabetes mellitus, renal failure, respiratory diseases, COPD, and function class of patients obtained from their documents or asked directly from patients. All patients had spirometry and if there were abnormal values on it, further evaluation including total lung capacity (TLC) and diffusion of the lung for Carbon Oxide (DLCO) were done. On operating room all patients had arterial blood gas profile (ABG) at room air and then 20 minutes after intubation and putting on ventilator with 100% O₂. All of them received general anesthesia and pump oxygenator during surgery and we had pump blood gas in regular interval. ABG obtained from arterial line on. Alveolar Oxygen Pressure (PA) estimated based on atmospheric pressure of 660 millimeter of mercury for our hospital height from sea level, fraction of O₂ (FIO₂) considered 21% and water vapor pressure 47 millimeter of mercury at alveoli and alveolar O₂ estimated based on these formula: $PIO_2 = PB - 47 \times FIO_2$ and $PAO_2 = PIO_2 - PaCO_2 \times 1.2$.

Where in PIO₂ means fraction of inspired O₂, PB mean Barometric Pressure and PaCO₂ mean Arterial pressure of carbon dioxide. We considered alveolar-arterial gradients (A-AG) as a physiologic marker and one probable denominator of lung function.

All surgeries performed via median sternotomy and patients. Cold-blood cardioplegia was used for cardiac arrest. In ICU, our patients were extubated when they were hemodynamically stable and able to breathe adequately. After extubating, oxygen saturation

(SPO₂) was maintained above 90% by supplemental oxygen and patients became out of bed as soon as general condition and patients tubing let.

Complete history taking, vital signs and clinical examination, chest X-Ray, pulse-oximetry, ECG, echocardiography, and complete blood tests, were done to detect respiratory and other potential problems. Blood culture and special evaluation was done if patient complicated and had to have that diagnostic tests or procedures.

To obtain the amount of total prevalence of complications, the frequency of all morbidity in 24, 48 and 72 hours after surgery, also after leaving the ICU and before discharge time were summed. Diagnosis of complications was based on following definitions:

“Atelectasis” approved by CXR, or CT scan based on our radiologist or pulmonologist report. Plate atelectasis, lobar, multi-lobar atelectasis or lung collapse considered as atelectasis. Hospital Acquired Pneumonia (HAP) or Ventilator associated Pneumonia (VAP) diagnosis were based on presence of new pulmonary infiltrates on chest X ray or CT scan, fever, cough or sputum after operation. Leukocytosis is common after these kinds of operation and we considered hospital acquired pneumonia (VAP) in our patient if they had at least two or more of the above findings besides leukocytosis. And if patient remained intubated more than 48 hours and get pneumonia, we accepted VAP. Diagnose and classification of ARDS was based on Berlin Definition of ARDS. Rule out of cardiac disease or valvular malfunction always done by echocardiography or trans-esophageal echo if it was indicated clinically. Diaphragm paralysis diagnosed if; significant permanent Diaphragm elevation was seen on CXR and or ultrasonography approved decreased or absence of diaphragm muscles contraction. Phrenic nerve NCV and Diaphragm EMG were not available in our center. Pleural effusion diagnosed based on Chest radiography, Sonography of the pleura, echocardiography or CT scan and appreciated if it was more than 2 intercostal spaces on radiography. We considered pulmonary emboli in our patient based on CT angiography and direct observation of clot on echocardiography.

Lung volumes (IVC and FEV₁) were measured by spirometry (GANSORN SPIROSCOUT and PWC-BODY+ plethysmograph). Spirometry was standardized according to American Thoracic Society

recommendations and was performed with the patient in a sitting position. Patients were asked to refrain from smoking and using bronchodilators for at least 8 hours before the testing. The value recorded was the best (the highest IVC, FEV1, and forced vital capacity (FVC) measurement) of 3 consecutive attempts. Predicted values for pulmonary functions were calculated from regression equations according to sex, age, and height. The accuracy of the spirometer for volume is claimed to be 2%, or 0.05 Litter, and the validation limit for flow is claimed to be 3%, or 0.07 Litter, according to the operating manual for Ganshorn spirometer.

Statistics

Statistical analysis was performed with SPSS 15 for Windows (SPSS Inc., Chicago, Illinois). Mean standard deviation (SD) and frequency was used as descriptive analysis. For evaluation the distribution of data one-sample Kolmogorov-Smirnov test was used.

To compare the mean variables between two groups, an independent t-test or Mann-Whitney U test was used.

A multivariate analysis was used to test the variables which can predict POPC. To determine the accuracy of A-AG100 and A-AG air for prediction of POPC, ROC curve was calculated and best cut-off points were analyzed.

Results

Patients evaluated in two groups of those with post op pulmonary complications (POPC), and those without POPC and data recorded in tables.

180 patients (92 males and 88 females) with a mean age of 49±15.9 were studied. Demographic and perioperative data are shown in Table 1.

Table1. Descriptive data of all patients (n=180)

Variables	M±SD, N (%)
Sex (male/female) %	51.1/48.9
Age	49.96±15.96
Surgery duration (hour)	4.99±1.06
Cross clamp time (min)	62.27±25.02
Pump time	1.37±0.48
Surgery type	MVR 119 (66.1%)
	AVR 46(25.6%)
	TVR 26(14.4%)
	PVR 24(13.9%)
History of respiratory disease	11(6.1%)
Cardiac risk factors	DM 27(15%)
	HTN 79(43.9%)
	FH 104(57.8%)
	HLP 50(29%)
	C/S 130(72.2%)

Table 2 shows the relationship between the lung volumes and postoperative pulmonary complications (POPC). FEV1, FVC and FEV1/FVC% were significantly decreased in patients with POPC (p-value 0.004 and 0.04 respectively).

Table 2. The relationship between lung volumes and postoperative pulmonary complications (POPC)

	With POPC	Without POPC	P-value
FEV1 (n=167)	2.35±0.86	2.53±0.77	0.07
FEV1 (%)	83.22±16.30	83.28±14.56	0.98
FVC (n=167)	2.82±0.98	2.94±0.92	0.42
FVC (%)	82.61±16.24	80.58±14.02	0.13
FEV1/FVC (n=167)	82.63±11.84	86.03±11.66	0.004
FEV1/FVC (%)	105.56±9.92	108.29±10.23	0.04
TLC (n=20)	16.21±21.87	10.64±13.89	0.96
TLC (%)	104±18.75	109.28±35.51	0.64
RV (n=19)	15.20±31.21	12.26±24.58	0.27
RV (%)	119±38.95	143.71±39.60	0.21
RV/TLC	3.10±6.67	3.32±7.62	0.69
TLCO (n=14)	6.62±2.14	6.81±2.41	0.90
TLCO (%)	86.22±45.67	75±17.87	0.52
PEFR (n=167)	6.08±2.25	6.18±2.26	0.77
PEFR (%)	80.46±21.91	80.74±20.91	0.80
MEFR (n=167)	1.88±1.46	2.01±1.44	0.26
MEFR (%)	75.33±30.82	83.69±36.67	0.19

POPC: post operation pulmonary complication, FEV1: forced expiratory volume at first seconds, FVC: forced vital capacity, TLC: total lung capacity, RV: reserve volume, DLCO: diffusion of the lung for Carbone monoxide, PEFR: peak expiratory volume, MEFR: Mid expiratory flow rate

Pressure of arterial Blood Gasses (pressure of O₂ and CO₂) with fraction of inspired oxygen of 100% and air (PO₂-100 and PO₂-air), were significantly different between patients with

POPC and patients without POPC (p-value 0.012 and 0.014 respectively). Indeed **PO2-100** and **PO2-air** were significantly lower in patients with POPC (Table3).

Table 3. The relationship between PaO₂-100, PaO₂-21, A-a gradient (A-AG100, and A-AG-air) and postoperative pulmonary complications

	With POPC	Without POPC	P-value
PaO ₂ -100	212.32±54.51	234.06±63.19	0.012
PaO ₂ -air	72.74±11.60	77.30±11.02	0.014
PaCO ₂ -100	32.53±6.25	31.15±5.59	0.411
PaCO ₂ -air	34.57±6.39	33.20±4.58	0.139
A-AG100	348.01±55.50	327.98±63.13	0.02
A-AG-air	14.60±10.12	11.48±7.76	0.02

A-a gradient: alveolar-arterial gradients, POPC: post operation pulmonary complication, PaO₂-100: pressure of arterial O₂ with 100% oxygen, PaO₂-Air: pressure of arterial O₂ on air, PaCO₂-100: pressure of CO₂ on 100% oxygen, PaCO₂-air: Pressure of arterial CO₂ at air, A-AG100: alveolar-arterial gradient of O₂ on 100% O₂, A-AG-air: alveolar-arterial gradient on air breathing

Alveolar-arterial gradients (A-AG) at **FIO₂-100(A-AG100)** and **air (A-AG21)** were compared between two groups of patients (Table 3). **A-AG100** (p-value: 0.02) and **A-AG21** (p-value: 0.02) were significantly higher in patients with POPC in comparison with patients without POPC.

ROC curve of A-AG100 and A-AG air for predicting POPC is shown in table 4 & 5. The AUC of A-AG100 for predicting POPC was

0.59 (95% confidence interval (CI) 0.51-0.67). The optimal cut point of A-AG100 was 311 and showed evidence of high relatively sensitivity of 80% and a negative predictive value of 61% (Table 4). The AUC of A-AG air for predicting POPC was 0.54 (95% confidence interval (CI) 0.50-0.67). The optimal cut point of A-AG air was 8.33 and showed evidence of high relatively sensitivity of 71% and a negative predictive value of 43% (Table 5).

Table 4. Diagnostic accuracy of A-AG100 in Cut of point of 311 for predicting POPC

	Cut of point of 311 for A-AG100	95%CI
Sensitivity	80%	70.25% to 87.69%
Specificity	32%	22.75% to 42.90%
Positive predictive value	54%	49.75% to 58.46%
Negative predictive value	61%	49.16% to 72.86%

Table 5. Diagnostic accuracy of for A-AG-air in Cut of point of 8.33 for predicting POPC

	Cut of point of 8.33 for AAG-air	95%CI
Sensitivity	71%	70.25% to 87.69%
Specificity	43%	22.75% to 42.90%
Positive predictive value	55%	49.75% to 58.46%
Negative predictive value	61%	49.16% to 72.86%

Discussion

The first aim of this study was to determinate the incidence of pulmonary complication after cardiac valvular surgery at a referral heart center, and then, find correlations of this complication with pulmonary function tests obtained before, during or after surgery.

The occurrence of major postoperative pulmonary complications is reported between 5 and 80% with variation attributed to preoperative, intra-operative and even post-

operative risk factors [4]. Some studies have reported a lower incidence rate of POPC; ranging from 3 to 16 percent following coronary artery bypass grafting and 5 to 7% following cardiac valvular surgery [2].

In our study, the incidence of postoperative pulmonary complications was 50% that look to be high. And as we discussed at previous article [9] it is somewhat depend on range of definition of complications. We included plate atelectasis, pulmonary edema and hypoxemia as complications and also our study was on patients

with valvular surgery at a tertiary center that do both complex multi-valvular operation and in more complicated patients. Valvular heart surgery has more complication and mortality in comparison with other kinds of cardiac surgery. It is especially higher in multi valvular heart surgery, which is a common surgery at our center.

In the current study, atelectasis occurred in 12.2% (22 of 180) of patients which is lower than other studies (17.3% and 36%) [3,4,7,10]. Our patients had 5 cm positive end expiratory pressure at the time of intubation and we also used incentive spirometry after extubation, to prevent atelectasis immediately after surgery in all patients. The incidence of postoperative pneumonia in the present study was 11 (6.1%), which was lower than several studies [3,11]. This difference might explained by presence of antibiotic prophylaxis in all patients, and strict pre-operation criteria for evaluation of patients. We also think that special focus of this study on valvular and multi-valvular heart surgery may explain the difference between this study and others, which often cover all kinds of cardiac diseases in their studies. These kinds of patients have complex pre-op evaluations in comparison with other simple cardiac surgeries.

In several studies, advanced age, excess weight (BMI), smoking, high pulmonary artery pressure (PAP), diabetes mellitus, abnormal results of pulmonary function tests, COPD and emergency surgery consistently were identified as risk factors for POPC after cardiac surgeries [6,8-11]. Increased age was directly related to an increase in major complications; hence patients older than 50 years old were most prone to major pulmonary complications, especially infectious complications [3,9,10]. In our study, patients with Hypertension had more POPC. Although increased number of POPC among patients with diabetes mellitus was clinically important but, it was not statistically significant. Besides that, in this study main objective was evaluation of pulmonary complication in valvular heart surgery, not all kinds of cardiac surgery. In our patients most common kinds of operation were mitral valve replacement surgery followed by aortic, tricuspid and then pulmonary valve replacement. It was bivalve or three valve operation in 48 patients.

We studied spirometry values like forced vital capacity (FVC), forced expiratory volumes at first second (FEV1), peak and mid flow rates on all patients and we did Total lung capacity study (TLC), and reserved volume (RV) and

diffusion of the lung for carbon monoxide (DLCO) measurement in patients with abnormal spirometry values. In this regard as it is shown in table [2] most powerful correlation was between FEV1/FVC percent ($P<0.004$). Despite some correlation with FEV1 in other measured values it were not significant ($P<0.07$). We concluded that presence of obstructive pattern of spirometry can predict post op pulmonary complications but other spirometry data have minimal correlation with post up pulmonary complication.

We also considered O₂ challenge test values and Alveolar-arterial gradient of O₂ as a marker of prediction of post op complication and put it on exam. Pulmonary complications (POPC) are common and often lead to morbidity, prolongation of hospital stay and sometime death. In addition, POPC are more commonly associated with death after surgery in comparison with cardiac and other complications [4]. Range of pulmonary complications may differ depending on the time of occurrence. Arterial hypoxemia, atelectasis, pneumonia, diaphragm dysfunction or paralysis, and ARDS may be seen during post op period.

Although it is usual to measure arterial O₂ pressure after giving 100% O₂ (Pa₁₀₀), to evaluate shunt in cardiac diseases, it may also be helpful for evaluation of lung function as routine practice in transplant centers before harvesting. Despite some challenges it is a criterion for selection of lung for organ donation so that values above 300mmHg considered as perfect lung for donation and below 250mmHg may discarded in majority of cases [12]. It is also notable that all patients undergoing open heart surgery have Pa₁₀₀ measurement routinely in operating room before start of anesthesia and we thought that consideration of this precious value beside Alveolo-arterial gradients (A-AG₁₀₀) may have benefit in predicting post op pulmonary complication. To evaluate this hypothesis we obtained A-AG₁₀₀ and A-AG₂₁, and Pa₁₀₀ and Pa₂₁ of all patients before operations and checked for correlation between this value and post op complications. As it is shown in table 3 there is significant correlation between these values and post op complications. With more lower the PaO₂-100 and higher A-AG₁₀₀, we found more post op pulmonary complications. In our experience there were no other studies that take these physiological data in to account. We propose that these data must be one of the basic issues to consider in patient who undergone complex valvular heart surgery.

It is possible to achieve 100 percent O₂ fraction without intubation of patient with non-rebreathing reservoir mask in ward.

ROC curve of A-AG100 and A-AG air for predicting POPC is shown in table 4&5. We found that the best area under curve (AUC) for A-AG100 for predicting POPC was 0.59 (95% confidence interval (CI) 0.51-0.67). The optimal cut point of A-AG100 was 311 and showed sensitivity of 80%. It means that with A-AG100 above 311 chance of post op complication is above 80 percent and perhaps for those patients with high A-AG100 (above 250-300) it would be better to thinking about alternative methods of treatment or special pre op consideration to reduce risk of post op complication and death.

Systolic PAP obtained by ECHO, is an important factor in cardiac surgery and often associated with increased morbidity and mortality. Prevalence of pulmonary hypertension in cardiac surgery patients will increase parallel with severity of illness [2,3,10].

In our studies, SPAP was associated with more complications after surgery even if it was due to back ward failure of heart and pulmonary congestion.

Recommendations: based on this article we found correlation between A-AG with Pa100 and air with post op complication in patients with cardiac valvular surgery but, this study was done on limited patients and only in valvular heart surgery and Obtained Arterial blood gasses were not under direct control. More precise evaluation of these variables in patients with other kinds of cardiac and thoracic surgery need to define practical position of these tests on pre op evaluation of patients. Therefore, another controlled study in all kinds of thoracic surgery may answer questions about correct position of these tests in routine practice.

Conclusion

Valvular heart surgery still has significant post op complication and mortality. There is significant correlation between A-AG100, A-AG21 percent, PaO₂100, and FEV₁/FVC with post op complications in these patients. We recommend measurement of these values in pre op evaluation of patient who need cardiac surgery.

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