

The Effects of Different Type Vasodilator Agents on Radial Artery Blood Flow: A Placebo-Controlled Clinical Study

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Abstract

Background: The radial artery (RA) is being used as a second arterial conduit in coronary artery bypass grafting (CABG) patients. Vasospasm during the harvesting is the most common problem, yet. Our goal of this research is to evaluate the effects of different vasodilators on RA blood flow. **Material and Method:** In our 250 CABG patients who were included into the study, patients were divided into five groups which have the same number of the patients. Before the harvesting of the RA, Allen test and modified Allen test were performed. In group 1, sodium nitroprusside (SNP) was administered via central line. In group 2, nitroglycerine was applied as a vasodilator agent. In group 3, diltiazem as a calcium channel blocker was used. In group 4, dobutamine was used with a dose of 3micro./kg/min. In the remaining patients, as a control group (CG), normal saline solution was used with the same protocol. RA length and radial artery flow, mean arterial blood pressure, central venous pressure, and heart rate were measured before and 10 minutes after drug administration. **Results:** No significant differences were found between the groups in respect to age, body surface area, cardiopulmonary bypass time, aortic cross clamp time. A multivariate general linear model was created and revealed the drug (specifically SNP and nitroglycerin) as a predictor to increase flow in the radial artery ($p = 0.001$ and $p = 0.002$), respectively. SNP has significantly decreased mean arterial pressure when we compared to nitroglycerin ($p < 0.001$). The blood flows of RA after dobutamine and calcium channel blocker administration has not changed significantly ($p > 0.05$). **Conclusions:** Our study showed that SNP and nitroglycerin are very effective agents to provide the increasing of RA blood flow. However, statistical comparisons exhibited that intravenous SNP was a very effective vasodilating agent for RA than nitroglycerin.

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Keywords

Radial Artery, Vasospasm, Coronary Artery Bypass Surgery

1. Introduction

The radial artery is the conduit of choice as an arterial graft for coronary artery bypass grafting by many of the surgeons. However, perioperative severe conduit spasm with insufficient early graft flow has previously been reported. Thus, vasospasm can be the cause of life threatening clinical condition perioperatively and postoperatively. Many studies have suggested that during the RA harvesting, perioperative flow decrease and spasm can be seen due to manipulation and false preparations of the arterial conduits. For inhibition of the conduit spasm, the authors used different systemic or topical vasodilators such as calcium receptor inhibitors after CABG operations [1]-[3]. In recent publications, some of the authors have suggested that vasodilator use has not provided vasodilator effect. But, there is no common consensus about the routine use of vasodilator agents. Thus, our goal of this study is to evaluate the effects of different vasodilators on flow after the harvesting of RA in our 250 CABG patients.

2. Patients and Methods

250 patients undergoing primary CABG were included in our study. Patients were included in the study if they met the following criteria: 1) age less than 70 years, 2) ejection fraction (EF) more than 50%, 3) no clinical evidence of congestive heart failure, 4) creatinine less than 1.2 mg/100 mL, 5) no evidence of significant chronic obstructive pulmonary disease, and 6) normal liver function. Each patient's physiologic monitoring included mean arterial pressure (MAP), heart rate (HR), and central venous pressure (CVP). Anesthesia was induced with fentanyl 0.015 to 0.01 mg/kg, midazolam 0.05 to 0.1 mg/kg, and nurocuron 0.1 mg/kg. Anesthesia was maintained with fentanyl, isoflurane, and nurocuron as needed.

3. Surgical Procedure

All patients were explored through a median sternotomy. Before the harvesting of the RA Allen test and modified Allen test was performed. The radial artery was dissected as a pedicle from the brachial fossa to the wrist. The artery was dissected with low voltage diathermy. Hemoclips were used to control side branches. Heparin, 300 units/kg, was administered intravenously before transection of the RA. The artery was then cut and allowed to bleed freely for 30 seconds into the cab. This was defined as preoperative RA blood flow. Simultaneously, MAP, HR, and CVP were measured and recorded as preoperative measurements. After then, depending upon the assigned group, the patient received either nitroprusside 0.2 to 2 microgr/kg/min for 10 minutes (Niprus; Schwarz Pharma, Mannheim, Germany), nitroglycerin a dose of 0.5 to 3 microgr/kg/min. for 10 minutes, dobutamine 1 to 3 microgr/ kg/min for 10 minutes, diltiazem 0.25 mg/kg over 2 minutes, and normal saline solution (0.9%) NaCl 10 mL/h for 10 minutes. Ten minutes after starting the drug, the blood flows of RA were measured again (postoperative flow). Hemodynamic measurements taken at the time were defined as postoperative measurement. The RA length, heart rate, MAP were recorded for each flow measurement. The time between flows 1 and 2 was recorded.

4. Statistical Analysis

Data are presented as mean \pm SD for continuous variables and as the number of occurrences for noncontinuous variables. Two-tailed Student's *t* test was used to compare differences between variables at time 1 and time 2 within each drug group. One way analysis of variance (ANOVA) or χ^2 were used as an appropriate to compare differences between groups. The influence of different potential variables on flow ratios were studied by a multivariate general linear model. A value of P less than 0.05 was used to indicate significance.

5. Results

The demographic and hemodynamic data of five groups are shown in **Table 1**. There were no significant

characteristics between the groups with respect to sex ratio, body mass index, RA length, MAP and CVP. When we compared MAP between the groups; there was no significant differences from preoperative measurement to postoperative measurement ($P > 0.05$). Thus, all groups had similar preoperative MAPs. A minimally increase in postoperative MAP was measured but not statistical significance in the dobutamine group ($P = 0.035$) as we expected. There was no difference among the groups for preoperative and postoperative HR. Dobutamine caused an minimally increase in HR from preoperative to postoperative measurements ($P = 0.042$). There were no significant differences among the groups for preoperative CVP. There were no significant differences among preoperative RA flow. The significant flow increase of RA blood flow in nitroglycerin and the SNP ($P < 0.05$).

A multivariate general linear model was created using drug, sex, age, body surface area, postoperative MAP/preoperative MAP, postoperative HR/preoperative HR, postoperative CVP/preoperative CVP as predictors, and radial flow as dependent variables. Drug was the only predictor of an increase of flow in the radial artery ($P = 0.001$). **Figure 1** is summarized as a graphyc the blood flows changes from the RA. Specifically, the use of sodium nitroprusside predicted an increased flow from RA ($P = 0.001$). Also, nitroglycerine predicted an increase flow in the radial artery ($P = 0.002$) (**Table 2**). In 8 patients from nitroprusside group, MAP decreased after the starting of vasodilator administration but in a few minutes it has been corrected with the volume loading. No mortality and myocardial ischemia was seen after operation. Postoperative cardiac enzyme analyses and electrocardiography was recorded from all patients. There was no evidence of myocardial ischemia after operation.

6. Discussion

In a number of studies, the high patency rate of ITA to LIMA anastomosis has been shown. The RA in CABG patients and its association with improved survival have reported from many of the surgeons in CABG which used full arterial revascularisation in last two decades [1]-[3]. Thus, RA use is accepted as an alternative arterial bypass conduit for CABG by a number of surgeons [1]-[4]. The most common problem with the use of RA was defined as a severe spasm of the RA, which can lead to acute myocardial ischemia after operation, and

Table 1. The preoperative demographic and hemodynamic data of all groups are summarized in this table.

Variables	Nitroglycerin	Nitroprusside	Diltiazem	Doputamine	Saline	P Value
Mean Age (years)	62 ± 2.1	59 ± 1.1	66 ± 4.4	61 ± 4.4	65 ± 3.2	0.89
Gender (M/F)	34/16	36/14	37/13	35/15	31/19	0.92
No. Of Graft	3.4 ± 1.2	4.1 ± 1.1	3.3 ± 1.1	3.4 ± 1.1	3.1 ± 1.3	0.49
Mean CPB time (min.)	69.6 ± 3.2	64.3 ± 5.2	63.4 ± 4.1	68.2 ± 5.1	65.4 ± 2.4	0.87
Mean AoXClamp Time (min.)	47 ± 5	42 ± 8	41 ± 9	49 ± 9	43 ± 6	0.7
Mean blood pressure(mm/Hg) Preop.	74.1 ± 3.4	68.6 ± 1.3	64.6 ± 2.4	67.8 ± 2.5	62.7 ± 3.2	0.3
Mean blood pressure(mm/Hg) Postop.	62 ± 7.4	63 ± 4.3	61.4 ± 4.2	70.2 ± 4.3	61 ± 3.9	0.4
RA length (cm)	18 ± 3	16 ± 2	17 ± 1	15 ± 8	16 ± 2	0.8
Preop HR	65.7 ± 6	70.1 ± 10.8	68.1 ± 4.9	70.2 ± 9.6	69.6 ± 4.1	0.97
Postop HR	66.8 ± 9.9	75.1 ± 11.7	76.5 ± 5.1	94.7 ± 11	70.8 ± 8.2	0.42

Abbreviations: M: Male; F: Female; CPB: cardiopulmonary bypass; AoX Clamp: Aortic cross clamp; P values of each pretreatment and post-treatment pair are based on paired *t* test. P values between treatment groups are based on one-way ANOVA for continuous variables and by χ^2 for sex. No any difference was found when we compared the characteristics of the patients. The mean arterial pressures are similar preoperatively for all groups ($P > 0.05$). A minimally increase in postoperative mean arterial pressure is detected in Dopamine Group ($P = 0.035$). No difference among the groups when we compared the preoperative and postoperative heart rate. But, in Dobutamine group, we seen that an minimally increase in heart rate after surgery ($P = 0.042$). There are no significant differences among the groups for preoperative central venous pressure and preoperative RA blood flow. The significant blood flow is detected from RA in nitroglycerin and the SNP group ($P < 0.05$).

Table 2. After drug administration, the flow rates from the RA.

	Nitroprusside	Nitroglycerin	Diltiazem	Doputamine	Saline Sol.
First flow	68.1 ± 20.7	55.8 ± 14.8	49.8 ± 11.6	51.0 ± 13.2	48.0 ± 13.2
Second flow	116.3 ± 17	74.3 ± 13.6	53.8 ± 13.6	54.3 ± 9.4	54.4 ± 11.9
P value	0.001	0.002	>0.05	>0.05	>0.05

MAP: mean arterial pressure. P values between treatment groups are based on one-way ANOVA.

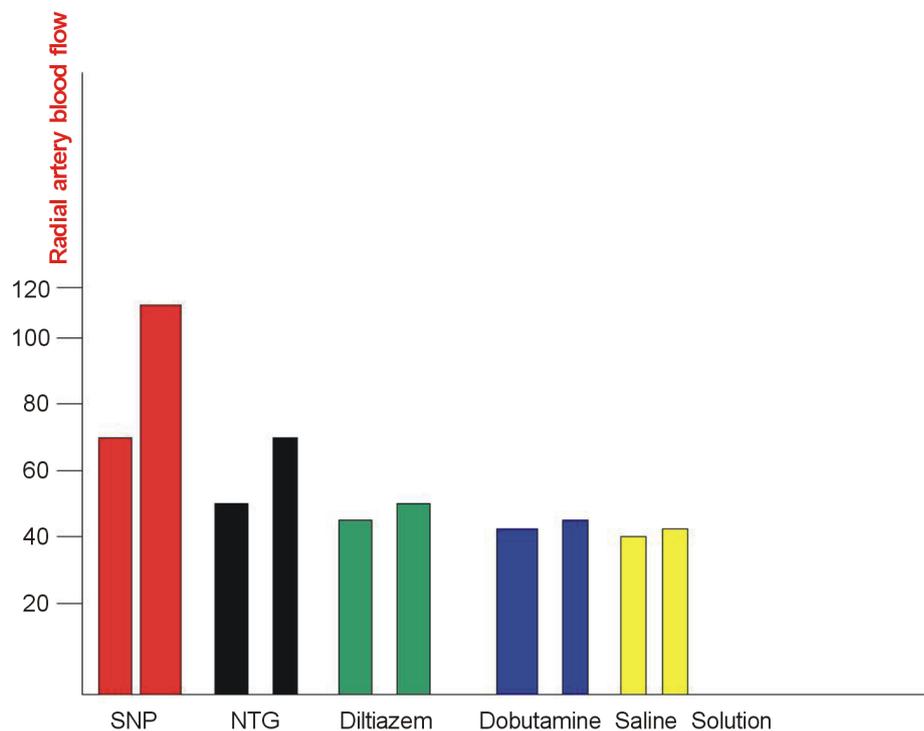


Figure 1. Shows that the change of blood flows as a graphic from the RA after the use of vasodilators and placebo.

may contribute to reduced late patency. In the previous report, Buxton *et al.* showed that the maximal vasoconstrictive response of the RA to noradrenalin is twice that of the IMA [4]. As we know, we see that over adrenergic response during and after CABG. Thus, resulting from this inevitable results, vasoconstriction of arterial grafts which is life threatening condition can be seen in some CABG patients. The effect of topical and systemic vasodilators on internal thoracic artery flow *in vivo* has been well investigated [5]-[8]. But, the effects of systemic vasodilators on *in vivo* radial artery flow have not been studied well. As we known that the radial artery is midsize musculoskeletal arteries with the potential for vasoconstriction [9] [10]. Thus, the purpose of this study was to evaluate the effects of systemic vasodilators on the radial artery blood flow using different systemic vasodilators. Histologically, the radial artery has a wider lumen but thicker media with many leiomyocytes [11] and deficiencies of the internal elastic lamina [4].

Pharmacologically, the response to vasoconstriction *in vitro* is greater in the radial artery than the mammary artery [12] [13]. The use of verapamil and nitroglycerin solutions on the harvested radial artery has been shown to cause vasodilation [12]-[14]. Dogan *et al.* have investigated the quantitative efficacies of the mixed solution, which included verapamil, nitroglycerin, and papaverine, on RA using a scanning electron microscope with a 3-dimensional anaglyph technique [13]. In this study, they have showed that the described vasodilator solution with heparinized autologous blood was to be very effective and it could be used as a pretreatment agent in CABG conduits [13]. *In vitro* studies have shown milrinone that is able to inhibit radial artery contraction by pretreatment and to relax a precontracted radial artery [14]. When using the RA during CABG, systemic vasodilators such as calcium channel blocker during surgery are considered to be important by most of the surgeons [4] [12] [13] [14].

Acar et colleagues have strongly recommended the use of calcium-channel blockers postoperatively when using the radial artery as a conduit in CABG (17). To the best of our knowledge, our study is the largest comparative study *in vivo* flow rates of the radial artery in CABG operations. The radial artery responds to systemic nitroprusside and nitroglycerin with an increase in flow. On the other side, nitroprusside seems to be more effective than nitroglycerin. We have previously shown this effect with mixed solution in our study involving the IMA [13], and the current findings reinforce the previous study's findings [14].

Zabeeda *et al.* previously reported that only nitroglycerin, as opposed to other vasodilators, had an *in vivo*

effect on the radial artery flow [14]. However, in our research, we found that nitroprusside was the more effective vasodilator to increase flow in the relatively muscular radial artery. It is noteworthy that SNP increased the flow of the RA arteries at very low doses. A larger dose of nitroprusside probably would have shown a statistical increase of flow in the radial artery in the multivariate analysis. However, in our opinion, because of the systemic hypotension caused by increased doses of nitroprusside, the dose of nitroprusside should start with a minimal dose and can be increased slowly during short time administration (about 10 min.). But we see that the colloid volume overloading is protecting the patients from severe hypotensive attack. If the radial artery blood flow is weak; though, suitable systemic blood pressure, the surgeons can use nitroprusside and/or nitroglycerin intravenously with the volume overloading. From our data appears that sodium nitroprusside as nitric oxide donor, which is known to have direct and indirect effect on smooth muscle relaxation. SNP was also superior to treatment with papaverine, glyceril trinitrate and saline. In our opinion, the effect of SNP may be continued after the operation when the patients' blood pressure is high. To provide RA graft vasospasm due to over-adrenergic responses after CPB, we propose SNP use in the ICU.

Vasoconstriction may be evoked by mechanical stimulation, as well as by various vasoconstrictor substances. In some patients who underwent treatment with SNP, the RA flow may be lower. But, if blood flow is weak when the completion of RA harvests, we should keep in mind that we can wait before the artery has made a fully spontaneous recovery from the spasm. Vasodilator treatment with the use of SNP may be helpful to provide suitable blood flow from the RA.

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