Evaluation of Arterial Stiffness in Cardiac Surgical Patients Using Applanation Tonometry

Abstract

**Context:** Applanation tonometry enables the noninvasive analysis of arterial pressure wave morphology. Applanation tonometry provides the augmentation index (AIx, %), an index of arterial stiffness that partially reflects arterial-ventricular (A-V) coupling. In addition, applanation tonometry provides the dP/dt (rate of intraventricular pressure variation over time), which reflects myocardial contractility, and the sub-endocardial viability ratio (SEVR, %), which is an indicator of myocardial oxygen supply and demand. There are no data on how cardiac surgery can modify these tonometry-derived indexes. **Aim:** The aim was to assess changes in AIx, dP/dt, and SEVR in patients undergoing cardiac surgery. **Subjects and Methods:** This observational study was conducted at the University Hospital of Siena. We studied 32 patients before cardiac surgery in intensive care unit (ICU) on admission and at ICU discharge. We measured AIx, dP/dt, and SEVR using applanation tonometry (SphygmoCor). Changes in variables over time were evaluated by analysis of variance for repeated measurements. **Results:** AIx decreased significantly from T1 [28.8%, interquartile range (IQR) 21.6–36.6%] to T2 (16.2% IQR 8.1–22.4%) and T3 (14.5% IQR 7.9–23.6%) (P = 0.01). dP/dt increased significantly from T1 (635 mmHg/ms, IQR 534–756 mmHg/ms) to T3 (751 mmHg/ms, IQR 651–1013 mmHg/ms; P = 0.03). The SEVR was lower at T2 than at T1, but returned toward T1 values by T3. **Conclusions:** Cardiac surgery was associated with an improvement in arterial stiffness, A-V coupling, and myocardial contractility as assessed using applanation tonometry. The results suggest, however, a transient imbalance between myocardial oxygen supply and demand in the immediate postoperative period.

**Keywords:** Arterial stiffness, arterial tonometry, arterial vascular tone, augmentation index, dP/dt, cardiac surgery

Introduction

In the human vascular system, the arteries can modify the pulsatile component of arterial blood pressure enabling the microvascular blood flow to be continuous.[1] However, this ability can be altered or lost when there is arterial stiffness. Arterial stiffness also causes a constant increase in left ventricular afterload with consequent ventricular hypertrophy and the potential development of heart failure. Increased arterial stiffness is widely used as an index of cardiovascular risk and has been directly related to a worse cardiovascular prognosis in various populations and at different ages, independent of other risk factors.[2] Arterial stiffness can be evaluated by applanation tonometry, a technique performed with an arterial tonometer that positioned perpendicular to the radial artery, allows a beat-to-beat and noninvasive analysis of blood pressure wave morphology, and provides an estimation of arterial stiffness and myocardial function.[3,4]

The arterial pressure wave changes in morphology when moving from the aorta to the peripheral arteries. After the first systolic peak, a second peak resulting from the sum of the reflected waves occurs centrally and peripherally, however, and is called the augmented pressure [Figure 1].[5] In healthy young patients, the augmented pressure facilitates coronary perfusion without increasing ventricular afterload. In the elderly (and also in patients with high blood pressure, cardiomyopathy, or diabetes), arterial stiffness causes an increase in blood pressure, interfering with left ventricular ejection and leading to ventricular hypertrophy and myocardial ischemia.[6,7]

The arterial tonometer provides a parameter that is a percentage of the augmented...
pressure: the augmentation index (AIx). The AIx is a widely described index of arterial stiffness in several pathological conditions, including hypertensive or ischemic cardiomyopathy, diabetes, or collagenopathies. Whether and by how much corrective heart surgery can modify arterial stiffness, and consequently AIx values, in patients with heart disease has still not been evaluated.

The aim of this study was, therefore, to assess the changes in arterial stiffness in patients undergoing heart surgery by analysis of the AIx and to evaluate the time-course of other noninvasive parameters of cardiac performance obtained with applanation tonometry.

**Subjects and Methods**

We performed a prospective study from December 2012 to March 2013 at the University Hospital of Siena. Ethical approval for this study (CEL AOUS 23/11/2012) was provided by the Comitato Etico Regione Toscana—Area Vasta Sud Est of Siena University Hospital, Siena, Italy (Chairperson Prof M. Martini) on 23 November 2012, and all patients gave their written informed consent.

The study included a convenience sample of 32 adult patients (≥18 years) undergoing coronary artery bypass surgery, heart valve repair or replacement surgery (aortic or mitral), combined interventions (valve replacement or valvuloplasty plus coronary artery bypass grafting (CABG)), or ascending aorta replacement. Patients were excluded if they underwent off-pump surgery, heart transplantation, or had cardiac arrhythmias or edema of the wrist and/or the forearm (course of the radial artery).

**Study protocol**

The study involved the noninvasive morphological analysis of the radial artery pulse wave using applanation tonometry. An arterial tonometer (SphygmoCor, AtCor Medical, Sydney, Australia) was placed on the skin, perpendicular to the radial artery being studied; a slight but constant pressure was applied to eliminate tangential vascular pressures and ensure the sensor was only exposed to the pressure within the vessel [Figure 2].

**Augmentation index**

The AIx is expressed as a percentage of the augmented pressure (augmented pressure/central pulse pressure × 100). It is a measure of increasing systolic blood pressure due to the reflected waves and is an indirect index of arterial stiffness. This parameter is influenced mainly by age, sex,
height, mean arterial pressure (MAP), and heart rate (HR). To increase the reproducibility of this parameter among groups, it has been suggested that the Alx normalized for a HR of 75 beats per minute (Alx@75) could be used.[9]

Other parameters from applanation tonometry

The tonometric technique provides two other parameters of interest: $dP/dt$ and SEVR. The $dP/dt$ (rate of intraventricular pressure variation over time) is an indirect index of myocardial contractility. The maximum velocity achieved ($dP/dt$ Max, peak of contractility) on a pressure–time graph can be calculated as the first derivative of the curve in its ascending phase [Figure 3a].[10]

The SEVR is a sub-endocardial perfusion index and is obtained from the ratio between the systolic and diastolic areas under the aortic pressure curve [Figure 3b]. This index estimates the arterial system’s capacity to satisfy the energy requirements of the heart. The diastolic area is correlated to cardic work, oxygen consumption, pressure, and duration of coronary perfusion.[11]

Data acquisition

After calibration of the device with patient height, weight, and blood pressure values measured with a brachial sphygmomanometer, the pressure sensor was positioned over the radial artery on the contralateral arm where radial arterial pressure was measured invasively. In accordance with the manufacturer’s directions, 30-s recordings of the pulse wave profile were carried out, evaluating the quality of the signal each time and repeating the measurement if it was not adequate (operator index <80%). Measurements were made at the bedside, in conditions of hemodynamic stability (absence of arterial pressure and HR variations >5% compared with the baseline values) at three different timepoints: the day before surgery (T1), on admission to the ICU (T2), at ICU discharge (T3) immediately before radial artery catheter removal. In each patient, three measurements were conducted at each timepoint and the average value was calculated. This average arterial pressure value along with demographic and anthropometric data (age, sex, weight, height, body surface area, body mass index) were recorded in an electronic database for subsequent analysis. The same arterial tonometer was used throughout the study period.

Statistical analysis

For all measured parameters, mean and standard deviation, or median and interquartile range (IQR) were calculated. For continuous data, a Student’s t-test was used and normal distribution evaluated using the Kolmogorov–Smirnov test. When appropriate, the analysis of variance (ANOVA) for repeated measures was used for the evaluation of data changes over time. Subgroup analyses of patients according to the duration of cardiopulmonary bypass (CPB; ≤180 min vs. >180 cm), type of surgical procedure (valvular surgery vs. others), use of inotropic or vasopressor agents, high lactate levels on ICU admission (≤2 vs. >2 mmol/L), and preoperative risk status (EUROscore ≤6 vs. >6) were also performed. Statistical significance was considered as a $P$ value of <0.05.

Results

A convenience sample of 32 patients who underwent cardiac surgery with CPB was included. Medical history, type of surgery, comorbidities, perioperative, and ICU admission data are shown in Tables 1 and 2. No patients received inotropic and/or vasoactive drugs at T1 and T3. All patients were alive at hospital discharge.

Alx was significantly lower at T2 (16.2% IQR 8.1–22.4) and T3 (14.5% IQR 7.9–23.6) than at T1 (28.8%, IQR 21.6–36.6%) [Figure 4; $P = 0.01$]. Conversely, Alx@75 values remained stable over time [Figure 4]. $dP/dt$ values were significantly higher at T2 (760 mmHg/ms, IQR 680–1008 mmHg/ms) and T3 (751 mmHg/ms, IQR 651–1013 mmHg/ms) than at T1 (635 mmHg/ms, IQR 534–756 mmHg/ms).
Table 1: Clinical data, type of surgery, comorbidity, and perioperative and ICU admission data of patients

| Clinical data                  |       |
|-------------------------------|-------|
| Age (years)                   | 68.4±21.2 |
| Weight (kg)                   | 78.2±17.7 |
| Sex (M/F)                     | 24/8  |
| Height (cm)                   | 168.9±7.8 |
| Body mass index (kg/cm²)      | 27.3±3.9  |
| Body surface area (m²)        | 1.9±0.2  |
| Ejection fraction (%)         | 56.5±3.5  |
| EUROScore (points)           | 6.5±3.5  |

| Type of surgery and CPB       |       |
|-------------------------------|-------|
| Aortic valve replacement      | 8     |
| Coronary artery bypass        | 5     |
| Ascending aorta replacement   | 4     |
| Ascending aorta + aortic valve replacement | 8 |
| Bypass + valve                | 7     |

| Cardiovascular comorbidities  |       |
| Arterial hypertension         | 24    |
| Dyslipidemia                  | 12    |
| Diabetes                      | 8     |
| Atherosclerosis (n)           | 15    |

| Intraoperative variables      |       |
| CPB time (min)                | 153.4±43.3 |
| Lactate (mmol/L)              | 2.9±1.6  |
| Hematocrit (%)                | 25.0±4.0  |
| Hemoglobin (g/dL)             | 7.9±1.2  |

| Variables at ICU admission    |       |
| Blood loss (mL)               | 300±175 |
| Nitrate, n (%)                | 17 (53) |
| Noradrenaline, n (%)          | 5 (16)  |
| Dopamine, n (%)               | 2 (6)   |

Data are expressed as means and standard deviations or numbers and percentages. EUROScore: European System for Cardiac Operative Risk Evaluation; CPB: Cardiopulmonary bypass.

Discussion

In this study, we observed that the AIx, and thus arterial stiffness, was significantly reduced in the immediate postoperative period after cardiac surgery. This effect was associated with a concomitant improvement in indices of ventricular afterload and cardiac work. These benefits appeared to be more pronounced in high-risk patients (EUROscore >6), who also had higher preoperative AIx values than lower-risk patients. However, the variation in this parameter could also be due to improved ventricular performance in patients undergoing CABG and to an improvement in V-A coupling in patients undergoing aortic valve and/or ascending aorta surgery. In addition, we observed that patients undergoing prolonged CPB (>180 min) had lower AIx values at T2 than patients with shorter CPB durations. It is possible that a longer CPB duration may have temporarily increased the systemic inflammatory response leading to vasodilation and reduced systemic vascular resistance.[13] Finally, the type of surgery, use of vasoactive drugs, and arterial lactate levels did not seem to affect AIx in our population.

The AIx@75 did not change significantly in our study, but it should be stressed that the physiological and statistical validity of normalizing the AIx to a HR of 75 beats per minute is debated. This index was proposed by Wilkinson and colleagues in two articles in which a correction factor was calculated based on linear interpolation.[10,14] Nevertheless, a subsequent review,[15] in which 12 studies comparing AIx and AIx@75 were analyzed, speculated that the use of linear interpolation could create an inferential error. The authors of this review suggested using the HR as an independent or covariate factor,[15] especially in longitudinal studies.

The significant increase in dP/dt values at T2 and T3 probably reflects the positive effect of the surgical procedure on the myocardium. In patients undergoing coronary artery bypass, the revascularization of hypoperfused myocardial areas results in an increase in oxygen transport and a subsequent improvement in ventricular performance.[16] Conversely, increase in dP/dt values in patients who undergo surgery for aortic stenosis or surgery involving the ascending aorta may represent an improvement in V-A coupling due to the reduction in afterload caused by the surgical resolution of the aortic pathology (indeed, tonometry measures dP/dt downstream with respect to the aortic valve). However, it is important to underline that there are controversial results about the correlation between the dP/dt values obtained by tonometry and those measured using echocardiography.[16,17] Therefore, dP/dt obtained from...
tonometry, similar to AIx, should be used with caution as index of left ventricular function in the perioperative evaluation of cardiac patients.

In our study, SEVR values showed a specific trend, being reduced at T2, but increasing back towards T1 values by T3. SEVR is a sub-endocardial perfusion index, therefore its reduction at T2 may be due to the effects that cardioplegia, intraoperative hypothermia, and ischemia-reperfusion have on the myocardium.\[^{[18]}\] Indeed, during aortic cross-clamping, cardiac metabolism undergoes profound modifications: the predominant anaerobic metabolism reduces the production of ATP, the redox power of the cells is depleted (time-dependent decrease in the levels of reduced glutathione),\[^{[19]}\] and finally, there is an increase in N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels, reflecting the degree of stress and myocardial dysfunction.\[^{[20,21]}\] Alternatively, the lack of a statistically significant increase in SERV values at T3 may have been related to the short follow-up period.

The study presents several limitations, related to the technique of arterial tonometry and to study design. The main limitation of tonometry is related to the detection site, the radial artery, because there is a change in arterial wave morphology between the aorta and the periphery.\[^{[5]}\] However, the use of the transfer function limits the impact of estimation errors.\[^{[4,22,23]}\] Furthermore, measurements with tonometry performed at the radial artery level, rather than at the carotid level, avoid the risk of baroreceptor activation or atheromatous plaque dislocation. A further limitation of the method is its operator dependence. To overcome this limitation, the device provides an online parameter (operator index) that estimates the adequacy of the single measurement and allows the operator to exclude a measurement and repeat it.

A study limitation is that the majority of the patients included in the study had normal cardiac function and only a few received inotropes or vasopressors in the perioperative period. As such, we could not analyze the effects of cardiovasoactive drugs on applanation tonometry-derived variables or the potential implications

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**Table 2: Hemodynamic and metabolic variables**

|          | T1              | T2              | T3              |
|----------|-----------------|-----------------|-----------------|
| SAP (mmHg)| 120.8±19.1      | 122.6±17.6      | 121.2±19.5      |
| DAP (mmHg)| 69.7±9.6        | 66.4±12.2       | 68.3±12.9       |
| MAP (mmHg)| 87.4±10.4       | 83.9±13.1       | 85.5±13.0       |
| HR (bpm)  | 64.7±11.4       | 85.0±10.9*      | 83.3±11.4*      |
| CVP (mmHg)| N/a             | 9.8±3.5         | 10.5±2.8        |
| ScvO\(_2\) (%)| N/a             | 65.7±7.4        | 63.2±7.2        |
| Hemoglobin (g/dL)| N/a             | 10.5±1.6        | 10.1±1.8        |
| Lactate (mmol/L)| N/a             | 2.2±1.4         | 1.4±0.4*        |

Data are expressed as means and standard deviations. SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; MAP: Mean arterial pressure; HR: Heart rate; CVP: Central venous pressure; ScvO\(_2\): Central oxygen venous saturation. T1: Day before surgery; T2: Admission to ICU; T3: Discharge from ICU. *P<0.05 compared to T1; **P<0.05 compared to T2 for the variables collected only at T2 and T3.
of our findings on clinical outcomes. In addition, we did not enroll patients undergoing off-pump coronary artery bypass (OPCAB) surgery. As a consequence, we could not assess the perioperative difference in tonometry-derived indexes changes in CABG patients undergoing CPB with respect to OPCAB patients. That would have allowed us to estimate the potential impact of systemic inflammatory response, triggered by CPB, on vascular tone and to prove that AIx and dP/dt max changes after CPB were more or less related to the actual improvement of the left ventricular performance or to the temporary V-A coupling changes triggered by CPB. By the way, a potential advantage of using applanation tonometry coupled to transesophageal echocardiography in OPCAB surgery, especially in high-risk patients with low ejection fraction, would be the continuous assessment of left ventricular performance and pressure wave-derived parameters changes by manipulating the heart during surgery, so that one may identify patients with significant hemodynamic instability and increased risk of tissue hypoperfusion. Of course, further studies would be warranted to prove this hypothesis. Unfortunately, we did not compare applanation tonometry data with those obtained using echocardiography (i.e., contractility parameters or AV coupling data); however, the aim of the study was not to compare echocardiographic and tonometry data but to assess the value of a simple and noninvasive method that requires a short learning curve.

The pulse wave velocity, which is an independent parameter of stiffness, was not measured in our study. Thus, changes in vascular stiffness might be due to either the large increase in HR or the surgical intervention. As such, it is possible that the improvement of vascular stiffness that we observed in our study might be related to reduced effects of peripheral wave reflection. Indeed, HR increased and MAP did not change. This might imply that peripheral resistance may have played a role in such an improvement (e.g., peripheral vasodilation). Finally, a wide range of surgeries and patients was included; indeed, the small sample size did not enable analysis of the change in parameters in some subgroups. Nevertheless, to the best of our knowledge, this is the first study in the literature to perform this type of analysis in patients undergoing cardiac surgery.

Conclusions

In conclusion, our findings showed that cardiac surgery has beneficial effects on arterial stiffness, A-V coupling, and myocardial contractility. However, the immediate postoperative period is characterized by a temporary imbalance between myocardial oxygen supply and demand. Applanation tonometry is a simple and feasible technique to noninvasively estimate A-V coupling, myocardial contractility, and coronary blood flow in patients undergoing cardiac surgery. Further larger studies are warranted to investigate the potential clinical implications of this study.

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Conflicts of interest

There are no conflicts of interest.

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Table S1: Univariate analysis of AIx in subgroups of patients accordingly to the duration of cardiopulmonary bypass (CPB), preoperative EUROscore, type of surgery, and postoperative variables

| Variables                                | AIx          | ANOVA | P     |
|------------------------------------------|--------------|-------|-------|
|                                          | T1           | T2    | T3    |       |
| CPB time <180 min (n=22)                 | 22.5±11.9    | 20.1±11.0 | 18.5±15.7 | 0.24 |
| CPB time >180 min (n=10)                 | 29.75±8.4    | 9.1±15.6* | 13.6±20.5 |       |
| EUROscore <6, (n=15)                     | 24.8±10.7    | 14.8±16.0 | 13.6±21.9 | 0.28 |
| EUROscore >6 (n=17)                      | 33.5±9.2*    | 18.8±9.7 | 20.8±8.7 | 0.38 |
| CABG (n=5)                               | 20.6±6.1     | 15.5±5.8 | 14.7±15.5 |       |
| Other type of surgery (n=27)             | 30.4±10.9    | 16.9±14.4 | 17.4±17.7 | 0.55 |
| Vasopressor or inotropic drugs (n=7)     | 28.9±5.7     | 14.8±12.6 | 12.3±19.2 |       |
| No vasopressor or inotropic drugs (n=25) | 28.9±12.0    | 17.2±13.8 | 18.3±16.7 |       |
| Lactate levels <2 at T2 (n=19)           | 28.0±11.7    | 18.0±13.4 | 18.8±15.6 | 0.70 |
| Lactate levels >2 at T2 (n=13)           | 30.2±9.7     | 14.8±13.7 | 14.3±19.5 |       |

Data are expressed as means and standard deviations. *P<0.05 at univariate analysis between the groups, CABG: Coronary artery bypass graft.