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# Association of Carotid Arterial Circumferential Strain With Left Ventricular Function and Hemodynamic Compromise During Off-Pump Coronary Artery Bypass Surgery

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***Background:*** Considering the importance of ventricular-vascular coupling, a measure of arterial stiffness may reflect global myocardial performance. We evaluated the predictive value of common carotid arterial circumferential strain (CCA CirS), measured with ultrasound speckle tracking, for hemodynamic deterioration during off-pump coronary artery bypass (OPCAB) and assessed its association with echocardiographic indices of myocardial function.

***Methods and Results:*** Patients with left ventricular ejection fraction (LVEF) ≥50% were enrolled. Intraoperative hemodynamic variables were compared in relation to CCA CirS tertiles. A total of 96 patients were analyzed. Mixed venous oxygen saturation ($SvO_2$) during left circumflex artery grafting and sternum closure were lower in the first tertile than in the third tertile. On univariate logistic regression female gender, ratio of early transmitral velocity to annular velocity, pulse pressure, and CCA CirS were predictors of hemodynamic deterioration (defined as decrease in $SvO_2$ ≥20%), while only CCA CirS remained as an independent predictor after multivariate analysis (OR, 0.27; 95% CI: 0.11–0.68). Area under the curve of CCA CirS for its prediction was 0.730 (95% CI: 0.608–0.852). CCA CirS was strongly associated with tissue Doppler-derived parameters of LV function.

***Conclusions:*** CCA CirS is a comprehensive marker reflecting LV function, and a predictor for hemodynamic deterioration during OPCAB in patients with preserved LVEF. (*Circ J* 2014; **78:** 2422–2430)

**Key Words:** Circumferential strain; Left ventricular function; Off-pump coronary artery bypass; Vascular stiffness

Multi-vessel off-pump coronary artery bypass surgery (OPCAB) is accompanied by inevitable periods of hemodynamic deterioration induced by mechanical heart displacement and cumulative regional myocardial ischemia-reperfusion injuries.[1,2] Although it is well tolerated in most patients, it may be severe enough to cause serious perturbations affecting outcome.[3,4] Its anticipation, however, is difficult on conventional preoperative assessment of cardiac status, especially in patients with preserved left ventricular ejection fraction (LVEF).

Large artery stiffness augments afterload imposed on the left ventricle (LV) while decreasing diastolic perfusion pressure.[5,6] Accordingly, it is related to LV dysfunction, making it a prominent cardiovascular risk factor in patients with coronary artery disease (CAD),[7,8] and has been described as a major determinant of coronary reserve and ischemic threshold.[9,10]

Among the available methods to assess vascular stiffness, circumferential strain (CirS), on speckle tracking analysis, has recently emerged as a useful tool to determine the elastic properties of the carotid artery.[11–13] It measures the circumferential change in the vascular morphology throughout a cardiac cycle, and the higher the value, the more compliant the vasculature.[12] In CAD patients, the CirS of the common carotid artery (CCA CirS) has been found to be more closely associated with severity and extent of coronary atherosclerosis, compared to the carotid intima-media thickness (IMT), a most widely used surrogate marker of vascular stiffening.[14]

Considering the importance of ventricular-vascular coupling, a sophisticated factor reflecting vascular stiffness may be useful as a comprehensive marker of global LV function, reflecting both systolic and diastolic function, and as a predictor of hemodynamic deterioration during mechanical heart displacement in OPCAB. The clinical relevance of CCA CirS, however, in patients undergoing OPCAB has not been validated as yet.

The aim of this study was to evaluate CCA CirS as a predictor for actual hemodynamic deterioration in patients undergo-

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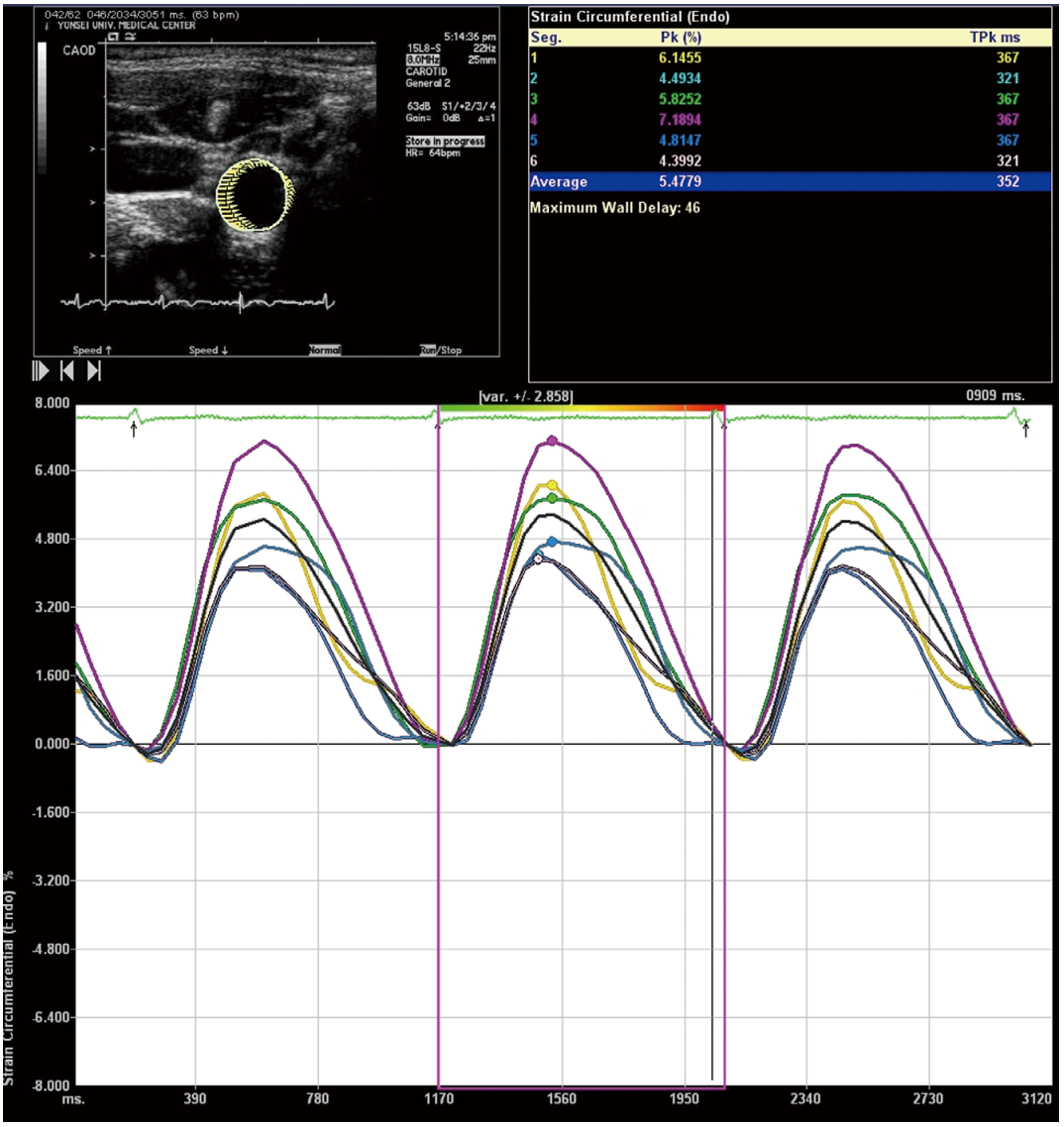


**Figure 1.** Measurement of common carotid artery circumferential strain on 2-D speckle tracking analysis. On the short-axis right common carotid artery 1 cm below the bulb, the luminal-intimal border was traced manually at the end-diastolic phase. After frame-to-frame tracking of ultrasound reflection (speckle) by software, the magnitude and direction of tissue velocities of 6 segments were obtained throughout the cardiac cycle. The peak systolic circumferential strain (%) of the 6 segments and their averages are shown.

ing multi-vessel OPCAB with preserved LVEF.

## Methods

### Subjects

After approval by Yonsei University Institutional Review Board and registration with ClinicalTrials.gov (registration number: NCT01840969), patients undergoing elective multi-vessel OPCAB between 2011 September and 2012 November were recruited, and gave written informed consent (clinical trial no. NCT01840969). One day before surgery, all subjects underwent medical interview and physical assessment including anthropometric measurements, electrocardiography, plasma and serum samplings, and blood pressure measurement. Blood pressure was measured on conventional oscillometry at the left brachial artery 5 times and averaged. Basic inclusion criteria were triple vessel disease, sinus rhythm, and LVEF ≥50%. Exclusion criteria were as follows: New York Heart Association functional class ≥3, pulmonary hypertension (defined as mean pulmonary artery pressure ≥25 mmHg), stenotic valvular disease, more than mild regurgitant valvular disease, serum creatinine ≥2.0 mg/dl, myocardial infarction within 1 week before surgery, and history of cerebral or peripheral arterial occlusive disease.

### Echocardiography

After physical assessment, transthoracic echocardiogram was done using commercially available equipment (Vivid 7; GE

Vingmed Ultrasound, Horten, Norway) in all subjects by cardiologists who were not aware of this study. LVEF was calculated from 2-D recordings using the modified Simpson's method. LV mass was calculated using Devereux's formula.[15] Left atrial volume was assessed on the prolate ellipse method and indexed by body surface area.[16] Using pulsed-wave Doppler, early mitral inflow velocity (E) was measured on apical 4-chamber view. On pulsed-wave tissue Doppler imaging of the septal mitral annulus, peak systolic velocity (Sm) and early diastolic velocity (Em) were measured from apical 4-chamber view with a 2–4-mm sample volume.

### Carotid Ultrasonography and CCA CirS

Upon arrival at the operating theatre and after 10 min of rest in the supine position, carotid ultrasonography was performed with a real-time, high-resolution, 8-MHz linear transducer (Sequoia C512; Siemens Medical Solutions USA, Mountain View, CA, USA) by 1 observer, blinded to the results of transthoracic echocardiogram. To evaluate the presence of plaque, a thorough scan of the right CCA, bulb, proximal internal and external carotid artery was done using manual delineation. Patients who had previously unknown carotid stenosis ≥50% were excluded from the current study.[17]

Optimal transverse and longitudinal images of the right CCA were obtained at approximately 1 cm proximal to the bifurcation. A cine-looped image of 1 cardiac cycle at a frame rate >20 frames/s were stored for later offline analysis. From the long-axis view, IMT of the far wall was measured at end-diastolic frame using automated edge detection (Syngo US Workplace; Siemens Medical Solutions USA). CCA CirS was obtained from digitally stored transverse images using the Syngo Velocity Vector Imaging technology (Siemens Medical Solutions USA Inc) by 2 other independent observers who were blinded to the clinical and echocardiographic data. The luminal-intimal border was traced manually from a still frame image at the end-diastolic phase, by locating 10 equidistant guiding points. The software then automatically tracked frame-to-frame movement of ultrasound reflections (speckles). The magnitude and direction of tissue velocities of 6 automatically divided segments were obtained throughout the cardiac cycle. The peak systolic deformation of the 6 segments was expressed as CirS (%) (**Figure 1**). Repeated tracing was performed for optimization of accurate border tacking. To assess the reproducibility of the measurements, analysis of the 20 random images was done twice by a single observer at a 1-month interval (for intra-observer variability). On the same 20 images, the measurements were carried out by a second observer who was blinded to the results of the first measurements (for inter-observer variability).

### Perioperative Management

After the carotid examination, all patients received standard anesthetic care, which we have described previously.[18] In brief, standard monitoring devices included transesophageal echocardiography and pulmonary artery catheter, which was connected to an analysis system (Vigilance TM; Edwards Lifesciences, Irvine, CA, USA) for continuous monitoring of cardiac index and mixed venous oxygen saturation ($SvO_2$). Anesthesia was maintained with a continuous infusion of sufentanil (0.2–0.3 $\mu g \cdot kg^{-1} \cdot h^{-1}$) with sevoflurane (0.6–2.0%). The major goal of hemodynamic management during grafting was to maintain mean arterial pressure between 70 and 80 mmHg and $SvO_2$ ≥60%. Norepinephrine was infused, if the target mean arterial pressure was not achieved despite the optimization of preload and hematocrit. Vasopressin (0.1–0.2U) was given when norepinephrine requirement exceeded 0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Milrinone was infused in the case of increase in mean pulmonary arterial pressure >30 mmHg with a development of moderate to severe mitral regurgitation and/or in the presence of persistently low $SvO_2$ (<60%) despite optimization of other determinants of cardiac output. Packed erythrocytes were transfused when hematocrit was <25%.

Surgery was performed by a single surgeon via median sternotomy. The heart was displaced using a posterior pericardial stitch and large gauze swabs. Anastomotic site was secured with a suction-type tissue stabilizer (Octopus Tissue Stabilization System®, Medtronic USA). The sequence of grafting in all patients was the left anterior descending artery (LAD) first, followed by the left circumflex coronary artery (LCx) and right coronary artery (RCA). The left internal thoracic artery was anastomosed to the LAD in all cases, while other grafts were performed using a composite graft consisting of radial artery or saphenous vein with the internal thoracic artery or proximal aorta. During grafting on the LAD and distal RCA, intracoronary shunt was used. All patients were transferred to the intensive care unit after surgery and received standardized postoperative care.

### Assessed Parameters

Assessed preoperative data included comorbidity (hypertension, diabetes, chronic kidney disease), smoking history, recent myocardial infarction (within 1 month), laboratory data, blood pressure and heart rate. Assessed transthoracic echocardiogram parameters were LVEF, left atrial volume index, LV mass, tissue Doppler imaging of septal mitral annular Sm and Em and ratio of early diastolic inflow and annular velocity (E/Em). Disease severity was assessed on proportion of patients with left main occlusion ≥70% and percent luminal narrowing of the LAD, LCx, and RCA. Assessed operative data included number of grafts performed, total graft reconstruction time, amount of infused norepinephrine during grafting, and number of patients who received milrinone during grafting. Hemodynamic variables including systolic, diastolic, and mean arterial pressure, $SvO_2$, cardiac index, systemic vascular resistance index, central venous pressure (CVP), and pulmonary capillary wedge pressure (PCWP) were recorded at 15 min after induction (baseline, T1), 10 min after stabilizer application for LAD (T2), LCx (T3), and RCA (T4) grafting, and 15 min after sternum closure (T5). The percent change in $SvO_2$ was calculated as follows: [($SvO_2$ at baseline–$SvO_2$ at LCx grafting)/$SvO_2$ at baseline]×100. Assessed postoperative data were morbidity endpoints including acute kidney injury (increase in serum creatinine >0.3 mg/dl or 50% of preoperative value), newly developed myocardial infarction (Tn-T >99th percentile upper reference limit in case of normal preoperative value; >5-fold above upper reference limit and the development of new pathological Q waves or new left bundle branch block, in case of abnormal preoperative value), permanent stroke, deep sternal wound infection, re-exploration for any reason, re-intubation due to respiratory problem, operative mortality, and composite of these outcomes.[19]

### Endpoints

First, the relationship between CCA CirS and actual hemodynamic changes during OPCAB grafting was investigated by comparing intraoperative hemodynamic variables in relation to the tertile distribution of CCA CirS. Additionally, the predictive value of CCA CirS for hemodynamic deterioration (defined as percent change in $SvO_2$ ≥20%) during mechanical heart displacement (LCx grafting) was evaluated. Second, to investigate the role of CCA CirS as a comprehensive marker of

**Table 1. Baseline Characteristics and Surgery Data**

| Variables | CCA CirS (n=96) | | | P-value |
|---|---|---|---|---|
| | 1st tertile (1.09–1.93) | 2nd tertile (1.93–2.90) | 3rd tertile (3.01–5.48) | |
| Age (years) | 67±7 | 65±9 | 61±9 | 0.010 |
| Female gender | 11 (34) | 5 (16) | 2 (6) | 0.013 |
| Body mass index (kg/m²) | 24.0±2.0 | 24.2±2.7 | 24.8±2.8 | 0.524 |
| Hypertension | 29 (91) | 21 (66) | 20 (63) | 0.021 |
| Diabetes | 13 (41) | 15 (47) | 11 (34) | 0.596 |
| Chronic kidney disease | 2 (6) | 4 (13) | 1 (3) | 0.495 |
| Recent MI | 6 (19) | 7 (22) | 4 (13) | 0.606 |
| Severity of coronary disease | | | | |
| Left main occlusion ≥70% | 5 (16) | 4 (13) | 4 (13) | 1.000 |
| % of LAD luminal narrowing | 88±12 | 82±11 | 81±14 | 0.052 |
| % of LCx luminal narrowing | 84±16 | 78±15 | 74±14 | 0.055 |
| % of RCA luminal narrowing | 84±14 | 80±17 | 76±15 | 0.107 |
| Preoperative medication | | | | |
| β-blocker | 18 (56) | 17 (53) | 17 (53) | 0.959 |
| Calcium channel blocker | 17 (53) | 13 (41) | 17 (53) | 0.513 |
| RAS blockers | 16 (50) | 17 (53) | 20 (63) | 0.578 |
| Statins | 7 (23) | 17 (53) | 21 (66) | 0.002 |
| Hematocrit (%) | 38±5 | 38±5 | 41±4 | 0.101 |
| SBP (mmHg) | 133±21 | 126±17 | 122±16 | 0.032 |
| DBP (mmHg) | 71±10 | 70±10 | 70±9 | 0.897 |
| Pulse pressure (mmHg) | 63±17 | 56±14 | 52±12 | 0.012 |
| Heart rate (beats/min) | 73±13 | 68±12 | 66±10 | 0.090 |
| Carotid IMT (mm) | 0.61 (0.53–0.82) | 0.68 (0.52–0.85) | 0.53 (0.45–0.65) | 0.012 |
| No. grafts per patient (3/4/5) | 16 (50) / 13 (41) / 3 (9) | 14 (44) / 15 (47) / 3 (9) | 18 (56) / 12 (38) / 2 (6) | 0.893 |
| Total graft reconstruction time (min) | 34±4 | 34±4 | 32±5 | 0.333 |
| Milrinone during grafting | 1 (3) | 1 (3) | 2 (6) | 1.000 |

Data given as mean±SD, median (IQR) or n (%). CCA CirS, common carotid arterial circumferential strain; DBP, diastolic blood pressure; IMT, intima-media thickness; LAD, left anterior descending artery; LCx, left circumflex artery; MI, myocardial infarction; RCA, right coronary artery; RAS, renin-angiotensin system; SBP, systolic blood pressure.

global LV function, the relationship between CCA CirS and echocardiographic parameters of LV function was assessed.

### Statistical Analysis

We determined that 96 patients would be required to detect a 4% difference in $SvO_2$ during LCx grafting among the tertile of CCA CirS with a standard deviation of 6% at an $\alpha$ level of 0.05 with 80% power.[18] For assessment of reproducibility, Bland-Altman plot and measure of interclass correlation coefficient were calculated using Medcalc Version 12.1.3 (Mariakerke, Belgium).

After Shapiro-Wilk test for normality, continuous variables among the tertiles were compared on 1-way ANOVA with Bonferroni post-hoc test or Kruskal-Wallis test with Dunn procedure as appropriate. Categorical variables were compared using the Fisher exact test or chi-squared test as appropriate. Hemodynamic data were analyzed on 1-way ANOVA for inter-group comparison and repeated measures of ANOVA for intra-group comparison with Bonferroni post-hoc test. For assessment of predictors of hemodynamic deterioration, between patients who did or did not have percent change in $SvO_2$ ≥20%, continuous variables were compared on t-test or Mann-Whitney U-test, and categorical variables were compared on Fisher exact test or chi-squared test as appropriate. Then, variables with P<0.1 were entered in univariate logistic regression analysis. After that, only variables with P<0.1 were further used in the multivariate logistic regression model. The ability of CCA CirS to discriminate between patients who did or did not have hemodynamic deterioration (percent change in $SvO_2$ ≥20%) during LCx grafting was evaluated on receiver operator characteristic (ROC) curve analysis. The optimal cut-off was defined as the point of CCA CirS providing the greatest sum of sensitivity and specificity. Assuming that relationships between variables were linear and dependent variables were normally distributed for independent variables, multiple linear regression analysis was used to determine the relationship of CCA CirS with echocardiographic parameters. In this model, age, sex, hypertension, diabetes, body mass index, systolic blood pressure, diastolic blood pressure, and heart rate were first entered as covariates. Then, presence of regional wall motion abnormality and left ventricular mass were additionally adjusted in turn.

Continuous variables are expressed as mean±SD or median (interquartile range). Categorical variables are expressed as number (%). Statistical analysis was done using SPSS version 19.0 (SPSS, Chicago, IL, USA), and P<0.05 was considered statistically significant.

## Results

One hundred patients who met the inclusion criteria had a carotid examination. In 3 of them, carotid stenosis ≥50% was newly diagnosed, and the image of an additional patient could

**Table 2. Intraoperative Hemodynamic Data**

| Hemodynamic variables in CCA CirS tertiles | T1 | T2 | T3 | T4 | T5 |
|---|---|---|---|---|---|
| Mixed venous $O_2$ saturation (%) | | | | | |
| 1st tertile | 81±4 | 74±7* | 68±8* | 71±9* | 74±6* |
| 2nd tertile | 82±6 | 77±8* | 72±9* | 75±8* | 78±7* |
| 3rd tertile | 83±6 | 79±7 | 74±8* | 76±7* | 83±6 |
| P-value (intergroup) | 0.488 | 0.035 | 0.011 | 0.048 | <0.001 |
| Cardiac index ($L \cdot min^{-1} \cdot m^{-2}$) | | | | | |
| 1st tertile | 2.6±0.4 | 2.1±0.4* | 1.6±0.3* | 1.9±0.5* | 2.3±0.3* |
| 2nd tertile | 2.6±0.3 | 2.3±0.4* | 1.8±0.3* | 2.0±0.4* | 2.4±0.3* |
| 3rd tertile | 2.6±0.4 | 2.2±0.4* | 1.8±0.4* | 2.0±0.3* | 2.3±0.3* |
| P-value (intergroup) | 0.900 | 0.149 | 0.019 | 0.428 | 0.409 |
| SVR index ($dyne \cdot s \cdot cm^{-5} \cdot m^{-2}$) | | | | | |
| 1st tertile | 2,061±433 | 2,527±609* | 2,773±483* | 2,659±646* | 2,251±296 |
| 2nd tertile | 1,978±424 | 2,299±511* | 2,520±457* | 2,361±461* | 2,144±299 |
| 3rd tertile | 1,940±316 | 2,479±559* | 2,534±482* | 2,394±483* | 2,237±293* |
| P-value (intergroup) | 0.455 | 0.243 | 0.061 | 0.056 | 0.299 |
| Systolic arterial pressure (mmHg) | | | | | |
| 1st tertile | 116±12 | 114±14 | 105±10* | 108±10 | 115±10 |
| 2nd tertile | 114±13 | 112±12 | 107±1 | 109±11 | 108±9 |
| 3rd tertile | 110±10 | 116±12 | 107±9 | 105±12 | 105±9 |
| P-value (intergroup) | 0.105 | 0.466 | 0.607 | 0.398 | <0.001 |
| Diastolic arterial pressure (mmHg) | | | | | |
| 1st tertile | 53±10 | 52±9 | 51±5 | 50±7 | 52±5 |
| 2nd tertile | 51±9 | 50±8 | 51±6 | 52±8 | 55±5 |
| 3rd tertile | 52±6 | 51±8 | 52±5 | 50±10 | 56±6 |
| P-value (intergroup) | 0.716 | 0.736 | 0.996 | 0.891 | 0.008 |
| Mean arterial pressure (mmHg) | | | | | |
| 1st tertile | 74±9 | 74±7 | 71±5 | 73±5 | 72±4 |
| 2nd tertile | 72±9 | 75±8 | 71±6 | 74±7 | 73±4 |
| 3rd tertile | 72±6 | 75±8 | 71±6 | 72±10 | 74±2 |
| P-value (intergroup) | 0.547 | 0.861 | 0.816 | 0.682 | 0.092 |
| Central venous pressure (mmHg) | | | | | |
| 1st tertile | 9±2 | 11±2* | 17±3* | 15±3* | 10±2 |
| 2nd tertile | 9±2 | 12±2* | 16±3* | 15±3* | 10±3 |
| 3rd tertile | 9±3 | 11±2* | 16±3* | 15±3* | 9±2 |
| P-value (intergroup) | 0.897 | 0.375 | 0.669 | 0.727 | 0.298 |
| PCWP (mmHg) | | | | | |
| 1st tertile | 13±3 | 15±3* | 20±4* | 18±4* | 14±2 |
| 2nd tertile | 13±3 | 15±2* | 19±3* | 18±3* | 13±2 |
| 3rd tertile | 13±3 | 15±3* | 19±4* | 18±4* | 13±3 |
| P-value (intergroup) | 0.661 | 0.747 | 0.682 | 0.587 | 0.068 |
| Norepinephrine during grafting ($\mu g$) | | | | | |
| 1st tertile | 3.0 (0–10.4) | 26.0 (9.3–68.5) | 82.1 (25.1–136.9) | 37.5 (12.8–37.5) | 12.5 (0–23.1) |
| 2nd tertile | 4.8 (0–13.0) | 28.2 (2.6–58.4) | 71.4 (19.9–120.5) | 42.4 (11.6–69.2) | 14.7 (0–32.3) |
| 3rd tertile | 7.7 (0–10.4) | 12.8 (1.3–28.2) | 50.7 (29.4–68.6) | 22.5 (10.4–36.0) | 13.0 (0–17.8) |
| P-value (intergroup) | 0.429 | 0.033 | 0.1 | 0.106 | 0.583 |
| Vasopressin during grafting | | | | | |
| 1st tertile | 5 (16) | 5 (16) | 11 (66) | 5 (16) | 1 (3) |
| 2nd tertile | 5 (16) | 0 (0) | 5 (16) | 5 (16) | 1 (3) |
| 3rd tertile | 4 (13) | 0 (0) | 3 (9) | 2 (6) | 1 (3) |
| P-value (intergroup) | 1.000 | 0.01 | 0.033 | 0.473 | 1.000 |

Data given as mean±SD, median (IQR) or n (%). All the hemodynamic variables except vasopressor requirement at T2–T5 were compared with T1 (intra-group comparison), and corrected P<0.05 was considered statistically significant (marked as *). PCWP, pulmonary capillary wedge pressure; SVR, systemic vascular resistance; T1, 15 min after induction; T2, 10 min after stabilizer application for left anterior descending artery; T3, 10 min after stabilizer application for left circumflex artery; T4, 10 min after stabilizer application for right coronary artery; T5, 15 min after sternum closure. Other abbreviation as in Table 1.

**Table 3. Thirty-Day Morbidity Endpoints**

| Variables | CCA CirS (n=96) | | | |
|---|---|---|---|---|
| | 1st tertile (1.09–1.93) | 2nd tertile (1.93–2.90) | 3rd tertile (3.01–5.48) | P-value |
| AKI | 13 (41) | 7 (22) | 6 (19) | 0.104 |
| AMI | 9 (28) | 4 (13) | 4 (13) | 0.177 |
| Permanent stroke | 0 (0) | 0 (0) | 0 (0) | 1.000 |
| Deep sternal wound infection | 1 (3) | 1 (3) | 2 (6) | 1.000 |
| Reoperation due to any reason | 1 (3) | 0 (0) | 0 (0) | 1.000 |
| Re-intubation | 1 (3) | 0 (0) | 0 (0) | 1.000 |
| Operative mortality | 0 (0) | 1 (3) | 0 (0) | 1.000 |
| Composite of morbidity endpoints | 20 (63) | 9 (28) | 7 (22) | 0.001 |

Data given as n (%). AKI defined as >0.3 mg/dl or 50% increase in serum creatinine from preoperative value. AMI defined as follows: Tn-T >99th percentile upper range limit, if preoperative TnT is within normal range. New onset left bundle branch block, CK-MB >5-fold upper reference limit, graft occlusion on angio-CT, if the preoperative TnT is over normal range. AKI, acute kidney injury; AMI, acute myocardial infarction. Other abbreviation as in Table 1.

**Table 4. Predictors of Hemodynamic Deterioration During LCx Grafting**

| Variables | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | OR (95% CI) | P-value | OR (95% CI) | P-value |
| Female gender | 3.50 (1.13–10.83) | 0.030 | 1.87 (0.52–6.82) | 0.341 |
| Diabetes | 1.94 (0.71–5.36) | 0.198 | | |
| Recent MI | 2.50 (0.79–7.87) | 0.117 | | |
| Sm | 0.75 (0.51–1.09) | 0.127 | | |
| E/Em | 1.22 (1.08–1.39) | 0.001 | 1.11 (0.95–1.30) | 0.206 |
| Hematocrit | 0.93 (0.84–1.02) | 0.133 | | |
| Pulse pressure | 1.05 (1.01–1.09) | 0.022 | 1.05 (1.00–1.10) | 0.062 |
| CirS | 0.27 (0.11–0.68) | 0.006 | 0.32 (0.12–0.90) | 0.031 |

Hemodynamic deterioration was defined as significant decrease (percent change ≥20% from baseline) in mixed venous $O_2$ saturation. CI, confidence interval; CirS, circumferential strain; E/Em, ratio of early diastolic inflow and annular velocity; OR, odds ratio. Other abbreviations as in Table 1.

not be analyzed due to ill-defined luminal-intimal border. None of the patients required insertion of intra-aortic balloon pump or emergency conversion to an on-pump procedure. Accordingly, data of the remaining 96 patients were included in the final analysis. The results of Bland-Altman analysis are as follows. The mean differences were 0.41% (95% confidence interval [95% CI]: –0.30 to 1.10%) for the same observer, and 0.31% (95% CI: –0.17 to 0.80%) for different observers. Intra-observer interclass correlation coefficient was 0.95 (95% CI: 0.53– 0.99) and inter-observer interclass correlation coefficient was 0.90 (95% CI: 0.76–0.96).

Patient characteristics and operative data according to tertile distribution of CCA CirS are summarized in Table 1. Patients in the first tertile were significantly older than those in the third tertile (P=0.008). Significantly more patients in the first tertile were female and had a history of hypertension compared to those in the second and third tertiles. Also, fewer patients in the first tertile had been taking statins compared to those in the higher tertiles. Pulse pressure in the first tertile were significantly higher than in the third tertile (P=0.009). Mean IMT measured at CCA in the first and second tertiles was larger than that in the third tertile (P=0.012 and 0.009, respectively). The number of grafts performed, graft reconstruction time, and the number of patients requiring milrinone during grafting were similar among the tertiles.

The hemodynamic data and vasopressor requirements during surgery are listed in Table 2. The baseline hemodynamic variables at T1 were not different among the groups. $SvO_2$ was significantly different among the tertiles at T2 (first tertile vs. third tertile, P=0.036), T3 (first tertile vs. third tertile, P=0.012), and T5 (first tertile vs. second and third tertile, P=0.027 and <0.001, respectively). When compared to its corresponding baseline value (T1), $SvO_2$ was decreased significantly during grafting (T2, T3, T4) in the first and second tertiles, and it did not return to its baseline value after sternum closure (T5). SvO2 in the third tertile was decreased at T3 and T4, but it was restored at T5 to its baseline value. Cardiac index was significantly lower in the first tertile than third tertile at T3 (P=0.036). When compared to its corresponding baseline value, cardiac index was significantly decreased during grafting (T2, T3, T4) and did not return to its baseline value after completion of surgery in all tertiles. CVP showed no significant intergroup differences among the tertiles, while it was increased during grafting (T2, T3, T4) in all tertiles compared to the corresponding baseline value. PCWP also showed no significant intergroup differences among the tertiles, while it was increased during grafting (T2, T3, T4) in all tertiles compared to the corresponding baseline value. Amount of norepinephrine required during LAD grafting (T2) was significantly larger in the first tertile than third tertile (P=0.008). Also, the number of patients who required vasopressin during LAD and LCx grafting (T2, T3) was significantly greater in the first tertile than in the second and third tertiles.

Among the 30-day postoperative morbidity endpoints, the incidence of composite of morbidity endpoints was significantly higher in the first tertile (Table 3).

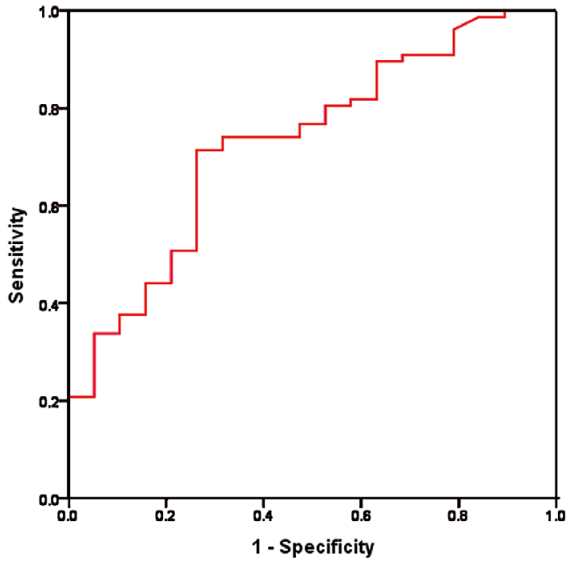


**Figure 2.** Receiver operator characteristic curve of the common carotid artery circumferential strain for hemodynamic deterioration during left circumflex artery grafting. Area under the curve was 0.730 and P=0.002, 95% confidence interval: 0.608–0.852. The optimal cut-off for hemodynamic deterioration was 2.016 (%) with a sensitivity and specificity of 71.4% and 73.7%, respectively.

On univariate logistic regression analysis to identify predictors of hemodynamic deterioration during LCx grafting, sex, E/Em, pulse pressure, and CCA CirS were significant (P<0.1). On multivariate analysis of these variables, only CCA CirS remained as an independent predictor (Table 4).

On ROC curve analysis, CCA CirS had an area under the curve of 0.730 (95% CI: 0.608–0.852, P=0.002). The optimal cut-off value for predicting hemodynamic deterioration was 2.016 (%) with a sensitivity and specificity of 71.4% and 73.7%, respectively (Figure 2).

CCA CirS and echocardiographic variables are listed in Table 5. CCA CirS was associated with Sm, Em, and E/Em with adjustment for age, sex, body mass index, hypertension, diabetes, blood pressure and heart rate measured at carotid examination. This association remained after additional adjustment for regional wall motion abnormality. After LV mass was added as a covariate, an association of CCA CirS with Em and E/Em was still present, but it was lost for Sm. LVEF was shown to be positively associated with CCA CirS after addition of regional wall motion abnormality as a covariate, but this was not seen before adjustment for it.

## Discussion

This prospective, observational study has shown that CCA CirS is superior to any other parameters of LV function in terms of prediction for actual hemodynamic deterioration in patients undergoing OPCAB. Moreover, a strong and consistent association was found, of CCA CirS with echocardiographic parameters reflecting LV systolic and diastolic function independent of known cardiovascular risk factors in CAD patients with preserved LVEF.

The influence of arterial stiffness on long-term cardiovascular outcome has been well elucidated in various subsets of patients,[20,21] while evidence regarding its clinical impact in surgical patients is scarce. Arterial stiffening is a comprehensive conceptual disease entity including an interaction between the heart and vasculature. In patients with reduced vascular compliance, net cardiovascular performance may not be solely dependent on the associated ventricular dysfunction per se, but rather on their interaction with each other. A tandem increase in ventricular stiffness combined with vascular stiffening may maintain effective cardiovascular performance at rest.[22] LV systolic stiffening, however, blunts contractile reserve, elevates cardiac metabolic demand, and causes diastolic function to deteriorate.[23] These subclinical abnormalities in ventricular function and limited reserve in myocardial performance present in patients with increased arterial stiffness may become evident under stressful conditions and yield a very poor prognosis.

In the same context, an extreme hemodynamic perturbation during OPCAB grafting is among the most critical situations that may require the maximum use of contractile reserve. During OPCAB grafting, transient impairment of cardiac function invariably occurs in various degrees mainly due to both systolic and diastolic dysfunction elicited by mechanical heart

**Table 5. CCA CirS and Echocardiographic Variables**

| | LVEF | Sm | Em | E/Em |
|---|---|---|---|---|
| Model I | | | | |
| $\beta$ (SE) | 2.49 (1.40) | 0.42 (0.21) | 0.51 (0.19) | −1.083 (0.5253) |
| P-value | 0.079 | 0.047 | 0.011 | 0.042 |
| $R^2$ of model | 0.122 | 0.174 | 0.289 | 0.220 |
| Model II | | | | |
| $\beta$ (SE) | 2.17 (0.98) | 0.43 (0.21) | 0.49 (0.19) | −1.08 (0.53) |
| P-value | 0.029 | 0.041 | 0.012 | 0.044 |
| $R^2$ of model | 0.577 | 0.201 | 0.314 | 0.221 |
| Model III | | | | |
| $\beta$ (SE) | 2.63 (1.00) | 0.41 (0.21) | 0.49 (0.20) | −1.24 (0.56) |
| P-value | 0.010 | 0.057 | 0.019 | 0.029 |
| $R^2$ of model | 0.618 | 0.220 | 0.357 | 0.266 |

Model I, age, sex, body mass index, hypertension, diabetes, SBP, DBP, and heart rate included as covariates; model II, presence of regional wall motion abnormalities was added to model I; model III, left ventricular mass was added to model II. Em, early diastolic mitral annular velocity; LVEF, left ventricular ejection fraction; Sm, peak systolic mitral annular velocity. Other abbreviations as in Table 1.

displacement.[1] In rare instances, an unacceptable condition requiring emergency on-pump conversion does occur, which increases perioperative morbidity and mortality.[3] Even if the surgery was completed successfully on a beating heart, significant hemodynamic instability during grafting tends to remain until the end of the surgery and leads to adverse postoperative consequences.[18,24] Several studies have been conducted to identify the risk factors, but none of these introduced a marker of vascular stiffening, which may reflect global myocardial performance.[18,24]

During OPCAB surgery in the present study, lower CCA CirS was an independent predictor of significant decrease in $SvO_2$, indicative of marked imbalance of global oxygen supply and demand.[25] Patients with lower CCA CirS should have had a relatively matched increase in arterial and ventricular stiffness, yet failed to augment pump efficiency to cope with extreme hemodynamic perturbation during the period of mechanical heart displacement. In terms of postoperative morbidity, patients with lower CCA CirS had a higher incidence of composite of 30-day morbidity endpoints. Of note, the decrease in cardiac index and $SvO_2$ persisted until the end of the surgery in patients with lower CCA CirS. Similar findings had been observed in patients with elevated filling pressure and diastolic dysfunction as assessed on preoperative E/Em,[18] which proved to be of prognostic importance in patients undergoing OPCAB.[26] But it is beyond the scope of this study to clarify the association of CCA CirS with persisting hemodynamic consequence and outcome, which merits further investigation with a larger sample size.

Strain is the percentage of spatial deformation relative to the original size, and CCA CirS using speckle tracking ultrasound that we tested in the present study has been validated as a reliable index of stiffness in diverse systemic arteriopathies.[27,28] The biggest benefit of CCA CirS is that assessment of the carotid artery has a great advantage for determination of vascular stiffening, based on its relative proximity to the heart and close interaction with cardiac performance, greater tendency for atheroma formation, and accessibility for ultrasonography.[12] Moreover, the superiority of CCA CirS, over carotid IMT and conventional measures of local stiffness of the carotid artery including elastic modulus, distensibility coefficient or $\beta$ stiffness index, as a diagnostic tool, has been reported.[11,14]

Another important finding of the present study is that CCA CirS is a comprehensive marker of global LV function in patients undergoing OPCAB surgery. Lower CCA CirS was related to compromised early phase relaxation (represented by Em) and increased filling pressure (represented by E/Em) of the LV. This relationship remained after adjustment of the LV mass, although myocardial hypertrophy is the main pathological process connecting arterial stiffening to diastolic dysfunction.[29] This supports the hypothesis that the heart responds to stiffened artery by a tandem increase in diastolic ventricular stiffness, regardless of the development of LV hypertrophy.[30] With regard to LV systolic function, CCA CirS was positively correlated with Sm, suggesting that subclinical LV contractile dysfunction may already be present in patients with preserved LVEF (>50%) when CCA CirS is decreased. Given the possible impact of regional wall motion abnormality, which is a common manifestation of CAD but which had not been considered before, we added it as a covariate. A positive relationship between CCA CirS and LVEF was then obtained despite the truncation of the distribution of LVEF at 50% on its lower side, which was reported to disturb the relationship in a previous study.[31]

There are limitations in this study. First, regarding the measurement of CCA CirS, we used the average of global wall strain without consideration of possible heterogeneity of local pressure applied by any transducer that may have existed. But it might not directly affect the results given that a previous study conducted on healthy subjects showed that segmental variation in CCA CirS was not significant.[32] Second, hemodynamic deterioration during grafting may also be a consequence of regional ischemia imposed by transient coronary hemostasis, which could confound the observed results. The influence of ischemic insult on the degree of hemodynamic deterioration, however, is usually subclinical and difficult to assess separately. Considering that all surgical procedures were performed by a single surgical team on patients with similar severity of CAD, and that changes in CVP and PCWP, which also partly reflect the degree of mechanical heart displacement, were similar without intergroup differences, we can only assume that the surgical loading on the heart during grafting was similar among the tertiles.

## Conclusions

The current study provides primary evidence regarding the role of CCA CirS, a novel indicator of arterial stiffness, as a sophisticated marker reflecting global LV function and a predictor for actual hemodynamic deterioration during OPCAB surgery in patients with preserved LVEF. Measurement of CCA CirS may allow integrated assessment of cardiac and vascular status in a highly feasible, reproducible, and simple manner, and provide more accurate risk stratification in CAD patients requiring surgical revascularization.

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