Journal of Anesthesia & Clinical Research
ISSN: 2155-6148

Danninger et al., J Anesth Clin Res 2013, 4:10
DOI: 10.4172/2155-6148.1000360

Research Article Open Access

The Effect of Incremental Airway Resistance on Cardiac Performance and Pulmonary Pressure in Spontaneously Breathing Volunteers

Thomas Danninger[1], Stephen Haskins[1], Ottokar Stundner[2], Yan Ma[3], Jemiel Nejim[1], Sean Garvin[1] and Stavros G Memtsoudis[1]*

[1]*Department of Anesthesiology, Hospital for Special Surgery, Weill Cornell Medical College, New York, USA*
[2]*Department of Anesthesiology, Perioperative Medicine and Intensive Care Medicine, Paracelsus Medical University, Salzburg, Austria*
[3]*Department of Biostatistics, Hospital for Special Surgery, Weill Cornell Medical College, New York, USA*

Abstract

Previous research suggests that increases in airway resistance are associated with a depression in a number of hemodynamic variables. In this study we evaluated the hypothesis that these changes may be in part associated and explainable with increases in pulmonary vascular pressures. We therefore examined the effect of increasing airway resistance on a number of cardiac parameters, and estimated pulmonary arterial pressures using transthoracic echocardiography (TTE) in spontaneously breathing healthy volunteers.

Methods: Subjects were connected to a bioreactance monitor capable of determining hemodynamic parameters including stroke volume (SV), and cardiac index (CI). Blood pressure (NIBP) was obtained non-invasively. Volunteers sequentially breathed for 2 minutes through endotracheal tubes (ETT) with decreasing internal diameters (ID) between 8.0 and 3.0 mm in order to simulate increasing airway resistance, while attached to spirometric equipment. A second measurement cycle was performed for validation. TTE was performed focusing on the estimation of pulmonary arterial pressures during the experiment. Statistical analyses were performed using the generalized estimating equations (GEE) method and Spearman correlation.

Results: All subjects were male, (mean age 29.8 years (SD 5.4), mean BMI 26.75 kg/m^2 (SD 4.8)). Mean baseline SV and CI were 117.48 ml (SD 14.0) and 3.72 l/min/m2 (SD 0.7); both, SV and CI decreased significantly vs. baseline when breathing through ETT ID 3.0 (111.50 ml (SD 15.3), p=0.0016 and 3.51 l/min/m^2 (SD 0.7), p=0.0007, respectively). For the same breathing cycles, no change in averaged systolic pulmonary arterial pressure (SPAP) was detected between baseline and ETT ID 3.0 (24.45 mm Hg (SD 5.1) vs. 24.87 mm Hg (SD 5.6), p=0.43).

Discussion: Although detecting hemodynamic alterations when simulating upper airway resistance in healthy volunteers, there was no significant change in systolic pulmonary arterial pressure (SPAP) seen. Further research is needed to investigate potential mechanisms associated to hemodynamic changes in response to increases in airway resistance.

Keywords: Obstructive sleep apnea; Transthoracic echocardiography; Stroke volume

Introduction

Obstructive Sleep Apnea (OSA) has become a major problem throughout the United States, affecting approximately 1 in 4 men and 1 in 10 women [1]. A number of studies have identified OSA patients to be at increased risk for perioperative complications. However, mechanisms to explain acute complications in this patient population remain largely unexplored. While many clinicians have focused on hypoventilation and desaturation events, some researchers point to the potential association of airway obstruction and adverse hemodynamic consequences as a reason for complications. While a number of studies describe and explain the long-term cardiovascular consequences especially on pulmonary arterial pressures associated with repeated airway obstruction [2,3], only limited data exist evaluating a direct, short-term relationship between increased airway resistance and changes in stroke volume (SV) and cardiac index (CI), respectively [4]. This is important as pre-existing pulmonary hypertension has been suggested to be a major risk factor for complications in the postoperative period, likely due to worsening of right heart strain [5]. In a previous trial, our study group could detect significant hemodynamic alterations during simulated upper airway obstruction in healthy volunteers [6]. However, no mechanism for our finding could be established at the time. In this study we therefore sought to identify if increases in pulmonary arterial pressures were associated with depression of cardiac hemodynamics during airway resistance breathing. Specific goals were (1) to examine the effect of increasing airway resistance on a number of cardiac parameters and (2) to determine if the detected hemodynamic alterations were associated with changes in estimated pulmonary arterial pressures obtained using transthoracic echocardiography (TTE).

Material and Methods

Ethics approval, demographics

After approval by the institutional review board (Hospital for Special Surgery), 16 healthy, male volunteers aged 18 or older without a history of cardiovascular and/or pulmonary disease were enrolled. Data on patient demographics (age, ethnicity, BMI) were recorded.

***Corresponding author:** Stavros G Memtsoudis, MD, PhD, FCCP, Department of Anesthesiology, Hospital for Special Surgery, Weill Cornell Medical College, New York, 535 East 70th Street, New York, NY 10021, USA, Tel: (212) 606 1206; Fax: (212) 517 4481; E-mail: MemtsoudisS@hss.edu

Received September 27, 2013; **Accepted** October 23, 2013; **Published** October 25, 2013

Citation: Danninger T, Haskins S, Stundner O, Ma Y, Nejim J, et al. (2013) The Effect of Incremental Airway Resistance on Cardiac Performance and Pulmonary Pressure in Spontaneously Breathing Volunteers. J Anesth Clin Res 4: 360. doi:10.4172/2155-6148.1000360

Data collection

After signing an informed consent form, subjects were asked to position themselves supine on a stretcher before being connected to a bioreactance monitor (NICOM, Cheetah Medical Inc, Vancouver, WA) capable of continuously recording stroke volume (SV), cardiac index (CI) and oxygen saturation (SpO_2) [7]. In order to monitor respiration-associated variables, an anesthetic circuit was set up in manual mode. A nose clip was applied and subjects were asked to breathe through a mouthpiece which was attached to a device recording spirometry data and ent-tidal CO_2 data ($EtCO_2$; Datex Ohmeda, Madison, WI). Blood pressure (NIBP) was obtained non-invasively using the integrated blood pressure cuff. Baseline data was collected for five minutes. Endotracheal tubes (ETT; Covidien, Mansfield, MA) with decreasing internal diameters (ID; 8.0, 6.0, 5.0, 4.0 3.0 mm) were used to simulate increasing airway resistance. After baseline measurement, subjects started breathing through the ETT beginning at ID 8.0 through size 3.0, 2 minutes each. After the first set of measurement, a five minute recovery period was allowed; subjects were breathing through the unobstructed respiratory circuit during this period. A second measurement cycle was performed.

Transthoracic Echocardiography (TTE)

TTE was performed with the focus on estimating pulmonary arterial pressures. The method entailed measuring Systolic Pulmonary Arterial Pressure (SPAP) non-invasively via TTE using either Continuous Wave (CW) Doppler assessment of the maximal tricuspid regurgitation (TR) jet velocity or, when a TR jet was not present, via Pulse-Wave Doppler assessment of Pulmonary Artery Acceleration Time (PAAT). Non-invasive measurement of TR jet velocities has been shown to best correlate with pulmonary arterial catheter measurements; however, not all patients have sufficient TR to accurately calculate the estimated peak systolic pulmonary arterial pressure (EPSPAP). In 2011, Yared et al. published a method demonstrating that in patients without a TR jet, PAAT can be accurately used to measure EPSPAP. The regression equation describing the relationship between PAAT and EPSPAP is as follows log10 (EPSPAP)=−0.004(PAAT)+2.1(P<0.001) [8]. Therefore, PAAT was utilized when CW assessment of TR jet velocities was not possible. Given the limited time frame during each of the individual breathing cycles, the TTE examination was focused solely on determining the SPAP or EPSPAP. Mean Pulmonary Arterial Pressures (mPAP) were calculated directly from the SPAP using the equation mPAP=0.61×sPAP+2 mm Hg [9].

Data recording and statistical analysis

Hemodynamic data were recorded every 60 seconds (five readings for basline, two readings for each level of airway resistance). All recorded data for both measurment cycles were then tabulated and averaged for each level/patient. Continous data is expressed as mean and standard deviation (SD). Multiple regression analyses based on the generalized estimating equations (GEE) method were conducted to assess changes from baseline for outcomes of interest, adjusting for age and BMI [10]. The GEE method is able to take into account correlations between repeated measures with different ETT tube sizes and does not require a particular distribution for data, leading to robust parameter estimation. Correlations between outcomes and ETT tube size were evaluated using Spearman rank correlation coefficient. P-values less than 0.05 were considered statistically significant.

Results

16 healthy, male volunteers were enrolled in the trial. Mean age was 29.8 years (SD 5.4), and mean BMI was 26.75 kg/m^2 (SD 4.8). All subjects completed the study without incident.

We found a significant change in CI between baseline and ETT ID 3.0 (3.72 l/min/m^2 (SD 0.7) vs. 3.51 l/min/m^2 (SD 0.7), p=0.0007). Similarly a decrease was seen for SV (117.48 ml (SD 14.0) vs. 111.50 ml (SD 15.3), p=0.0016, Figures 1 and 2). Mean values for $EtCO_2$, HR, NIBP and SpO_2 are presented in Table 1. No major differences were found for the variables across all tube sizes except for $EtCO_2$ and HR.

There was no significant change found for SPAP between baseline and ETT ID 3.0 (24.45 mm Hg (SD 5.1) vs. 24.87 mm Hg (SD 5.6), p=0.43, Figure 3) or any other tube sizes; similarly, no significant change was seen for estimated mPAP (16.90 mm Hg (SD 3.1) vs. 17.17 mm Hg (SD 3.4), p=0.41).

Correlation analysis revealed a significant correlation between ETT tube size and EtCO2 (r=0.30, P=0.0025), however there was no other significant correlation found for the recorded parameters (Table 2).

Discussion

In this volunteer study simulating increased airway resistance, we were able to show significant hemodynamic alterations in CI, SV, HR and a significant increase in $EtCO_2$ while NIBP and SpO_2 remained unchanged. However, we did not observe any significant changes of

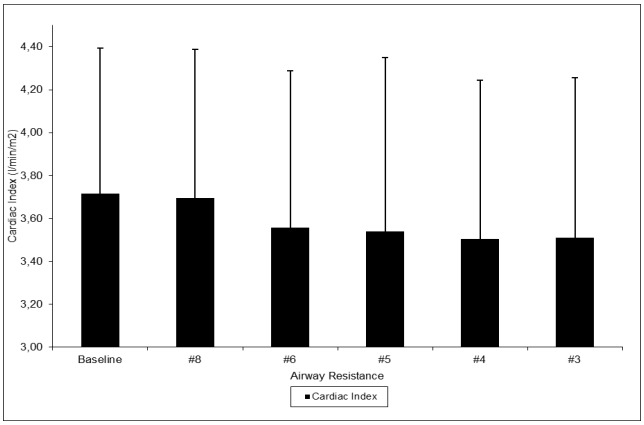

Figure 1: The figure displays cardiac index during discrete level of increased external airway resistance.

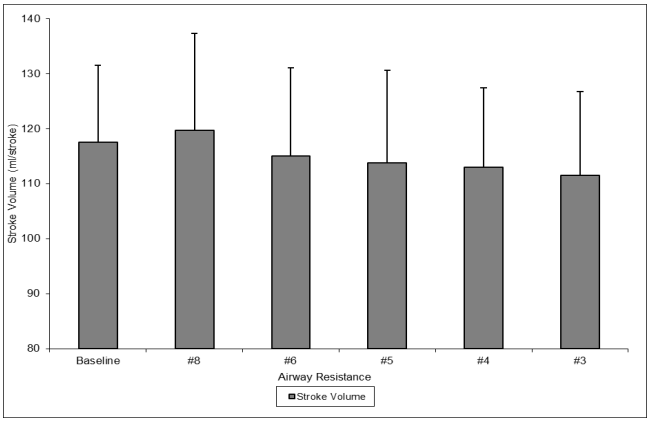

Figure 2: Stroke volume during discrete level of increased external airway resistance.

	Baseline	#8	#6	#5	#4	#3
End-tidal CO_2 mm Hg; mean ± SD (*p-value*)	39.45 ± 5.40	40.13 ± 5.70 (*0.1805*)	40.86 ± 6.15 (*0.027*)	42.9 ± 5.48 (*<0.0001*)	44.40 ± 4.80 (*<.0001*)	42.45 ± 5.85 (*0.0005*)
Heart rate bpm; mean ± SD (*p-value*)	65.79 ± 8.50	64.45 ± 9.11 (*0.0001*)	64.27 ± 9.21 (*<0.0001*)	64.49 ± 9.26 (*0.0008*)	64.44 ± 9.17 (*0.0002*)	65.43 ± 9.18 (*0.4063*)
Mean arterial pressure mm Hg; mean ± SD (*p-value*)	84.95 ± 8.17	84.87 ± 7.76 (*0,4113*)	85.41 ± 7.12 (*0,8994*)	85.31 ± 8.05 (*0,8206*)	86.03 ± 7.99 (*0,8353*)	87.38 ± 9.58 (*0,8591*)
SPO_2%; mean ± SD (*p-value*)	98.58 ± 0.80	98.72 ± 0.64 (*0.231*)	98.79 ± 0.66 (*0,2884*)	98.71 ± 0.77 (*0,3127*)	98.69 ± 0.75 (*0,1017*)	98.42 ± 0.86 (*0,2413*)

Table 1: Changes in various (Hemodynamic) parameters [end-tidal CO_2, heart rate, mean arterial blood pressure and oxygen saturation (SPO_2)] across different levels of airway resistance.

	Spearman correlation	95% Confidence intervals		p Value
End-tidal CO_2	0.30331	0.109477	0.474913	0.0025
PSAP	0.00782	-0.192973	0.207975	0.9399
mPAP	0.00848	-0.192337	0.208607	0.9349
CI	-0.10543	-0.299583	0.097109	0.3075
HR	-0.0175	-0.217224	0.18363	0.866
SV	-0.1664	-0.35504	0.035264	0.1053

Table 2: Correlation analysis for pulmonary systolic arterial pressure (PASP), mean pulmonary arterial pressure (mPAP) and various hemodynamic parameters across different levels of external airway resistance. (CI=cardiac index, HR=heart rate, SV=stroke volume).

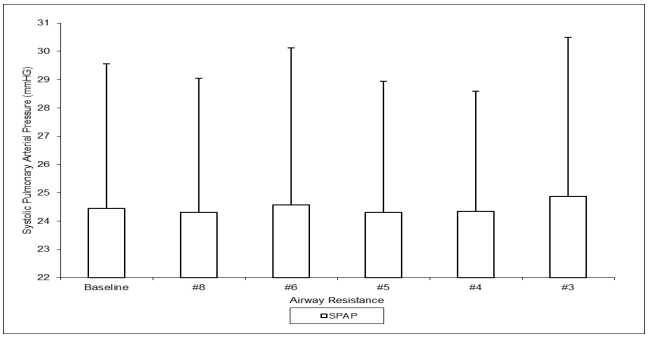

Figure 3: Systolic pulmonary arterial pressure during discrete level of increased external airway resistance.

systolic or mean pulmonary arterial pressure with increases in airway resistance.

The significant decrease in CI and SV observed in this study is consistent with results of previously published data [6]. This model has several advantages compared to the Mueller maneuver which have been discussed extensively in the latter article. The key advantage of our model lies in the possibility of discretely increasing airway resistance allowing a continuous and repetitive assessment of hemodynamic changes. Furthermore, it considers the expirational component of the breathing cycle, specifically important to patients suffering from partial airway obstruction. We could also detect a significant change in $EtCO_2$ which may reflect the impaired exhalation of carbon dioxide during increased airway resistance. When performing Spearman's correlation analysis, $EtCO_2$ was not surprisingly found to have a highly positive correlation with a decrease in tube size. It has been suggested that mechanisms frequently found in patients with OSA, including carbon dioxide retention, may be contributors to the development of cardiac diseases (e.g. artrial fibrillation) [11,12]. However, a number of different patient populations, including patients undergoing procedural sedation or patients in an intensive care unit when increases in resistance occur with various airway devices (e.g. mucus plug in tracheostoma), is known to frequently suffer from periods of increased airway resistance. It remains speculative if the changes observed in our trial would have a clinically significant impact on those patient populations.

The further evaluation of pulmonary arterial pressures using TTE revealed no significant changes during increases in airway resistance. It is therefore unlikely that the hemodynamic alterations can be explained by an acute change in pulmonary pressures, at least in healthy volunteers with no previous history of pulmonary hypertension. Therefore, other factors have to be taken into consideration. Orban et al. demonstrated a decrease in left atrial volume and an increase in left ventricular end systolic volume acutely in response to high negative intrathoracic pressure resulting in a decrease in SV, cardiac output and ejection fraction using TTE [4]. The influence of intra- and extrathoracic as well as changes in transmural pressure on this finding have been discussed extensively over decades [13-15]. Although using Mueller's maneuver to simulate high negative intrathoracic pressure has been shown to closely simulate changes in OSA patients [14,16], a major disadvantage consists in the all or nothing change in airway resistance not accounting for the expirational component of the breathing cycle in partial airway obstruction. Unfortunately, given the limited time for the capture of TTE images and the focus of our exam, we were not able to analyze cardiac filling patterns and obtain necessary views and measurements.

Additional limitations to this study have to be addressed. Firstly, we have performed this investigation in healthy, male volunteers with a mean age of approximately 30 years and an average BMI of 26.75 kg/m^2. Therefore, we cannot determine if our results would have been different in other populations such as females, obese patients and those with preexisting diseases including sleep apnea or pulmonary hypertension. The absence of major comorbidities is crucial because e.g. ischemic heart disease or heart failure are very likely to alter cardiac performance [17]. Therefore, our results derived from the TTE have to be interpreted with caution, as it may be possible that patients with comorbidities or reduced cardiac performance may show different alterations in pulmonary pressures. Moreover, and as mentioned previously we were not able to determine and analyze atrial or ventricular filling patterns. Thirdly, our study period consisted of two minutes per tube size only. This may have been an insufficient period of time to capture changes in pulmonary arterial pressures.

In conclusion, in healthy, male volunteers the change in hemodynamic parameters, such as CI or SV, was not accompanied by changes in systolic pulmonary arterial pressure. Therefore, other possibly causative reasons have to be investigated to further understand hemodynamic alterations. Observational studies in patients with comorbidities such as OSA and cardiac disease may address limitations of this proof of concept analysis.

Acknowledgement

The authors declare no conflict of interests.

Dr. Memtsoudis is funded by the Anna Maria and Stephen Kellen Career Development Award.

Dr. Ma's research was partially supported by grant number R01HS021734 from the Agency for Healthcare Research and Quality.

References

1. Young T, Peppard PE, Gottlieb DJ (2002) Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 165: 1217-1239.
2. Yang SQ, Han LL, Dong XL, Wang CY, Xia H, et al. (2012) Mal-effects of obstructive sleep apnea on the heart. Sleep Breath 16: 717-722.
3. Minai OA, Ricaurte B, Kaw R, Hammel J, Mansour M, et al. (2009) Frequency and impact of pulmonary hypertension in patients with obstructive sleep apnea syndrome. Am J Cardiol 104: 1300-1306.
4. Orban M, Bruce CJ, Pressman GS, Leinveber P, Romero-Corral A, et al. (2008) Dynamic changes of left ventricular performance and left atrial volume induced by the mueller maneuver in healthy young adults and implications for obstructive sleep apnea, atrial fibrillation, and heart failure. Am J Cardiol 102: 1557-1561.
5. Memtsoudis SG, Ma Y, Chiu YL, Walz JM, Voswinckel R, et al. (2010) Perioperative mortality in patients with pulmonary hypertension undergoing major joint replacement. Anesth Analg 111: 1110-1116.
6. Stundner O, Danninger T, Kao I, Gerner P, Memtsoudis S (2013) Hemodynamic Response to Dynamic Changes in Upper Airway Impedance–A Volunteer Study. J Anesthe Clinic Res 4: 317.
7. Keren H, Burkhoff D, Squara P (2007) Evaluation of a noninvasive continuous cardiac output monitoring system based on thoracic bioreactance. Am J Physiol Heart Circ Physiol 293: H583-H589.
8. Yared K, Noseworthy P, Weyman AE, McCabe E, Picard MH, et al. (2011) Pulmonary artery acceleration time provides an accurate estimate of systolic pulmonary arterial pressure during transthoracic echocardiography. J Am Soc Echocardiogr 24: 687-692.
9. Chemla D, Castelain V, Provencher S, Humbert M, Simonneau G, et al. (2009) Evaluation of various empirical formulas for estimating mean pulmonary artery pressure by using systolic pulmonary artery pressure in adults. Chest 135: 760-768.
10. Ma Y, Mazumdar M, Memtsoudis SG (2012) Beyond repeated-measures analysis of variance: advanced statistical methods for the analysis of longitudinal data in anesthesia research. Reg Anesth Pain Med 37: 99-105.
11. Rossi VA, Stradling JR, Kohler M (2013) Effects of obstructive sleep apnoea on heart rhythm. Eur Respir J 41: 1439-1451.
12. Lopez-Jimenez F, Sert Kuniyoshi FH, Gami A, Somers VK (2008) Obstructive sleep apnea: implications for cardiac and vascular disease. Chest 133: 793-804.
13. Buda AJ, Pinsky MR, Ingels NB Jr, Daughters GT 2nd, Stinson EB, et al. (1979) Effect of intrathoracic pressure on left ventricular performance. N Engl J Med 301: 453-459.
14. Somers VK, Dyken ME, Skinner JL (1993) Autonomic and hemodynamic responses and interactions during the Mueller maneuver in humans. J Auton Nerv Syst 44: 253-259.
15. Santamore WP, Bove AA, Heckman JL (1984) Right and left ventricular pressure-volume response to positive end-expiratory pressure. Am J Physiol 246: H114-119.
16. Bradley TD, Tkacova R, Hall MJ, Ando S, Floras JS (2003) Augmented sympathetic neural response to simulated obstructive apnoea in human heart failure. Clin Sci (Lond) 104: 231-238.
17. Scharf SM, Bianco JA, Tow DE, Brown R (1981) The effects of large negative intrathoracic pressure on left ventricular function in patients with coronary artery disease. Circulation 63: 871-875.