

Research Article

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May Transient Positive End-Expiratory Pressure Ameliorate Hemodynamic Setting and Outcome After Aortic Surgery?

Enrico Giustiniano¹, Nadia Ruggieri^{1*}, Gian Michele Battistini¹, Nadia Fusilli¹, Francesco Pellegrino¹, Pierluigi Giorgetti², Maria Grazia Bordini³, Valentina Bellato⁴ and Giovanni Bordone⁵

¹Department of General Anesthesia and Intensive Care Unit-IRCCS Humanitas Clinical Institute, Italy

²Chief of Vascular Surgery Unit I-IRCCS Humanitas Clinical Institute, Italy

³Chief of Vascular Surgery Unit II-IRCCS Humanitas Clinical Institute, Italy

⁴Chief of Perioperative Medicine Unit-Department of General Anesthesia and Intensive Care Unit-IRCCS Humanitas Clinical Institute, Italy

⁵Chief of Department of General Anesthesia and Intensive Care Unit-IRCCS Humanitas Clinical Institute, Italy

Abstract

Study objective: Patients submitted to major vascular surgery often match Metabolic Syndrome's (MetS) risk factors and consequently they are affected by high postoperative risk of cardio circulatory, respiratory and renal dysfunctions, which can worsen the outcome. Hemodynamic variations occurring during aortic surgery may expose patients at risk for cardiac complications, particularly myocardial ischemia. Positive end-expiratory pressure applied to mechanical ventilation only during clamping phase may protect heart against stress due to augmented blood return when aorta is clamped and may reduce the sudden lowering of blood pressure if it is discontinued when circulation is restored. Further it may reduce postoperative complications rate.

Design: Randomized controlled trial

Setting: Vascular surgery operative room.

Patients: 124 patients (ASA 2-4) were divided into two groups: ZEEP (zero end-expiratory pressure, control group) and PEEP (positive end-expiratory pressure, treated group). They underwent vascular surgery operation for elective abdominal aortic reparation.

Interventions: When aorta was clamped, we applied PEEP 10 cm H₂O to mechanical ventilation. When surgeon removed the clamp, we discontinued PEEP.

Measurements: Blood pressure, Heart rate, Blood-gas analysis, Fluid balance, Cardiac output, Stroke volume variation, Brain Natriuretic Peptide, Serum Creatinine and Troponine I, outcome (length-of-stay, complications rate).

Main results: After unclamping, blood pressure of ZEEP-group fell more than in PEEP-group (SAP -21.4 ± 22.8% vs -5.5 ± 21.5%, p=0.000; MAP -18.6 ± 23.6% vs -5.8 ± 23.5%, p=0.003). In treated group, a significant lower number of patients with MetS risk factors experienced postoperative complications than in control group (p=0.005).

Conclusions: Application of PEEP when abdominal aorta is clamped and its discontinuation just when circulation is restored may guarantee a better hemodynamic setting and a safer postoperative outcome.

Keywords: Positive end-expiratory pressure; Aortic surgery; Metabolic syndrome

Introduction

Metabolic Syndrome (MetS) consists of several inter-related risk factors: obesity, atherogenic dyslipidemia, hypertension, insulin resistance and pro-inflammatory prothrombotic state. Preventive treatment of each risk factor may improve postoperative outcome [1,2]. Cardiac events, Acute Kidney Injury (AKI), stroke, infections are some potential complication of MetS, [1]. Patient's submitted to major vascular surgery often match MetS risk factors and consequently they are affected by high postoperative risk of cardiocirculatory, respiratory and renal dysfunctions, which can worsen the outcome. Intra-operative management of hemodynamic setting during major vascular surgery can be challenging because aortic cross-clamping produces rapid variations of vascular resistances. When aorta is occluded, the after load of left ventricle (LV) increases and the preload of right ventricle (RV) rise too, due to augmented venous blood return. As cross-clamping are replaced vascular resistances abruptly falling, and the patient may experience hypoperfusion. These hemodynamic variations may expose patients at risk for cardiac complications, particularly myocardial ischemia, [3,4]. Effects of PEEP on circulatory assessment are well known: the rising of intrathoracic pressure may limit venous blood return to the right atrium and finally cardiac output decreases [5-9]. We hypothesized that PEEP application to mechanical ventilation just when aorta is occluded may limit the preload and its discontinuation, just before cross-clamp releasing, favouring the venous blood return

to right atrium, may assure a better cardiac performance and a safer hemodynamic setting without fluid overloading. Furthermore, we investigated whether PEEP may reduce postoperative complications related to Metabolic Syndrome.

Materials and Methods

The study was approved by the Independent Ethics Committee of Humanities Clinical Institute and each patient gave written informed consent to be enrolled in the trial that was performed according to CONSORT Statement advices [10,11].

Patients were randomly divided into two groups: ZEEP-group (control group) where ZEEP stands for Zero End-Expiratory Pressure

***Corresponding author:** Nadia Ruggieri, Department of General Anesthesia and Intensive Care Unit-IRCCS Humanitas Clinical Institute, via Manzoni 56-20089 Rozzano, Milano, Italy, Tel: +390282244115; Fax: +390282244190; E-mail: docnadia76@gmail.com

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and treated group (PEEP-group) whose patients received PEEP 10 cm H₂O.

Exclusion criteria

Age <18years, ruptured aortic aneurysm, pregnancy and potential childbearing, pulmonary bullous emphysema (diagnosed by preoperative CT-scan). Primary end was a lesser lowering of blood pressure when aorta was unclamped (T2=one minute after clamp removing). Secondary end-point was intra-hospital outcome: Length of Stay (LOS), Intensive Care Unit (ICU) admission and staying, perioperative complications. Preoperatively, plasmatic BNP was tested and we collected non-invasive blood pressure (NIBP), heart rate (HR), left-ventricle ejection fraction (EF), serum creatinine (sCr), haemoglobin (Hb) and haematocrit (Ht). General anaesthesia started with Propofol 2.5 mg/kg + Fentanyl 1-2 mcg/kg and patients were intubated after Succinyl-Choline 1 mg/kg i.v. administration. A gas mixture including Air, Oxygen (FiO₂ 0.50) and Sevoflurane 1-2% was administered for anaesthesia maintaining. No-depolarizing myorelaxant drug (Atracurium 0.5 mg/kg or cis-Atracurium 0.15 mg/kg boluses, and repeated top up doses as needing) was administered and subjects were connected to mechanical ventilator (Tidal Volume 6-8 ml/kg; Respiratory Rate 10-12 apm; Peak Respiratory Pressure limit 35 cm H₂O). Fentanyl 1-2 mcg/kg bolus was re-administered after 30 and 60 minutes.

Fluid input included

Crystalloid solutions 15-20 ml/kg before aortic clamping crystalloid solutions 10 ml/kg and Hydroxy-ethyl-starch 130/0.4 (Voluven®) 5-10 ml/kg when requested by hemodynamic performance, during aortic clamping. Target Hb was 8-10 g/dl reached by hemo transfusion and/or administration of collected-blood processed by red cells saver. After aorta, unclamped, fluid input was administered according the anaesthesiologist judgement.

Intraoperative monitoring included

D2 and V5 electrocardiogram tracks, HR, NIBP, and Invasive Blood Pressure (IBP), Peripheral Oxygen Saturation (SpO₂), End-tidal Carbon Dioxide (EtCO₂), Diuresis. Cardiac Output (CO), Cardiac Index (CI) and Stroke Volume Variation (SVV) were monitored by FloTrac/Vigileo™ (Edwards Lifescience, Irvine, CA). Data collection and Blood Gas Analysis were performed before aortic clamping (T0), close 1 minute after cross-clamping (T1), just 1 minute after clamp was replaced (T2) and after awakening in Recovery Room (T3) where a blood sample was taken to test BNP, serum Troponine I, sCr and C-Reactive Protein (CRP). When surgeon was going to clamp aorta, Positive End-Expiratory Pressure 10 cm H₂O was applied in PEEP-group patients. Just before surgeon removed the clamp, PEEP was zero. When bifurcated prosthesis was inserted, “unclamping” meant for the first reperfused prosthetic branch, generally the left one. In control group, patients received ZEEP mechanical ventilation throughout the whole operation. For post-operative pain control we administered intravenously a 50 ml saline-solution containing Morphine 30-40mg+Ketorolac 60-90 mg, starting intra-operatively (2.1 ml/h).

Statistical analysis

A simple randomization was performed, without stratification. Using a level of 0.05 and a power of 0.90, with a two sided design we needed a total of 122 patients (Rosner B. “Fundamental of Biostatistics”, 1982). Statistical analysis had been performed with SigmaStat 3.5 (Copyright©2006 Sistat Software Inc.): t-Student’s test for quantitative data or Wilcoxon Signed Rank Test when appropriate; χ^2 -Test or Fisher’s Exact Test were performed for qualitative data. Results were statistically significant if p<0.05.

Results

We enrolled 124 consecutive cases randomly divided into the two groups: ZEEP (control) and PEEP (treated). Patients’ sample results homogeneous (Table 1). Results are listed in Table 2. When aorta was clamped, in ZEEP group blood pressure did not change (p=0.967); in PEEP group it reduced significantly (p=0.164). After unclamping, IBP of ZEEP-group fell more than in PEEP-group (SAP -21.4 ± 22.8% vs -5.5 ± 21.5%, p=0.000; MAP -18.6 ± 23.6% vs -5.8 ± 23.5%, p=0.003). CO and CI did not change; SVV% was greater in PEEP-group. The pO₂/FiO₂ ratio was higher in treatment group than control. T2-Serum Lactate was little higher in PEEP group, although without statistical significance (p=0.124). As expected, in treated group EtCO₂ was lower than control group at T1 (p=0.066). Airways pressure never reached the limit of 35 cm H₂O. Fluid load and balance did not show significant difference between the two groups; bleeding was little greater in treated patients (p=0.179). Analogue diuresis resulted in the two groups (p=0.936). When aorta was unclamped, in control group blood pressure fell more often than treated patients; on the contrary, in PEEP group it more often raised (Table 3). Post-operative blood sample tests did not show any significant difference between the two groups (Table 4). We did not find difference about outcome between the two groups, both in terms of ICU admissions and Length-of-Stay (LOS). Nevertheless, starting from a similar incidence of subjects with more than 3 risk factors for MetS (19 vs 15 patients, respectively), despite preoperative BNP plasmatic levels were not different, we found significant difference about complications incidence related to Metabolic Syndrome (Table 5): cardiovascular events and acute kidney injury (AKI). Patients with MetS risk factors who had plasmatic BNP ≤ 200 pg/ml and treated with PEEP application during mechanical ventilation did not experience any complication; conversely, in ZEEP group, 8 of 15 patients with MetS risk factors experienced a complicated postoperative outcome (Table 6). Regression test confirmed that PEEP can reduce the postoperative complications rate in patients with metabolic syndrome’s risk factors (p=0.005).

Discussion

Intra-thoracic pressure affects the hemodynamic setting of mechanically ventilated patients during general anesthesia or ICU treatment for critical illness. In a recent study Fougères and co-workers stated that PEEP administration in ARDS produces a decrease in cardiac index associated with an increased right ventricle after load instead of a reduced venous blood return to right atrium; the effect vanished when central blood volume was increased by passive leg raising [12]. This conclusion contrasts with our hypothesis that PEEP may reduce the overload of right heart’s sections due to aortic clamping by limiting the venous blood return. But we consider that our study and Fougères’ results are not comparable as the typology of patients was different. Our results indicate that transient PEEP, only applied during the clamping phase, limited the blood pressure raising and its falling after clamp removed. It might assure a better tissue perfusion associated with a better oxygen supply. In agreement with previous

	ZEEP (n=60)	PEEP (n=64)	p
Male	54 (90.0%)	54(84.4%)	0.506
Age (years)	69.0 ± 8.2	69.1 ± 7.7	0.944
Age range (years)	47-83	49-88	
ASA	2-4	2-4	
Body Mass Index (kg/m ²)	25.6 ± 3.2	26.4 ± 3.1	0.160
MetS Risk Factors >3	19 (31.6%)	15 (23.4%)	0.094

Table 1: Population.

	T0			T1			T2			Recovery Room		
	ZEEP	PEEP	p	ZEEP	PEEP	p	ZEEP	PEEP	p	ZEEP	PEEP	p
Systolic Arterial Pressure (mmHg)	130 ± 26.2	135 ± 23.4	0.294	132 ± 21.8	126 ± 23.1	0.147	106 ± 18.8	131 ± 20.7	0.000	125 ± 22.5	135 ± 21.3	0.018
Mean Arterial Pressure (mmHg)	88 ± 18.3	93 ± 17.8	0.133	86 ± 14.6	84 ± 14.6	0.494	71 ± 12.1	77.9 ± 14.5	0.007	90 ± 20.1	93 ± 17.6	0.394
Heart Rate (bpm)	63 ± 11.8	66 ± 17.4	0.183	63 ± 11.9	67 ± 16.4	0.672	66 ± 14.5	68 ± 14.5	0.467	65 ± 11.2	67 ± 14.6	0.373
EtCO ₂ (mmHg)	28.8 ± 3.2	28.3 ± 3.0	0.371	26.9 ± 3.1	25.9 ± 2.9	0.066	29.5 ± 4.8	30.2 ± 4.2	0.388	-	-	-
pH	7.43 ± 0.1	7.43 ± 0.1	1.000	7.42 ± 0.1	7.42 ± 0.1	1.000	7.36 ± 0.1	7.34 ± 0.1	0.277	7.35 ± 0.1	7.34 ± 0.1	0.586
pCO ₂ (mmHg)	37.6 ± 6.0	38.9 ± 4.9	0.188	36.5 ± 7.2	37.4 ± 4.8	0.412	41.0 ± 5.5	42.6 ± 6.1	0.128	41.7 ± 4.9	43.3 ± 4.1	0.050
pO ₂ /FIO ₂	347 ± 168	343 ± 150	0.889	297 ± 111	300 ± 109	0.880	318 ± 104	362 ± 92	0.014	333 ± 110	350 ± 119	0.411
Serum Lactate (mmol/L)	0.85 ± 0.4	1.0 ± 1.4	0.425	0.98 ± 0.5	1.2 ± 1.3	0.222	1.8 ± 0.9	2.2 ± 1.8	0.124	2.1 ± 1.4	2.2 ± 1.9	0.741
Base Excess (mmol/L)	2.2 ± 7.1	2.3 ± 6.2	0.933	-0.4 ± 2.6	-0.4 ± 3.0	1.000	-2.0 ± 2.5	-2.5 ± 2.4	0.258	-2.2 ± 2.9	-2.3 ± 2.4	0.834
Hematocrit (%)	37.2 ± 6.1	37.9 ± 6.0	0.534	34.7 ± 5.3	35.2 ± 6.2	0.631	31.3 ± 5.3	31.9 ± 5.6	0.542	36.7 ± 4.9	37.0 ± 6.3	0.769
Cardiac Output (L/min)	5.0 ± 0.9	4.8 ± 1.0	0.245	5.6 ± 1.3	5.5 ± 2.1	0.752	5.5 ± 1.3	5.7 ± 1.4	0.412	-	-	-
Cradiac Index (L/min/m ²)	2.6 ± 0.5	2.4 ± 0.8	0.100	3.0 ± 0.7	2.9 ± 0.9	0.493	2.9 ± 0.8	3.0 ± 0.7	0.460	-	-	-
Stroke Volume Variation (%)	8.9 ± 4.4	9.3 ± 3.0	0.553	7.9 ± 4.2	14.9 ± 3.6	0.000	9.1 ± 4.9	11.3 ± 5.6	0.022	-	-	-

Table 2: Results.

	ZEEP (n=60)	PEEP (n=64)	p
Systolic Arterial Pressure <90mmHg (n)	6	7	0.902
Systolic Arterial Pressure lowering >10% (n)	37	27	0.047
Total n (%)	43(71.6%)	34 (53.1%)	0.052
Mean Arterial Pressure <60mmHg (n)	7	8	0.894
Mean Arterial Pressure lowering >10% (n)	34	23	0.033
Total n (%)	41 (68.3%)	30 (46.9%)	0.026
Systolic Arterial Pressure increasing 0-10% (n)	7	11	0.537
Systolic Arterial Pressure increasing >10% (n)	2	14	0.005
Total n (%)	9 (15.0%)	25 (39.1%)	0.005
Mean Arterial Pressure increasing 0-10% (n)	5	8	0.643
Mean Arterial Pressure increasing >10% (n)	5	16	0.026
Total n (%)	10 (16.6%)	24 (37.5%)	0.017

Table 3: Blood pressure variations after aortic unclamping (T2).

	ZEEP (n=60)	PEEP (n=64)	p
Serum Creatinine (mg/dl)	1.27 ± 1.1	0.98 ± 0.4	0.051
Serum Troponine I (mcg/L)	0.02 ± 0.03	0.05 ± 0.22	0.297
C-Reactive Proteine (mg/dl)	11.5 ± 7.5	12.1 ± 6.0	0.623
Serum BNP (pg/ml)	156.8 ± 291.1	136.6 ± 164.6	0.642

Table 4: Post-operative blood sample tests.

	RF MetS >3	Preoperative BNP (ng/dl)	LOS (days)	ICU pat (%)	ICU days (%)	Pat with complications*
ZEEP	19/60 (31.6%)	195.2 ± 300.0	10.1 ± 5.2	4/19 (21.1%)	18/192 (9.4%)	11/19 (57.9%)
PEEP	15/64 (23.4%)	203.4 ± 318.9	11.5 ± 4.9	4/15 (26.6%)	19/172 (11.0%)	3/15 (20.0%)
p	0.094	0.942	0.457	0.327	0.134	0.025

RF: Risk Factors; LOS: Length of Stay; ICU: Intensive Care Unit; Pat: Patients.

*AKI and Cardiac events

Table 5: MetS risk factors and outcome.

studies, it happens despite no significant differences in cardiac output [8].

We noted a greater SVV in treated group, probably due to “residual” hemodynamic effects of PEEP. Further, at unclamping PEEP was discontinued but the vascular resistances falling might overrun the venous blood return. Another mechanism may contribute to explain the higher SVV in PEEP group. As recently reported, high PEEP may compress peri-alveolar pulmonary vessels and increase extra-alveolar vessels capacitance as lung volume increases. With hypovolemia and

during hyperinflation, blood is stored in extra-alveolar vessels limiting the blood return to the Left Ventricle [13]. Although preceding studies reported a cutoff value of 10% to discriminate patients needing volume expansion, SVV not always reached the most accepted threshold to surely identify a “fluid-responder” patient (SVV 15%) [14-16]. Finally, as we recorded data just within one minute after unclamping, higher values of SVV may be due to the recording timing: it might be too early. The reduction of splanchnic oxygen delivery in ALI/ARDS patients receiving mechanical ventilation with PEEP may be due to increased thoracic pressure which may cause splanchnic hypo

		BNP ≤ 200ng/dl	BNP 201-400ng/dl	BNP >400ng/dl
ZEEP group	N	49	6	5
	Pat with MetS risk factors	15/49 (30.1%)	1/6 (16.7%)	3/5 (60%)
	Pat with complications	8/15 (53.3%)	1/1 (100%)	3/3 (100%)
PEEP group	N	54	7	3
	Pat with MetS risk factors	11/54 (20.4%)	3/7 (42.8%)	1/3 (33.3%)
	Pat with complications	0/11 (0%)	2/3 (66.7%)	1/1 (100%)
p	Pat with MetS risk factors	0.089	0.293	0.428
	Pat with complications	0.016	0.600	0.533

Table 6: Complications rate and BNP.

perfusion [17-22]. Conversely, Kiefer and co-workers found that PEEP did not affect splanchnic blood flow provided cardiac index is stable [23]. Nevertheless, PEEP may guarantee a sufficient oxygen delivery to splanchnic organs [24]. As PEEP did not impaired cardiac output in our subjects and Serum Lactate levels were not significantly higher than in control group, we may consider that abdominal organs were adequately perfused.

Finally, despite a similar number of patients with more than three risk factors for MetS in the two groups, complications related to metabolic syndrome in control group occurred more often than in treated group. The regression test about complications' rate in patients with more than three risk factors related to MetS and preoperative serum BNP under hazard level showed that PEEP may guarantee a safer postoperative outcome. May it be due to the smaller hemodynamic variation when we applied PEEP? We consider that further trials on this particular issue are desirable. Our study has some limitations. First, we cannot know which the best timing to record data is after clamping and unclamping. We arbitrarily decide to collect data just one minute after aortic occlusion and blood flow restoration: it may be too early or too late. It is hard to establish "when appropriate". A second limit is that blood pressure and cardiac output may be not sufficient to assess the hemodynamic status of a patient who experiences the circulatory effects of open aortic surgery. The third limit is the lacking of data about vascular resistances variations in the two groups as we did not measure central venous pressure (CVP), as requested by Vigileo monitor to calculate systemic vascular resistances. Finally, we arbitrarily consider "normal" BNP plasmatic level ≤ 200 pg/ml. Our decision was guided by data reported in specific literature. About outcome and MetS' complications, despite results indicated that the treatment with PEEP was safer, our data may be not sufficient for definitive conclusions. A wider trial about this issue is desirable.

Nevertheless, according to our experience, in patients submitted to open aortic surgical repair, PEEP 10 cm H₂O during aortic clamping and its withdrawal at clamp removing may limit the hemodynamic impairment, reducing the risk for postoperative cardiovascular events and renal impairment.

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