Original Article

Low Systemic Vascular Resistance State Following Off-Pump Coronary Artery Bypass Grafting

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Objective: To determine the prevalence, hemodynamic characteristics, and risk factors for low systemic vascular resistance (SVR) state following after off-pump coronary artery bypass (OPCAB).
Patients and Methods: SVR data could be obtained for 116 OPCAB patients. Low SVR was defined as an indexed systemic vascular resistance (SVRi) of <1,800 dyne·s/cm^5·m^2 at the end of operation. Hemodynamic data were recorded preoperatively, at the end of operation, just after entering ICU, and the following morning.
Results: Low SVR state was noted in 54 of 116 patients (53%). The SVRi values in low-SVR and non–low-SVR patients were 1,406±253 and 2,326±509 dyne·s/cm^5·m^2 at the end of operation (*p*<0.0001). Increased CI level, decreased MAP level, but unchanged CVP level was observed postoperatively in the low-SVR patients. The increase in CI and decrease in MAP were maximal at the end of operation. Patients with low SVR were more likely to have a higher body mass index (24.5±3.6 vs. 22.9±2.9; *p*=0.013) and to be male (82% vs. 62%; *p*=0.036) than no–low-SVR patients. In low-SVR patients, fluid balance was more positive intraoperatively (3,537±1,411 vs. 3,068±1,597; *p*=0.09), but more negative at 6 hours postoperatively (–136±978 vs. 234±844; *p*=0.034) and 12 h postoperatively (–282±1,321 vs. 268±1,238; *p*=0.024).
Conclusions: Low SVR state, a probable manifestation of systemic inflammatory response (SIRS), is common in patients who have undergone OPCAB. For these patients it is more reasonable to maintain MAP with vasopressors by restoring vascular tone, than by volume loading. (Ann Thorac Cardiovasc Surg 2008; 14: 15–21)

Key words: off-pump, coronary artery bypass grafting, hemodynamics

Introduction

Performance of off-pump coronary artery bypass grafting (OPCAB) has come to be widely accepted in the past decade.[1–8] Many previous studies have disclosed the equivalent quality of OPCAB to conventional coronary artery bypass grafting, which is performed with cardiopulmonary bypass (CPB).[9,10] One of the most important advantages of OPCAB is its reduction of systemic inflammatory response to CPB.[11–14]

The systemic inflammatory response syndrome (SIRS) commonly occurs after cardiac surgery.[15] The most important characteristic of SIRS is decrease in vascular tone, which presents as a decrease in systemic vascular resistance (SVR) clinically.[16]

Many previous studies have revealed that the clinical instability caused by SIRS is result of post-perfusion syndrome. However, even in the OPCAB era, we have encountered some patients who exhibit low SVR in the early postoperative stage. This suggests the possibility that some

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type of inflammatory cascade occurs even after OPCAB. However no previous studies have noted a low SVR state in the patients who have undergone OPCAB.

The aim of the present study was to evaluate the prevalence, background factors, hemodynamic characteristics, and risk factors for a low SVR state in patients who have undergone OPCAB.

Patients and Methods

One hundred fifty consecutive patients underwent OPCAB between January 2000 and May 2006 in our institution. Of these, 116 patients, for whom SVR could be calculated using the pulmonary artery flotation catheter, were included in this study.

The mean age was 66.6±9.7 years and 74.2% (*n*=86) of the patients were male. The mean duration of follow-up was 28±16 months. All preoperative medications, including beta blockers, angiotensin receptor blockers (ARB), angiotensin-converting enzyme (ACE) inhibitors, and calcium antagonists, were continued up to the day of operation, with the exception of non-steroidal anti-inflammatory drugs, which were discontinued one week before surgery, and Digoxin, which was discontinued 3 days before surgery.

All the operations were performed without CPB. Heparin 1.5 mg/kg was administered, and ACT (anticoagulation time) was maintained above 200 s. Anesthetic techniques and medications were similar in all patients. Anesthesia was induced with fentanyl, propofol, and neuromuscular paralytic drugs, and maintained with total intravenous anesthesia using the same drugs. All the operations were performed by median sternotomy. We prefer multiple and complete coronary revascularization with composite or sequential grafting, and prefer *in situ* arterial grafts, in particular. We used a cell saver device for all the patients but did not use anti-fibrinolytic drugs throughout the operation. To prevent arterial spasm, continuous intravenous infusion of Diltiazem (0.5–1.0 μg/kg) or Nicardipine (0.1–0.2 μg) was used intraoperatively and during the first 16 h after the operation. Diltiazem (100 mg/day) or Amlodipine (2.5–5.0 mg/day) was then administered orally together with aspirin (81 mg/day), beginning the following morning.

For each patient, we recorded CI (cardiac index), MAP (mean arterial pressure), central venous pressure (CVP) and core body temperature. A pulmonary artery flotation catheter was inserted just before surgery. CI was measured using the thermodilution technique with the pulmonary artery flotation catheter. MAP was monitored by a radial arterial catheter inserted preoperatively. CVP was obtained using the proximal port of the pulmonary artery flotation catheter. Core body temperature was obtained from the thermometer at the tip of the pulmonary artery flotation catheter. These values were collected preoperatively, at the end of operation, just after entering the ICU, and the following morning. Indexed systemic vascular resistance (SVRi) was calculated at each of these times using the following equation: SVRi = (MAP–CVP) × 80/CI. In this study, low SVR was defined as an SVRi of <1,800 dyne·s/cm^5·m^2 at the end of operation.

Baseline demographic and clinical data were available for all patients. Initial data were collected from case notes. We recorded the following preoperative variables: gender, age, body mass index (BMI), preoperative ejection fraction, use of angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, β blockers, calcium blockers, or Digoxin, and the presence of diabetes mellitus, hypertension, hyperlipidemia, chronic renal failure, cerebrovascular disease, chronic obstructive pulmonary disease, and severe mitral regurgitation. We also recorded echocardiographic data obtained both preoperative and postoperatively. Preoperative and postoperative ejection fraction were measured by angiography.

We recorded the following intraoperative variables: operative time, number of anastomoses, performance of blood transfusion, and the use of bilateral internal thoracic arteries. We also noted the duration of postoperative use of an inotropic agent (dopamine) and a vasopressor (noradrenalin). We measured fluid balance intraoperatively as well as 6 and 12 h postoperatively, as well as length of postoperative stay. The incidences of atrial fibrillation, wound dehiscence, postoperative respiratory dysfunction, late incidence of heart failure, and late death were determined as well.

Institutional approval for this study was obtained and each patient within the study gave informed consent to serve as a subject.

Statistical methods

All data were reviewed retrospectively. Values of all continuous variables are expressed as mean ± SD. Differences between the two patient groups were tested with univariate analysis (the χ^2 test, the two-tailed *t* test, and the Mann-Whitney U test, as appropriate). Values of $p<0.05$ were considered significant.

Results

According to our criteria, a postoperative low SVR state occurred in 54 of 116 patients (46.8%) Overall mean values for SVRi, MAP, CI, CVP, and core body temperature are shown in Table 1. Figure 1 shows the changes in SVRi. Preoperatively, SVRi was similar in low and non–low-SVR patients. SVRi was significantly lower in low-SVR patients (1,406±253 dyne·s/cm^5·m^2) than in non–low-SVR patients (2,326±509 dyne·s/cm^5·m^2) at the end of operation (p=0.0001). This difference between groups persisted until entering the ICU (2,420±520 vs. 1,476±243 dyne·s/cm^5·m^2; p=0.0001) but gradually decreased by postoperative day 1 (2,337±570 vs. 2,094±488 dyne·s/cm^5·m^2; p=0.021). The decrease from preoperative state to the end of operation was significantly greater in low-SVR patients than in non–low-SVR patients. The nadir of SVRi was observed at the end of operation in both groups.

Figures 2, 3, and 4 show the changes in mean CI, MAP, and CVP, respectively.

CI was significantly higher in low-SVR patients (3.91±0.76 L/min/m^2) than in non–low-SVR patients (2.64±0.44 L/min/m^2) at the end of operation (p=0.0001). Similarly, MAP was significantly lower in low-SVR patients (75.9±4.7 mmHg) than non–low-SVR patients (81.5±11.9 mmHg), and CVP was significantly higher in low-SVR patients (7.9±3.5 mmHg) than non–low-SVR patients (p=0.045, p=0.045). The changes in core body temperature are displayed in Fig. 5. There was no difference in this variable between groups or across time points.

Preoperative, intraoperative, and postoperative data are displayed in Tables 2, 3, and 4, respectively. The low-SVR patients were more likely to be male (p=0.036) and had a higher body mass index (BMI) (p=0.014). Age at operation did not differ between the low-SVR and non–low-SVR groups (p=0.26). Operative time did not differ significantly different the groups (p=0.7816).

In examination of fluid balance, input volume did not differ between groups intraoperatively but was significantly greater in low-SVR than in non–low-SVR patients 6 h (1,047±426 vs. 1,245±488; p=0.023) and 12 h postoperatively (1,842±544 vs. 2,071±692; p=0.047). Net fluid balance was slightly more positive intraoperatively in low-SVR patients (3,537±1,411) than in non–low-SVR patients (3,068±1,597) (p=0.10). On the other hand, net fluid balance was more negative in the low-SVR group 6 h postoperatively (–136±978 vs. 234±844; p=0.034) and 12 h postoperatively (–282±1,321 vs. 268±1,238; p=0.025). The duration of postoperative usage of dopamine was slightly longer in non–low-SVR patients (p=0.10), while that of noradrenaline was slightly shorter in non–low-SVR patients (p=0.40).

The incidence of neither atrial fibrillation (p=0.23) nor wound dehiscence (p=0.99) differed between the groups. Postoperative stay was slightly shorter in the low-SVR

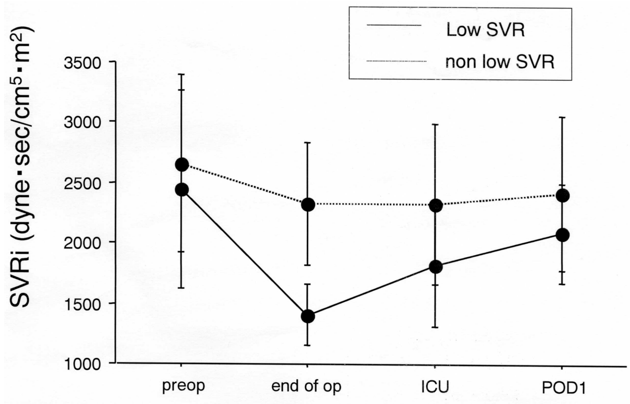

Fig. 1. Changes in SVRi.

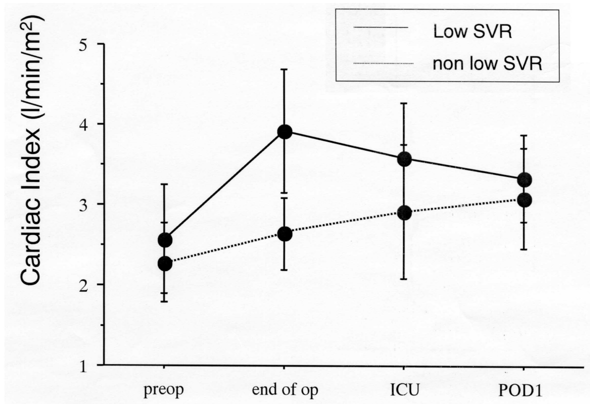

Fig. 2. Changes in CI.

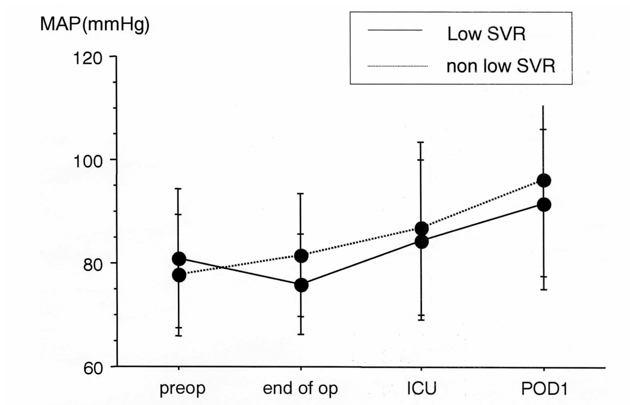

Fig. 3. Changes in MAP.

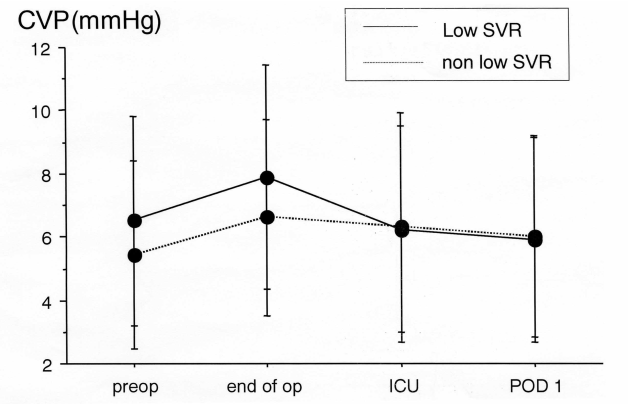

Fig. 4. Changes in CVP.

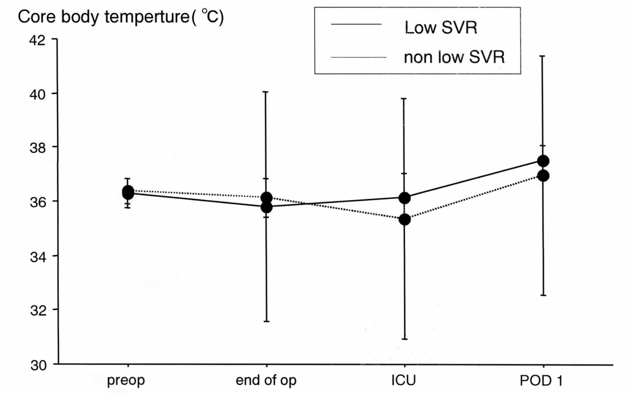

Fig. 5. Changes in core body temperature.

group (p=0.09). Respiratory dysfunction occurred in one low-SVR patient (1.6%), and 3 (4.9%) non–low-SVR patients (p=0.25). During follow-up, major adverse cardiac events occurred in 2 patients (3.7%) in the low-SVR group and 3 patients (4.9%) in the non–low-SVR group (p=0.99). Late cardiac death occurred in only one patient of the low-SVR patients group.

Discussion

Previous studies reported that cardiac surgery using CPB sometimes causes low SVR state due to SIRS-like phenomenon.[16] The present study revealed that a low SVR state is common in the early postoperative period, even in patients who have undergone coronary artery bypass grafting without CPB.

A definition of SIRS was proposed by the members of the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) consensus conference as a condition meeting two or more of the following criteria[17]: (i) temperature greater than 38°C or less than 36°C; (ii) heart rate greater than 90 beats per min; (iii) respiratory rate greater than 20 per min or $PaCO_2$ less than 32 Torr; and (iv) white blood cell count greater than 12,000 or less than 4,000 cells/mm^2 or including more than 10% bands. It is not appropriate to apply these criteria to our study group, since in the early postoperative period, all patients had ventilator assistance. Therefore, conclusions regarding the presence of SIRS in the present study can be no more than speculative. Notably, as Pittet et al. reported, it is possible that almost every patient in the surgical ICU has SIRS.[18] They also concluded that, because of its poor specificity, SIRS is not helping predicting outcome, including mortality and morbidity. Similarly, we found that the postoperative stay of low-SVR patients was shorter than that of non–low-SVR patients, and that there were no differences between groups in incidence of other postoperative complications.

The hemodynamic definition of low-SVR state is difficult to clearly determine. We used a criterion of SVRi <1,800 dyne·s/cm^5·m^2 to identify patients with low-SVR in accordance with the report by Kristof and Magder.[16] This value is equal to two standard deviations SD below the mean in the published normal reference range.[15] It is clearly necessary to determining the presence of SIRS to measure subsets of mediators or component factors. As Bone described previously, even if cytokine levels are elevated, systemic cytokine release can occur in a variety of disorders without producing organ dysfunction.[19]

In our study, low SVR state was predominantly observed in male patients. This result is the same as reported by Kristof for patients undergoing CPB. We also found that patients with higher BMI were more likely to exhibit a low SVR.

In this study, we hypothesized that low SVR patients with a high CI and low MAP exist even among OPCAB patients. We also examined differences between groups in perioperative characteristics including fluid balance and vasopressor usage and outcome. Basically in patients with postoperative hemodynamic instability, dopamine and adequate fluid administration were performed first, and noradrenaline was used to ensure that MAP remained above 50 mmHg. In this study, compared with non–low-SVR patients, low SVR patients had more positive fluid balance intraoperatively but more negative postoperative phase fluid balance. In addition, the duration of noradrenaline administration was significantly longer for low-SVR than for non–low-SVR patients. This difference in postoperative characteristics is theoretically reasonable, since low SVR can be stabilized by vasopressors but not

Table 1. Hemodynamic variables

	Non–low-SVR	Low-SVR	*p* value
Preoperative SVRi	2,656±733	2,450±819	0.16
Preoperative CI	2.27±0.49	2.57±0.66	0.0087
Preoperative MAP	77.7±11.6	80.8±13.4	0.20
Preoperative CVP	5.45±2.95	6.50±3.30	0.077
SVRi (end of op)	2,326±509	1,406±253	0.0001
CI (end of op)	2.64±0.44	3.91±0.76	0.0001
MAP (end of op)	81.5±11.9	75.9±9.7	0.0059
CVP (end of op)	6.6±3.1	7.9±3.5	0.045
SVRi (ICU)	2,330±664	1,816±499	0.0001
CI (ICU)	2.92±0.83	3.57±0.69	0.0001
MAP (ICU)	86.7±16.6	84.5±15.5	0.47
CVP (ICU)	6.3±3.6	6.2±3.2	0.90
SVRi (POD 1)	2,420±638	2,090±409	0.0012
CI (POD 1)	3.07±0.63	3.33±0.53	0.022
MAP (POD 1)	96.2±21.1	91.5±14.2	0.16
CVP (POD 1)	6.0±3.2	5.9±3.2	0.85

SVRi, indexed systemic vascular resistance; CI, cardiac index; MAP, mean artery pressure; CVP, central venous pressure; POD 1, postoperative day 1.

Table 2. Preoperative variable

	Non–low-SVR	Low-SVR	*p* value
Male (%)	35 (64.8%)	51 (82.2%)	0.036
Age (years)	67.6±9.7	65.6±9.5	0.26
Preoperative EF (%)	51.7±14.4	55.7±13.3	0.14
Body mass index	22.9±2.9	24.5±3.6	0.014
NYHA	2.35±0.93	2.33±0.80	0.93
Use of ARB (%)	12 (22%)	18 (29%)	0.11
Use of ACE inhibitors (%)	12 (22%)	11 (18%)	0.64
Use of beta blockers (%)	26 (48%)	31 (50%)	0.85
Use of Ca blockers (%)	21 (39%)	27 (44%)	0.58
Use of Digoxin (%)	4 (7%)	1 (1.6%)	0.19
Diabetes mellitus (%)	32 (59%)	35 (56%)	0.85
Hypertension (%)	31 (57%)	40 (65%)	0.45
Hyperlipidemia (%)	29 (54%)	37 (60%)	0.58
Chronic renal failure (%)	6 (11%)	6 (9.7%)	0.99
Cerebral vascular disease (%)	8 (15%)	7 (11%)	0.59
COPD (%)	3 (5.6%)	1 (1.6%)	0.34
Severe mitral regurgitation (%)	3 (5.6%)	3 (4.8%)	0.99

EF, ejection fraction; ARB, angiotensin receptor blocker; ACE, angiotensin converting enzyme; COPD, chronic obstructive pulmonary disease.

Table 3. Intraoperative variables

	Non–low-SVR	Low-SVR	*p* value
Operative time	359±86	354±101	0.78
Number of anastomoses	2.57±0.92	2.62±0.83	0.73
Blood transfusion	42 (78%)	33 (54%)	0.27
Use of bilateral ITA	40 (74%)	49 (79%)	0.66
Preoperative use of IABP	7 (13%)	11 (18%)	0.073

ITA, internal thoracic artery; IABP, intra-aortic balloon pump.

Table 4. Postoperative variables

	Non–low-SVR	Low-SVR	*p* value
Duration of postoperative use of dopamine	13.6±16.9	9.28±10.5	0.095
Duration of postoperative use of noradrenalin	1.01±3.2	1.87±6.8	0.41
Postoperative EF (%)	55.2±13.3	58.1±13.3	0.31
Postoperative stay (days)	25.0±9.6	22.3±6.9	0.09
Postoperative atrial fibrillation (%)	14 (26%)	23 (37%)	0.23
Wound dehiscence (%)	3 (5.6%)	4 (6.5%)	0.99
Early postoperative LOS (%)	0	1 (1.6%)	0.99
Early postoperative respiratory dysfunction (%)	0	3 (4.8%)	0.25
Hospital death (%)	0	1 (1.6%)	0.99
Late cardiac death (%)	1 (1.9%)	0	0.47
MACE during follow-up (%)	2 (3.7%)	3 (4.8%)	0.99

EF, ejection fraction; LOS, low output syndrome; MACE, major adverse cardiac event.

Table 5. In-out volumes and net volume balances

	Non–low-SVR	Low-SVR	*p* value
Intraoperative input	4,451±1,804	4,772±1,384	0.28
Intraoperative blood transfusion	845±824	610±807	0.13
Intraoperative urine output	1,061±715	842±524	0.06
Intraoperative bleeding	1,168±721	993±804	0.22
Intraoperative balance	3,068±1,597	3,537±1,411	0.10
Input (6 h after op)	1,245±488	1,047±426	0.023
Blood transfusion (6 h after op)	333±395	228±455	0.20
Urine output (6 h after op)	1,054±567	1,129±540	0.47
Bleeding (6 h after op)	289±174	283±286	0.89
Balance (6 h after op)	234±844	–136±978	0.034
Input (12 h after op)	2,071±692	1,842±514	0.047
Blood transfusion (12 h after op)	463±624	283±600	0.12
Urine output (12 h after op)	1,818±883	1,908±785	0.56
Bleeding (12 h after op)	447±258	499±515	0.51
Balance (12 h after op)	268±1,238	–282±1,321	0.025

by fluid loading.

Limitations

We examined a small number of patients in only a single institution, and in retrospective fashion. In addition, we did not measure cytokine levels, and were unable to definitively give a diagnosis of SIRS.

Conclusions

Low SVR state, a probable manifestation of SIRS, is common in patients who have undergone OPCAB. For patients with a low SVR, it is more reasonable to maintain MAP with vasopressors in order to restore vascular tone, than to perform volume loading.

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