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The Effect of Positive Pressure Volume Control Mechanical Ventilation On Arterial Stiffness Measured By Carotid-Femoral (Aortic) Pulse Wave Velocity In Patients Who Operated For Coronary Artery Bypass Surgery

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ABSTRACT

Coronary artery bypass surgery is the most commonly performed heart surgery. After operation, at a certain time, patients are followed in mechanical ventilator support at intensive care units. Pulse wave velocity (PWV) is one of the most important parameters to evaluate elastic properties of great arteries. Increased values of PWV is an indicator of diffuse atherosclerosis. Mechanical ventilation induces cyclic changes in vena cava blood flow, pulmonary artery blood flow and aortic blood flow. In this context, respiratory changes in aortic blood flow are reflected by swings in blood pressure. In this study, the effect of mechanical ventilation on arterial stiffness measured by carotid-femoral (aortic) PWV in patients who operated for coronary artery bypass surgery were investigated.

A total of 20 patients who are operated for coronary artery bypass surgery, followed at intensive care units and applied mechanical ventilation, were enrolled in this study. Aortic PWV measurements were performed twice, including preoperative and postoperative times, from patients. Aortic PWV was determined by using an automatic device, the Complior Colson (France), which allows online pulse wave recording and automatic calculation of PWV. PWV is calculated from measurements of pulse transit time and the distance travelled by the pulse between two recording sites, according to this formula: PWV (m/s) = Distance (m) / transit time (s).

Preoperative measured systolic, diastolic and mean blood pressures, PWV values higher than according to the values measured postoperative (respectively $p=0.014$, $p<0.001$, $p<0.001$, $p=0.001$); PWV propagation time and heart rate (respectively $p=0.033$, $p=0.006$) values were higher at postoperative care.

In conclusion, in our study, the effect of positive pressure volume control mechanical ventilation on the patients who operated for coronary artery bypass surgery was caused by a decrease in PWV.

Key Words: Arterial stiffness, Coronary artery bypass surgery, Positive pressure volume control mechanical ventilation, Pulse wave velocity

Introduction

Bypass surgery of coronary artery is the most common heart surgery. After the operation, patients are followed up for a certain time in intensive care units with the support of mechanical ventilators (MV) (1). Mechanical ventilation conducives cyclic changes in the inferior-superior vena cava, pulmonary artery and aortic blood flows (2). The important components of artery expandability determined by pulse wave velocity (PWV) are blood pressure and heart rate (3).

PWV is one of the most significant parameters in evaluating the elastic properties of large arteries (3,4). PWV is measured by two transcutaneously fixed ultrasonic or pressure sensitive transducers on the trace of a double of arteries separated to a certain distance, such as the carotid artery and femoral artery (3). The index of artery wall

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stiffness is measured by PWV and it is inversely proportional to artery distensibility or relative artery compliance calculated with the classical formula of Bramwell-Hill [(dV / V) / dP] (dV= Volume difference, V= Volume, dP= Pressure difference) (4). PWV and its distensibility index are also dependent on blood pressure, like artery compliance. After ventricular ejection, an PWV is created along the arterial tree. Modifications in the thickness and lumen diameter of the artery wall are the main factors in PWV measurement. This subject can be expressed as a mathematical formula; according to Moens-Korteweg equation PWV = √Eh / 2δR or according to the Bramwell-Hill equation PWV = √ΔP.V / ΔV.δ (E: Young's modulus of the artery wall (E =ΔP.D/ h.ΔD (cm3mmHg-1)), h:Wall thickness, R:Arterial radius, δ:Blood density, ΔP:Pressure change, ΔV:Volume change ΔD:Diameter change.)

Increased values of PWV demonstrates the diffuse atherosclerotic process (5). PWV is a marker of increased arterial stiffness; arterial PWV progression time is inversely proportional to arterial extensibility and arterial compliance (3,4). While arterial PWV increases at increasing heart rates (6); arterial extensibility and compliance may decrease

Blood pressure, heart rate, volume and autonomic nervous system changes that can be observed during mechanical ventilation may affect large arterial mechanics such as arterial stiffness (2). Increased aortic stiffness can lead to increased resistance to left ventricular ejection, decreased effective coronary blood flow and consequently increased myocardial ischemia.

In current study, we explored the effect of MV application on arterial stiffness measured by arterial PWV in patients undergoing coronary artery bypass surgery.

Material and Methods

This clinical study was carried out at Istanbul University Cardiology Institute Cardiovascular Surgery and Anesthesiology and Reanimation Departments in 2015. 20 patients who underwent coronary artery bypass surgery due to coronary artery disease, followed up in the intensive care unit and underwent mechanical ventilation were included in the study. Patients with peripheral artery disease, serious cardiac valve disease, severe carotid artery disease and patients with BMI (Body Mass Index) ≥ 35 kg / m2, waist-hip ratio ≥ 1 and atrial fibrillation on the surface ECG, as it may affect the measurement results for technical reasons, were excluded from the study. Written informed consent was obtained from all participants stating that they participated in the study with their own consent. At the same time, the approval of the ethical committee required to conduct the study was obtained from the Istanbul University Cardiology Institute Clinical Research Ethics Committee.

All patients underwent a standard anesthesia protocol and cardiovascular surgery protocol.

Anesthesia Protocol: Anesthesia induction was achieved with 1 mg/kg 2% lidocaine (Arithmal, Biosel), 0.2-0.3 mg/kg midazolam (Dormicum, Roche), 5 µg / kg fentanyl (Fentanyl Citrate, Abbott) and 1 mg / kg rocuronium (Esmeron, Organon). Intraoperative artificial respiration was initiated in VC mode (FiO2: 45%, TV: 6-8 mL / kg, PEEP: 5 cmH2O) and frequency was adjusted as 12-14 / min to keep the end-tidal carbon dioxide pressure in the range of 35-40 mmHg. (Servo Ventilator 900C, Siemens-Elema, Sweden). The maintenance of anesthesia was achieved with TIVA (Total Intravenous Anesthesia) with 0.25 µg / kg / min remifentanil and 100 µg / kg / hour propofol according to hemodynamic status.

Cardiovascular surgery protocol: In all cases, surgery was realised with a median sternotomy. In all cases, the left internal mammarian artery was preferred as the graft for revascularization of the left anterior descending artery, and the saphenous vein was preferred for the revascularization of other coronary vessels.

Roller pump, hollow-fiber oxygenator (Affinity NT, Medtronic, USA), polyvinylchloride tubing set and two-stage venous cannula were used for cardiopulmonary bypass. Prime volume was created with 1600 mL of ringer, 150 ml of mannitol, 1 g of cefazolin sodium and 2500 IU of heparin. Cardiopulmonary bypass was performed under mild systemic hypothermia (33-34 ° C) and using a non-pulsatile pump flow of 2.6 L / min / m2. During the cardiopulmonary bypass, hematocrit was kept between 22-25% and the mean arterial pressure was tried to stabilize between 50-70 mmHg. Anticoagulation was achieved with heparin (300-400 U / kg) just before the onset of cardiopulmonary bypass and with activated clotting time> 450 sec. Following the aortic cross clamp, the myocardium was protected by antegrade and retrograde cold blood cardioplegia combined with a 4: 1 blood-crystalloid ratio. Distal anastomoses were performed using the cross-clamp and proximal anastomoses were performed using the side-clamp. N-acetyl cysteine (900mg) was applied

Table 1. Demographic and anthropometric measurements of patients

Variables	Mean± SD	Minimum value- Maximum value
Age (year)	55 ± 7.12	44-68
Height (cm)	170.05 ± 7.95	150-185
Weight (kg)	78.25 ± 11.97	55-104
Waist circumference (cm)	98.25 ± 6.22	89-112
Hip circumference (cm)	104.9 ± 4.59	97-114
Waist-hip ratio	0.93 ± 0.00	0.87-0.99
BMI(kg/m²)	26.9 ± 3.13	21.5-34

BMI: Body Mass Index,SD: Standard deviation

before the cross clamp was removed. When the esophageal temperature reached 36 ° C and the cardiac filling pressures and systemic arterial pressure were at the optimal level, the cardiopulmonary bypass was terminated. After the pump, hemodynamic optimization was achieved with adequate intravascular volume and appropriate dose inotrop (Dopamine 5-10 µg/kg/hour, Adrenaline 0.01-0.05 µg/kg/hour, Dobutrex 5-10 µg/kg/hour). After termination of the cardiopulmonary bypass, anticoagulation was neutralized using 1 mg of protamine for each 100 IU heparin dose.

Intensive Care Unit: The patients were transferred to intensive care unit with artificial respiration, under the postoperative sedation (propofol-remifentanil). Artificial respiration settings in intensive care; In VC mode, FiO2: 45%, TV: 6-8 mL/kg, PEEP: 5 cmH2O and frequency (12-14/min) parameters to keep the end-tidal carbon dioxide pressure in the range of 35-40 mmHg. (Servo Ventilator 900C, Siemens-Elema, Sweden)

Measurement of Arterial Blood Pressure: The first measurement of arterial blood pressure from the patients was done at the bedside in the service approximately 24 hours before the operation, and the second measurement was done half an hour after the transfer to the intensive care unit with positive pressure volume controlled ventilation. Before the operation, arterial blood pressure was measured in a supine position with a standard mercury manometer after a 10-minute rest. After the operation, arterial blood pressure was measured by invasive monitoring from the radial artery cannula. PP = SBP– DBP, MBP = SBP + 2 X DBP/3 formulas were used.

Measurement of Arterial Expandability and stiffness: Arterial stiffness was calculated by aortic PWV, using the Complior device (Createch Industrie, France), which permits automatic real-time recording of pulse wave and automatic calculation of PWV. The coefficient of correlation of the automatic evaluation method between the observers and the measurements of an observer at different times was reported as >0.9. Carotis communis artery and femoral artery pressure wave shapes were measured noninvasively using by pressure sensitive transducer, TY-306 Fukuda (Fukuda, Japan). Evaluations were repeated in more than 10 different heart cycles and the mean value obtained was used for result analysis. PWV is automatically calculated by the device with the formula ($PWV = \Delta D / \Delta t$). [ΔD: Distance (meters) traveled on the body surface by the pulse wave between two recording points. Δt: Pulse wave transit time (seconds) automatically determined by the Complior device].

Statistical Analysis: Statistical analysis SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL) made using a package program. Categorical variables as numbers and percentages, continuous variables as mean ± standard deviation specified. Significance between the measurements of preoperative and postoperative values of the same participant was determined using the non-parametric Wilcoxon Signed Rank test. The relationship between PWV and other variables was evaluated by Pearson correlation test.

Results

18 (90%) of 20 patients were male and 2 (10%) of 20 patients were female. Demographic features and anthropometric measurements of the patients are shown in Table 1 and hemodynamic and ventilation parameters, before (1) and after (2) operation, measurements of patients are shown in Table 2.

5 (25%) of 20 patients had Type 2 DM. Hypertension was detected in 18 (90%) of 20 patients. Fourteen (70%) patients had hyperlipidemia. The number of smokers was 15 (75%). In 8 (40%) patients, family history was positive in terms of coronary artery disease.

Table 2. Hemodynamic and ventilation parameters, preoperative and postoperative, measurements of patients

	Mean± SD	Minimum value- Maximum value
Preoperative SBP (mmHg)	137.75± 11.86	110-160
Postoperative SBP (mmHg)	124.5± 20.6	80-170
Preoperative DBP (mmHg)	80± 7.43	70-100
Postoperative DBP (mmHg)	61± 7.88	40-75
Preoperative MBP (mmHg)	98.95± 7.95	83-120
Postoperative MBP (mmHg)	81.8±10.72	53-96
Preoperative PP (mmHg)	57.75±9.79	40-80
Postoperative PP (mmHg)	63.5±17.55	40-110
Preoperative CAB (beat/min)	76.05±11.07	59-94
Postoperative CAB (beat/min)	84.95±8.85	69-98
Frequency (respiratory rate/min)	11.65±0.67	10-13
InsMV (l/min)	6.35±1.22	4.5-10
EMV(l/min)	6.04±1.16	4.2-9.3
ITV (ml/kg)	541.05±102.4	400-850
ETV (ml/kg)	521.85±100.37	390-845
PAP (cmH2O)	20.77±3.09	16-27.5
PAUSE-P (cmH2O)	16.45±2.56	11-20.5
MAP (cmH2O)	8.25±1.23	5.4-10.2
PEEP (cmH2O)	5±0	5-5
Preoperative PWV (m/sec)	10.79±1.23	8.61-12.77
Postoperative PWV (m/sec)	10.26±1.37	7.31-12.60
Preoperative PWVPT (m/sec)	62.35±8.31	47-78
Postoperative PWVPT (m/sec)	65.10±11.30	46-97

(SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Average blood pressure, PP: Pulse pressure, CAB: Cardiac apex beat, InsMV:Inspiratory minute volume, EMV: Expiratory minute volume , ITV:Inspiratory tidal volume, ETV: Expiratory tidal volume, PAP: Peak Airway Pressure, PAUSE-P: Pause Airway Pressure, MAP: Mean Airway Pressure, PEEP: Positive End Expiratory Pressure)

SBP, DBP, MBP, PWV values measured before the operation were higher than the values measured after the operation (respectively, $p = 0.014$, $p < 0.001$, $p < 0.001$, $p = 0.001$); PWVPT and CAB (respectively $p = 0.033$, $p = 0.006$) were higher after operation. There was no statistically significant difference in PP value ($p = 0.346$) (Table 3) (Figure 1-2-3).

A significant positive correlation was found between preoperative PWV and age; A negative correlation was found between preoperative PWV and preoperative PWVPT (Table 4).

A significant positive correlation was found between postoperative PWV and age; A negative correlation was found between postoperative PWV and postoperative PWVPT (Table 5).

There was no statistically significant relationship between PWV values with gender, height, weight, BMI, waist circumference, hip circumference, waist-hip ratio, SBP, DBP, MBP, PP, CAB, frequency, InsMV, EMV, ITV, ETV, PAP, PAUSE-P, MAP and PEEP ($p>0.05$).

Discussion

In current study, the effect of MV application on arterial stiffness measured by arterial PWV was investigated in patients undergoing coronary artery bypass surgery.

Based on the data we obtained from this study, there was a statistically significant decrease in arterial PWV measured before and after surgery.

PWV can be affected by different blood pressure values such as age, heart rate, SBP, DBP, MBP and PP (7-9). In current study, a significant positive correlation was found between PWV and age; a negative correlation was found between PWV and PWVPT. As it can be understood from the formula ($PWV=\Delta D/\Delta t$) [ΔD: Distance traveled on the body surface by the pulse wave

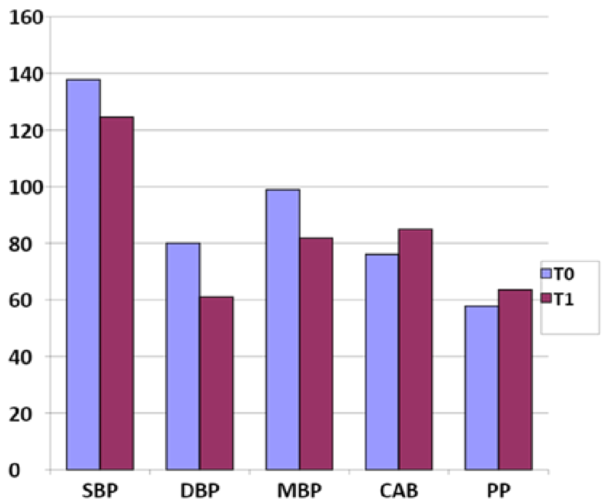

Fig. 1. SBP, DBP, MBP, CAB and PP values measured before Operation (T0) and After Operation (T1)
SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean arterial blood pressure, CAB: Cardiac apex beat, PP: Pulse pressure

Fig. 2. PWV values measured before surgery (T0) and after surgery (T1)

PWV: Pulse wave velocity

between two recording points (meters), Δt: Pulse wave transit time (seconds) automatically determined by the Complior device], there is an inverse relationship between PWV and PWVPT; this situation explains the negative correlation in the findings. There was no statistically significant relationship between PWV values and heart rate.

In the study, the heart rate increased in the post-operative period; this may be due to increased sympathetic activity and used inotropic agents.

Age and arteriosclerosis affect the artery tree to varying degrees, more prominently on central and elastic arteries. As the age gets older the stiffness of the aorta increases and its extensibility decreases. As the age progresses, the structure of aortic elastic fibers changes, the elastic tissue gradually decreases and is replaced by collagen tissue. In the both genders the wave velocity of the aortic pulse (carotid-femoral or trunk PWV) values increase with the age (7,8). It is also known

Fig. 3. PWVPT values measured before surgery (T0) and after surgery (T1)

PWVPT: Pulse wave velocity progression time

that PWV increases with increasing intra-arterial pressure (9). In this study, after the coronary artery bypass surgery, the decrease in arterial pressure values (SBP, DBP, MBP), as well as a decrease in PWV, thus an improvement in arterial elasticity are observed.

MVs are devices designed to do all or part of the work of the respiratory muscles. These devices support the functions of the respiratory system in any respiratory failure, respiratory muscle fatigue. The main purpose in mechanical ventilation is to continue breathing without harming the patient, to ensure gas exchange and hemodynamics and to save time for the repair of the lungs. For this purpose, various MV variables such as respiratory frequency and PEEP are used in the clinics. Mechanical ventilation induced cyclic changes in vena cava blood flow, pulmonary artery blood flow and aortic blood flow (10). At the inspiratory phase, first of all vena cava blood flow decreases, followed by decreases in pulmonary artery blood flow and then aortic blood flow. Decreases in vena cava blood flow, especially venous return; It is associated with compression of the vena cava as a result of both an increase in the right atrial pressure and an inspiratory increase in pleural pressure during mechanical ventilation (11-16). According to the mechanism of Frank-Starling, inspiratory decline in the right ventricular preload causes in a decrease in right ventricular output and pulmonary artery blood flow, that causes in a decrease in left ventricular filling and output (17). Quintao et al. (18) investigated the acute effect of continuous positive airway pressure non-invasive ventilation on the pulse pressure in patients with chronic cardiac failure and found that it improved arterial mechanics. Also this practice has been shown to help improve nocturnal blood pressure in patients with sleep-apnea syndrome, thereby improving arterial stiffness (19). The results of

Table 3. Evaluation of postoperative and preoperative SBP, DBP, MBP, PP, CAB, PWV and PWVPT values with Wilcoxon test

		Mean±SD	p
SBP	Postoperative-preoperative	124.5±20.6 - 137.75±11.86	0.014
DBP	Postoperative-preoperative	61±7.88 - 80±7.43	<0.001
MBP	Postoperative-preoperative	81.8±10.72 - 98.95±7.95	<0.001
PP	Postoperative-preoperative	63.5±17.55 - 57.75±9.79	0.346
CAB	Postoperative-preoperative	84.95±8.85 - 76.05±11.07	0.006
PWV	Postoperative-preoperative	10.26±1.37 - 10.79±1.23	0.001
PWVPT	Postoperative-preoperative	65.10±11.30 - 62.35±8.31	0.033

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Average blood pressure, PP: Pulse pressure, CAB: Cardiac apex beat, PWV: Pulse wave velocity, PWVPT: Pulse wave velocity progression time

Table 4. Relationship between preoperative PWV with age and preoperative PWVPT values

	r value	p value
Preoperative PWV - Age	0.570	0.009
Preoperative PWV - Preoperative PWVPT	- 0.896	<0.001

PWV: Pulse wave velocity, PWVPT: Pulse wave velocity progression time

Table 5. Relationship between postoperative PWV with age and postoperative PWVPT values

	r value	p value
Postoperative PWV - Age	0.527	0.017
Postoperative PWV - Postoperative PWVPT	- 0.912	<0.001

PWV: Pulse wave velocity, PWVPT: Pulse wave velocity progression time

these studies are compatible with the current study results, in terms of decreased arterial stiffness. In addition, long-term non-invasive ventilation may decrease the arterial compliance by causing an increase in systemic inflammatory markers such as human neutrophil peptide, interleukin-6. Paone et al. (20) found that in individuals with chronic obstructive pulmonary disease, long-term home non-invasive mechanical ventilation causes an increase in systemic inflammatory response. Mechanical ventilation has been shown to increase the inflammatory response in animals with lung contusion (21). In the current study, acute hemodynamic effects have been investigated but inflammatory markers have not been studied.

PEEP application prevents the airways and especially the alveoli from closing by keeping the pressure above atmospheric pressure during the expiratory phase of ventilation. Opening the collapsed alveoli improves the functional residual volume, improves V/P ratio and oxygenation, reduces the patient's respiratory work. All these effects increase oxygenation and allow the reduction of FiO2 level. In addition, PEEP increases the average airway pressure and creates a pressure difference for oxygen to flow into the blood. If the lung disease is mild and oxygenation is sufficient in patients who are intubated and connected to the mechanical ventilator, it is sufficient to apply 3-4 cmH2O PEEP. High PEEP values are needed in the presence of atelectasis, pneumonia or pulmonary edema. The basic point is to apply PEEP level which will increase oxygenation by decreasing FiO2 below 0.6 without creating a change in the cardiovascular system (22). However, PEEP application can reduce cardiac output, thereby reducing the expected benefits of oxygen (23). The harmful haemodynamic effects of PEEP occur with an increase in pressure of pleura by reducing right ventricular filling and an increase in transpulmonary pressure by increase in afterload of right ventricle. A decrease in cardiac output may be associated with a decrease in blood pressure. This situation may appear as a decrease in arterial stiffness in the acute period.

Based on this study data, patients who undergo coronary artery bypass surgery and who are connected to a mechanical ventilator and who undergo PEEP have reduced PWV values in the acute period, thereby reducing arterial stiffness values.

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