

The effect of milrinone on blood flow of the Y-graft composed with the radial and the internal thoracic artery in patients with coronary artery disease

Sungwon Na

Department of Medicine

The Graduate School, Yonsei University

The effect of milrinone on blood flow of the Y-graft composed with the radial and the internal thoracic artery in patients with coronary artery disease

Directed by Professor Yang-Sik Shin

The Master's Thesis submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree of Master
of Medical Science

Sungwon Na

December 2005

This certifies that the Master's Thesis of
Sungwon Na is approved.

Thesis Supervisor: Yang-Sik Shin

Thesis Committee Member: Young-Lan Kwak

Thesis Committee Member: Hyoung Woo Park

The Graduate School Yonsei University

December 2005

Acknowledgements

This research is truly the work of many people. At first, I would like to express special appreciation to Professor Yang-Sik Shin for his encouragement to accomplish this study. Without his firm guidance and helpful critiques, I would not have been able to complete this paper.

I owe a great debt of gratitude to Professor Young-Lan Kwak and Professor Hyoung Woo Park. Their valuable comments helped me very much to improve the quality of this paper. I especially appreciate their advices.

My colleagues gave me special encouragements not only in academic activity but in real life. I am most grateful for their help.

Finally, I thank my family for all the supports that they gave. My parents gave me all the possible support in every aspect. My wife, Soo Ji inspired me to do my best. My Son, Jung Woo and my daughter, Yoo Jin are the reasons why I live. I need to mention my brothers and sisters, as they are important in keeping my mind moderate.

Written by writer

Table of Contents

ABSTRACT	1
I . INTRODUCTION	3
II . MATERIALS AND METHODS	5
III . RESULTS	9
IV . DISCUSSION	16
V . CONCLUSION	21
REFERENCES	23
ABSTRACT (IN KOREAN)	27

LIST OF TABLES

Table 1. Patients' Characteristics	11
Table 2. Hemodynamic Changes after Milrinone Administration	12
Table 3. Changes in Y-graft Flows after Milrinone Administration	13
Table 4. Changes in Graft Vascular Resistances after Milrinone Administration	15

ABSTRACT

The effect of milrinone on blood flow of the Y-graft composed with the radial and the internal thoracic artery in patients with coronary artery disease

Sungwon Na

Department of Medicine

The Graduate School, Yonsei University

(Directed by Professor Yang-Sik Shin)

Objective: Milrinone has been known to dilate the internal thoracic artery (ITA) and the radial artery (RA). The effect of milrinone, however, on respective graft flows is unclear when the left ITA (LITA) and the RA compose a Y-graft. This study evaluated the changes in blood flows of a composite Y-graft using the LITA and the RA in response to milrinone.

Methods: Thirty-two patients, undergoing isolated coronary artery bypass graft surgery using arterial composite Y-graft of the LITA in which a free RA graft was attached to the proximal side of the LITA, were included. Graft flow was measured by opening the graft end freely for thirty seconds, and was converted in the form of 'ml/min'. Graft flow and hemodynamic data were recorded before and 10 min after intravenous milrinone (50 µg/kg) administration.

Results: Milrinone significantly increased the RA graft flow measured with clamping the LITA

graft end and total Y-graft flow. The flows of respective grafts were not increased by milrinone when both clamps were released simultaneously, in spite of significant decrease in resistances of both grafts. The ratio of the RA and the LITA graft flows was not changed by milrinone.

Conclusion: Milrinone significantly reduced resistances of the RA and the LITA composing a Y-graft and increased the total Y-graft flow. Milrinone might dilate respective arterial grafts in a different degree. Milrinone, however, did not change the ratio of the RA to LITA graft flows when they were measured simultaneously, therefore, it would not divert graft flow to one side significantly in a composite Y-graft.

Key words: milrinone, Y-graft flow, radial artery, internal thoracic artery

<본문>

The effect of milrinone on blood flow of the Y-graft composed with the radial and the internal thoracic artery in patients with coronary artery disease

Sungwon Na

Department of Medicine

The Graduate School, Yonsei University

(Directed by Professor Yang-Sik Shin)

I . INTRODUCTION

Because of superior long-term patency of the arterial graft to the saphenous vein,^{1,2} total arterial revascularization has been increased in coronary artery bypass graft surgery. The expanded use of the left internal thoracic artery (LITA) as a Y configuration with the radial artery (RA) conduit, which allows maximal arterial graft economy and sufficient length of the grafts, has been performed with excellent clinical results.³ However, the RA possesses a pronounced medial layer and is known to be highly vasoreactive,^{4,5} contrary to the internal thoracic artery (ITA) which possesses a thin medial layer with few smooth muscle cells and has little vasoreactivity.⁶ Various procedures have been attempted to prevent vasospasm such as no

touch technique,⁷ topical or systemic vasodilator injection,^{8,9} and maintaining intraluminal pressure of a graft.

Milrinone, a phosphodiesterase inhibitor, is an inotropic agent with vasodilatory activity.¹⁰ A few studies revealed vasorelaxant effect of milrinone on the RA,⁴ the ITA,^{11,12} and the coronary vasculature itself.¹³ However, those studies evaluated the effect of milrinone on a respective, independent arterial graft not on a composite arterial Y-graft. When Y-graft is composed of the LITA and the RA that have different anatomical characteristics, both grafts compete with each other for the proximal LITA flow and milrinone could affect both the LITA and the RA graft flow in a different way. Thus, we evaluated the effect of milrinone on the respective flow of the LITA and RA graft composing a Y-graft.

II. MATERIALS AND METHODS

The study was approved by the Yonsei Institutional Review Board. All participants provided written form of informed consent. Thirty-two patients, who underwent elective coronary artery bypass graft surgery using an arterial composite Y-graft in which a free RA graft was attached to the proximal side of the LITA, were included in this prospective study between April 2005 and September 2005. All Y-grafts were created by the same surgeon to minimize the bias associated with surgical skill. Patients with left ventricular ejection fraction less than 40% and significant dysrhythmia were excluded.

All regular cardiovascular medications, except diuretics and digitalis, were continued up until the morning of surgery. Patients were premedicated with intramuscular morphine (0.05-0.1 mg/kg). Five electrocardiogram leads were placed; and leads II and V₅ were continuously monitored. Arterial pressure was monitored through a RA catheter in the dominant hand. A pulmonary artery catheter (Swan-Ganz CCombo-CCO/SvO₂[®], Edwards Lifesciences LLC, Irvine, California, USA) was inserted via the right internal jugular vein to monitor cardiac performance continuously including central venous pressure (CVP), pulmonary artery pressure (PAP), cardiac output (CO) and right ventricular volumetric parameters. Anesthesia was induced with intravenous injection of 1.5–2.5 mg of midazolam, 1.5–3.0 µg/kg of sufentanil, and 50 mg of rocuronium. Anesthesia was maintained with intravenous infusion of sufentanil

(0.5–1.5 µg/kg/h) and inhalation of isoflurane (0.4–0.6 %) with oxygen and air (fraction of inspired oxygen 0.6). Cardiac performance was also monitored by transesophageal echocardiography after anesthesia induction.

All patients explored through median sternotomy. The LITA was harvested with a pedicle using diathermy and hemoclips to control the side branches. The RA was harvested without skeletonization. The RA conduit was flushed with heparinized arterial blood. Mechanical dilatation was not applied. After the RA harvest and the LITA dissection, heparin 150 U/kg was injected intravenously. The RA was anastomosed to the proximal part of LITA after confirming the activated clotting time was over 300 seconds.

After Y-graft construction, respective grafts free flows were measured directly against no resistance. Blood was collected for 30 seconds and graft flow was calculated from the blood volume in the form of 'ml/min'. At first, the surgeon measured the RA flow (RA-fl1) or the LITA flow (LITA-fl1) with clamping the opposite graft end. And the respective grafts flows were simultaneously but separately measured by releasing both vascular clamps (RA-fl2 and LITA-fl2, respectively). Total Y-graft flow was calculated by the sum of RA-fl2 and LITA-fl2. The order which graft flow was measured firstly was determined on the basis of a computer-generated table of random numbers. During this process, the anesthesiologist collected the hemodynamic data. The following hemodynamic variables were measured: cardiac index (CI),

heart rate (HR), mean arterial pressure (MAP), mean PAP (MPAP), CVP, and pulmonary capillary wedge pressure (PCWP). Myocardial oxygen demand (MvO_2 , $HR \times$ systolic blood pressure), resistance of each graft blood flow, systemic vascular resistance (SVRI), and pulmonary vascular resistance (PVRI) were calculated from known data (Pre-milrinone). Then milrinone (50 μ g/kg, Primacor[®] Sanofi-Synthelabo Korea, Seoul, Korea) was administered intravenously for 10 minutes. The grafts flow measurements were repeated on 10 minutes after milrinone injection (RA-fl1, LITA-fl1, RA-fl2, LITA-fl2) and hemodynamic variables were recorded and calculated as stated above (Post-milrinone). Grafts resistances were calculated as follows: $RA-resist1 = MAP/RA-fl1$, $LITA-resist1 = MAP/ LITA-fl1$, $RA-resist2 = MAP/ RA-fl2$, $LITA-resist2= MAP/ LITA-fl2$, Total resistance = $MAP/Total Y-graft flow$. Blood lost during grafts flow measurements was collected by Cell Saver (Cell Saver[®] 5 System, Haemonetics, Braintree, MA, USA) and retransfused after surgery. To minimize the effect of anesthetics and hemodynamics on data, anesthetic settings (the concentration of inhalation anesthetics and the infusion rate of intravenous anesthetics) and fluid administration rate were not changed and no vasoactive drug was used during data gathering.

Statistical analysis was performed with SPSS 11.5 (SPSS Inc, LS, USA). All data are presented as mean \pm standard deviation or number of patients (percent). Continuous data were compared by paired t-test. Wilcoxon signed ranks test was used when variables did not show

normal distribution. Normalities of continuous data were analyzed by Kolmogorov-Smirnov test.

P < 0.05 was considered as statistically significant.

III. RESULTS

The demographic data, preoperative medication, comorbid diseases, and coronary angiographic findings are presented in Table 1.

Milrinone increased HR, CI and MvO_2 but did not change MAP, MPAP, and PVRI. Milrinone administration resulted in a statistically significant decrease in CVP and SVRI (Table 2).

The RA graft flow with clamping the LITA graft (RA-fl1) and total Y-graft flow were significantly increased after milrinone administration. However, the LITA graft flow with clamping the RA graft (LITA-fl1) was not significantly changed with milrinone. Milrinone did not increase simultaneously measured the LITA and the RA graft flow (LITA-fl2 and RA-fl2, respectively). RA-fl1 was significantly greater than LITA-fl1 before and after milrinone administration. The graft flow divided by cardiac output (the proportion of graft flow in cardiac output) significantly increased after milrinone administration only in the RA graft with clamping the LITA. The ratio of RA-fl2 to LITA-fl2 did not demonstrate significant change by milrinone. Milrinone did not change the respective graft flows divided by total Y-graft flow (Table 3).

The resistances in all circumstances (RA-resist1, LITA-resist1, RA-resist2, LITA-

resist2, and Total resistance) were significantly decreased after milrinone administration.

Milrinone did not change the ratio of RA-resist2 to LITA-resist2 (Table 4).

The Kolmogorov-Smirnov normality test demonstrated normal distribution of all the continuous data except RA-resist2 and RA-resist2/LITA-resist2 before milrinone administration.

With Wilcoxon signed ranks test, RA-resist2 significantly decreased after milrinone administration compared to before milrinone administration ($P = 0.012$).

Table 1. Patients' Characteristics

Age (yr)		64 ± 7
Gender (M/F)		7/ 25
BSA (m ²)		1.72 ± 0.17
LVEF (%)		64 ± 10
Preoperative medications	nitrates	19 (59%)
	calcium channel blockers	24 (75%)
	β-blockers	25 (78%)
	ACE inhibitors	9 (28%)
Diabetes mellitus		9 (28%)
Hypertension		22 (69%)
Recent myocardial infarction		4 (13%)
Coronary angiography	left main	15 (47%)
(luminal narrowing > 50%)	LAD	30 (94%)
	LCx	28 (88%)
	RCA	28 (88%)

All values are expressed as mean ± standard deviation or number of patients (percent). BSA:

body surface area, LVEF: left ventricular ejection fraction, ACE: angiotensin converting enzyme,

LAD: left anterior descending coronary artery, LCx: left circumflex coronary artery, RCA: right

coronary artery.

Table 2. Hemodynamic Changes after Milrinone Administration

	Pre-milrinone	Post-milrinone
HR (beats/min)	60 ± 6	70 ± 10*
MAP (mmHg)	74 ± 10	71 ± 11
MPAP (mmHg)	18 ± 4	18 ± 6
CVP (mmHg)	7.0 ± 2.1	6.6 ± 2.4*
CI (L/min/m ²)	3.1 ± 0.6	3.4 ± 0.8*
MvO ₂ (beats · mmHg/min)	6982 ± 1280	8270 ± 1972*
SVRI (dynes · sec · m ² /cm ⁵)	1793 ± 519	1635 ± 475*
PVRI (dynes · sec · m ² /cm ⁵)	143 ± 57	163 ± 92

All values are expressed as mean ± standard deviation. Pre-milrinone: before milrinone administration, Post-milrinone: 10 minutes after milrinone (50 µg/kg) administration, HR: heart rate, MAP: mean arterial pressure, MPAP: mean pulmonary arterial pressure, CVP: central venous pressure, CI: cardiac index, MvO₂: myocardial oxygen demand (HR × systolic blood pressure), SVRI: systemic vascular resistance index, PVRI: pulmonary vascular resistance index.

* $P < 0.05$ versus Pre-milrinone value by paired t-test.

Table 3. Changes in Y-graft Flows after Milrinone Administration

	Pre-milrinone	Post-milrinone
Flow 1		
RA-fl1 (ml/min)	91 ± 41 [†]	110 ± 49 ^{*†}
LITA-fl1 (ml/min)	66 ± 31	73 ± 35
RA-fl1/CO (‰)	0.18 ± 0.10	0.21 ± 0.11 [*]
LITA-fl1/CO (‰)	0.14 ± 0.08	0.14 ± 0.08
Flow 2		
RA-fl2 (ml/min)	85 ± 43	90 ± 46
LITA-fl2 (ml/min)	53 ± 32	60 ± 24
Total Y-graft flow (ml/min)	138 ± 55	150 ± 55 [*]
RA-fl2/LITA-fl2	1.98 ± 1.12	1.69 ± 0.98
RA-fl2/Total Y-graft flow	0.61 ± 0.17	0.58 ± 0.14
LITA-fl2/Total Y-graft flow	0.39 ± 0.17	0.42 ± 0.13
RA-fl2/CO (‰)	0.17 ± 0.10	0.16 ± 0.11
LITA-fl2/CO (‰)	0.11 ± 0.07	0.11 ± 0.05
Total Y-graft flow/CO (‰)	0.28 ± 0.14	0.28 ± 0.14

All values are expressed as mean ± standard deviation. Pre-milrinone: before milrinone administration, Post-milrinone: 10 minutes after milrinone (50 µg/kg) administration, **Flow 1**: flow measured with clamping the opposite graft, RA-fl1: the radial artery (RA) graft flow with clamping the left internal thoracic artery (LITA) graft, LITA-fl1: the LITA graft flow with clamping the RA graft, CO: cardiac output, **Flow 2**: flow measured with releasing both clamps simultaneously, RA-fl2: the RA graft flow measured simultaneously with the LITA flow, LITA-fl2: the LITA graft flow measured simultaneously with the RA flow, Total Y-graft flow: the sum of RA-fl2 and LITA-fl2. * $P < 0.05$ versus Pre-milrinone value by paired t-test, [†] $P < 0.05$ versus

LITA-fl1 by paired t-test.

Table 4. Changes in Grafts' Vascular Resistances after Milrinone Administration

	Pre-milrinone	Post-milrinone
Resistance 1 (N·sec/cm ⁵)		
RA-resist1	0.82 ± 0.53	0.64 ± 0.33*
LITA-resist1	1.15 ± 0.74	0.92 ± 0.37*
Resistance 2 (N·sec/cm ⁵)		
RA-resist2	1.02 ± 1.10 [†]	0.80 ± 0.56 [‡]
LITA-resist2	1.48 ± 0.94	1.09 ± 0.45*
RA-resist2/LITA-resist2	0.95 ± 1.35 [†]	0.84 ± 0.59
Total resistance	1.09 ± 0.45	0.50 ± 0.23

All values are expressed as mean ± standard deviation. Pre-milrinone: before milrinone administration, Post-milrinone: 10 minutes after milrinone (50 µg/kg) administration,

Resistance 1: graft's vascular resistance measured with clamping the opposite graft, RA-resist1: vascular resistance of the radial artery (RA) graft with clamping the left internal thoracic artery (LITA) graft, LITA-resist1: vascular resistance of the LITA graft with clamping the RA graft,

Resistance 2: graft's vascular resistance measured with releasing both clamps simultaneously, RA-resist2: vascular resistance of the RA graft with releasing both clamps simultaneously, LITA-resist2: vascular resistance of the LITA graft with releasing both clamps simultaneously,

Total resistance = MAP/Total Y-graft flow. * $P < 0.05$ versus Pre-milrinone value by paired t-

test, [†] Data did not show normal distribution by Kolmogorov-Smirnov test, [‡] $P < 0.05$ versus

Pre-milrinone value when compared using Wilcoxon signed ranks test.

IV. DISCUSSION

In a composite Y-graft using the RA and the LITA, milrinone increased the free blood flow of the RA graft when the LITA graft was clamped and total Y-graft flow in patients undergoing coronary artery bypass graft surgery. Milrinone, however, did not significantly change the respective RA and LITA flow and the ratio of the RA flow to the LITA flow when both arterial grafts were released simultaneously, although vascular resistances of both arterial grafts were significantly decreased. Accordingly, it could be expected that milrinone would not divert graft flow to one side of a Y-graft.

Coronary blood flow is closely matched to myocardial oxygen demand.¹⁴ Thus myocardial metabolism is the most important determinant of coronary perfusion and many other factors also contribute to the regulation of coronary blood flow, for example, aortic pressure, autoregulation, neurohumoral, and endothelial influences.¹⁵ In patients with coronary artery disease, flow is known to become pressure-dependent because of exhausted coronary vascular reserve.¹⁶ It is not clear, however, whether regulation mechanisms of coronary blood flow described above can be applied to a bypass graft, especially a composite arterial Y-graft.

Lemma et al.¹⁷ reported that Y-graft may significantly increase its blood flow in response to increased MvO_2 . They regarded, however, myocardial oxygen demand as the multiplication of systolic blood pressure by heart rate. Since blood pressure affect graft flow and

myocardial oxygen demand simultaneously, it may be inappropriate that a Y-graft flow is controlled just by myocardial oxygen demand. Sakaguchi et al.¹⁸ demonstrated that Y-graft improved regional myocardial blood flow at rest, but it was not as effective as independent grafts for improving coronary flow reserve measured at two weeks after myocardial revascularization. Since the Y-graft is under different neurohumoral milieu from coronary vasculature, there is a possibility that not only myocardial metabolism but also vascular tone of grafts regulate the Y-graft flow. However, effect of hemodynamics on a composite arterial Y-graft flow is not well established. He et al¹⁹ classified all arterial grafts into 3 types: type I; somatic arteries, type II; splanchnic arteries, type III; limb arteries. The RA which belongs to the type III is more spastic than the type I artery such as the ITA. The proximal and distal portion of the ITA is a musculoelastic artery and the middle portion is an elastic artery.⁶ Its vasoreactivity is less than that of the RA due to a thin medial layer with few smooth muscle cells. The ITA dilates in response to milrinone and does not vasoconstrict in response to norepinephrine.²⁰ After Acar C et al.²¹ reintroduced the RA as a conduit for coronary revascularization, it has been reported to have superior long-term patency to saphenous vein.² However, the RA is very susceptible to vasospasm due to its pronounced medial layer.^{4,5} Therefore, vasodilator administration, especially calcium channel blockers has been used to prevent vasospasm of the RA.²²

We supposed that a phosphodiesterase inhibitor, milrinone, an inotropic agent with vasodilator activity would increase Y-graft flow by reducing vascular tone of grafts and/or increasing CO but its effect on them might be different because of the anatomical difference of both grafts and competition against each other for proximal LITA flow. Although, there were studies that revealed vasorelaxant effect of milrinone on the RA⁴ and the ITA,^{11,12} the in vivo effect of milrinone on Y-graft was unclear. In contrast to previous studies reported that milrinone dilated the ITA further comparing the RA,^{23,24,25} vasodilatory effect of milrinone was more prominent in the RA graft in this study. This discrepancy may result from the different experimental conditions. Most of previous studies investigated vasoreactivity of precontracted artery in vitro or graft flow after cardiopulmonary bypass that would result in vasoconstriction. However, we investigated the flow of Y-graft without vasoconstrictor pretreatment. Baseline condition of arterial graft before treatment of vasoactive drug was known to affect the degree of graft's response to the drug.²⁴

In this study, the free RA flow (RA-fl1) was greater than the free LITA flow (LITA-fl1) before and after milrinone administration. This finding is reasonable because diameter of the RA is greater than that of the ITA.²⁶ Furthermore, milrinone could increase the RA-fl1 but it failed to increase the LITA-fl1. The proportion of RA flow to CO also increased after milrinone that means the increase in RA graft flow did not just result from increased CO.

Regarding blood flow competition for proximal LITA flow between the RA and the LITA graft, the respective grafts' flows (RA-fl2 and LITA-fl2) were not significantly changed by milrinone in spite of significant decrease in vascular resistance in both grafts. But total Y-graft flow, namely the sum of RA-fl2 and LITA-fl2 showed significant increase after milrinone administration. In the Y-graft, proximal portion of LITA might represent the flow-limiting segment of the RA graft²⁷ and it was likely to be associated with that result. The respective grafts' flow are thought to demonstrate statistical significance with greater sample size.

According to these findings, there is a concern that milrinone may divert blood flow toward the RA graft rather than LITA graft in patient receiving coronary artery bypass graft surgery using a Y-graft. It may raise serious issue because the LITA is usually anastomosed to the coronary artery that perfuses most critical myocardial region. As a composite Y-graft was reported to provide a 2.3 fold reserve of flow to the coronary vascular bed through the grafts,²⁷ there is a possibility that milrinone can divert more proximal LITA flow to the RA side than the LITA side of a composite Y-graft with concomitant increase of MvO₂. However, regarding the fact that milrinone did not change the graft flow ratio of the RA to the LITA in anesthetized patients, milrinone is not likely to cause graft flow diversion from the LITA to RA. Therefore, vasodilatory effect of milrinone on the RA and LITA graft in clinical situation may not be different from the result of this study. The LITA graft flow is dependent on the perfusion

pressure. Although systemic blood pressure was not changed with milrinone in this study, milrinone can cause hypotension occasionally. Hypotension and use of vasopressor would affect respective graft flow but it was not evaluated in this study.

There are some limitations in this study. Firstly, since this study was aimed to investigate the effect of milrinone on vascular tones and free graft flows of the RA and the LITA, myocardial oxygen demand did not affect the result. The effect of milrinone, therefore, on the RA and LITA graft flow would be different from the result of this study according to the change in myocardial demand. The setting of this study is, however, closer to clinical situation than other previous studies regarding a composite Y-graft flow using LITA and RA. Secondly, applications of vascular clamp to measure graft flow could damage grafts. It can affect the lately measured graft flow and attenuate the vasodilatory effect of milrinone, although its effect on the both grafts is unknown. But these manipulation of the vessels did not harm to the result of surgery since distal portion of both grafts were excised before graft anastomosis.

V. CONCLUSION

Effect of milrinone on a composite arterial Y-graft using the LITA and the RA was investigated in patients with coronary artery disease. Free grafts flows of respective arterial graft were compared before and after milrinone administration. The present study demonstrated as follows.

1. Milrinone increase the RA graft flow but not LITA graft flow in a composite Y-graft when the opposite side graft was clamped.
2. Milrinone increased total Y-graft flow but not each graft flow when they measured simultaneously in spite of significant reduction in resistances of both grafts, which seems to be associated with the flow limitation at proximal portion of LITA. The ratio of the RA graft flow to the LITA graft flow was not changed with milrinone.
3. The proportion of graft flow in cardiac output was increased by milrinone only in the RA graft flow when the LITA graft was clamped. Milrinone did not change the proportion of total Y-graft flow in cardiac output.
4. These results imply that there is a possibility that milrinone can change LITA and RA graft flow composing a Y-graft in a different degree, especially when the proximal LITA flow has reserve and hypotension occurs with milrinone. However, milrinone demonstrated identical changes in the RA and the LITA graft flow when both grafts flows were measured

simultaneously and it is not likely that milrinone diverts Y-graft flow toward the RA graft significantly in clinical situation.

References

1. Cooper GJ, Underwood MJ, Deverall PB. Arterial and venous conduits for coronary artery bypass. A current review. *Eur J Cardiothorac Surg* 1996;10:129-140.
2. Zacharias A, Habib RH, Schwann TA, Riordan CJ, Durham SJ, Shah A. Improved survival with radial artery versus vein conduits in coronary bypass surgery with left internal thoracic artery to left anterior descending artery grafting. *Circulation* 2004;109:1489-1496.
3. Royse AG, Royse CF, Raman JS. Exclusive Y graft operation for multivessel coronary revascularization. *Ann Thorac Surg* 1999;68:1612-1618.
4. He GW, Yang CQ. Vasorelaxant effect of phosphodiesterase inhibitor milrinone in the human radial artery used as coronary bypass graft. *J Thorac Cardiovasc Surg* 2000;119:1039-1045.
5. Chardigny C, Jebara VA, Acar C, Descombes JJ, Verbeuren TJ, Carpentier A, et al. Vasoreactivity of the radial artery: comparison with the internal mammary and gastroepiploic arteries with implications for coronary artery surgery. *Circulation* 1993;88:II 115-127.
6. van Son JA, Smedts F. Histology of arterial conduits as a predictor of their long-term patency as coronary bypass conduits. *Eur J Cardiothorac Surg* 1993;7:277-278.
7. Galvin IF. Mammary artery grafts: a new no-touch technique for anastomosis. *Ann Thorac Surg* 1991;51:500-503.
8. He GW, Buxton BF, Rosenfeldt FL, Angus JA, Tatoulis J. Pharmacologic dilatation of the

internal mammary artery during coronary bypass grafting. *J Thorac Cardiovasc Surg* 1994;107:1440-1444.

9. Cooper GJ, Wilkinson GA, Angelini G: Overcoming perioperative spasm of the internal mammary artery: Which is the best vasodilator? *J Thorac Cardiovasc Surg* 1992;104:465-468.

10. Alousi AA, Stankus GP, Stuart JC, Walton LH. Characterization of the cardiotonic effects of milrinone, a new and potent cardiac bipyridine, on isolated tissues from several animal species. *J Cardiovasc Pharmacol* 1983;5:804-811.

11. Salmenpera MT, Levy JH. The in vitro effects of phosphodiesterase inhibitors on the human internal mammary artery. *Anesth Analg* 1996;82:954-957.

12. Liu JJ, Doolan LA, Xie B, Chen JR, Buxton BF. Direct vasodilator effect of milrinone, an inotropic drug, on arterial coronary bypass grafts. *J Thorac Cardiovasc Surg* 1997;113:108-113.

13. Monrad ES, Baim DS, Smith HS, Lanoue A, Brauwald E, Grossman W. Effects of milrinone on coronary hemodynamics and myocardial energetics in patients with congestive heart failure. *Circulation* 1985 ;71:972-979.

14. Sethna DH, Moffitt EA. An appreciation of the coronary circulation. *Anesth Analg* 1986;65:294-305.

15. Konidala S, Gutterman DD. Coronary vasospasm and the regulation of coronary blood flow. *Prog Cardiovasc Dis* 2004;46:349-373.

16. Epstein SE, Cannon RO 3rd, Talbot TL. Hemodynamic principles in the control of coronary blood flow. *Am J Cardiol* 1985;56:4E-10E.
17. Lemma M, Mangini A, Gelpi G, Innorta A, Spina A, Antona C. Analysis of Y-graft blood flow and flow reserve in conditions of increased myocardial oxygen consumption. *Ital Heart J* 2004;5:290-294.
18. Sakaguchi G, Tadamura E, Ohnaka M, Tambara K, Nishimura K, Komeda M. Composite arterial Y graft has less coronary flow reserve than independent grafts. *Ann Thorac Surg* 2002;74:493-496.
19. He GW. Arterial grafts for coronary artery bypass grafting: biological characteristics, functional classification, and clinical choice. *Ann Thorac Surg* 1999;67:277-284.
20. Gitter R, Anderson JM Jr, Jett GK. Influence of milrinone and norepinephrine on blood flow in canine internal mammary artery grafts. *Ann Thorac Surg* 1996;61:1367-1371.
21. Acar C, Jebara VA, Portoghese M, Beyssen B, Pagny JY, Grare P, et al. Revival of the radial artery for coronary artery bypass grafting. *Ann Thorac Surg* 1992;54:652-659.
22. He GW, Yang CQ. Comparative study on calcium channel antagonists in the human radial artery: clinical implications. *J Thorac Cardiovasc Surg* 2000;119:94-100.
23. Zabeeda D, Medalion B, Jakobshvilli S, Ezra S, Schachner A, Cohen AJ. Comparison of systemic vasodilators: effects on flow in internal mammary and radial arteries. *Ann Thorac Surg*

2001;71:138-141.

24. Wei W, Yang CQ, Furnary A, He GW. Greater vasopressin-induced vasoconstriction and inferior effects of nitrovasodilators and milrinone in the radial artery than in the internal thoracic artery. *J Thorac Cardiovasc Surg* 2005;129:33-40.

25. Onomoto M, Tsuneyoshi I, Yonetani A, Suehiro S, Matsumoto K, Sakata R, et al. Differential pharmacologic sensitivities of phosphodiesterase-3 inhibitors among human isolated gastroepiploic, internal mammary, and radial arteries. *Anesth Analg* 2005;101:950-956.

26. Chamiot-Clerc P, Copie X, Renaud JF, Safar M, Girerd X. Comparative reactivity and mechanical properties of human isolated internal mammary and radial arteries. *Cardiovasc Res* 1998;37:811-819.

27. Royse AG, Royse CF, Groves KL, Yu G. Blood flow in composite arterial grafts and effect of native coronary flow. *Ann Thorac Surg* 1999;68:1619-1622.

ABSTRACT (IN KOREAN)

관상동맥질환자에서 요골동맥과 내흉동맥을 이용한 Y자이식편 혈류에 Milrinone이

미치는 영향

<지도교수 신 양식>

연세대학교 대학원 의학과

나 성원

연구배경: Milrinone은 phosphodiesterase III 억제제의 하나로서 혈관확장과 양성 변력

작용을 동시에 나타내는데 요골동맥과 내흉동맥을 확장시킨다고 알려져 있다. 그

러나 milrinone이 해부학적 구조가 다른 Y자이식편 각각의 혈류량에 대해 미치는

영향에 대해서는 아직 알려진 것이 적으므로 그에 대해 알아보하고자 한다. **대상**

및 방법: 요골동맥과 내흉동맥으로 이루어진 Y자이식편을 사용하는 관상동맥우회

술을 시행받는 환자 32명을 대상으로 milrinone (0.05 mg/kg)을 정주하고 투여 전과

투여 10분 후의 각각의 이식편혈류량과 혈액학적 변수들을 측정하였다. 이식편혈

류량은 30초간 이식편 끝을 열고 모은 혈액량으로부터 ‘ml/min’ 형태로 환산하였

다. 요골동맥이식편 혈류량을 내흉동맥이식편을 차단한 채 측정하고 내흉동맥이

식편 혈류량을 요골동맥이식편을 차단한 채 측정하였다. 그 후 양쪽 이식편을 동

시에 개방하여 각각의 혈류량을 측정하였다. **결과 및 결론:** Milrinone은 Y자이식편

의 양쪽의 혈류를 함께 측정하였을 때 전체혈류량을 유의하게 증가시켰다. 또한

Y자이식편의 내흉동맥측 혈류를 차단했을 때 측정된 요골동맥이식편의 혈류량을 증가시켰다. 그러나 요골동맥측 혈류의 차단 여부와 무관하게 내흉동맥이식편의 혈류량은 증가시키지 못했다. 이식편혈류의 저항은 모든 경우에 유의한 감소를 보였다. 본 연구 결과 milrinone은 동맥이식편혈류를 증가시킬 수 있으며 내흉동맥 보다는 요골동맥의 혈류량에 미치는 영향이 더욱 크다는 것을 알 수 있었다. 하지만 두 이식편을 모두 열었을 때 측정된 양측 이식편의 혈류의 비와 저항의 비는 milrinone에 의해 변화하지 않았으므로 실제 임상적으로 milrinone이 Y자이식편 혈류의 편향을 심화시킬 가능성은 적다고 할 수 있겠다.

핵심되는 말: milrinone, Y자이식편, 요골동맥, 내흉동맥