IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 10 Ser.4 (October. 2020), PP 52-58
www.iosrjournals.org

A Study To Predict Post Cross Clamp Venous Oxygen Saturation By Transpulmonary Gradient In Chronic Obstructive Pulmonary Disease Patients Undergoing On Pump Coronary Artery Bypass Grafting.

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ABSTRACT
Title : *A Study To Predict Post Cross Clamp Venous Oxygen Saturation By Transpulmonary Gradient In Chronic Obstructive Pulmonary Disease Patients Undergoing On Pump Coronary Artery Bypass Grafting*.
Context : *Patients with COPD are at increased risk of coronary artery disease (CAD) and, conversely, CAD is associated with the diagnosis and severity of COPD . Due to secondary pulmonary hypertension, right ventricular hypertrophy and ischaemia are known to occur in COPD. The purpose of our study is to compare a preoperative echocardiographic parameters; Transpulmonary Pressure Gradient (TPG), to quantify RV dysfunction to predict post surgery decreased venous oxygen saturation in COPD patients undergoing CABG.*
Aims : *To find out the correlation of* TPG *with the changes of venous oxygen saturation after release of cross clamp.*
Settings and design: *After obtaining institutional ethics committee clearance and informed consent from each* 30 *COPD* patients *undergoing on-pump CABG for CAD,* were included in *this* study over a period of one and half years.
Material and methods:After institution of general anaesthesia TPG was measured before any incision. SvO2 *was measured before going on bypass and one hour after release of cross clamp.*
Statistical analysis used: D*ata w*ere *analyzed using standard statistical software Epi Info (TM) 7.2.2.2.*
Result and conclusion: TPG has a *predictive accuracy of 91.67% in* to predict low *SvO2 after coming out of bypass, following CABG.*

Key-words : COPD , *TPG, SvO*2.

Date of Submission: 28-09-2020 Date of Acceptance: 10-10-2020

I. Introduction

Patients with COPD are at increased risk of coronary artery disease (CAD) and, conversely, CAD is associated with the diagnosis and severity of COPD [1,2]. Due to secondary pulmonary hypertension right ventricular hypertrophy and ischaemia are known to occur in COPD patients **.** Many patients with COPD with or without significant pulmonary hypertension, soon develop RV failure and end up with end stage heart disease. Smoking, respiratory muscle strength and lung function (independent of the effect of smoking) and inflammatory markers, predisposes a patient of COPD towards CAD. Even precipitating factors for acute exacerbation of COPD like infections, hyperglycaemia, or enzyme matrix metalloproteinase (MMP) have a role to play in acute coronary syndrome[3]. So COPD patients posted for CABG constitute a high risk group due to existing preoperative right ventricular dysfunction. The aim is to find out the correlation of TPG with the changes of venous oxygen saturation after release of cross clamp.

II. Materials and Methods

Patients aged between 35 to 70 years, both sex with COPD (FEV1/FVC < 70% as per Global Initiative for Chronic Obstructive Lung Disease) undergoing on-pump CABG for CAD were included.

Patients with other respiratory or cardiac problems, CAD in a setting of moderate to severe aortic stenosis, contraindications for TEE probe insertion and an inability to perform PFT were also excluded.

After obtaining institutional ethics committee clearance and informed consent from each patient this trial was conducted at N.R.S. medical college and hospital, Kolkata, over one and half years on a study population that consists of 30 patients.

After admission all the patients were nebulised with inj. duolin (levosalbutamol sulphate and ipratropium bromide) 4 hourly and advised to do incentive spirometry at least for 3 preoperative days. On the day of operation, patients maintaining proper fasting guideline, were shifted to preoperative holding area. Standard ASA monitors were attached. Following intravenous access, radial artery catheterization was done under local anaesthesia for measurement of arterial blood pressure and blood sampling for arterial blood gas analyses .

After shifting patients to OT , all standard ASA monitors attached. Induction was done with inj. midazolam (0.05mg/kg), inj. fentanyl (5 to 10 µg/kg), followed by sleep dose of inj. etomidate . Induction was done monitoring BIS. Intubation was achieved following inj. vecuronium (0.1mg/kg) . Bilateral air entry was checked. TEE probe was inserted. Anaesthesia was maintained by oxygen and nitrous oxide with isoflurane at 1 MAC to maintain BIS between 40-60, along with intermittent intravenous top up doses of injection fentanyl (1-2 µg/kg) and injection vecuronium(0.02µg/kg).

Multilumen internal jugular catheter was inserted for measurement of central venous pressure, and for fluid/medication administration. ScvO2 was measured in each patient after putting in a central line. Urinary catheterization was done after intubation .

EV1000 clinical platform was used to maintain a note on cardiac output, systemic vascular resistance and stroke volume variation. Inotropes, inodilators and vasodilators were infused to maintain a mean arterial pressure of around 20% of the initial value.

Before incision a transesophageal echocardiography (Vivid^{TM}E 95/ Version 202/ model no. GE 000500) was done in each patient to record TPG. TPG was calculated by subtracting the left atrial pressure from the mean pulmonary artery pressure(mPAP).[4]

Mean pulmonary artery pressure(mPaP) can be known from the following equation:

$mPaP = 4(Vearly\ PI)^2$ + central venous pressure[5]

Pulmonary regurgitation can be easily be assessed with doppler from upper esophageal aortic arch short axis view.

Left atrial pressure (LAP) can be calculated from the following equation:

LAP = Systolic blood pressure $- 4(VMR)^2$ [5] where MR is mitral regurgitation. Doppler assessment of mitral regurgitation was done in mid-esophageal long axis view.

And if there was no MR jet then it was calculated by the Nagueh formulae:

$LAP = 1.9 + (1.24 * E/e')$

CABG was done on cardiopulmonary bypass in selected patients. Just after going on cardiopulmonary bypass SvO2 was measured from the venous line blood and PaO2 was measured at the same time from the arterial blood .One hour after release of cross clamp, while the patient was still on bypass mixed venous oxygen saturation was measured with simultaneous measurement of PaO2 from arterial blood.

Anaesthesia and monitoring was continued till the patients were shifted to ITU with stable haemodynamic parameters.

Statistical analysis:

Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC).

Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (s.d.). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (χ^2) test was performed to find the associations. Odds Ratio (OR) with 95% confidence interval (CI) had been calculated to find the risk factors. Diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value were calculated to compare the findings of different diagnostic tools. $p<0.05$ was taken to be statistically significant.

III. Results

TABLE 1: Demographic characteristics; Investigations and monitoring parameters.

Descriptive Statistics	Mean±sd	Median	Range
Age	53.70±6.59	54	36 – 67
BMI	23.60±4.55	22.86	14.5 - 37.2
BSA	2.55±0.45	2.455	1.6 - 3.6
Descriptive statistics	**Mean±Sd**	**Median**	**Range**
Haematocrit	37.53±3.65	38	30 – 45
Hb(gm/dl)	13.54±1.55	13.6	10.3 - 16.7
TC	7364.98±1635.20	7269	4600 – 11456
FBS	96.68±28.68	89	57 – 166
ESR	20.20±5.77	18	13 – 34
PLATELET COUNT	2.31±0.82	2.225	1.3 - 4.4
INR	1.33±0.23	1.3	1.0 - 1.7
Heart rate	71.3±15.78	69	45 – 102
SpO2 at room air	96.8±2.17	97	90 – 99
Systolic blood pressure at the time of calculating MR Vmax	97.2±7.34	96	84 – 121
CVP at the time of measuring mPAP	9.5±1.41	9	6 – 13
CO	3.42±0.77	3.5	2.1 - 4.7
SV	44.62±7.51	46	30 – 58
SVR	1518.97±385.81	1453	1124 - 3283

TABLE 1 , shows,the mean age (mean ± s.d.) of the patients was 53.70±6.59 years with range 36 – 67 years and the median age was 54 years. 88.3% and 11.7% of the patients were males and females respectively with ratio male:female as 7.5:1.0. Proportion of males (88.3%) was significantly higher than that of females (11.7%) ($Z=10.74; p<0.0001$). All the investigations and monitoring parameters median range were within normal range

TABLE 2: Showing TPG of patients according to GOLD classification.

	No. of patients	TPG
GOLD I	27	7.57mm Hg
GOLD II	29	12.35 mm Hg
GOLD III	4	14.55 mm Hg

TABLE **2** showing mean TPG of patients of GOLD I COPD was 7.57mm Hg; TPG of patients of GOLD II COPD was 12.35 mm Hg; and TPG of patients of GOLD III COPD was 14.55 mm Hg

Table 3: Final parameters for investigations.

Descriptive statistics	Mean±Sd	Median	Range
TPG pre-incision	10.38±3.36	11.24	2.3 - 15
SvO2 1 hour after release of cross clamp	57.60±8.13	60.2	38 - 69
PaO2 1 hour after release of cross clamp	379.8±31.72	379	286 - 464

Table 3 shows , the median TPG was 11.24 mm Hg . The median post bypass SvO2 was 60.2 % and post bypass PaO2 is 379mm Hg. TPG was more than 12 mm Hg in 46.7% of patients .

Table4 : Relationship between ScvO2 and SvO2 just after starting bypass

Descriptive statistics	Mean	Range
ScvO2	66.05	61 – 71
SvO2 pre cross clamp	66.95	61 – 73

Table 4shows that pre incision ScvO2 was almost similar to pre cross clamp SvO2

Figure 1: Post cross clamp release SvO2 in our group of patients.

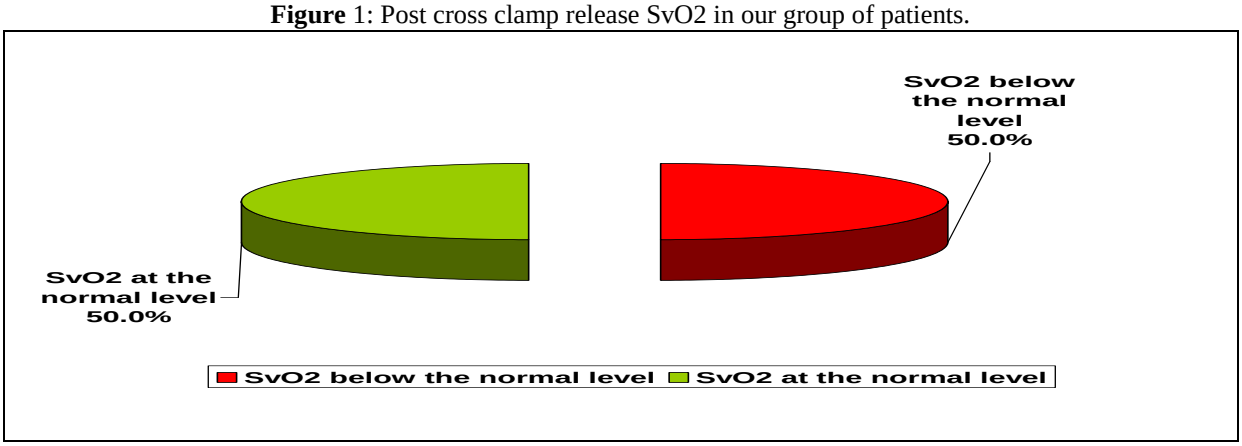

Figure1: One hour after release of cross clamp, 50% of patients had SVO2 more than 60%,whereas, rest of the 50% of study population showed less than 60%.

Table 5 : Correlation between TAPSE, TPG with different parameters

	Pearson Correlation (r) and p-values	$SvO_{2\ post\ cross\text{-}clamp}$	$PaO_{2\ post\ cross\ clamp}$
TPG	R	-0.719	-0.133
	P	<0.001 S	0.313 NS

Table 5 shows , Pearson Correlation was used to correlate TPG with SvO2 and PaO2 . S-Statistically Significant; NS- Statistically not significant. The level of TPG was significantly negatively correlated with the level of SvO2 ($p<0.0001$). Thus the level of SvO2 decreased significantly with the increasing level of TPG.

Figure2 : Correlation between TPG and SvO2

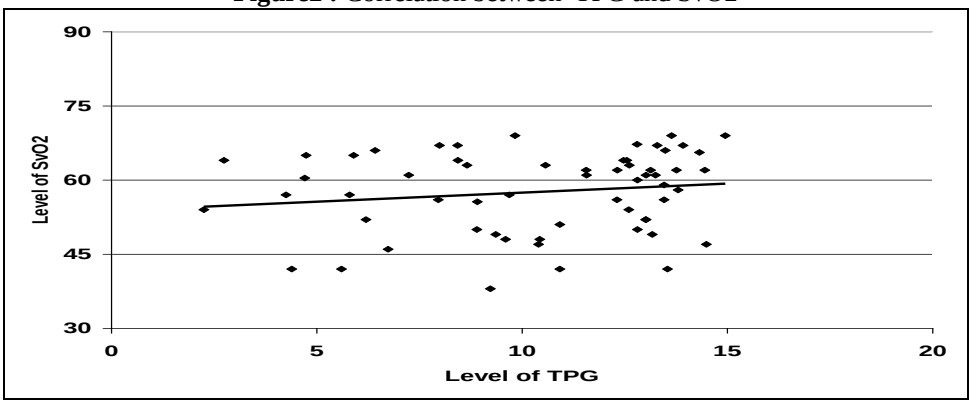

Figure**2** : shows that the level of TPG was significantly negatively correlated with the level of SvO2 ($p<0.0001$). Thus the level of SvO2 decreased significantly with the increasing level of TPG.

Table 6: Comparison of Prediction of post -cardiopulmonary bypass venous oxygen saturation in COPD patients undergoing on pump CABG surgery through TPG

Parameters related to prediction	TPG before skin incision
Diagnostic Accuracy	91.67%
Sensitivity	89.66%
Specificity	93.55%
Positive Predictive Value	92.86%
Negative Predictive Value	90.63%

Table6 shows that, from the above it revealed that TPG can superiorly predict post -cardiopulmonary bypass venous oxygen saturation in COPD patients undergoing on pump CABG surgery.

IV. Discussion

Several studies have shown a significant interaction with COPD and CABG.[6,7,8,9] The spectrum of cardiovascular disease in COPD includes right ventricular (RV) dysfunction, pulmonary hypertension (PH), coronary artery disease (CAD), and arrhythmias. Impairments of right ventricular dysfunction and pulmonary vascular disease complicate the clinical course of COPD and related to their survival. Because of alteration in gas exchange and vascular change, as well as structural changes of the pulmonary vasculature and several mechanical factors leads to pulmonary vascular disease in COPD patient. Severity of pathology of COPD & CAD may be enhanced by systemic inflammation reaction from CPB. Management strategies from preoperative evaluation for prediction of postoperative outcome for the care of patients throughout the intra and post op period has paramount importance.

Pulmonary hypertension is defined by a mean pulmonary arterial pressure (P_{pa}) ≥25 mmHg at rest. Small proportion of COPD patients may present with "out-of-proportion" pulmonary hypertension, defined by a mean pulmonary artery pressure >35–40 mmHg and a relatively preserved lung function .

GOLD classification is valuable in terms of differentiation of airway disease severity.[10] This study included CAD with COPD patients having FEV1/FVC < 70% as per Global Initiative for Chronic Obstructive Lung Disease undergoing on-pump CABG. This prospective observational study aimed to correlate TPG with the changes of venous oxygen saturation (SvO2) after release of cross clamp.

A direct way to measure the pulmonary pressure is the transpulmonary pressure gradient (TPG). The TPG is a flow-independent variable, as increases in pulmonary flow will distend the vessels by increasing transmural pressure, thereby diminishing PVR without altering TPG .[4,11] TPG of >12 mmHg would result in a diagnosis of "out of proportion" pulmonary hypertension. TPG-derived diagnosis of "out of proportion" pulmonary hypertension may not always agree with clinical context. This value is arbitrary, because the gradient is sensitive to changes in cardiac output and both recruitment and distension of the pulmonary vessels.

In the present study after analysis this has been seen that, mean TPG of patients of GOLD I COPD was 7.57mm Hg; TPG of patients of GOLD II COPD was 12.35 mm Hg; and TPG of patients of GOLD III COPD was 14.55 mm Hg; as shown in TABLE **2**. Therefore it has been found that, as the GOLD stages increases, TPG was getting worse.

When adequacy of tissue oxygenation is a key issue, the balance between oxygen delivery and oxygen consumption must be considered. SvO2 reflects this balance directly while cardiac output does not. Measurements of ScvO2 are often readily available, since a thoracic central line is often needed as part of care in critically ill patients. Attention to placement of the tip of the central line near or at the right atrium increases the accuracy of ScvO2 in reflecting SvO2 .[12]

SvO2 can help to determine whether the cardiac output and oxygen delivery is high enough to meet a patient's needs after CPB. It can be very useful if measured before inotropic support are used after coming out of bypass. SvO2/ScvO2 (mixed or central venous oxygen saturation) is an important yet frequently misunderstood hemodynamic parameter.[13] Scheinman and co-workers were the first to demonstrate changes in ScvO2 and SvO2 in haemodynamically stable patients and those in shock. [14]

All ScvO2 was more than 60% indicating that all SvO2 will also be more than 60% . In the present study the pre-incision ScvO2 was almost similar to the pre cross clamp SvO2 as shown in table **4** ; where mean ScvO2 was 66.05 % (ranging from 61% to 71%) and mean SvO2 was 66.95% (ranging from 61 to 73).

Mixed venous oxygen saturation has been known as the gold standard indication for knowing the balance between systemic oxygen delivery and demand. SvO2 monitoring from venous return line of CPB can be used as a measure of circulatory adequacy. Continuous monitoring of SvO2 was earlier measured with the use of a pulmonary artery catheter. But the use of PA catheter is also associated with several complications.[15,16,17,18]

Only a few studies are there correlating ScvO2 and SvO2 during intraoperative period , particularly cardiac surgery undergoing cardiopulmonary bypass. Our study showed that ScvO2 and SvO2 before application of cross-clamp were very relatable and that one hour post cross clamp release SvO2 was reduced to less than normal values in half of the patients who all required a strong support of inotropes and vasopressors to maintain haemodynamic stability. These denotes a decrease in global oxygen delivery to the body and it has been revealed from the present study that all were having a higher TPG value ie more than 12 mm Hg. in the preoperative setting.

This study collected venous blood sample for SvO2 after one hour release of cross clamp, so as to exclude the effects of hypothermia, reperfusion injury. The hemodynamic variables affect VO_2 in different ways, depending on the phases of CPB. Their influence is maximal during rewarming and minimal during the cooling period. This implies that lower peripheral arterial resistances, together with higher perfusion flow rates and lower arterial pressures, are desirable conditions to achieve an optimal whole body oxygen metabolism, when the patients are in hypothermic conditions, but especially when they are rewarmed and then weaned from cardiopulmonary bypass.[19]

Outcome after cardiac surgery is to a large extent determined by the preoperative status of the patient. However, the outcome is also influenced by events during surgery and anaesthesia and the patient's prognosis at arrival to ICU may differ markedly from the preoperative evaluation. Early reevaluation on admission to ICU is desirable for a proactive management plan.

With the advent several cardiac output monitoring, use of pulmonary artery catheter has declined dramatically. ScvO2 measurements obtained from internal jugular or subclavian catheters are often used and interpreted in the same manner. An ScvO2 refers to a central venous sample. A ScvO2 measurement is a surrogate for the SvO2. It may be used to identify changes in a patient's tissue oxygen extraction.

In this study while making comparison of for prediction of post -cardiopulmonary bypass venous oxygen saturation in COPD patients undergoing on pump CABG surgery through TPG, it has been found that , TPG has a better diagnostic accuracy (91.67%),better sensitivity (89.66%) ,better specificity (93.55%) and better positive (92.46%) and negative predictive(90.63%) value in predicting a low SvO2 (< 60%) after release of cross clamp.

Patients with SvO2 below 60% had significantly higher postoperative mortality and morbidity.

A low cardiac output does not necessarily imply that tissue oxygenation is jeopardized. Under normal circumstances cardiac output is primarily determined by the metabolic rate. Due to the prognostic value of SvO_2 measurements and its specificity with respect to cardiorespiratory problems, Swan Ganz catheters can be reserved for high risk patients. Intermittent SvO_2 measurements by this method can contribute to cost containment in perioperative care.

Development of pulmonary hypertension in patients with left heart disease, chronic interstitial lung disease and chronic obstructive pulmonary disease is associated with worse outcome. However , well-designed clinical studies are lacking for results of TPG for the group of GOLD 2,3 and 4 COPD patients . There is no consensus monitoring strategy other than spirometric value , which is important to consider for critically compromised coronary artery disease patients with COPD posted for CABG.

V. Conclusion

Measurement of pre-induction ScvO2 and pre cross clamp SvO2 was found to be normal in all the COPD cases. While the TPG came to be different. According to this study , TPG has a better diagnostic accuracy ,better sensitivity, better specificity and better positive and negative predictive value in predicting a low SvO2 (< 60%) after release of cross clamp.

Limitations of the study

We didn't measure diastolic pulmonary pressure gradient, so we can't say whether it were cases of combined pre-capillary and post-capillary pulmonary hypertension.

The study is single-centred and multicentric studies with more number of patients is required to validate my results.

Also it was a non-blinded study. Blinding was not feasible in our operating room set-up since the vaporizers and anesthetic gas monitors could not be masked from the echocardiographer.

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Dr Soumyadip Pal, et. al. "A Study To Predict Post Cross Clamp Venous Oxygen Saturation By Transpulmonary Gradient In Chronic Obstructive Pulmonary Disease Patients Undergoing On Pump Coronary Artery Bypass Grafting." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(10), 2020, pp. 52-58.