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

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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.


Main results: After unclamping, blood pressure of ZEEP-group fell more than in PEEP-group (SAP -21.4 ± 22.6% 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 cardio-circulatory, 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 afterload 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 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 and Outcome After Aortic Surgery.
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 (NIHBP), 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 Succinil-Choline 1 mg/kg i.v. administration. A gas mixture including Air, Oxygen (FiO₂ 0.50) and Sevoflurane 1-2% was administered. 50 ml saline-solution containing Morphine were administered. Myorelaxant drug (Atracurium 0.5 mg/kg or cis-Atracurium 0.15 mg/kg boluses, and repeated top dose by need) was administered. After aorta, unclamped, fluid input was administered according to the anesthesiologist judgement.

Intraoperative monitoring included

D2 and V5 electrocardiogram tracks, HR, NIHBP, 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 Troponin 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).

Fluid input included

Crystalloidal solutions 15-20 ml/kg before aortic clamping crystalloidal 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 autotransfusion. When blood volume was reduced by clamping aorta we administered 5 ml/kg boluses of colloid-blood processed by red cells saver. After aorta, unclamped, fluid input was administered according to the anesthesiologist judgement.

Intraoperative monitoring included

D2 and V5 electrocardiogram tracks, HR, NIHBP, 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 Troponin 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: χ²-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 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).
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
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 H\(_2\)O during aortic clamping and its withdrawal at clamp removing may limit the hemodynamic impairment, reducing the risk for postoperative cardiovascular events and renal impairment.

### References


### Table 6: Complications rate and BNP.

<table>
<thead>
<tr>
<th></th>
<th>BNP ≤ 200ng/dl</th>
<th>BNP201-400ng/dl</th>
<th>BNP &gt;400ng/dl</th>
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<tr>
<td><strong>PEEP group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>49</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Pat with MetS risk factors</td>
<td>15/49 (30.1%)</td>
<td>1/6 (16.7%)</td>
<td>3/5 (60%)</td>
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<tr>
<td>Pat with complications</td>
<td>8/15 (53.3%)</td>
<td>1/1 (100%)</td>
<td>3/3 (100%)</td>
</tr>
<tr>
<td><strong>PEEP group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>54</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Pat with MetS risk factors</td>
<td>11/54 (20.4%)</td>
<td>3/7 (42.6%)</td>
<td>1/3 (33.3%)</td>
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<tr>
<td>Pat with complications</td>
<td>0/11 (0%)</td>
<td>2/3 (66.7%)</td>
<td>1/1 (100%)</td>
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<tr>
<td><strong>p</strong></td>
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<td>Pat with MetS risk factors</td>
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<td>0.428</td>
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<td>Pat with complications</td>
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